OCULAR THERAPEUTICS

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ACCORDING TO THE MOST RECENT DISCOVERIES

BY

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TRANSLATOR'S FOREWORD.

This more or less literal translation has been made from the second edition of Dr. A. Darier's *Leçons de thérapeutique oculaire.* In presenting it to the medical profession I feel that no apology is called for, inasmuch as the author enters into new remedies and methods of treatment that are yet scarcely known in this country, besides describing fully the better understood treatments commonly adopted for the cure of eye disease. Indeed, it may be safely said that even the most experienced ophthalmic surgeon has something to learn about the treatment of eye disease from a perusal of Dr. Darier's book.

The almost purely personal character of the Lectures has been criticised in some quarters. It is mainly accounted for by the fact that they are the outcome of Dr. Darier's own researches into the action of the remedies he deals with. In my opinion, it is a good rather than a bad point.

Dr. Darier has been kind enough to revise the proof-sheets of this translation, and, in doing so, has made important additions to many of the sections. He has, moreover, added two new chapters (XXII and XXV), which have not yet appeared in the original work. They cannot but add to the completeness and value of the book.

The metrical system adopted in the original work has been retained unaltered in the translation.

Finally, it should be noted that *Leçons de thérapeutique oculaire* has been awarded the Desportes Prize (1902) by the French Academy of Medicine as "the best work published on practical therapeutics."

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AUTHOR'S PREFACE.

To my Readers.

This book is not large, so that you may perhaps find time to read it through. It embodies the result of twenty years' ophthalmological study and practice. It may therefore, as I hope, help to enrich our therapeutic arsenal. Most of the ideas it contains are my own, or at least have become mine by a process of intimate and lengthened assimilation—there are few things which were not produced, spoken of, or thought of before our time.

May those of my teachers who peruse this modest book see in it a manifestation of my gratitude by the fact that they will recognise the fruit of their teachings.

To those who are no more I will pay a tribute by propagating their cherished ideas. Their names matter little, provided the work goes on and is accomplished. May everybody contribute to it by his own personal labours.

For us practitioners our part, above all others, is to learn how to cure disease.

A. D.

Paris.

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OCULAR THERAPEUTICS.

LECTURE I.

SUMMARY.

Personal views based upon twenty years' study and experience.—The eye lends itself better than any other organ to experimental therapeutics.—The unceasing progress of chemistry has furnished us with a host of new and important medicaments.—Classification of local remedies according to their physiological action upon the eye.—The facts acquired by clinical observation and experimental therapeutics should be confirmed in the laboratory.—The poverty of ocular therapeutics until recent times.—Atropine, silver nitrate, and mercury formed up to now the omnipotent triad.

GENTLEMEN,—

In these few Lectures, the character of which will be eminently simple and practical, I have no intention of covering the whole ground of ocular therapeutics, for that is more suitable to systematic treatises on the subject.

I wish simply to initiate you into my personal practice, based upon nearly twenty years' study, clinical observation, and experimental therapeutics.

Before going deeply into the subject, permit me to make some **general remarks** which will prove to you that the study of ophthalmology is important, not only to the specialist, but still more so to the student, the practitioner, and especially to the therapist.

The eye is the most delicate, precious, and exact of all the organs of sense. The educator and purveyor of our intellect and judgment, it is, literally and figuratively, an extension of the brain—a mirror reflecting the state of the mind, as modern novelists say.

For us as practitioners, however, side by side with these psychological claims, we find in the eye, physically and physiologically, an

inexhaustible source of scientific information, along with clinical and therapeutic observations of the highest importance.

Has not the exquisite sensibility of the eye—and above all of the cornea—always been appealed to as a test of the more or less complete anæsthesia of the individual?

Has not the pupillary reaction served to betray the existence of cerebral lesions, and even aided in their localisation? Do not physiologists employ the same means for testing the sensibility of animals under experiment?

Has not this same pupillary response given valuable information with regard to the action of many drugs? Does it not serve as a diagnostic sign of intoxication by belladonna and atropine? Does it not also show us the degree of narcosis when chloroform, etc., is administered?

Does not the examination of the fundus of the eye with the ophthalmoscope daily furnish us with exact information as to the state of the vessels and circulation, and make us acquainted in some cases also with changes in the blood itself? It is, however, needless to labour this interesting subject.

Does not the observation of entoptic phenomena give us useful information with regard to the capillary circulation, permitting us to see, as under a microscope, the red corpuscles and the leucocytes of the blood?

The possibility of perceiving by transparency one's own crystalline lens,* allows a very interesting study to be made of the development of cataract; perhaps it may further give us the chance of studying the absorption of lenticular opacities under the influence of this or that treatment.

In brief, our incessant researches and our daily observations, checked, as they are, by physiological experiments, have allowed us to make valuable contributions to pathology and to general therapeutics, thanks to what I may call our *réactifs oculaires*, of which we shall speak again presently.

Having spent my first few years of medical study in a physiological laboratory, I have always felt an inclination towards experiment. But (I admit the fact) the clinician is not always in a position to control his observations in the laboratory. On the other hand, he should take careful note of the modern advances of physiology, bacteriology, and of experimental pharmacodynamics.

* Darier, *De la possibilité de voir son propre Cristallin*, Société Française d'Ophtalmologie, 1895.

Moreover, chemists nowadays understand that the new products given to the medical profession must have been studied, not alone from the standpoint of their chemical reactions, but also and especially with regard to their physiological and even bacteriological reactions.

Clinical experiment—or, better, therapeutic experiment—has at last entered upon a more scientific phase, rich not only in promise but also in performance, and accompanied by an almost complete change in our pharmacological arsenal.

Without mentioning the changes brought about in medicine and surgery by the memorable discoveries of Pasteur, we have seen, in the last few years, a multitude of new products, almost all of which are organic compounds, obtained usually by synthesis—as, for example, sodium salicylate, aspirine, antipyrine, phenacetine, iodoform, protargol, and so forth.

How many new alkaloids have appeared in the productive end of the last century, when some have even predicted the bankruptcy of science? Would that our financiers were able to conduct their affairs as well as we can conduct our own!

Then, what about the organic juices? These we owe, in point of fact, to Brown-Séquard, who was jeered at when he introduced spermine. Do they not constitute a source of new therapeutic inspiration? It is probable that we shall soon have definite chemical products in place of thyroidine, adrenaline, and the remaining glandular extracts. Meanwhile, we already know that these organic products are possessed of great physiological and therapeutic importance.

To cure is our constant aim, and the word "incurable" should be the most dreadful of nightmares to a medical man. The most redoubtable diseases will little by little find their prophylactic or their remedy. Smallpox has become very rare through the influence of vaccination and re-vaccination; typhoid fever has become uncommon in face of good sanitary arrangements. Tuberculosis, that most formidable enemy, is already less fatal, and the introduction of new tuberculines may perhaps end by triumphing over the scourge. Meanwhile, it is certain that a fair proportion of tuberculous subjects are now cured, thanks to the advances made in therapeutics and hygiene.

Carcinoma itself will find its antidote when the nature and pathogeny of the disease are better understood.

Ah! in atrophy of the optic nerve, when all perception of light is extinct, we find ourselves faced by a really incurable evil. But so long as a little sight remains, it is our duty to fight strenuously with all the means at our command. And if the classical measures remain

without effect we must search for new ones, never forgetting the ancient Hippocratic dictum, *Primum non nocere.* Who can tell? It is perhaps reserved for one of us to discover a plan of checking the fatal atrophic process.

Seek, always seek—that should be the greatest aim of every progressive man. But one must know how to seek. In order to seek well, one must possess a firm will, a faith strong enough to overcome many difficulties—the tangled brushwood that always bars the road to innovators.

Every great mind has been a seeker consecrated by success.

How did Pasteur discover the vaccine of hydrophobia? How did Behring find the serum of diphtheria? To enter upon our own domain of ophthalmology, how did von Graefe find a plan for curing glaucoma, a malady looked upon as hopeless before his time?

It was not by physiological experiments, nor by calculations, nor by theoretical deductions that he found the remedy for an affection of which, even to-day, we can scarcely be said to know the exact explanation.

Von Graefe had seen his teacher, Desmarres, perform iridectomy in iritis, chronic irido-choroiditis, etc., conditions often associated with glaucomatous symptoms. An intrepid investigator, because well informed, Graefe was the first to practise this delicate surgical operation upon an eye affected with glaucoma.

Truly, when faced by a disease hitherto deemed incurable, every attempt, even the most hazardous, is allowable—nay, commendable—to the therapist really worthy of the name. But von Graefe was an observer and an experimentalist of the first rank. Read, for example, his numerous works upon iridectomy. You will then see with what care he studied the action of the operation in pathological ways which have nothing to do with glaucoma, but on which that operation exercised a favourable influence, without it being always possible to explain the why and wherefore. Von Graefe tried, and was crowned with success. It is often thus. *Audaces fortuna juvat.*

It would occupy too long to report all the other discoveries made upon such lines. In the course of these Lectures we shall see how therapeutic experiment led Secondi to discover the remarkable curative properties of subconjunctival injections of corrosive sublimate. Physiologists may reason from their experiments on animals that mercury does not penetrate the media of the eye. When faced by numerous and well-recorded observations, however, they can point only to negative facts.

On the other hand, we shall see that experimental physiology has

introduced into the realm of ocular therapeutics the wonderful cocaine, and a host of other valuable alkaloids, such as euphthalmine, scopolamine, those interesting mydriatics, eucaine, holocaine, acoine, and dionine, ocular anæsthetics which in some respects are superior to cocaine itself.

It is by bacteriological experiment that we have learnt the undisputed superiority of the organic salts of silver as compared with the over-caustic, though useful, silver nitrate. Among these agents, protargol (proteinate of silver) deserves a place of honour; and it is not one of the smallest merits of experimental therapeutics that the latter has produced a local remedy possessing nearly all the advantages of silver nitrate without any of its drawbacks, of which some may be serious.

Experimental therapeutics is prolific, not only in immediate discoveries, but is often the cause of indirect discoveries, which finally may come to possess a more important bearing than the fact originally sought. Thus, it was while studying the action of dionine upon the circulation of the eye that the analgesic properties of that medicament in painful ocular affections was discovered quite by chance.

It is very probable that the anæsthetic properties of cocaine as regards the cornea were found when studying its action upon the pupil, a discovery that has led to a complete change in operative work.

But, Gentlemen, before leaving this interesting subject, allow me to add a few words more. I fail at this moment to recall the name of the author who said, "Nobody can be a good doctor who has never himself been ill."

For my own part, I have believed in this axiom ever since an attack of typhoid fever at the end of my medical studies.

I learnt more perhaps during that illness, philosophically speaking, than I did during the course of my professional studies. Never before did I enter into the great importance of the physician's *rôle*. It is with a feverish impatience that one awaits his coming—that one hopes, after a consolatory word, that he will give a promise of cure, or, at least, confirm an improvement.

Let us therefore treat our patients as we would like to be treated ourselves, and we shall gain as much that way as our patients themselves.

It was during and after my illness that I was seized with a taste for self-experimentation, invaluable for the right appreciation of the therapeutic properties of this or that remedy.

Take advantage (believe me when I say so) of all the sad occasions that nature may offer you in order to study seriously the action of remedies which you yourself prescribe.

If we glance back over the last twenty years, you cannot fail to be struck, as I am, with the trivial nature and the monotony of the remedies adopted at that time by oculists the whole world over.

A genius, they say, often swallows up the whole intellectuality of a family, and may even weaken or paralyse the effects of an entire generation. The influence of von Graefe has been immense and fertile, but at last, nobody daring to do otherwise than the great master, stagnation was produced in ocular therapeutics, a stagnation that Graefe would himself have condemned had he not died so young.

Ten years ago, when I was sent by the Minister of Public Education to study the practice of ophthalmology in the Universities of Central Europe, I was struck by two facts; first, by the same therapeutical poverty as prevailed in France; and, secondly, by the admirable development and the surprising flights taken by the various eye establishments or institutions. Their organisation was complete; the arrangement of the wards, operating theatres, and laboratories, where so many students worked, left nothing to be desired, and might serve as models for our *cliniques*. Tuition was carried out methodically, with a science conscious of itself, and was seconded by practical demonstrations calculated to hold the attention of the students. The last were numerous, considering that they were not compelled to attend the course of lectures. I have been present at many lectures and consultations where, after an academic description of the etiology, pathogeny, and anatomy of the disease, when came the important chapter of treatment, one was astonished with the simplicity, poverty, and trivial nature of the means placed at our disposal by a science organised so admirably. In these circumstances, how many times have I heard the conclusion, couched in good Latin, but opposed to all medical progress, namely, *Therapia nulla!*

To know how to avow one's ignorance, indeed, is a proof of profound philosophy, and medical men are apt to err in the opposite way. But if impotence be admitted before students, to whom one should endeavour to pass on the sacred fire of science, one should at least soften the avowal by making it clear that the rising generation, with improved means, may do much better than its predecessors, which should always be the case.

The measures of twenty years ago are still to be found in many

French and foreign *cliniques*—in sum, the omnipotent triad: **mercury, silver nitrate,** and **atropine.**

Indeed, the last-named agent had acquired such an importance that it was prescribed in almost every case; it could almost be said that every oculist had become an atropinomaniac, to the detriment of the patients, who were thereby deprived of the function of accommodation.

However, there is but one indication for the use of **atropine,** *viz.* the fear of posterior synechiæ. Whenever you dread any complication as regards the iris, it becomes necessary to secure a marked dilatation of the pupil as quickly as possible. That is the principal *rôle* of atropine, the direct consequence of its mydriatic powers. Atropine still retains an important place in ocular therapeutics.

As to the alleged antiphlogistic properties of atropine, they are illusory, and do not compensate for the great inconvenience which the drug produces in depriving patients of their accommodative power.

There are, it is true, some cases where such deprivation is useful and even necessary; for example, in myopia produced by spasm of accommodation, and in certain cases of convergent squint—above all, when occurring in children too young to wear spectacles. Nevertheless, the foregoing are therapeutic exceptions.

In phlyctenular keratitis, which was and still is often treated with atropine, we seldom employ mydriatics. Adrenaline, as an antiphlogistic, or, rather, as a vaso-constrictor, and yellow ointment, as a local remedy almost specific in this malady, bring about the speedy cure of these superficial forms of keratitis, when the general health is not too seriously involved. Atropine is reserved exclusively for cases where the keratitis is central and persistent.

When the substance of the cornea is deeply involved, as in parenchymatous keratitis and certain deep inflammations, atropine is indicated, inasmuch as the iris may become affected, and synechiæ must be prevented at all hazards.

Concerning **silver nitrate** I can speak no ill, for it is one of the most potent antiseptic local applications. It has, until recently, rendered such good service in all forms of conjunctivitis that a garland should be woven for the one who introduced it into eye work.

But, as we shall see later, the incessant progress of organic chemistry has given us still more valuable agents, since while they are as active as, they are less harmful and are managed more easily than, silver.

We shall study this subject at some length when we come to

speak of the treatment of the various forms of conjunctivitis with protargol, ichtargan, etc.

With regard to **mercury**, for want of something better it still remains our supreme resource in most of the affections of the deeper structures of the eye.

In the course of the present work we shall go carefully into the study of mercurial medication. We believe that mercury should not be regarded exclusively as an antisyphilitic remedy. The ancients were right in attributing to it an alterative and potent resolutive action, the existence of which we cannot deny.

Moreover, we nowadays recognise in mercury antiseptic virtues, which place it in the front rank with the salts of gold and silver amongst the most powerful microbicides. On this account it renders us yeoman service in operative work, as well as in the treatment of infectious eye diseases.

We shall have, therefore, to study at some length the different forms of mercurial medication—inunctions, absorption by the digestive tract, hypodermic injection of soluble and insoluble salts,* of watery and oily solutions, etc.

Lastly, we shall enlarge upon intra-venous injections, which we recommend more especially under the form of subconjunctival injections of cyanide of mercury.

How seductive this new therapeutic idea! It allows us to apply to the eye itself, as it were autonomously, this or that remedy indicated by the nature of the local mischief.

A new horizon unfolds itself before the clinician, an horizon the more brilliant insomuch that it can be seen only from afar through the prism of enthusiasm and novelty.

After ten years of contradictory observation and experience have been passed through the sieve of scientific criticism, we are in a position to form a relatively exact idea of the true value of subconjunctival injections and the chief indications for their use.

The study of these indications (which we shall pursue together) will give us the chance of discussing in detail the treatment of traumatic infections of the eye, simple wounds, penetrating wounds, erosions and infectious ulcers of the cornea, deep and parenchymatous keratitis. In these last cases we shall insist upon the importance of general treatment based upon an exact knowledge of the etiology of the affection.

We shall next pass to diseases of the iris and ciliary processes. They will naturally bring us to the interesting study of sympathetic

* The last are little to be recommended.

ophthalmitis, on the nature of which the progress of bacteriology has cast a new light.

Glaucoma, its pathogeny and treatment, will detain us for some little time.

We shall see, as we go along, that many affections of the retina and choroid, which can scarcely be said to have been locally treated until recent times, may now and then be much benefited by subconjunctival injections.

By its ocular reagents ophthalmology has already furnished pathology and therapeutics with much valuable information. These may be divided into:

1. Agents that modify superficial sensibility, or **anæsthetics**, such as cocaine, eucaine, and holocaine.

2. Agents that modify deep sensibility, or **analgesics**, as dionine and other derivatives of morphia.

3. Agents that modify muscular tone, such as atropine and euphthalmine (**mydriatics**), or eserine and pilocarpine (**myotics**).

Lastly, experimental therapeutics has recently placed us in possession of powerful **modifiers of the vascular tone**, which render signal service not only as therapeutic but also as diagnostic agents, allowing us to recognise certain pathological states difficult to detect until now.

The extract of supra-renal capsule is the most potent vaso-constrictor known to us. Applied to the conjunctiva, it provokes a profound anæmia of the whole ocular surface; injected under the conjunctiva, it produces a marked reduction of intra-ocular pressure. The latter fact finds its explanation in contraction of the vessels and other anatomical elements of the ciliary body, the secretion of which is, as it were, suspended. The supra-renal capsule extract is indicated in strumous affections of the cornea and conjunctiva, spring catarrh, episcleritis, glaucoma, etc.

Lymphatism may be considered as a lymphatic and capillary atony, possibly due to a functional inadequacy of the supra-renal capsules. Supra-renal opotherapy has given encouraging results in rickets.

Dionine, on account of its profound analgesic properties, has quite recently made us comprehend vaso-dilatator properties lying unsuspected until the present time. The capillaries, under its influence, become three or four times bigger than usual, while the capacity of the lymphatic vessels becomes increased tenfold.

All people do not react in the same way to dionine. Healthy adults show merely a marked conjunctival hyperæmia without chemosis; while those who suffer from arterio-sclerosis, Bright's

disease, or cardiac affections present a chemosis sometimes of marked degree. Among children and young persons dionine may serve to diagnose lymphatism and scrofula, since, in such subjects, the reaction is as pronounced as in the pathological conditions mentioned above as attaching to an inadequacy of vascular tonus. We shall later return to this reaction, as interesting as it is new.

Anæsthetics, as well as the new class of ocular analgesics, present an extremely attractive subject for study. We shall discuss them carefully, as well as the different myotics, mydriatics, and so forth.

Antiseptics and various local applications will lead us up to the study of conjunctivitis, one of the most important questions for the practitioner. We shall then consider the differential diagnosis of maladies affecting the conjunctiva and the edges of the eyelids.

Our therapeutical studies will terminate by the consideration of some physical agents, such as heat, cold, electrotherapy, etc.

Massage of the eye, in its different forms, will also be discussed. You will see that its mechanical action exerts a great influence upon the tonus and nutrition of that organ. Traumatic myopia shows us that pressure on the cornea is able to modify refraction materially, so as to transform, for the time being, a hypermetropic into a myopic eye. Indeed, well-applied massage is one of our most powerful and interesting mechanical agents, of great value in affections of the cornea and conjunctiva, and even in glaucoma.

You see, Gentlemen, that our programme is interesting. I shall endeavour to explain my ideas as simply, clearly, and practically as possible. Should I succeed in inciting you to pursue experimental therapeutics, and the means of curing disease better and more quickly than our predecessors, then shall I have reached more than the end at which I aim.

LECTURE II.

Summary.

Oculists are, above all, interested in one method of general therapeutics. Mercurial medication; its importance, and the abuses to which it has been put.—Different ways of administering mercurials: mercurial inunctions; absorption by the stomach; hypodermic injection of soluble and insoluble salts.—Brilliant future of intra-venous and of subconjunctival injections.—Importance of local treatment in eye work.

We have seen in our first Lecture what an important place is occupied by **mercury** in the treatment of diseases of the deeper membranes of the eye.

Empiricism possesses a distinct value, and one must not deny its worth because one can understand its action, or can explain it but imperfectly. In fact, mercurial medication, despite the abuses to which it has been subjected in ocular therapeutics, is nevertheless, when well administered, one of the most precious arms of our arsenal.

Empiricism (which we nowadays term clinical observation) is, it must never be forgotten, our great master, even more so than the laboratory and the microscope. Experimentation should compel us to verify the facts presented to us by clinical work.

To-day, with modern pathogenic theories, we are in a position to form a more exact idea of the therapeutic action of mercurials. The latter act as topical applications when we employ them against keratitis, as in yellow ointment, calomel, etc.; as wound-disinfectants, as in solution of sublimate, of cyanide, etc.

As a general remedy, mercury often acts as an antisyphilitic, but in many instances it has a bactericidal or microbicidal action, a very pronounced antiseptic provoking an abundant production of phagocytosis; we ought to attach the greatest importance to these last and important properties of mercurials.*

* It is not correct to believe that mercury always exercises a general lowering action on the system. In small doses, it exercises, on the contrary, a tonic action on the heart, increases the blood-pressure, enhances the number of red blood-cells, and augments the weight of the body. It acts, however, otherwise when given in large doses. In this case its effect on the heart is incontestably weakening, the blood-pressure is lowered, the number of red cells is diminished, and the amount of hæmoglobin is reduced.

There is yet another mode of action, which was admitted by the ancient writers, and has certainly its interest. They attributed to mercurials an alterative action, whereby they were able to dissolve exudations of different kinds.

We have to-day the proof of this dissolving power, both by clinical experience and by experiment. In fact, in the calcareous infarcts of the kidneys seen in mercurial intoxication, are we not able to see a dissolved osseous substance arrested by the renal filter?

Experiments upon animals have shown, in fact, that nephritis consecutive to mercurialism is due to an irritation of the excretory elements by the calcareous salts transported by the blood.

The number of ways in which mercury can be applied is as great as it is varied. We shall pass in review the principal ones only. **Frictions** have survived all the other mercurial applications, so strange and so curious, employed by the ancients; they constitute, however, the quickest and most efficacious way of arriving at mercurial saturation. They are therefore indicated when it is important to obtain in as short a time as possible an intense mercurialisation of the whole body, as in certain cases of iritis, irido-cyclitis, irido-choroiditis, accompanied by violent inflammatory phenomena, whether due to syphilis or to some traumatic infection, as in sympathetic ophthalmitis.

Apart from this, the main indication for friction is in cases where it is impossible to administer subcutaneous or intra-venous injections, either because the patient refuses them or for some other reason. In order to act more quickly one may, however, combine the two methods, local mercurial frictions and hypodermic injections; while, for my part, I sometimes do not fear to make at the same time sub-conjunctival injections when the latter are indicated by the gravity of the local accidents.

Frictions have a prompt and efficacious action when carried out under the direction of a medical man, but they are liable to have the contrary effect when left to the discretion of the patient himself, who always feels a certain repugnance towards a treatment as dirty as it is troublesome.

Under these circumstances, we cannot recommend too highly *mercurial lanoline*, which undergoes little change, and which is absorbed more easily than Neapolitan ointment. Four grammes of this medicament are prescribed daily.*

Let us leave on one side the **administration of mercury by the**

* MM. Chaumel, chemists in Paris, prepare gelatine *ampoules*, each containing four grammes of mercurial lanoline, which keep indefinitely.

stomach. We are far from denying that this method is devoid of efficacy. On the contrary, it has furnished its proofs, and has its fervent disciples. Indeed, it even possesses some practical aspects that cause it to be preferred by de Wecker, Abadie, and others, in the treatment of the choroiditic complications of myopia. Sublimate pills, in fact, often yield satisfactory results in these particular cases.

At one time tiny doses of calomel had a great vogue in eye work, but we know better now, and this mode of administration, although valuable, no longer presents indications except in special cases.*

Administration by the stomach has the grave inconvenience of being untrustworthy and irregular, because the amount of mercury absorbed depends entirely upon the state of the digestive tract and upon the quantity that is able to traverse the liver without being eliminated in doing so. The liver, amongst its other functions, serves as a filter for everything absorbed from the digestive tract, as I have often seen in the laboratory of my venerated master, Professor Schiff. This interceptive function of the liver is a fact that henceforth we must reckon with seriously in therapeutics; it explains why there is now a growing tendency to administer medicine hypodermically.

That is, in point of fact, the most practical way of giving medicine which keeps the patient under the immediate and continuous control of the medical man. The doses are always graduated exactly, and the administration takes place at regular intervals. The patient cannot possibly deceive the physician with respect to the doses taken.

Many different mercurial preparations have been employed as **hypodermic injections**, salts soluble and insoluble.

The employment of insoluble salts ought to be, if not completely rejected, at least adopted with great precaution. One must commence with small doses, in order to feel one's ground. There exist, in fact, idiosyncrasies with which one must reckon under penalty of serious poisoning and even death. Seventeen cases of death following the injection of insoluble salts have already been published. Instances of pulmonary and of cerebral embolism have also been related. Speaking for myself, I never practise massive injections before I have proved the tolerance of the patient by increasing injections of soluble salts.

* In eye affections, probably of an acute infectious origin, the following formula will be found of service if a purgative is needed:

Calomel	0·20 to 0·60 centigramme.
Scammony	0·20 to 0·60 „

S.—*In one dose to be taken late in the evening.*

As I have myself observed several instances of intolerance towards mercurial medication, I will say a few words on the subject.

It is useless to speak of cases where mercurial frictions or small doses of calomel caused, in a few days, violent stomatitis with gastric disturbance. That would be merely commonplace. I desire simply to cite a fact which struck me. It occurred in the days when sympathetic ophthalmitis was treated exclusively by enucleation and by mercurial frictions to excess.

A young girl treated in this way had, as the result of long-continued mercurial frictions, complications as regarded her kidneys, which placed her life in serious danger (probably parenchymatous nephritis by calcareous infarcts, proceeding from the decalcification of bone induced by the mercurial treatment). However, she retained the sight of the affected eye.

During the last eighteen years, since we have adopted hypodermic injections, on the recommendation of M. Abadie, to whom belongs the credit of having generalised this mode of treatment, we have practised them daily, and have never met with a serious accident. The latter may be readily understood, since one sees the patients daily or on alternate days, and so can always interrupt the treatment if the same is badly borne. The urine should be frequently examined.

In this case the symptoms first complained of by the patient include abdominal pains, colic, cramps in the stomach, sometimes bloody diarrhœa, and sometimes vomiting. The first cases of intolerance which we observed manifested themselves after about ten hypodermic injections of one centigramme of sublimate in two gouty subjects, who both showed the same symptoms of colic and sanguineous diarrhœa. Since the occurrence of the foregoing facts our attention has been directed to this aspect of the question, and we have observed in all five or six cases amongst several hundred patients.

Young subjects, in full health, may present this intolerance towards mercury under whatever form it may exist. What would happen to such patients if, instead of an ordinary dose of a soluble mercurial salt, an injection had been made of a massive dose of calomel or yellow oxide? Death would be the probable consequence.

It may be well to add that experience has recently shown that the intolerance is relative only, and that one can easily accustom the patients to bear large quantities of mercury by commencing with small doses and by progressively increasing them. I will cite only two cases as examples.

The first was a child of 8 years affected with a bilateral parenchymatous keratitis, associated with obvious hereditary syphilis.

Children, as a rule, bear mercurial treatment admirably, so without any hesitation I made a first injection of 0·008 of cyanide of mercury in 3 c.c. of saline water. The patient had a little diarrhœa. Two days after a second injection was made of 0·006, and this was followed by bloody diarrhœa. The treatment had to be stopped for several days.

The condition of the patient underwent a notable improvement. One point had struck the mother—namely, that since the two injections the child had been free from hæmoglobinuria,* a concomitant affection from which he had suffered for more than a year. The mother was accordingly inclined to adopt the treatment again.

Injections were made of 2, 3, and then 4 milligrammes of the cyanide. The tolerance was perfect, and the little patient was cured completely, both of his parenchymatous keratitis and also of his hæmoglobinuria, which had resisted all measures for more than a year.

The second case occurred in a woman affected with specific choroiditis, a disease which was cured despite the very alarming intolerance to mercury shown at first.

It is true that such marked instances of intolerance are rare. It is, however, necessary to recognise their existence, and to reject the advice of those who claim that you may inject at once 5 centigrammes of sublimate.

In certain very grave cases I have gone by progressively increased doses so far as to use 5 centigrammes of sublimate or of cyanide of mercury, but I have rarely been able to keep up that dose without provoking colic and diarrhœa, which at once caused me to reduce the amount.

It is well to note that in almost every case these toxic effects have not remained without benefit, since, on the contrary, improvement of the eye disease has always been more rapid and evident.

Many soluble salts have been employed. They are all good, and there is nothing much to pick amongst them. Above all, we have used with Abadie peptonate of mercury and corrosive sublimate.

The injections of oil with bi-iodate of mercury, to which Professor Panas has given the preference for some years, have also yielded me good results, but they are neither less painful nor more efficacious than injections of cyanide, of which we shall speak later. They are, in return, less easy to render aseptic.

* This is a curious bit of internal evidence pointing to the truth of the view, now held by certain authorities, that the cause of paroxysmal hæmoglobinuria is congenital syphilis.—TRANS.

During the past ten years we have given the preference to *cyanide of mercury*, on account of its solubility, its rapid absorption, and the trifling amount of pain caused by its injection. Moreover, there is the additional advantage that, unlike sublimate, it does not precipitate cocaine, a point which allows us to make our injections practically painless by using the following solution :

Cyanide of mercury . .	0·30 gr.*
Hydrochloride of cocaine . .	0·15 „
Distilled water . . .	30 „

The injections are supported very well, and if care is taken to inject them each time into a different part of the body, induration is never observed. To obtain a rapid, intensive effect, they are repeated daily, and it may surprise some of our *confrères* if we state that we thereby get effects as rapid as with the most energetic frictions, and without any serious inconveniences. But one must never neglect to question the patient with regard to the state of his bowels. As soon as ever the least colic arises, the dose must be reduced. Colic and diarrhœa, sometimes bloody, are the first signs that the maximum dose has been reached. I have rarely seen stomatitis ; the intestinal accidents are instantly cured by an injection of morphine or by a dose of paregoric.

The patient ought to be shielded from these mishaps. The perfect resorption of the injected liquid—which is, in fact, artificial serum—allows of rapid diffusion through the entire organism, while elimination is facilitated by the mass and the temperature of the liquid, which is always injected at 30° to 35° C.

Rapid and intense action and prompt elimination—such are the advantages of injections of cyanide of mercury. All injections allow of a dosage precisely adapted to the desired results, from the slightest to the most energetic, while avoiding the phenomena of intoxication.

The **intra-venous injection** of soluble mercurial salts, and especially of cyanide of mercury, *constitutes the last word on the application of mercury*. I am in a position to say that I am a partisan of the plan, and it is nowadays to intra-venous injection that I have recourse almost exclusively.

It is evidently a delicate proceeding in unskilful hands, but practised by a surgeon trained in the principles of asepticism and of serious clinical experimentation, it presents advantages of the first

* Thanks to a new therapeutic agent, *Acoine*, which has a longer and more profound anæsthetic action than cocaine, it is now possible to render injections of cyanide of mercury almost completely painless (*see* Lecture V).

rank—absence of all pain and of all local changes such as infiltrations, nodosities, with a certain and rapid action.

The solution should be very pure and aseptic, and, above all, free from cocaine, or any other analgesic which might act too quickly upon the heart and the nervous centres. Here is the formula which I recommended at first:

Cyanide of mercury . . .	0·10
Chloride of sodium . . .	0·08
Sterilised distilled water . .	30 gr.

Three centimètre cubes of this solution, containing one centigramme of $Hg(CN)_2$, is to be injected into one of the veins at the bend of the elbow. One knows also, serving oneself of the principle of abundant and dilute injections, how to use solutions of 1 : 300 or 1 : 500, always with 8 per 1000 of chloride of sodium; one injects, then, 3 to 5 cubic centimètres of one of these solutions, taking care to push the injection slowly, especially if the liquid has not been warmed. If stronger doses are needed, you may use more concentrated solutions.

For my part, I have made thousands of intra-venous injections without the least complication, except occasionally a little periphlebitis when a trace of the liquid had passed outside a vein. Even the penetration of big bubbles of air into the vein of the arm is devoid of danger.

Nervous subjects may experience, on the first occasion, a certain amount of fear. This readily makes them feel faint, especially if the injection is forced too rapidly into the vein. But this trifling drawback is compensated by the great advantages of intra-venous injections.

In order to make the vein stand out well, one applies one or two turns of a bandage tightly around the lower part of the biceps muscle, and, while the venous stasis is brought about, cleanses the spot where the injection is to be made with a pledget of wool steeped in chloroform. Then, the fine needle of iridised platinum having been heated, one plunges it into the vein with care, and, before injecting, one aspires lightly for the purpose of seeing if blood rises in the syringe. In this event one is certain of not having made a false passage. The bandage is removed, and nothing remains to be done except to push the liquid gently into the vein. The patient mentions a sensation of coolness, and sometimes a taste as of almonds in his mouth. The needle should be withdrawn gently, and light pressure applied with a tampon of wool over the site of the puncture, and the imperceptible orifice is then closed hermetically with a drop of

collodion. After a certain number of injections, one must change the vein, or return to hypodermic injections, in order to give rest to the veins, which might otherwise become occluded.

Whether one resorts to hypodermic injections or to the intra-venous injection of cyanide of mercury, one must never omit to ask the patient, before each fresh prick, if he has experienced any colic or diarrhœa after the last injection. In such an event, the doses must be diminished or the injections made less frequently.

After a first series of twenty to thirty injections, it is good practice to prescribe a month's rest prior to taking a second or even a third series. In certain relapses of slow and uncertain evolution, as in parenchymatous keratitis, irido-choroiditis, and choroiditis, one may be forced to give, in the course of two or three years, more than two hundred injections.

There are also cases where the ordinary doses may have to be raised to an extraordinary degree. Thus, I have now and then found it necessary to inject $Hg(CN)_2$ two or three times a week, in order to check the progressive loss of sight in cases of malignant syphilitic choroido-retinitis. In such circumstances we must thoroughly understand the physiological, or, rather, the toxic, reactions of the drug. Contrary to what obtains in the other forms of mercurial medication, stomatitis rarely interferes with treatment by intra-venous injection. A little salivation and gingivitis may be seen at the beginning, especially in smokers, but tolerance is rapidly established. The earliest toxic reaction, the real touchstone of intoxication, is furnished by intestinal disturbances. That fact once grasped, our therapeutic activity can easily be regulated.

Is it always necessary to saturate the entire organism with mercury for the purpose of curing an affection absolutely localised to the eye?

The further we advance, the more exact we become, the more we seek to apply the remedy to the affected organ itself, while confining, as much as possible, the strife of the medicament against the pathogenic agent to the infective point itself.

The thing is easy when the seat of the evil is accessible and when its destruction is possible without harming the sick organism. But, as a rule, when dealing with the eye we must content ourselves with rendering the environment unsuitable for the life of the pathogenic agent, by irrigating the neighbouring lymphatic territory with an antiseptic such as we believe to be the most fatal to our enemy.

Many ocular affections may thus be treated locally, perhaps by injecting the remedy into the eyeball itself (as M. Abadie was the

first to do), or, perhaps, by simply injecting the remedy beneath the conjunctiva. **Intra-ocular injections** have their special indications. They are suited for those grave cases where anything may be tried in the hope of saving an eye which we believe to be absolutely lost. They are, unhappily, sometimes associated with serious consequences, which makes one hesitate to apply them currently.

It is by no means the same with **subconjunctival injections,** which merely entail a little pain, and never lead to the loss of an eye. They irrigate the lymphatic spaces of the eye with a 1 : 5000 solution of cyanide of mercury or of some stronger solution.

The local therapeutics, which we have followed for several years,* is not based solely on empiricism. It rests upon important anatomical and physiological laws, as set forth in a communication made in 1892 to the Ophthalmological Society of Paris. We shall in this place insist only upon certain points.

Local therapeusis is now the order of the day, not alone in ophthalmology, but in all the branches of medicine. Whenever it is possible to strike at a morbid focus of disease, the surgeon lays claim to a considerable share in the treatment of maladies once supposed to belong exclusively to the domain of medicine.

In dermatology, perhaps more than anywhere else, local treatment has assumed more and more importance, while the great diathetic doctrines are little by little despoiled of many of their attributes, to the advantage, therefore, of those local infections which appertain principally to local treatment.

Even affections dependent upon a general malady, as syphilis, tuberculosis, and rheumatism, have, side by side with their general indications, local indications of the highest importance.

If marked manifestations show themselves in different organs at the same time, general treatment is the first indication. If, on the contrary, the accidents are absolutely localised to a single point, local applications should be adopted.

This law is better able to be applied to eye maladies. These often manifest themselves as unique phenomena, which we connect with a general diathesis of a more or less problematical character. The fact is that we do not know the true explanation.

We have always been guided in our researches by the following idea :—*whenever a primary or secondary affection is localised in an organ as important as the eye, it becomes of the greatest consequence to prevent and extinguish the infection locally, if possible, without*

* Darier, *Bull. de la Soc. d'Ophtal. de Paris,* 1888.

losing sight of the general indications. When this can be effected surgically, by the knife or the cautery, the end is quickly attained; but if the lesions are not superficial, or involve tissues which it is important to preserve, what local means then remain to us?

Sublimate dropped into the conjunctival sac (already practised by Scarpa) has been recently reinstated in honour by Gallenga,* who obtained by these means the cure of four cases of sympathetic ophthalmitis.

Secondi has tackled the subject in a more scientific way, *viz.*, by injecting sublimate under the conjunctiva. I had myself in 1888, starting from the arguments advanced above, injected quicksilver, asepticised as well as possible, under the conjunctiva of the lower cul-de-sac. At the end of several days, however, a small abscess formed, from which, when incised, escaped a globule of mercury and a little pus. I had not dared to inject sublimate, because it was thought too caustic.

Inject the antiseptic into the infectious focus itself or into its immediate surroundings in such a way as to irrigate and to asepticise the whole of the lymphatic territory in which the morbid process has lodged itself. Such appears to us to be the end of all treatment of every well-localised infectious malady.

* Gallenga, *Atti Reale Accademia di Medicina di Torina*, 1887.

LECTURE III.

Summary.

The mode of action and of penetration of substances injected beneath the conjunctiva.—Absorption by the cornea and the conjunctiva.—The penetration of fluoresceïn into the media of the eye.—Clinical work and experimentation.—Cyanide of mercury and chloride of sodium.—Trophic and antiseptic action.—The technique of subconjunctival injections.—They may be rendered painless by acoine.—Clinical indications and contra-indications.

The eye lends itself admirably to local therapeutics, because of the arrangement of its lymphatic system, which is made up of spaces communicating readily one with another.

It is well known that atropine, even in feeble solution, instilled into the conjunctival sac, is resorbed by the ocular lymphatics, and penetrates into the contents of the anterior chamber. Mydriasis may, we know, be induced in a second animal by putting into its eye a few drops of this aqueous humour.

Pflüger has proved the same thing by injecting under the conjunctiva a solution of fluoresceïn, a stain having great powers of diffusibility. He has observed, under such circumstances, that not only does the aqueous humour become tinged, but also the cornea and the crystalline lens.

Bellarminof, by simple instillations into the conjunctival sac, has also been able to colour the aqueous humour with fluoresceïn.

But it has been objected that salts of mercury form with the albuminoids of the body insoluble compounds unable to penetrate into the ocular media. In order to prove the point, one has made subconjunctival injections of sublimate or of cyanide of mercury in the rabbit, and several hours afterwards has failed to find any trace of mercury in the aqueous humour.

But the seeking for a mercurial reaction in a solution as dilute as it must be in the aqueous humour is a thing which is yet beyond the powers of our chemists and actual micrography.

It is the same as regards atropine, which we could never recognise

in the aqueous humour by its chemical reactions, but which we trace by its physiological reaction as a mydriatic.

As to fluoresceïn, its power of diffusibility is so great, and its colouring properties so intense, that an infinitesimal particle is enough to produce colouration of the aqueous humour.

For mercury, a chemical reaction is impossible under 1 : 100,000, but who can say what fraction of a millionth suffices to bring about a physiological reaction of a therapeutic nature in the tissues of the eye?

Do you know that gummata of the iris disappear rapidly under the influence of mercurial frictions, or of hypodermic injections, or of intra-venous injections? Well, has it never occurred to any observer to seek, after the gumma has vanished, whether the aqueous humour contains a ponderable amount of mercury?

When this reaction has been made by the experimenters who are so severe in their observations on the rabbit, I shall attach some value to their negations.

Negative facts have never been allowed to invalidate positive facts, well and duly observed.

What would these controversialists say when faced by a case of this kind?—a gumma of the iris as big as a grain of wheat; three subconjunctival injections of two drops of a solution of sublimate, 1 : 1000, caused the gumma to disappear completely in six days. No other treatment had been applied.

Is that not a clinical experience worth a hundred negative analyses carried out on the rabbit?

This fact is not the only one. I have seen many cases of this kind, the last one only a month ago. I have arrived at the point of thinking that this treatment is deceptive in one respect, namely, that the local disease is so quickly cured by it that the patient stops all treatment when he should undergo a prolonged mercurial cure to prevent ulterior accidents.

Better still—when Mellinger published his first criticisms upon the subconjunctival injection of mercurial salts, holding that chloride of sodium acted better than sublimate, a syphilitic patient consulted me with chorio-retinitis in the two macular regions. I could scarcely hope to find a more favourable subject for experiment. I practised injections of chloride of sodium, 4 per cent., on the better eye, and on the other eye injections of cyanide of mercury, 1 : 1000. After five injections the sight in the latter eye became normal; in the former not only did the sight fail to improve, but the time wasted by this experience hindered the therapeutic effect of the subconjunctival

injections of mercury applied too late. General treatment by hypodermic injection of cyanide of mercury was equally without effect.

One must not forget, as you know, that the gravity of macular lesions lies in the time that has elapsed since their appearance. Just as it is easy to recall to life retinal elements which have been compressed but momentarily, so is it just as difficult to resuscitate those which have been completely atrophied.

In science we must not act the partisan and see but one side of the question. Mellinger has related very interesting observations where he noted great improvement following the injection of saline water. I have also employed these simple and anodyne injections in many cases where mercury was not indicated—as, for example, in simple corneal infiltrations, the choroidal complications of myopia, certain troubles of the vitreous humour, etc.

But when trying to stay the course of an endogenous or ectogenous ocular infection, one must always have recourse to subconjunctival injections of cyanide of mercury, as well as in all specific affections of the eye, superficial or deep.

We may note in passing an interesting observation, which, so far as I know, has not hitherto been mentioned. Between the ocular and periocular lymphatics there exists an intimate communication with the intra-cranial lymphatics.

This conclusion I arrived at while engaged in making my researches upon the deep ocular analgesics.

Having placed in the conjunctival sac 2 to 3 milligr. of pure morphine, which dissolved with difficulty in the lacrymal fluid, I was surprised to observe at the end of an hour very violent symptoms of intoxication—pallor, faintness, then abundant cold sweats, followed by vomiting, which lasted at least two hours, despite the repeated administration of strong infusion of coffee.

These phenomena must be explained by the absorption of the morphine by the conjunctiva, nasal canal, and the pharynx.

But a subconjunctival injection of 4 to 5 milligr. of hydrochloride of heroine (the diacetic ether of morphine), having produced toxic symptoms of as marked a character cannot fail to cause surprise; for in hypodermic injections 20 to 30 milligr. of heroine were certainly necessary to produce emesis and so prolonged a state of prostration.

But this was not all. In two other cases, after a simple instillation of two or three drops of a 5 per cent. collyrium of heroine, slighter signs of intoxication manifested themselves, as pallor, dazzlings, vertigo, and a state of nausea.

That cannot be by an action upon the eye itself. One can only

explain these phenomena by assuming a direct penetration of the morphine into the cranial cavity, very probably by the intermediation of the ocular and intra-cranial lymphatic spaces, which are closely connected.

Vascular absorption is not admissible in this case, since no action was noted on the centres through the great veins and the sinus; and one knows that in a hypodermic injection at least one or two centigrammes of these salts of mercury must be used in order to provoke such signs of intoxication.

Penetration by the lymphatic channels explains the remarkable action of **subconjunctival injections** in certain forms of retro-bulbar neuritis.

Is it not then logical to conclude that the surest means of getting soluble medicamentous substances to penetrate into the interior of the eye is to inject them under the conjunctiva or into Tenon's space?

Our personal experience has proved that it is a matter of indifference whether the injection is made under the conjunctiva or into Tenon's space. The substance penetrates with the same rapidity into the ocular media.

How could it be otherwise, since, as we have already said, a simple instillation into the conjunctival cul-de-sac brings about a rapid absorption of atropine, which one can find in the liquid of the anterior chamber a few minutes afterwards? That fact has been known for many years.

The idea of subconjunctival injections was anterior to Secondi. Rothmund (of Munich) had practised subconjunctival injections of saline water for the purpose of dissolving, by imbibition, certain leucomata of the cornea. M. de Wecker has formerly vaunted the subconjunctival injections of saline solution to cure detachment of the retina. We ourselves in 1888 practised subconjunctival injections of pure mercury. Perhaps other observers have—before or after—made similar experiments, without their names, for various reasons, having reached us.

We do not claim any priority. We shall be only too happy if, by our prolonged researches, we have popularised the principal indications for the local treatment by subconjunctival injections in many affections of the eye against which one had until lately no other resources than general medication, which often went beyond the end, and sometimes failed to reach it, or reached it too late.

Now local treatment is called for every time when it is necessary to act with promptitude and energy.

We should not find a better example than that afforded by

sympathetic ophthalmitis, of which the only treatment until recently consisted of enucleation or mercurialisation.

Whatever the theory accepted, if general mercurial treatment is efficacious, then the local application of mercury must be even more so, a fact known to and proved by Gallenga, Secondi, Raymond, Abadie, Rogman, Coppez, ourselves, and Sourdille.

Subconjunctival injections have established, under certain conditions, the curability of sympathetic ophthalmitis, a therapeutic conquest of a very valuable kind.

In infections—secondary, late, traumatic, or post-operative—coming about through vicious or cystoid cicatrices, subconjunctival injections have yielded us results which we have never before obtained under the older methods of treatment. We have published many facts of this kind, which have been recently confirmed by several writers. In some way these facts constitute an experience of the purest and most conclusive description, proving the potency of antiseptics injected beneath the conjunctiva in localised infections not complicated with concomitant phenomena able to confuse observation.

Leaving on one side inflammations of the conjunctiva (against which local therapeutics has furnished its proofs), without, on that account, attributing a primordial influence to any general treatment, the simplest infection of the globe of the eye itself is that produced by an infected corneal erosion.

The infectious ulcer of the cornea is the commonest form. In the numerous cases which we have observed, we have invariably found that subconjunctival injections of cyanide of mercury practised for several days all around the cornea produced the surest and most efficacious antisepticism. This is not the outcome of our own experience alone, for Secondi (of Turin), Dufour (of Lausanne), Van Moll (of Rotterdam), Gepner (of Varsovie) have obtained admirable results by the same means. Further on we shall study the action of sodium chloride.

With the galvano-cautery and subconjunctival injections of mercury cyanide, or of sodium chloride, every infectious ulcer of the cornea, taken in time, can be promptly cured, which was not the case under the older methods of treatment.

That which we have claimed for the late traumatic infection is still more true for septic wounds of the eye, where ocular abscess is imminent.

If suppuration has not already spread to the deeper parts, subconjunctival injections of mercury cyanide, practised *larga manu* repeatedly, will often allow us to avoid enucleation.

If we look at the essential maladies of the deeper membranes of the eye—irido-choroiditis, retinitis, neuritis, etc.—we shall be surprised to see that even in these deep affections, of which the etiology is often very obscure, and where syphilis, rheumatism, and the most varied auto-intoxications play an important *rôle*, subconjunctival injections have in many cases given results that may, without exaggeration, be called astonishing.

At one of the last Congresses of Ophthalmology we were happy to hear Professor Pflüger (of Berne) confirm our words, saying that he had himself found that subconjunctival injections exerted, as it were, a selective action upon the choroid.

We have published many cases of choroiditis, where local treatment showed itself efficacious, while general treatment had miscarried or had become impotent.

In central choroiditis or choroido-retinitis, recent and not too deep, one is able to study, almost mathematically, the truly remarkable action of subconjunctival injections. In fact, the metrical types allow us to check exactly the progressive bettering of the visual acuity. On the other hand, the ophthalmoscope shows us with precision how the anatomical lesion advances or recedes.

We are happy to have been the first to establish this fact in an incontestable way, for we foresaw it theoretically. Physiologically the thing is easily explicable by the intimate communication existing between the choroidal lymphatics and the subconjunctival or Tenonian spaces.

We believe that it will be the same for diseases of the optic nerve; but there anatomical considerations, which are too long to discuss here, tell us that we cannot expect the restitution *ad integrum* when a certain number of the nerve-fibres have undergone atrophy. A certain therapeutic effect cannot then be expected except in cases where the optic fibres have only been compressed or weakened momentarily —in a word, one can hope for cure only in cases where the infectious inflammatory process is of recent date, and has terminated without having entailed complete atrophy.

Our researches upon this subject have been long and laborious. After a series of successes obtained in certain cases of infectious retro-bulbar neuritis, we tried what could be done in the different kinds of atrophy of the optic nerve.

In grey, tabetic atrophy the results have been negative. In white atrophy, due to former inflammatory processes, we have sometimes succeeded in improving sight, but only in a feeble degree. In optic neuritis, symptomatic of a serious intra-cranial affection,

the effect of subconjunctival injections of sublimate, although sometimes very manifest, has almost always been ephemeral. It is necessary to discover the cause of the malady in order to destroy its effects.

To finish the series of indications for using subconjunctival injections, we must speak of diseases of the iris and the ciliary body.

We have seen that in ectogenous traumatic infections, characterised by iritis, irido-cyclitis, and even by irido-choroiditis, the effects obtained by local treatment were superior to everything yet offered to us by general treatment.

We should not dare to affirm that it would be the same in all endogenous infections, proceeding from a diathesis, or rather from a general infectious malady, such as syphilis, tuberculosis, rheumatism, etc., or from a reflected or metatastic affection, as in blennorrhagia or in certain cases of metritis, etc.

Our studies upon this debatable subject are far from completed; but we are able already to affirm that in many of these affections, subconjunctival injections, if they do not constitute by themselves a complete treatment, often form a valuable auxiliary to general therapeutics.

In the different syphilitic manifestations of the iris and the ciliary body, marvellous results from the subconjunctival injections of cyanide of mercury may be rightly anticipated.

Several gummata of the iris treated by this means have been very quickly cured, as have also certain cases of chronic irido-choroiditis, which resisted long-continued general treatment. With regard to acute syphilitic iritis, real and violent, we must recognise that general treatment is the first indication. For the rest, we believe it is the same for all acute, violent, inflammatory processes of the iris and the ciliary circle, whatever be their etiology—specific, rheumatismal, or otherwise.

Prolonged clinical observation of facts of this kind, coming to oppose our first ideas, have led us to the conclusion that subconjunctival injections are contra-indicated, for the time being at all events, whenever the absorption of the medicament by the obstructed lymphatic channels is rendered difficult or impossible by a circulatory stasis. Cyanide of mercury injected beneath the conjunctiva then plays the part of an irritant body, more harmful than useful, giving rise to intense pain and marked chemosis.

This important contra-indication once established, we have often been able to prove that by following with care the clinical indications and by choosing the opportune moment, one is able not alone to

avoid the vexations mentioned above, but also to obtain very favourable results.

The **technique of subconjunctival injections** is very simple: A Pravaz syringe, with a fine needle of iridised platinum, which can be passed through the flame immediately before us, is needed. The liquids for injection must also be sterile, a point on which there is no need to insist. It is always advisable to boil the solution, which is then allowed to cool to 32° or 36° C. In this way it becomes less painful, and more easily resorbed.

No instrument is needed—neither speculum nor forceps, which merely serve to frighten patients without having any compensating advantages. The patient is directed to look strongly downwards and inwards, and pushing the upper eyelid upwards with the thumb of the left hand one exposes the equatorial supero-external part of the eyeball, which presents the largest conjunctival surface and is the least sensitive to the prick. The needle is then introduced superficially under the conjunctiva, as far as possible from the cornea and tangentially to the surface of the globe. The liquid must not be allowed to return to the limbus, where it is able to detach or to obstruct the pericorneal circle of vessels. It is after these pericorneal injections that trophic troubles of the cornea and conjunctival eschars have been observed. Moreover, when it is needful to inject a syringeful of liquid, it is necessary to enter the needle deeply and so to inject the solution behind the equator into the retro-bulbar tissue. Thanks to cocaine and a fine and well-sharpened needle, the prick is often not felt.

The addition of a few drops of a 1 per cent. solution of acoine to the liquid to be injected beneath the conjunctiva renders the injection painless for a period which varies directly with the amount of acoine and inversely with the strength of the solution injected.

Acoine is precipitated by the least alkalinity, a fact that renders the employment of this salt rather a delicate thing. In order to obtain clear solutions, all the glass utensils must be washed with acidulated water. It is, above all, with saline solutions that acoine precipitates. Sodium chloride, in fact, often has an alkaline reaction, which must be neutralised when acoine solutions are made. Acoine being much less toxic than cocaine, it should be easy to add to the solution to be injected under the conjunctiva enough acoine to render the pain almost *nil*.

The simplest plan is always to have ready a 1 per cent. solution of acoine (acoine 0·10; NaCl 0·08; distilled water, 10 gr.), of which one mixes then and there the amount desired with the solution for

injection. By adding one-third of the syringe* to two-thirds of a solution of mercury cyanide, 1 : 1000, one obtains a solution of 1 : 1500, which is almost painless. A 20 per cent. to 30 per cent. solution of sodium chloride, which causes atrocious pain, may be rendered painless by the addition of one-third of a solution of 1 per cent. acoine. A cloudy precipitate forms in the syringe, and the liquid must be injected at once if one does not wish the needle to become blocked by the condensation of this precipitate. In order to render painless solutions of cyanide, 1 : 3000 or 1 : 5000, or solutions of sodium chloride, 2 per cent. to 4 per cent., it is enough to add to them a few drops of solution of acoine.

To resume, in eye affections where general mercurial medication is indicated, the preference should be given in general to the *hypodermic injection* of soluble salts, and in particular to mercury cyanide. The injections should be repeated every other day or every day, according to the urgency of the case.

The same solutions employed as *intra-venous injections* give even superior results, with this additional advantage, that the injection leaves not the least pain behind it.

When it is impossible to keep the patient under personal control, and no doctor is available to practise the injections, *mercurial frictions* are indicated. They give good results if their proper method of application is explained to the patient.

As to *intra-ocular injections*, they are above all called for in grave affections of the vitreous body, profound traumatic infections, advanced sympathetic ophthalmitis, and serious syphilitic affections which have resisted general treatment and subconjunctival injections.

Briefly, subconjunctival injections have many indications.

1. They are the promptest and the most powerful means of producing antisepsis in traumatic or operative infections, and in infectious ulcers of the cornea associated with hypopyon.

2. They have a powerful resolutive action upon torpid parenchymatous keratitis, upon choroidal exudations and certain cases of plastic iritis, when the venous stasis is not too marked.

3. As an antisyphilitic, they have a rapid and intense action upon specific ocular manifestations at all stages.

4. The injections of sodium chloride have a powerful action upon the intra-ocular nutritive changes, quickening the absorption of corneal infiltrations, subretinal exudations, etc.

The chief contra-indication to subconjunctival injections lies in an

* The Pravaz syringe used by Dr. Darier is capable of containing 1 c.c. of fluid. It is divided into twenty divisions.—TRANS.

engorgement of the pericorneal circle of vessels. Resorption then takes place too slowly, and the injection gives rise to a violent irritation, more startling, however, than serious.

Many liquids have recently been proposed for subconjunctival injection.

Professor Pflüger, after the trichloride of iodine, has praised the good effects of **Hetol** (cinnamate of sodium), of which a 1 per cent. solution is used. This salt should possess, more than any other, the power of provoking very marked phagocytosis, a condition favourable to the absorption of exudations, toxines, and microbes themselves. The solution ought to be borne well and be scarcely painful.

I have had occasion to inject Hetol, which (with a little cocaine) is absolutely painless. The injections can be repeated frequently, as no induration follows the injection of half a syringeful of the solution. I have obtained by this means good results in some cases of parenchymatous keratitis, of tuberculous origin. It is possible that precise indications for the use of Hetol will be found in tuberculous affections of the eye, in herpes of the cornea, etc.

A new **physiological salt**, prepared by Merck, of Darmstadt, representing exactly all the salts contained in blood, has been used by Poehl, apparently with excellent results.*

But, until such time as we are better informed, we may claim that with solutions of NaCl, of different degrees of concentration, we can provoke a powerful phagocytic, lymphagogue, eutrophic, and exosmotic action; while with solutions of $Hg(CN)_2$ we can set up antiseptic, resolutive, and antisyphilitic effects of a pronounced kind.

Hetol appears to be indicated in herpetic and in tuberculous keratitis.

Poehl's **Sal physiologicum** is a white substance soluble in water. It contains the whole of the osmotically active constituents of blood-serum. It is supplied by Merck in the form of compressed tablets each containing 1 grm. Merck's *Annual Report*, March, 1900, p. 129.—TRANS.

LECTURE IV.

Summary.

Collyria employed from extreme antiquity.—Dry collyria: powders (calomel, iodoform, etc.).—Moist collyria: ointments.—Liquid collyria, their mode of action and of penetration through the lymphatic spaces into the media of the eye and cranium.—Demonstration by fluoresceïn, atropine, and dionine.—Asepsis of collyria.—Sterilisation by heat.—Aseptic collyria and stable *ampoules*.—Ocular anæsthetics.—Discovery of cocaine.—Its marvellous properties.—Revolution brought about both in eye and in general surgery.—Anæsthesia by subcutaneous, subconjunctival, and by intra-rachidian injections.—Inconvenience of cocaine, its toxity; means for preventing accidents.—Substitutes for cocaine.—Eucaine.—Tropacocaine.—Holocaine.—Orthoform, etc.

Before undertaking in detail the study of the various diseases of the eye and of their treatment, we must first of all pass in review the principal therapeutic agents used in eye work. You should thoroughly understand the different applications of these agents in the most varied pathological conditions.

In speaking to you at some length of mercurial treatment, I showed you that quite a school attached the greatest importance to the local manifestations of a general diathesis. We shall not pause for these considerations, which have to do with general pathology, a subject that you know so well that I have little to teach you on the matter.

First, if you please, the study of collyria, local applications, ocular antiseptics, etc.

From extreme antiquity, the most various medicaments have been applied to the eye under the different forms of **dry collyria** or powders blown into the eye, **moist collyria** or ointments, and lastly, **liquid collyria.**

To-day we still employ all these means. Calomel is the dry collyrium most commonly employed; iodoform, airol, protargol, and many other powders insufflated over corneal, conjunctival, or cutaneous wounds, are excellent measures for preventing suppuration and hastening healing.

Xeroform recommends itself to us especially on account of its perfect pulverescence, which renders insufflations very easy; tribromophenol and bismuth, which enter into its composition, render this therapeutic agent an antiseptic of the first rank, as well as an astringent or anti-purulent of an efficacious description.

Ointments, under many different names, are in everyday use in cases of blepharitis, keratitis, etc. Among them all, the yellow ointment, called after Pagenstecher,* enjoys a great reputation, since it has a specific action in lymphatic conjunctivitis, and, above all, in phlyctenular keratitis, which is always, more or less, connected with scrofula or lymphatism.

Ointment can be readily used, and, thanks to vaseline and lanoline, a number of substances are thus conveniently applied to the eye. In certain circumstances ointments possess a superiority over liquid applications. By their means one can place in the conjunctival sac stronger doses, which consequently have a more durable action.

Ointment should then be substituted for a liquid collyrium for all substances whenever there is any reason whatever for doing so; always, for example, when insoluble substances are prescribed.

One ointment I desire to mention specifically on account of the services it has rendered me is mercurial lanoline. This I employed at first with excellent results, combined with massage, in certain corneal or pericorneal infiltrations, interstitial keratitis, episcleritis, and spring catarrh. It was these attempts that gave me the idea of subconjunctival injections, in order to make a certain quantity of mercurial solution penetrate the lymphatic system of the eye. We shall speak later of massage.

As to oily collyria, we have personally but such an imperfect experience of their properties that we shall say nothing further about them. Theoretically, the same objections can be raised to them as to oily hypodermic injections; but they should have some advantages, since certain authors prefer them to watery solutions, so simple and easy to manage, and within everybody's reach.†

* In order to be non-irritating, this ointment should be prepared with great care. The precipitated or yellow oxide of mercury ought to be obtained by liquid process and used quite fresh and intimately pulverised so that with the microscope one can no longer find large particles. Under such circumstances the ointment is well borne even when as strong as 1 in 10, which we always use. Unless one is certain that the ointment is well made, its use at the patient's house should never be advised.

† The oily collyrium of eserine, 1 per cent., has the great advantage of keeping for an indefinite time, and of being better borne by the patient than the watery solution.

So far as we are concerned, the best collyria for every-day work are those having distilled water or artificial serum as the menstruum.

Small quantities of liquid only should be prescribed for domestic use, because the solutions readily undergo changes. Five grammes of the collyrium is nearly always ample.

In clinical work, the sterilisation of collyria is simple when we have to deal with ordinary solutions which are not altered by boiling. Even cocaine (no matter what some people say) stands boiling well enough.

But when dealing with wounds of the eye or with operations, we imagine that the best means of sheltering ourselves from infection by collyria is to employ during and after the operation (before matters little) only collyria sterilised in *ampoules* * such as those that M. Vignes and I were the first to present to the Parisian Ophthalmological Society in 1893.

In hospital, as in town and country, with a box of these tubes assorted and hermetically sealed, containing cocaine, atropine, eserine, dionine, etc., one can satisfy all the contingencies likely to arise during the course of the most unforeseen operation. Every practitioner can thus have in his cupboard, or even in his instrument case, the chief collyria without any fear that their composition will undergo change.

We shall not at this point say much about the mode of action of collyria; it must suffice to know that a crowd of substances can be resorbed by the ocular surface.

Some writers make out that absorption takes place only through the cornea, the conjunctiva not allowing itself to be traversed. We do not share this view, the falsity of which we shall demonstrate when speaking of dionine.

We have already proved that atropine dropped into the conjunctival sac penetrates into the aqueous humour, inasmuch as a drop of the latter, placed in another eye, produces mydriasis. It is also recognised that by repeated instillations of a solution of fluoresceïn the intra-ocular liquids can be tinged. This means has even been recommended by E. von Hippel to establish the early diagnosis of alterations of the membrane of Descemet. The reaction comes about in the same way as for superficial ulcers of the cornea—that is to say, the part, deprived of its protective epithelium, allows itself to be penetrated by the colouring agent, and shows itself as a clear greenish spot, isolated from the rest of

* These *ampoules* are simply small lengths of glass tubing, the ends of are drawn out fine and sealed by heat. They are most convenient.—TRANS.

the tissue. In the other case it is the aqueous humour which, holding in suspension the colouring substance, is imbibed by the affected spots on the posterior surface of the cornea.

It is certain that the degree of diffusibility is very different according to the substance; alkaloids have a great power of penetration; fluoresceïn is resorbed by the conjunctiva, and, if you wish a proof of that fact, you have only after the application of fluoresceïn to provoke by dionine a conjunctival chemosis, when you will be surprised to see that the subconjunctival lymph is coloured a yellowish green. This yellow colour is quite different from that observed in jaundiced persons, where conjunctival œdema takes equally a particular yellowish hue.

A soluble substance, therefore, placed in the conjunctival sac, is able to penetrate to the media of the eye through absorption by the cornea and conjunctiva. The underlying idea is of the greatest importance as regards the local treatment of diseases of the eye.

Without stopping to discuss the different local applications employed in superficial affections of the eye—as astringents, caustics, and antiseptics, which we shall study when speaking of conjunctivitis, keratitis, blepharitis, etc.—we shall address ourselves at once to that important class of medicaments which relieve pain, and on that account are of interest to the practitioner and, above all, to the patient. These we have called **ocular anæsthetics** and **analgesics**, and their discovery constitutes one of the greatest therapeutical conquests in modern eye work and even in general treatment.

Prior to the discovery of cocaine, the only local calmatives were belladonna and opium and its derivatives. So precarious were these means that it was always necessary to have recourse to general medication in order to relieve the agonising pain caused by an affection of the conjunctiva, cornea, iris, etc.

Now we have cocaine, acoine, and dionine, to quote only the three chief ocular analgesics or anæsthetics.

Cocaine calms almost instantly superficial pains, but it must be admitted that the duration of this analgesia is very short, about twenty minutes.

Acoine, in man, acts in instillations only when there exists a solution in the continuity of the corneal or conjunctival epithelium, but its analgesic action may last several hours, so that its use is valuable in burns of the conjunctiva and traumatic erosions of the cornea.

Dionine we may term a profound analgesic of long duration, putting the whole eye to sleep, so to say, for a sufficiently lengthened period. We shall study in detail all these valuable agents.

A drop of a 2 or 3 per cent. solution of **cocaine** placed in the eye provokes at first, as you know, a sensation of smarting, little to the liking of some and very disagreeable to the sensations of other patients.

If you wish to spare your patient this slight pain, you have only to tell him to look strongly upwards; at the same time you pull down the lower eyelid, so as to evert it somewhat. You then place the drop of cocaine on the border of the eyelid, taking care that it does not come into contact with the cornea until several seconds after the conjunctival surface has been well impregnated with the fluid. This little trick will render you real service in practice, for it is always advisable to hurt your patient as little as possible.

The smarting, however, does not last long. It is followed by a sensation of warmth in the eye, which can be scarcely closed. The eye appears larger, and is so, in fact. The palpebral fissure is wider open and the eye is prominent, a little thrust forward. One can then touch the cornea without giving rise to pain, and practise many operations without the patient betraying the least suffering.

The degree of anæsthesia varies according to (*a*) the subject, (*b*) the number of instillations, and (*c*) the strength of the solution employed.

There are people refractory to cocaine, just as there are others very sensitive to its action. It is the same with those who are intoxicated with infinitesimal doses, but it is necessary to be aware of these rare exceptions in order to be on one's guard against them.

Originally, when the way of using cocaine was not perfectly understood, there were many inconveniences, which it is enough to point out to avoid them. At first, a deleterious action upon the corneal epithelium was attributed to cocaine; but it is simpler to see in the loss of corneal polish, provoked by cocaine, a drying of that membrane by evaporation, the eye remaining widely open and insensitive to external irritants. In fact, as soon as one took the precaution of keeping the eye closed, these corneal complications were seen no longer, excepting only the infectious ones which may follow the others.

At the end of about twenty minutes the drug provokes a moderate dilatation of the pupil. That is one of the inconveniences of cocaine, but it is also a relative advantage, since the slight mydriasis has allowed us to make many ophthalmoscopic examinations which otherwise would have been difficult.*

The mydriatic action of cocaine may prove useful in the simple

* Now we possess a better means of dilating the pupil for ophthalmoscopic purposes in **Euphthalmine.** With this agent the pupil is dilated *ad maximum* in fifty minutes without appreciable alteration in accommodation.

extraction of cataract without iridectomy; but it has the grave inconvenience of provoking, amongst predisposed subjects, attacks of glaucoma, which may entail the most serious consequences. Cocaine, however, is far from being an agent which raises the tension of a normal eye, since one often observes after its application a lowering of tension, which, in certain subjects, may proceed so far as to give rise to an almost alarming collapse of the eyeball, following some operations for cataract, especially amongst very aged people. It is doubtless upon such facts as these that Groenow has proposed to combat glaucoma by instillations of strong doses of cocaine.

Injected subcutaneously, cocaine may provoke toxic accidents grave enough to cause even death.

It is therefore very important to employ only feeble doses and diluted solutions of cocaine, above all when operating upon the eye or the face. Certain predisposed subjects experience, after simple conjunctival instillations, uncomfortable nervous symptoms, such as agitation, palpitations, loquacity, subdelirium, and dyspnœa.

One should employ only 2 per cent. solutions and 1 per cent. hypodermic injections.

This toxity of cocaine has incited chemists to find other substances possessing similar anæsthetic properties but devoid of toxic qualities.

We shall be brief with regard to substitutes for cocaine, and, without stopping to consider **theine, caffeine,** and **erythrophleine,** the oldest and the least active, we shall pass to :

Eucaine B possesses the anæsthetic virtues of cocaine without dilating the pupil, and is, moreover, easily sterilisable. On the other hand, it gives rise to marked hyperæmia, and a smarting more lively than that of cocaine. Its toxity is but half that of cocaine.

Tropococaine appeared at one time likely to supplant its half-sister, but to-day we speak of it no longer. To begin with, it was as irritating as cocaine, even although a physiological solution of salt was used as its menstruum. However, tropococaine promised much; it produced a prompter and more profound anæsthesia than cocaine; the mydriasis and the toxity were less marked. Speaking for myself, I have put this medicament on one side simply because its advantages did not seem to me to compensate the fact that it was more painful than cocaine.

As to **holocaine,*** it has been much praised during the last few

* A 1 per cent. or 2 per cent. watery solution of the **hydrochloride of holocaine** now enjoys considerable popularity as an ocular anæsthetic, especially in America. It has no action upon pupil, tension, or corneal epithelium, and possesses distinct bactericidal properties.—TRANS.

years, but I am bound to admit, to my shame, that I have not yet tried it. It should have an anæsthetic power at least equal to that of cocaine, and much superior to that of eucaine; it does not dilate the pupil; it possesses certain antiseptic properties; and can without inconvenience be sterilised by boiling.

But holocaine, which is much more toxic than cocaine, cannot be employed as a subconjunctival or subcutaneous injection—or at least only in extremely diluted solutions. In glaucoma, a subconjunctival injection of 1 per cent. holocaine rendered iridectomy painless.

Upon the whole, we may say that cocaine, used with precaution and in moderate doses, still remains the most serviceable local anæsthetic. For him who understands its faults and knows how to avoid them, cocaine is able to render inestimable services in obtaining the local anæsthesia necessary for all surgical interference with the eyeball or eyelids.

The action of cocaine is too well known nowadays for it to be useful to dwell longer upon the subject.

One may only ask whether solutions stronger than 2 or 3 per cent. should be employed as collyria. It is better to repeat the applications oftener, which has only the disadvantages of causing one to be nearer the patient and of preventing the desiccation of the corneal epithelium. For intra-dermic, subcutaneous, or subconjunctival injections, solutions of only 1 per cent. are employed, or associated with acoine, which has no appreciable toxity, one has never, as it were, complications to dread.

It was hoped, at first, that cocaine rendering the eye insensitive would calm or suppress the pain provoked by any pathological condition of the ocular surface, conjunctival or corneal. That hope has scarcely been realised. The action of cocaine is too superficial and too fugitive. All the same, it is easy to quiet for several minutes the pain set up by the presence of a foreign body on the cornea or conjunctiva, or by an erosion or superficial ulceration of the cornea; the patient, until then unable to open his eye, is able without difficulty to look about him for a short time.

It is especially in affections of the cornea that cocaine is able to render the most signal services.

In affections of the conjunctiva or of the deeper parts of the eye, the results are almost nothing, more especially when the conjunctiva is very hyperæmic. Everybody knows, from personal experience, that a markedly inflamed eye is influenced only with difficulty by cocaine.

We believe that, thanks to adrenaline, which provokes a marked anæmia of the conjunctiva, it is now sometimes possible to obtain a

relative anæsthesia by means of cocaine; but this anæsthesia lasts a shorter time than in the normal state.

Is it not already a splendid result to have rendered painless almost all the operations that are performed on the eye?

But why should we not succeed in calming, by simple local applications, ocular pains caused by different pathological states of the eye, whether superficial or deep?

Many efforts have tended towards this end. For my own part, I have tried a considerable number of means, and I have found two or three which mark the first steps in the discovery of ocular local analgesics.

Already, in April, 1899, I had published a communication on **orthoform**, the conclusions of which may be related here:

Many works have already been printed upon orthoform in the treatment of wounds, of painful ulcers, and of burns, etc. We have recently observed a case where the analgesic action of orthoform was so remarkable and so durable that it gave us the idea of trying the remedy in certain affections of the eye. In the case just mentioned, which has nothing to do with ophthalmology, there was a large wound of the thoracic wall artificially produced by a blister. Everybody is aware how exquisite is the pain set up by these large surfaces deprived of epidermis and in continual contact with the dressings, or even with the clothes. Cocaine ointment in such cases has little action, and if it so happens to produce an analgesia more or less marked, this is of very brief duration. This is why the idea occurred to us of applying the following ointment:

Orthoform . . .	4 grammes.
Vaseline . . .	30 grammes.

This ointment, spread upon a sheet of waxed taffeta, was applied directly to the ulcerated surface. The patient immediately experienced a sensation of heat, of burning, and of violent smarting; but complete and lasting analgesia supervened at the end of two or three minutes. The dressing was changed night and morning, and the patient felt his blister no more than if it had never been applied.

We have tried orthoform in the following affections of the eye:—relapsing ulcers of the cornea, episcleritis, chemical burns of the conjunctiva, burns of the eyelids, etc.

The first case was that of a lady affected with a relapsing ulcer of the cornea of a species so painful that cocaine merely led to a transitory dulling of the pain. The patient passed almost the whole day in bed, incapable of opening her eye. Cocaine, quinine, bromide, sodium salicylate, remained absolutely without effect, as did hot compresses and the compressive bandage.

Orthoform ointment, 4:30, was then prescribed, a morsel the size of a grain of wheat being placed between the eyelids after the instillation of several drops of cocaine. Lastly, the application of an occlusive dressing that the patient raised only when the pain became intolerable. Despite the previous instillation of several drops of cocaine, the sensation of smarting was very lively at the time of the application of the ointment; but all pain soon disappeared, and the bandage was not taken off until the following morning. The patient passed a much better night than before, and cure was complete at the end of several days of this treatment. There has been no relapse since four months.

In two cases of rebellious episcleritis, the same ointment was applied in the same way, not so much to calm the pain as to create a revulsion. The effect was excellent in the first case, which was cured in a few days. The second still remains under treatment, but is much better. Each time the ointment is applied one should practise through the eyelid massage at the level of the affected spot. After the initial smarting, the patient experiences a sensation of relative comfort.

In a case, associated with rather violent pain, where the conjunctiva and cornea had been burned by liquid caustic potash, applications of orthoform ointment were at first, despite cocaine, followed by severe pain, so much so that the patient was afraid of repeating the application. It was nevertheless certain that analgesia was produced speedily, and that it lasted as long as the bandage was kept over the eye. As soon as the corneal epithelium was reproduced, the pains were much less lively than at the time of the application of ointment, when the membrane was still ulcerated.

In burn of the conjunctiva and of palpebral border by a spark of red-hot iron, the effect of an orthoform dressing was very favourable, without there being anything else in particular to note about the case. Several burns of the eyelids were also treated with orthoform successfully. It would be interesting to multiply these experiences, for if cocaine has a potent anæsthetic action it is too fleeting in many cases, so that if we find in orthoform an analgesic of prolonged action, that will be a rich conquest for ophthalmology.

But everything points in the direction that we shall discover better agents than orthoform. Acoine and dionine put us, without doubt, upon the track of profound analgesics.

To resume briefly the respective merits of the various ocular anæsthetics, we may say with Schmidt:*

* *Deutsche Med. Zeitung*, 1899.

1. From the point of view of the rapidity of the anæsthetic action tropococaine ranks first, then holocaine, cocaine, eucaine A and B, and, lastly, orthoform.

2. From the point of view of the duration of the anæsthesia, orthoform, cocaine, eucaine B and A, holocaine, and tropococaine.

3. Intensity of the anæsthesia: cocaine, tropococaine, eucaine B and A, and orthoform.

4. Analgesia when the eye is inflamed: *Ibid.*

5. Mydriatic action: cocaine, tropococaine, eucaine A and B, and holocaine.

6. Conjunctival ischæmia: *Ibid.*

7. Vascular dilatation: eucaine A and B, tropococaine, and holocaine.

8. Irritation: orthoform, eucaine, cocaine, tropococaine.

9. Antiseptic power: orthoform, holocaine, eucaine B, tropococaine, and cocaine.

10. Toxity: holocaine, cocaine, eucaine B, tropococaine, and orthoform.

LECTURE V.

Summary.

Ocular analgesics.—Profound anæsthesia may entail analgesia; but the reverse is not always true.—Antipyrine, phenacetin, injections of morphine, etc., are the general analgesics.—The first ocular analgesics are orthoform, acoine, and, above all, dionine.—Acoine, without having an anæsthetic action upon the human eye, renders almost completely painless subconjunctival or subcutaneous injections of irritating substances, such as mercury, iodine, etc.—Acoine gives a longer anæsthesia than cocaine for intra-dermic or subcutaneous injections, and has the advantage over the latter that it is not toxic.—Mode of employing acoine.

In our last Lecture the different ocular anæsthetics were passed in review, and we saw that they all possessed a superficial action of brief duration.

One of them, however, has shown itself to possess a calmative action of a more prolonged kind as regards burns of the cornea and conjunctiva, namely, orthoform; but that agent sets up lively pain when it is applied. Nevertheless, we consider this medicament as one of the best **ocular analgesics.**

This word "analgesic" may appear to be a pleonasm, since often anæsthesia implies analgesia; but for that it is necessary that anæsthesia be profound and even general, such as is given by ether, chloroform, and all the general anæsthetics.

We all know that one part of the skin may be anæsthetic, even when violent and profound pain may be felt in the same place.

Cocaine and the other local anæsthetics, as eucaine, holocaine, etc., act only upon the nervous elements. They may well induce an anæsthesia comprising analgesia, as, for example, injections of cocaine along the sciatic nerve, and, again, intra-spinal injections during parturition, or in the course of operations upon the lower two-thirds of the body.

But you never succeed by instillations of cocaine in calming the violent and profound pains which attend irido-cyclitis, glaucoma, and episcleritis. Rather you increase the pains by complicating them with insomnia, while you not infrequently succeed in dulling them by repeated applications of **dionine.**

On the other hand, dionine seldom if ever produces anæsthesia; an eye, freed from profound pain by dionine, feels easily enough a touch, a prick, a nip, or cauterisation by silver nitrate, whereas with cocaine exactly the contrary is the case. Besides, cocaine is a stimulant to the psychomotor centres at the same time that it extinguishes peripheral sensibility; while dionine, like most of the derivatives of morphine, has, on the contrary, a sedative, narcotic action of a very pronounced kind. It is well known that morphine itself is an analgesic devoid of the least anæsthetic properties, at least if the dose is not strong enough to induce a profound slumber. Indeed, one often observes in a patient under the influence of morphia a certain degree of cutaneous hyperæsthesia and cerebral excitement, with insensibility to pain or analgesia.

Analgesics, therefore, are not invariably anæsthetics, and *vice versâ.*

But if we return to local anæsthesia of the eye, its difference from analgesia is easy enough to determine. An eye that has become analgesic suffers no longer, although it feels readily enough the contact and the pain when it is touched or pinched; whilst an anæsthetic eye is deprived of all peripheral sensation, yet may continue to suffer from a deep-seated pain. In two words: an anæsthetic allows one to operate without pain; an analgesic suppresses a pre-existing pain, without destroying sensibility.

In the painful affections of the eye, therefore, a new class of local analgesics is now *à l'ordre du jour,** and we must be encouraged in our researches towards this end by the numerous and brilliant series of ocular anæsthetics that we already possess. In point of fact, what is needed? Simply a cocaine that shall have a more durable and lasting action.

Numerous essays have already been made, but the most interesting are certainly those of Trolldenier, of the Veterinary Institute of Dresden.*

The author, in collaboration with Dr. Hesse, undertook a series of experiments on the anæsthetic properties and the therapeutic uses **of acoine.**

Acoine is a medicament discovered by Heyden's chemical factory, at Radebeul, near Dresden. It is an alkyloxyphenylguanidine.

* Trolldenier, *Therapeutische Monatshefte*, i, 1899.

To begin with, the non-toxity of acoine as compared with cocaine was demonstrated by experiments on dogs.

Cocaine introduced in capsules into the empty stomach produced, in a dose of 18 centigrammes, violent nervous troubles, which betrayed their existence by abnormal movements, dulness of the senses and of the will, and a notable elevation of the temperature, inspirations, and cardiac pulsations. A dose of 25 centigrammes of cocaine killed a dog weighing 4½ kilos. with violent tetanic cramps.

Acoine did not give rise to these toxic symptoms. No trouble was observed after a dose of 50 centigrammes; in a stronger dose it acted as a caustic upon the stomach and intestines, and in that way might bring about death.

Concentrated solutions of acoine, instilled into the eye of a rabbit, produced an anæsthesia lasting several days, and at the same time a lively irritation of the cornea and conjunctiva. Very interesting results have been obtained with dilute solutions.

The lower eyelid of a rabbit was held away from the eyeball, and into the conjunctival sac thus enlarged were placed several drops of a solution of acoine, which was kept in contact with the eye for several minutes.

According to the concentration of the solution, anæsthesia was brought about at once or at the end of a few moments, and lasted for a longer or shorter time. One can thus, according to need, induce an anæsthesia depending upon the strength of the solution lasting a short or a long time, as under:

1 : 1000	.	Anæsthesia for 15 minutes.
1 : 400	.	„ 30 „
1 : 200	.	„ 60 „
1 : 100	.	„ 40 to 80 „
1 : 40	.	„ more than a day.

The last-named strength irritates the eye a good deal, but gives rise to no permanent trouble. The more dilute solutions are quite exempt from all inconvenience, and provoke an anæsthesia as complete as can be wished by any operator.

Moreover, it is important to note that one may in a simple manner notably augment the effect of a feeble solution, perhaps by keeping it for longer than a minute in contact with the eye, perhaps by making a fresh instillation. In this way an anæsthesia of the same duration can be got as easily as by employing a stronger solution. Nevertheless, a 1 per cent. solution may be employed without hesitation whenever a prolonged anæsthesia is desired.

At the Anatomico-Pathological Veterinary Institute of Dresden, cocaine has for some time been replaced by acoine. The last is employed especially for anæsthetising the eye of the rabbit in cases where intra-ocular inoculations are performed, and one can only congratulate oneself upon its prompt and immediate action. In the dog subcutaneous injections of a 6 per cent. solution of acoine have a purely local action. Despite this large dose, the least cerebral trouble has never been observed. On the other hand, around the site of injection the skin necroses and a slough comes away in a few days when more than 3 c.c. of this concentrated solution has been injected. Necrosis is not seen with feebler doses. An insensitive zone is produced all around the puncture after the injection.

After the harmlessness of acoine had been demonstrated by the means mentioned above, injections were made upon man after the method of Schleich.

After rendering the skin insensitive by means of ethyl chloride, experiments were commenced by injecting Schleich's original solution. The first prick of the needle gave rise to no pain, but the injection into the frozen tissues was much more painful than if the spray had not been used. The pain of the needle-prick is nothing compared with the pain set up by the injection, and so the employment of ethyl chloride was abandoned. Instead of cocaine, acoine was used, according to the formula given below :

Acoine	0 gr. 10.
Morphine hydrochloride . .	0 gr. 02.
Sodium chloride . . .	0 gr. 10.
Distilled water . . .	100 gr.

This solution was injected into the skin according to the precepts of Schleich. The prick and the formation of the first vesicle (*cloque*) are alone painful, and then, if one takes care to inject very softly, pain is minimal.

The vesicle thus formed is wholly insensitive, and one can enlarge at will the infiltrated surface by new injections, which cause no pain. There are no consecutive pains. But around the infiltrated zone is a red aureole, associated with slight swelling of the parts.

These slight inconveniences disappear as soon as one replaces the sodium chloride at 20 centigrammes by a stronger dose of 80 centigrammes. With this formula even the injections were completely painless.

To explain the part played by the morphine in this solution a solution of morphine containing 2 centigrammes per 100 was injected

beneath the skin. There followed a lively pain of some duration without anæsthesia. The morphine was accordingly put on one side, and the following formula was employed:

Acoine	0 gr. 10
NaCl	0 gr. 80
Distilled water	100 gr.

With the foregoing solution many subcutaneous injections have been made without any inconvenience. The reaction consecutive to the injection was, without contradiction, more feeble and shorter than formerly. Above all, the anæsthesia lasted longer than with the solution recommended by Schleich. For forty or fifty minutes after the injection it maintained the same extent of influence (*étendue*), and then the zone of sensibility gradually approached the centre of the injected area. For example, if a surface one centimètre in width was rendered insensitive, after an hour and a half or two hours one still found an insensitive band one to three millimetres in size. Even more diluted solutions (5 centigrammes of acoine per 100) still gave rise to an anæsthesia of about thirty minutes.

The solutions, which are very antiseptic, should be kept in the dark. It is, however, better to prepare the solution immediately before it is used.

Experience has proved that acoine is much less toxic than cocaine, and perhaps may be used in a less concentrated form. Its action is more rapid and lasts longer. The caustic action of concentrated solutions of acoine contra-indicates its employment in that form.

How far experiments upon the eyes of animals can be applied to man, and in what conditions acoine employed as a subcutaneous injection is capable of rendering services to the oculist and to the surgeon, we must learn by experience. It cannot be too often repeated that acoine in concentrated solutions, owing to the caustic action, must not be used for subcutaneous and endemic injections.

In all cases we may be certain that the following solution is superior in every sense to the solution of morphia and cocaine recommended by Schleich:

Acoine	0 gr. 10.
NaCl	0 gr. 80.
Distilled water	100 gr.

Prescriptions for the Preparation of Solutions of Acoine.—Cold water dissolves 6 per cent. of acoine; but diluted solutions, especially those of 1 per cent., are convenient in actual work.

These solutions are prepared by shaking the desired amount of acoine with a proportional quantity of freshly distilled water; the solution is ready in an instant.

If one has failed to use water freshly distilled and quite pure, or has placed the liquid in a flask made of bad glass, with an alkaline reaction, an opalescent solution is obtained, since the base acoine is insoluble in water, and is precipitated by the least trace of an alkaline substance (soap, etc.). The flask intended to contain the solution must therefore be washed with nitric acid and afterwards with distilled water before it is used. The opalescent solution may be rendered transparent by filtering it after it has stood for several hours.

The transparent solution, not too concentrated, placed in a blue flask and stored in the dark, keeps for several days or even several weeks.

Hot water must not be employed for making the solutions; a warm solution must not be diluted with cold water.

I have explained as well as I am able the experiences of Trolldenier, since they are most interesting from several points of view.

First, you see that an agent has been found which, when tested on the eye of a dog or rabbit, has an anæsthetic action persisting for an entire day.

What joy Trolldenier must have experienced when he obtained this first result, but what a bitter experience when he found that, upon the human eye, acoine had no anæsthetic action! You will soon see that he was mistaken, and that acoine in reality is a precious therapeutic agent when employed in certain well-determined conditions.

You see also, what cannot be repeated too often, that experiences upon the dog and rabbit cannot serve as an absolute criterion for experimental therapeutics as regards man. I have never ceased from quoting this fact to my opponents with respect to subconjunctival injections.

When I wrote to the firm von Heyden for the purpose of obtaining a little acoine for experimental purposes, I was told that acoine had no action upon the human eye. But I was myself convinced, by intuition, that I could count upon the therapeutic end I sought even in man. By insisting, I at length received a gramme of acoine, and I had the immense satisfaction of obtaining in my first attempt a result exceeding even my best hopes.

I obtained, in fact, that which I had long sought for—

i. e., the possibility of rendering subconjunctival injections almost completely painless, of which you already know the therapeutic value.

In order to get this result, it was enough to add to the solution for injection a few drops of a 1 per cent. solution of acoine, prepared in accordance with the directions given above (*see* page 46).

To explain to myself the exact effect of acoine upon the human eye, I began by instilling a drop of a 1 per cent. solution into my right eye, while I instilled a drop of a 3 per cent. solution of cocaine into my left eye. This is what I observed :

Right Eye.	*Left Eye.*
8.5.—Acoine, 1 per cent., 1 drop; rather lively smarting; lacrymation.	Cocaine, 3 per cent., 1 drop; lively smarting; lacrymation.
8.10.—Sensation of heat and of constriction; slight hyperæmia.	Sensation of intra-ocular tension and of enlargement of the eye; insensibility.
8.15.—No insensibility.	Complete insensibility of the cornea.
8.20.—Relative insensibility; I feel the contact, which, without being painful, is disagreeable.	Complete insensibility of the cornea; dilated pupil.
8.27.—Sensation of numbness of the eye, with slight temporal pain.	Pupil dilated more in the direction where the drop was instilled; sight a little clouded; insensibility.
8.35.—2 drops of acoine; very severe smarting.	2 drops of acoine; severe smarting, sensibility.
8.45.—Relative insensibility; clear vision.	Pupil always dilated; troubled vision; sensibility.
9.5.—Sensibility returned; instillation of 2 drops of acoine; very lively smarting.	Pupil dilated; sensibility; vision a little clouded.

9.15, R.E., the conjunctiva is almost insensitive, while the corneal sensibility is almost normal. Conjunctival and palpebral redness; pupil not dilated; sight absolutely normal.

After this experience upon myself, I believed myself justified in trying the effect of acoine upon patients, for foreign bodies, corneal ulcers, etc., but I did not obtain, as in the physiological state, encouraging results. Alone, or combined with cocaine, acoine did not present any advantage over cocaine only, as regards conjunctival instillations.

I was already despairing of obtaining any result by means of subconjunctival injections; the more so as the chemist who had furnished me with the product had first of all informed me that acoine, although very active on the eye of the dog or rabbit, was without action upon the human eye.

At length, upon a patient who had been treated for six weeks by frequent subconjunctival injections for disseminated choroiditis, I injected a quarter of a syringe of the following solution:

$Hg(CN)_2$	0·01
NaCl	1·00
Aq.	50·00

to which I added, besides, some drops of a 1 per cent. solution of acoine, and I kept the patient under observation for four hours.

This client, who had suffered much after each injection, stated that he experienced not the least pain during the time he remained at my *clinique*, although the conjunctiva was more swollen than usual. I made at an interval of some days five other injections, each one stronger than the other, in the same patient, who asserted that these injections were not at all comparable with those that had been formerly practised. He felt only the prick of the needle and the discomfort produced by the chemosis, which appeared to be more marked than without acoine.

I have repeated this experience many times in different affections, and amongst the most sensitive persons, but always with the same success. Absolute and unfailing insensibility must not, however, be expected, because human nature is so diverse in its individual reactions, in pathology as in therapy, that we must never be too absolute in our affirmations.

The dose of acoine will vary with the strength of the solution to be injected. Thus, to make a subconjunctival injection of a syringe full of 2 per cent. NaCl, one must add to it two divisions of the syringe; for a 4 per cent. injection, three or four divisions.* Pain is then, in most cases, absolutely abrogated, if the conjunctiva has been well cocainised beforehand and if the puncture is made with delicacy and lightness.

Even atrociously painful injections of sodium chloride, 15 and 20 per cent., which are indicated in the treatment of detached retina, are rendered quite painless if enough solution of acoine is added to them. In this case one must add almost as much acoine as saline solution. The liquid becomes milky on account of the precipitation of the acoine. The injection must be performed without delay, before the formation of clots which may obstruct the needle of the syringe.

Injections of cyanide of mercury are rendered equally painless by acoine. To inject without pain a half syringe of a 1 : 5000 solution, two or three divisions of acoine must be added. For a solution

* See foot-note on page 29.—TRANS.

1 : 1000 it will, of course, be necessary to add more—say about one-third of the solution to be injected.*

It is curious to observe how, even when precipitated by these solutions, acoine preserves its anæsthetic qualities.

It is also possible, thanks to acoine, to make subconjunctival or subcutaneous injections with all liquids, even the most irritating, including amongst them iodine and iodated solutions.

Acoine should therefore give, in man, an anæsthetic action of a very marked kind, which lasts three or four hours or more, longer than that produced by cocaine. As a matter of fact, cocaine incorporated with liquids injected under the skin or the conjunctiva renders them painless only for about half an hour.

But why should acoine not act upon the human cornea when it has so profound and durable an effect upon the cornea of the rabbit? That is a thing impossible to explain at present. Doubtless, the epithelial covering of the human eye does not allow itself to be penetrated by the same solutions of acoine; but should there be epithelial desquamation, the acoine would probably penetrate and produce analgesia.

Starting from this theory, I treated painful chemical burns of the conjunctiva and the cornea with an ointment of acoine, 0·50 : 10.

You know how eminently painful are these wounds, especially when the burned cornea is rubbed by a conjunctiva, which itself is deprived of its protective epithelium. Experience justified this prevision, but I admit that my experiences are still too recent to allow absolute and firm conclusions to be reached. All that I can say at the moment is that I have succeeded in procuring in my cases an almost complete cessation of the pain for several hours, and there can be no doubt that it was actually the acoine which produced the analgesia, since at the end of this time the pain returned with violence and persisted until the ointment was again applied.

Trolldenier, you see, was wrong when he said that acoine was without action on the human eye. I feel confident that, if we search carefully, we shall soon find the means, by a new combination, of rendering acoine active in normal and pathological eyes by simple instillations. Let us search and we shall find.

We have seen in the last Lecture that orthoform has a durable

* M. Naline, chemist, at Saint Denis (Seine), and M. Jacquet, 269, Rue Boileau, Lyons, prepare solutions of acoine put up in *ampoules* with sodium chloride 4 per cent., and with $Hg(CN)_2$ 1 : 1500, 1 : 3000, 1 : 5000. With these absolutely sterile solutions subconjunctival injections may be practised anywhere and everywhere almost without pain.

analgesic action upon ocular burns, but we have had to recognise the fact that its application is very painful.

Acoine is less painful, and its employment is rendered easier by several preliminary instillations of cocaine. We need not despair; the chemists will understand how to discover new products, less painful and more active, which will enable us to calm the superficial ocular pains set up by all kinds of keratitis and conjunctivitis.

As to deep ocular pains proceeding from iritis, irido-choroiditis, glaucoma, etc., we can nowadays generally calm them, thanks to the recent discovery of the powerful analgesic properties of dionine.

It is in deep and very painful affections of the eye that all the local anæsthetics remain without effect, and we have recourse to general medicine, which places at our disposal its great store of narcotics, analgesics, and other medicaments acting upon the central nervous system. Antipyrine, phenacetine, and their derivatives, quinine, sodium salicylate, and, above all, hypodermic injections of morphine, are the surest and most rapid means of calming the violent pains of acute iritis, irido-cyclitis, glaucoma, etc.

Locally, in the slighter cases we may attenuate the pain by the use of atropine or eserine, but when these agents, even combined with cocaine, fail in their purpose, we are locally disarmed, as it were, and must needs fly to general anæsthetics.

Perhaps we shall some day possess a special category of ocular analgesics, endowed with a power of producing profound insensibility lasting for a long time.

LECTURE VI.

Summary.

The deep ocular analgesics were discovered by the chances of experimental therapeutics.—The pain of iritis is generally calmed by several instillations of dionine.—In glaucoma dionine has a marked calmative action.—In certain cases of episcleritis, keratitis, and a crowd of other painful affections, dionine often causes the pain to disappear.—Other ocular analgesics, as morphine, codeine, peronine, and heroine.—Dionine is the only non-toxic agent, and is the best of the morphines (hydrochloride of ethylmorphine).

General therapeutics are certainly of the greatest importance, and should precede all other intervention when dealing with an affection of which the etiology is well known; but the element of pain, absolutely independent of the cause of the malady, is one of the most pressing symptoms to combat.

General analgesics have this inconvenience, that they upset the digestive canal and shake the nervous system of the patient, who needs all his vitality to bear up against a disease which is often of long duration. Morphine injections, so valuable on many occasions, have another disadvantage—morphinomania. It is, therefore, of great importance to discover local analgesics the action of which is profound and lasting.

Contrary to what happened to me in the case of acoine, where, against the opinion of its discoverer, I had predicted the action of that alkaloid, it was chance that caused me to find out the powerful analgesic properties of **dionine.**

In a communication published in December, 1899,* on dionine, I related the curious properties of this alkaloid, a precious substitute for morphine, to which Wolffberg attributed a lymphagogue action comparable to that produced by subconjunctival injections of salt solution.

The conclusions of my paper were rather negative from this special point of view, but observing that Wolffberg re-affirmed his

* *La Clinique Ophtal.*, No. 23, 1899.

conclusions, I reasoned thus: I am either placed in bad conditions, or else I have not experimented upon favourable cases. Let us begin again.

I therefore undertook, with the assistance of Dr. Daulnoy, of Nancy (who was very desirous of working under my direction), a new series of clinical observations upon the same subject. It was during the course of these researches that I was struck by the analgesic effects produced by dionine, upon which Wolffberg had not himself particularly insisted, but which constituted, to my mind, its most important qualities.

This is how the chances of experiment led me to discover deep analgesics:

One day a lady suffering from rheumatic iritis of hyperacute and very painful form, not allowing her to rest at night, was brought to me by her medical attendant. The pupil was not dilated, although atropine had been applied for several days; the eye was very hyperæmic and sensitive to light. For an hour I myself used atropine to the inflamed eye without result. In order to assist the action of the atropine, it occurred to me to place in the conjunctival cul-de-sac some dionine powder, a piece as big as the head of a pin. The patient was at first frightened by a very violent smarting; then a sort of numbness of the eye came on, with a difficulty in moving the eyeball, which was swollen and very œdematous. Two leeches were applied to the temple for the purpose of reducing the congestion. One hour afterwards the pupil was dilated *ad maximum*, and the patient was much relieved. Two days later the patient returned, and told me that she had not experienced the least pain and had passed two excellent nights without having taken the packets of sodium salicylate that I had prescribed for her. The pupil was dilated completely and evenly, and traces of ancient synechiæ could be seen on the anterior capsule of the lens; there was a little perikeratic hyperæmia; the fundus of the eye was still very congested, the papilla very red, and the retinal veins tortuous. From that day cure was assured.

This observation, taken by itself, presents no interest, because all of us have seen cases of this kind cured quickly under the influence of some treatment or other, especially when the painful phenomena have already lasted for a certain time.

But at the same time that the above patient was under my care, two old clients came to me for serious relapses of iritis, a disease which had given me much trouble on former occasions.

disappear

from the first application of dionine. These two observations have been published by Dr. Daulnoy.*

I merely wish to add a few words about M. C—, aged 51 years, a rheumatic subject, whom I had already looked after during several relapses. Before coming he had used salicylate and atropine, but his pain becoming worse, he consulted me on the eighth day. He was much worse than on the preceding occasions; the eye was red, watering much, and very sensitive to light; the pupil was imperfectly dilated; the cornea was striated; and there was a little hypopyon and Descemetitis. I introduced into the inferior cul-de-sac about as much dionine as would equal a millet seed. The patient experienced a violent smarting, and before long there was an intense, lardaceous chemosis with swelling of the eyelids, necessitating the application of a bandage, but the patient had no more pain.

Two days afterwards M. C— returned, and stated that he had slept well and experienced no more pain; the pupil was dilated *ad maximum*, the hypopyon had disappeared, the striæ *en grillage* in the cornea were less marked, but several spots of Descemetitis could still be perceived. Dionine was again applied. Briefly, after the first application of dionine the pains definitely disappeared, while in eight days the cornea became completely clear, the pupil free, the eye free from redness and photophobia; but the papilla was still cloudy, and the retinal vessels tortuous.

This patient, at the time of his former attack, was six weeks under treatment, but the iritis was then nothing like so severe as on the present occasion.

The third patient (who also returned for the third or fourth time) was relieved of his sufferings and cured in eight days, and saw me in all three times only.

May we conclude from these three facts that dionine is an infallible analgesic in iritis? Alas! no; for in a case of double iridocyclitis with total synechiæ of both eyes, I was able to do practically nothing with dionine. It is right to add that in this case dionine produced scarcely any chemosis, and the patient seemed refractory to the medicament. Iridectomy alone brought about an improvement.

On the other hand, one must always be on one's guard against an undue enthusiasm. We know that often enough an intervention by anodynes at the opportune moment is sufficient to provoke a kind of crisis, and to bring about a cure that may be attributed to the remedy last employed, while often it is nature, or general medica-

* Daulnoy, *La Clinique Ophtal.*, No. 7, 1900.

tion, which is really the first cause of the favourable turn of the illness.

But in the following case it is easy to discern the part played by dionine, for no other application had been used except atropine, and that remained without effect.

A schoolmaster applied to me on March 1st complaining of very violent pains of the right eye, preventing sleep for a fortnight. Having formerly suffered from rheumatic iritis, he had applied atropine for fourteen days to the eye. The eye was exceedingly red, slightly thrust forward, very sensitive to light, and watering a good deal; the iris was infiltrated and swollen; the pupil was not dilated; and there was blood in the anterior chamber. A morsel of dionine, as big as a millet seed, was applied, and followed by lively smarting and moderate chemosis. At the end of half an hour the patient could open his eye spontaneously, despite the swelling of the eyelids and the chemosis. Under the influence of atropine the pupil began to dilate. Next day, without any other treatment than the instillation of atropine, the pupil was dilated to 6 mm., while the eye was less red and painful. The blood had disappeared from the anterior chamber. The patient had slept well the first time for a fortnight. It was only towards the morning that the eye had become a little painful. A fresh application of dionine was made without any general treatment. On March 3rd the amelioration was considerable; the exophthalmos had disappeared, and ciliary redness only was present. The pupil was well dilated, and sight had become appreciable. On March 5th, not having had dionine for two days, the patient began to suffer. It was evident that dionine by itself would not bring about a complete cure. I therefore prescribed three to six packets of aspirine, each of 0·60 centigr., which usually yields me better results than sodium salicylate. I did not neglect to apply dionine again to the eye, and this soon produced its analgesic effect.

I have also treated a fourth case of double iritis, accompanied by violent pain, calmed on one side on the fifth day and on the other on the second day by dionine. This observation has been published by Dr. Daulnoy.

Since the publication of my first communication on the profound analgesic action of dionine, many *confrères*, having had their attention directed to the point, have amply confirmed my first assertions—some as regards iritis, others as regards glaucoma, and others, lastly, in all sorts of ocular affections.

Iritis is not the only painful affection of the eye. The violent

pains of glaucoma are also in most cases rapidly calmed by dionine, it may be for the moment or it may be permanently.

In the *Bollettino d'oculistica* for January, 1901, Dr. Simi has published three cases of glaucoma with violent pains, which were rapidly calmed by a 6 per cent. collyrium of dionine. One of the patients had suffered so much that he wished to lay violent hands upon himself.

I have lately published in detail * an exceedingly interesting case of acute glaucoma cured without operation, where the orbital and cephalic pains were dissipated by the first applications of dionine. I have since seen other similar cases.

Dr. A. Terson,† in a case of hæmorrhagic glaucoma associated with violent pain, for which enucleation had been suggested, had the good fortune to rid the patient of the pains completely by several instillations of dionine. The pain had not returned even after several months.

We shall return to the discussion of these facts when treating of glaucoma in a later lecture.

In a case of double vascular keratitis, associated with violent pain and intense photophobia, I had the idea to apply dionine on one side only. The pain and the photophobia disappeared entirely from that side after the production of a lively smarting and a marked chemosis; the next day that eye was still painless. Some dionine was placed in the other eye, and on the third day there was no more suffering. Under the influence of protargol and yellow ointment, the cornea and the conjunctiva soon assumed their normal aspect.

Among several children affected with pustular keratitis and photophobia, I have employed dionine, but I must admit that in babies it is difficult to study the analgesic action of the medicament; yet in most of the cases the children opened their eyes better. It was the same in acute parenchymatous keratitis with photophobia. The children became quieter and slept better.

In a child of seven years I obtained so rapid a bettering of a specific parenchymatous keratitis that I am unable to deny a certain influence to dionine in the case, applied conjointly with hypodermic injections of mercury cyanide.

In a man of forty years affected with a diffuse infiltration of the cornea, simulating a parenchymatous keratitis, coming on after a violent traumatism, the pain was so intense that the patient had not slept for several nights, despite 50 centigr. doses of quinine sulphate.

After a single application of dionine the patient passed a perfect

* *La Clin. Ophtal.*, No. 8, 1901.

† *Soc. d'Ophtal.*, Paris, 1901.

night, but having remained away for two days, intense pain reappeared, which was again calmed by dionine.

On the other hand, in many other cases of keratitis dionine has remained without effect. Why? Those are clinical points to be settled by future investigations.

Rheumatic episcleritis also sometimes sets up painful crises of a violent character. This was so in the case of Madame R—, who was confined to her couch for two months by nodose rheumatism. She called me on account of lively pain, which often seized her in the middle of the night and lasted for two hours or longer. For a week I prescribed salicylate, but both the pain and the episcleritis persisted. I then applied dionine to the worse eye. A startling chemosis was the result. When I returned two days later, the patient asked me about my *poudre de feu*, which had burned her eye so much that she had suffered no more pain. I made two other applications, and not only the pain but the episcleritis disappeared. I should add that in another case of episcleritis the action of dionine was doubtful.

Another affection that is often painful is the relapsing ulcer of the cornea, met with oftenest among rheumatic subjects. It is called by some the "arthritic ulcer" and by others "herpes of the cornea," and it sometimes assumes the arborescent form, all forms, however, being so far but imperfectly differentiated from one another.

In a couple of cases of this kind, already treated by me, dionine caused the pain to cease immediately.

Madame X— came to see me a year ago for a superficial ulcer of the cornea of rheumatic origin. She was cured on that occasion by two subconjunctival injections and salicylate of soda internally. This time, feeling a return of the same symptoms, she administered salicylate to herself and applied cocaine and leeches, but without the least result. I at once made an application of dionine powder. An hour later the pains left her, never to return. Two days afterwards I saw the patient again. The ulcer was healed, and nothing remained beyond a slight leucoma, not staining by fluoresceïn.

In a second patient—whom I had treated several times for the same malady—there was an arthritic ulcer of the cornea, for which salicylate had been taken, without result, for several days. In this case, also, I was able to prove the analgesic effects of dionine. But in this patient there had been two or three relapses, always calmed by dionine, which showed that the product in question has not always a curative action equal to its analgesic powers. Even the latter, as we have said above, may also be wanting.

But dionine may not be the only alkaloid which possesses this analgesic action upon the eye. In fact, the first agent employed by Wolffberg, who followed Buffalini, was **peronine**, equally a derivative of morphine.

I have tried peronine; it also provokes chemosis, but its lack of solubility makes it act for a long time on the eye like a foreign body, thereby causing more pain than comfort. I was forced on this account to renounce it.

Heroine, also a derivative of morphine, has not given me convincing results, on account of its scanty solubility. The hydrochlorate of heroine, which is more soluble, is also more likely to be accompanied by symptoms of nausea.

With regard to **morphine** itself, it sets up also a marked chemosis and a certain degree of analgesia; but, in one case, I have observed alarming symptoms of intoxication—as, for example, cold sweats, faintings, and vomiting—lasting two or three hours. With dionine, on the other hand, I have never seen the least complication of this kind.

Bloch* (as I have found by consulting the bibliography upon dionine) has praised this incontestable superiority of dionine over morphine, ... because it never gives rise to any unpleasant symptoms. It calms the pain caused by cough in phthisical persons without causing the latter to sleep; allows those with sciatica to go home without being incommoded by the vomiting or sleep produced by morphine, etc.

I have injected under the conjunctiva a solution of dionine with the same analgesic and chemotic results upon the eye. It is probable that a hypodermic injection would also exert a powerful calmative effect.

But many patients who refuse to allow a needle-prick to be made have no objection to a little dionine being placed in the conjunctival sac, especially after previous cocainisation.

Wolffberg, without insisting upon the profound analgesic properties of dionine, noted, however, in several of his observations, that after traumatisms the patients felt much relieved by the application of dionine.

I noticed this fact equally in several cases where the cornea had been wounded.

How is ocular analgesia brought about by dionine? This is difficult to explain. According to Buffalini and Wolffberg, peronine and dionine render the cornea insensitive; I have never been able

* *Therapeutische Monats.*, August, 1899.

to obtain this anæsthesia in a clear manner. The sensibility was possibly a little dulled on the side where the dionine had been applied, but there was never a true anæsthesia of the cornea.

Therefore one cannot say that dionine is an anæsthetic. While suppressing pain, it does not suppress sensibility.

The lymphatic stasis which manifests itself by the production of chemosis, sometimes of a very marked character, appears to take a share in the efficacy of the medicament, for the therapeutic action is often in direct relation with what Wolffberg has called the lymphagogue action of dionine. Have the terminations of the sensory nerves of the eye been deadened by the alkaloid contained in the liquid diffused through the conjunctiva? Has the lymphatic depletion diminished the compression or irritation of the sensory nerves? Or has the dionine acted upon the central nervous system by simple absorption through the conjunctiva and lacrymal passages?

The last hypothesis is not tenable, since, when both eyes are diseased, it is only the one that has had dionine applied that becomes analgesic.

Besides, the symptoms of general intoxication produced by morphine applied to the conjunctiva show distinctly that a medicament, thus applied, may act directly upon the central nervous system.

Perhaps the action of dionine upon the lymphatic circulation has a potent modifying influence upon the nutrition of the eye.

Lastly, until such time as experiment has given us a precise explanation of the way in which dionine acts, it is enough for us to know that we are now in possession of a powerful ocular analgesic, often capable of calming for hours the most violent pain in iritis, irido-cyclitis, ulcers, keratitis, and glaucoma; and that it is to experimental therapeutics alone that we owe this important discovery, of which I was proud to offer the firstfruits to the Ophthalmological Society of Paris.

How to employ Dionine as an Analgesic.—My first trials with dionine as an analgesic were made with the powder applied as such to the surface of the conjunctiva. I did not think it necessary to seek during my first series of experiments another mode of application before I had accumulated a sufficient number of facts. The objections raised on the difficulties of dosage attending the application of dionine powder thus applied were judicious, and indeed I had made them for my own guidance.

Subconjunctival injections certainly seemed to be the surest means of appreciating exactly the amount of dionine necessary to produce a complete and durable analgesia. I practised it in several cases; but

I should admit that certain patients refused to submit to the method.

There remained the instillation of concentrated solutions. I tried at first those of 10 per cent., but they are too concentrated and not stable enough. The 5 per cent. solution is that which has yielded me the best results. Two or three drops, instilled in the conjunctival sac, provoke a sensation of smarting, more lively than that caused by cocaine, and a little more prolonged. After a few minutes fresh instillations are practised until there appears a notable chemosis, which is, in general, the sign of a commencing analgesia, although I have never been able to note a clearly marked anæsthesia of the cornea. The instillations may be repeated a certain number of times if the chemosis is not very pronounced.

The application of a 5 per cent. collyrium has the advantage that patients can employ it at home. But they should be advised to apply the collyrium only when they are in great pain.

When pain is too violent one should always have recourse to the application of the powder or to subconjunctival injections of the 5 per cent. solution. Half a centigramme of dionine may thus be injected with impunity and without the least inconvenience.

In a patient affected with rheumatic iritis, with extremely violent nocturnal crises, the application of dionine having failed to stop the night pain, which was influenced alone by morphine injections, it occurred to me to prescribe a 5 per cent. collyrium of dionine to be dropped into the eye at the moment of the painful crises. From that time the patient, who had already acquired a taste for morphine, was able to put aside that dangerous means of analgesia. He even stated that the instillations of dionine quieted the pain more quickly than the morphine injections, although the duration of the analgesia lasted perhaps a shorter time. It is so easy to repeat the instillations, however, that this inferiority of dionine is more apparent than real.

To avoid the pain produced in patients by dionine in concentrated solution or in powder, our excellent *confrère* and friend, Dr. Jocqs, has prescribed very feeble collyria of 0·5 per cent. to 1 per cent. dropped very frequently into the eye during the day. This method lends itself to many different combinations in prescribing combined collyria according to the clinical indications, as with atropine, eserine, pilocarpine, cocaine, zinc sulphate, etc.

LECTURE VII.

Summary.

Agents that modify the vascular tonus.—In addition to its analgesic properties, dionine has a powerful vaso-dilator action, bearing not only upon the blood-vessels but also upon the lymphatic vessels and spaces.—Lymphatic stasis and chemosis (sometimes enormous) are produced with the greatest intensity in strumous subjects, and those suffering from arterio-sclerosis, Bright's disease, cardiac affections, etc.—in short, in subjects with defective circulation.—It may, perhaps, some day serve as a touchstone in the diagnosis of circulatory insufficiencies predisposing to stasis.—Lymphatism is characterised by a capillary atony.—Dionine, by its lymphagogue properties, exerts a resolutive and resorbent action on hyphæma, subconjunctival hæmorrhages, corneal infiltrations,—upon iridic synechiæ, vitreous troubles, and even upon choroidal or retinal exudations.—Unfortunately, the action of dionine is of very brief duration.—The lymphagogue action of dionine is exhausted at the end of two or three days.—Mode of applying dionine; formulæ.

We have finished with ocular anæsthetics and analgesics, but we have not yet done with dionine, which possesses not only a profound and lasting analgesic power, but has also a very favourable action upon a morbid process itself; it facilitates the dilatation of the pupil when this is slow under the action of atropine; it assists the resorption of pupillary exudations; and, lastly, it diminishes tension in cases of glaucoma.

Therapeutic experimentation, without giving us a precise explanation of the mode of action of dionine, has nevertheless shown us its importance in hastening nutritive changes, and in exciting the resorption of all kinds of pathological infiltrations.

We could not begin the study of topical applications to the eye with a better subject than dionine. What new vistas open themselves before the attentive observer through the multiple manifestations provoked by the application of this interesting modifier of the vascular tonus!

We must attribute to Wolffberg, of Breslau, if not the invention of dionine, at all events its application to the therapeutics of the eye; but the product is older than one thought at first. Krijewski

(*Thèse de Paris*, 1900) said, in fact:—"Towards 1880, a Frenchman, Grimaux, was the first to bring forward the merits of ethylmorphine or codethyline, as he called it, as it is a homologue of codeine."

Dionine is the hydrochloride of ethylmorphine. Its chemical formula is $C_{19}H_{23}NO_3HC_1H_{20}$. It occurs as a white, crystalline powder, of a moderately bitter taste. It is easily soluble. One hundred parts of water, at the ordinary temperature, dissolve fourteen parts of dionine.

Dionine owes its introduction into therapeutics to the fact—as experience has shown—that the ethylic compounds are superior from the point of view of their pharmacodynamic action, to the non-alkyliques and to the methylic compounds. M. J. von Mering, starting from this consideration, studied the pharmacological and clinical action of dionine, and thus entirely confirmed the theoretical previsions mentioned above. Dionine, therefore, was shown to be a good and agreeable substitute for morphia. It is more readily soluble in water than the hydrochloride of codeine.

Dionine was first introduced into practice by Schroeder and M. J. Korte in phthisis, chronic bronchitis, and pulmonary emphysema, and was shown in the hands of those authors to be an excellent and certain agent for combating the cough of irritation. Under its influence this cough became calmed, dyspnœa disappeared, the attack of asthma ceased, and the expectoration was influenced very favourably. Dionine is distinguished from morphine, according to Schroeder and Korte, by its insignificant action upon the digestive tract, as well as by the absence of all unpleasant associations. In general, it further seems to have an action more energetic and persistent than that of codeine; it produces a better and more peaceable sleep; and it considerably facilitates expectoration.

Dionine, employed as a subcutaneous injection, constitutes an excellent sedative, both in states of excitement, in melancholia, and in states of depression in the course of the precocious dementia of periodical insanity.

Dionine must be looked upon as a very valuable substitute for morphine in the treatment of morphinism by suppressing the toxic agent. At first it provokes neither euphoria nor any analogous state, which shields the patient from the danger of habit, and, secondly, on account of its ready solubility, it is rapidly eliminated.

Let us now examine the effects of dionine, first in the simplest pathological affections of the eye.

In subconjunctival ecchymoses, which are resorbed in eight to ten days according to their size, passing, as they do so, through various

colours, if a little dionine is applied to the conjunctival sac on the day of their appearance, more or less chemosis is soon produced. It is noteworthy that if the hæmorrhage is still fresh, you will see the conjunctival infiltration assume a rose colour, instead of being clear and transparent, as chemosis usually is. There is imbibition of the sanguineous exudation by the fluid infiltrated in the lymphatic spaces. This liquid, in the process of resorption, sweeps away the colouring matter of the blood, and perhaps dissolves the altered red corpuscles and revives the leucocytes, so that all traces of hæmorrhage soon disappear.

I have confirmed the foregoing observation on many occasions. It is certainly a matter worthy of discussion and criticism. You may say to me that ecchymoses do not always get resorbed in the same period of time—that is obvious even as regards two cases apparently similar; that there are individual conditions acting in one sense or the other, etc. Alas! clinical observations are not based upon mathematical data, but upon our senses and, alas! our judgment; and, as you know, *judicium difficile.*

But when the same fact recurs in the majority of cases, one is justified in concluding in favour of the repeated observation.

We have already seen that dionine sometimes exercises its lymphagogue action little or not at all, so that there is little if any chemosis. Under these conditions we have found that the analgesic action and the power of resorbing superficial infiltrations are but slightly marked.

In a case of bulbar ecchymosis where dionine remained without effect, no chemosis being produced, it occurred to me to make a control experiment, which fully confirmed the clinical observation. If it is true that the serosity poured out beneath the conjunctiva dissolves and resorbs the extravasated blood, then the same result should be brought about by injecting under the conjunctiva a syringe full of artificial serum. This is what I did, and the same phenomena came about as after the simple application of dionine, when the latter was followed by marked chemosis; the resorption of the subconjunctival hæmorrhage was extremely rapid.

To my mind, this is a therapeutic experience of a more conclusive nature than all of those which have been practised on the dog or the rabbit. For the rest, I have since learned that M. Haitz proposed to hasten the absorption of peribulbar hæmorrhages by subconjunctival injections of sodium chloride.

Hæmorrhages into the anterior chamber also tend to more rapid absorption under the influence of dionine, a fact observed by myself,

by Wolffberg, and by other authors. I have related, moreover, a case of this kind *à propos* of the analgesia produced by dionine in iritis.

In another peculiar case, experimental therapeutics confirmed the foregoing data. This occurred in a patient recovering from jaundice. The conjunctiva had an icteric colour, still sufficiently well marked, and this was clearly reduced by several applications of dionine. It would be interesting in this case to have kept one eye as a control. It is evidently necessary that the jaundice should be declining and that the blood should no longer include the colouring matter of bile, for the observation to possess any value. The yellow, icteric colour of the chemosis produced by the 5 per cent. dionine was truly remarkable.

When speaking of the absorption of collyria by the conjunctiva, I communicated this experience to you: a few minutes after fluoresceïn had been applied to the cul-de-sac, dionine was instilled, with the consequence that a yellowish-green chemosis was set up. The fluoresceïn had penetrated into the subconjunctival lymphatic spaces, and was placed in evidence by the thick layer of fluid contained in the chemosis.

In certain forms of chronic conjunctivitis (diplobacillary conjunctivitis) in which I had the idea of utilising the lymphagogue, detersive, and eliminatory action of dionine, I was surprised to see a chemosis of a dirty yellow colour. It would be interesting to study this subconjunctival lymph from the point of view of any toxines that it might include.

In every case of conjunctivitis the effect of dionine, from a therapeutic standpoint, has constantly been favourable. The considerable afflux of blood and of serosity provokes that which Wolffberg has so well termed a lymphatic inundation (*Lymphüberschwemmung*), the detersive action of which is incontestable. The use of any local application whatever has a much more remarkable effect after this lymphatic washing. It also appears as if the pain of cauterisation lasted for a shorter time; but this last observation is not yet fully established. This much is certain, *viz.*, that the sedative effect nearly invariably shows itself by a better night with good sleep. I have already spoken of this narcotic effect of dionine (*see* page 55).

The lymphagogue action of dionine may be especially checked in corneal infiltrations. It even exercises a curative action in the slighter cases. This may render us great service, and it will be studied in detail when dealing with corneal ailments and their treatment.

The remarkable action upon the cornea produced by dionine

betrays itself at first by a more marked brightness of that membrane, which appears to be more transparent, and is so in reality, for often in the course of several minutes, sight is bettered by one or two points. This improvement only comes about, it is true, when the visual acuity has been reduced by a slight and recent lesion of the cornea. In certain traumatisms I have observed that effect in an obvious way. In simple contusions of the cornea, accompanied by a slight more or less diffuse cloudiness, which may sometimes be confused with a commencing parenchymatous keratitis, I have seen dionine produce a notable clearing of the cornea and bettering of the sight. This comes about in so rapid a way that the resolutive action of dionine cannot be doubted in such cases.

The same is true of recent infiltrations of the cornea, set up by a slight scratch, a foreign body, etc., infectious infiltrations, the most often, on which dionine has a very rapid and favourable action in virtue of its antiseptic and lymphagogue properties.

These different observations are, as it were, physiological experiences which show us the peculiar action of dionine.

No other medicament has so far manifested properties of so interesting a kind. It is greatly to the credit of Wolffberg to have introduced into eye work this valuable agent, and to have praised it as a most powerful resolutive.

For the first few days dionine has an appreciable action upon the corneal infiltrations at the beginning of an attack of parenchymatous keratitis. Unfortunately the effect is of too short a duration. At the end of several days, dionine, in fact, has scarcely any action. All the same, it has produced in this short space of time a therapeutic effect such as we cannot obtain by any other local application, unless it be with subconjunctival injections. The latter, however, constitute, as it were, a method of surgical intervention, and we should congratulate ourselves in having at our disposal a more anodyne measure, which may be used before this last resource.

Dionine having irrigated the whole lymphatic region of the conjunctiva, paves the way, so to speak, for the action of subconjunctival injections. The two medicaments, by well-arranged alternations, are able to support one another; but we need not broach here this important chapter, which will form the subject of the next Lecture.

To expect to clear old leucomata by dionine appears to me to exaggerate the importance of its action. An appreciable bettering of sight, however, has been noted in some cases. It is probable that it then acts upon very slight nebulæ, encroaching little upon the pupillary area of the cornea. By absorption of the most peripheral

infiltrations, it may clear the sight by suppressing the circles of diffusion.

In abscess and ulcers of the cornea, good results are often obtained by stimulating the nutrition of the cornea and facilitating the regeneration of the epithelium, without our being in a position to speak of a true curative action.

We have already noted the remarkable effect produced by dionine in iritis, where it acts as an analgesic, hastens the absorption of the exudations, and dilates the pupil. In glaucoma we have seen, and shall still see, the favourable effect of dionine.

By quickening absorption, dionine favours the clearing of the pupillary field after operation for cataract or discission of the crystalline lens in myopes, but one must act alternately in order to avoid tolerance to dionine, so rapidly manifested by patients. In choroiditis, retinitis, and vitreous troubles, one often witnesses, after several instillations of dionine, a notable improvement, although most frequently this is transitory; and here, again, it is better to alternate applications of dionine with subconjunctival injections of sodium chloride (*see* page 26 and chapter on Choroiditis).

Recently, in a case of retro-bulbar neuritis due to cold, and associated with a very marked central scotoma, I saw vision clear so rapidly that I could not believe that dionine was able to produce such an effect; at the most, it was able to give a fillip to the subsiding morbid process. In every case that is always an agreeable coincidence to prove, but it is well to guard against attributing the effect to a medicament applied once only.

Wolffberg assigns to dionine a very favourable influence upon the cicatrisation of the corneal wounds made in the different operations, especially after cataract extraction. This fact I have been able to confirm many times. But it must not be forgotten that the sneezing set up by the lacrymation induced by dionine may counterbalance the healing effect by reopening the wound, and even causing a prolapse of the iris. I observed several days ago a reopening of the anterior chamber one hour after operation as the result of violent sneezing provoked by dionine, but fortunately there was no prolapse of the iris.

Let us endeavour to explain the **resolutive action of dionine.**

We may remark that the longer and stronger the chemosis, the more pronounced is this resolutive action. The irritation of dionine, when it comes into contact with the conjunctiva and the cornea, produces redness and very marked vascular dilatation with abundant

lacrymal secretion, often accompanied by sneezing; the lymphatic channels then become so distended and dilated as to attain ten times their original dimensions (Vermes*). The conjunctiva thus becomes enormously swollen, forming a great pad around the cornea, and having the characteristic aspect of conjunctival œdema or chemosis. The eyelids themselves may be notably swollen, and the eye is sometimes so puffed up as to make its state appear alarming, especially in elderly persons with embarrassed circulation, *but there is no danger to be apprehended.*

Does dionine act hygroscopically, manifesting its resolutive action by a subtraction of pathological fluid, which is then immediately replaced by purer blood?

This is the effect, pure and simple, of a blister, aside from pain, for dionine is painful only for several minutes after its application; as soon as chemosis appears, pain is replaced by a simple sensation of discomfort (chemosis); and if the eye was originally painful, a certain degree of analgesia is speedily produced.

This explanation of the action of dionine by an effect of revulsion or of vesication is not quite exact, since an analgesic effect is often brought about without there being any marked revulsion.

Therefore let us admit, until we have better proof, that a stimulating action upon the lymphatic and vascular circulation lies at the root of the resolutive virtues of dionine. We have already studied the analgesic action of the drug.

Its antiseptic action is obvious.

The therapeutic indications of dionine are very numerous, on account of its diverse and curious properties. In sum, it is a powerful stimulant, a lymphagogue, and a resolutive; it possesses, moreover, antiseptic properties of a direct and an indirect nature, by the afflux of fluids and an increase of the phagocytic action. Further, it is in many cases a powerful analgesic.

Dionine is therefore a general therapeutic remedy suitable for many different pathological processes. These we have passed in brief review, but we shall wait to study them in detail in their proper place.

Dionine may some day serve as a physiological reagent, furnishing us with valuable indications with regard to the state of the circulation in certain subjects. In fact, cardiac and some gouty patients, and those affected with Bright's disease and arterio-sclerosis, respond to dionine with remarkable intensity.

* Vermes, *Woch. f. Therap. u. Hyg. d. Augen*, Feb. 7th, 1901. Histological examinations of sections of the conjunctiva.

On the other hand, the action of dionine shows much variation in young and lusty persons. Among obviously scrofulous and lymphatic subjects the chemosis set up by dionine, as a rule, is extremely pronounced, although it is less so than amongst those with cardiac or Bright's disease.

Mode of employing Dionine.—I wish merely to transcribe certain useful formulæ and methods likely to render you help in your researches in experimental therapeutics and in your daily practice.

To begin with, you should always have ready the mother-solution of 5 per cent., which will serve for your early experiments:

Dionine	0 gr. 50.
Distilled water	10 gr.

I have renounced almost completely the application of dionine in powder, which is not easily measurable, and which provokes lively pain. There is, however, one exception, *viz.*, when the 5 per cent. collyrium remains without effect, and when one is not afraid to set up violent phenomena of reaction, or when it is the proper thing to produce the latter, or when their revulsive action is thought likely to prove useful.

It is advisable never to prescribe dionine for home use before having personally tested the particular sensibility of the subject, for if one chances across a patient who has a violent reaction he will probably be so frightened that one runs a risk of never seeing him again. On the other hand, if you have shown him the chemosis and demonstrated its use to him he will be reassured.

Before applying the agent for the first time it will be wise to instil a drop of cocaine, in order to lessen the sense of lively smarting caused by dionine. A drop of a 5 per cent solution* is then placed in the lower cul-de-sac, the patient meanwhile looking strongly upwards; in this way the cornea comes but little into contact with the liquid, and as the cornea is infinitely more sensitive than the conjunctiva, the smarting is much less pronounced.

In aged persons, as in lymphatic subjects, a small drop only should be used at first, and the dose should not be repeated until several minutes have elapsed without any effect having been produced.

In subjects with a good circulation, the lymphagogue action of dionine is much less marked; there are even cases where true

* In very nervous subjects, in scrofulous persons, or in those suffering from cardiac disease—briefly, in all cases where one has reason to dread a violent reaction—it will be wise to begin with a 2 per cent. solution, and then if at the end of half an hour the effect is insufficient, to instil two drops of the 5 per cent. solution.

chemosis cannot be obtained. At most, one observes a slight swelling of the conjunctiva, with dilatation of blood-vessels, and always a peculiar brilliancy of the cornea.

The first application of dionine invariably has a more marked effect than the second, made next day. If several days are allowed to escape between two applications, reaction may be the same. It must never be forgotten that tolerance to dionine is very rapid, so that after its use for four or five days scarcely any reaction is produced.

Once you know the way in which your patient will react, you may prescribe for home use whatever formula you think best adapted to the case.

In slight scratches, trivial traumatisms of the cornea, you order to be instilled five or six times a day into the affected eye one or two drops of the following collyrium:

Dionine	0·10 gr.—0·20 gr.
Cocaine hydrochlor. . . .	0·10 gr.
Cyanide of mercury, 1 : 2000 .	10 gr.

When the wound is already infected, the solution of cyanide of mercury must be stronger, 1 : 1500 or 1 : 1000, and the instillations must be prescribed hourly or every half-hour. With this collyrium I have obtained very brilliant results in already advanced infectious traumatisms, especially with the 1 : 1000 solution of the cyanide of mercury. In these cases the instillations must be repeated every half hour, and if improvement lags behind, the treatment must be completed by galvano-cauterisations and by subconjunctival injections.

The foregoing solution is equally indicated in the corneal infiltrations of slight parenchymatous keratitis, etc. In this case I have found it well to add 2 per cent. of sodium chloride, for the purpose of augmenting the eutrophic action of dionine:

Dionine	0·10 gr.—0·20 gr.
Cocaine hydrochloride . .	0·10 gr.
Sodium chloride . . .	0·20 gr.
$Hg(CN)_2$, 1 : 1000 . .	10 gr.

When the iris is, or may be, involved, atropine in a quantity proportionate to the gravity of the iritis should be added to the collyrium:

Dionine	0·10 gr.—0·20 gr.
Cocaine hydrochloride . .	0·10 gr.
Atropine sulphate (neutral) .	0·02 gr.—0·05 gr.
Distilled water . . .	10 gr.

The applications must be more or less frequent, according to the indications.

The above formula is that which we prescribe daily in iritis and irido-cyclitis.

Where the pupil is to be contracted, eserine or pilocarpine may be easily incorporated with the collyrium, following the indications:

Dionine	0·10 gr.
Cocaine hydrochloride . .	0·10 gr.
Pilocarpine hydrochloride .	0·03 gr.—0·10 gr.
Distilled water . . .	10 gr.

If the case is one of glaucoma, you must carefully avoid cocaine, and prescribe:

Pilocarpine hydrochloride . . .	0·05 gr.
Eserine sulphate	0·02 gr.
Dionine	0·10 gr.
Distilled water	10 gr.

S.—*One drop to be placed into the affected eye five or six times a day.*

This collyrium has the advantage of stopping promptly the painful phenomena of glaucoma, at the same time that it diminishes the intra-ocular tension, provokes contraction of the pupil, and hastens the clearing of the cornea. Its employment is favourable for preparing the eye for operation in all forms where the phenomena of irritation are too violent to permit of immediate surgical intervention.

LECTURE VIII.

Summary.

Agents that modify the vascular tonus (*continued*).—Adrenaline or extract of supra-renal capsule is the most perfect type of vaso-constrictor; it forms exactly the opposite to dionine.—The intense conjunctival ischæmia produced by adrenaline facilitates and augments the action of cocaine, atropine, etc.—It is a powerful anti-hæmorrhagic in operations upon the conjunctiva.—In glaucomatous subjects, adrenaline lowers the intra-ocular tension.—It acts in the same way in rabbits, as Wessely has proved by manometric observations.—In subconjunctival injections, the vaso-constrictor action of adrenaline is so potent as to slacken the production of the aqueous humour and to lower the intra-ocular nutrition.—Adrenaline has not yet been studied enough therapeutically, but it appears to act favourably in glaucoma, incipient iritis, scrofulous kerato-conjunctivitis, spring catarrh, episcleritis, etc.

Continuing to pass in review the agents that are most used in local ocular therapeutics, we have just studied the anæsthetics and the ocular analgesics, so well represented by cocaine, acoine, and dionine. The interesting properties of the last product gave us the occasion to occupy ourselves with the physiological reagents, so valuable in experimental therapeutics.

Dionine has upon the eye the most powerful vaso-dilator and lymphagogue action that we have ever seen.

We shall study to-day a vaso-constrictor, which we consider useful, in the other sense, in ocular therapeutics.

The **extract of supra-renal capsule,** when injected into the veins, shows its powerful vaso-constrictor properties, bearing mainly upon the smallest vessels; the consequence of the injection is an augmentation of the blood-pressure. Its application to the mucous membranes provokes a local ischæmia of a very marked nature.

At the Heidelberg Congress in 1896, after Bates, of New York, and L. Dor, of Lyons, I related some interesting facts relative to the vaso-constrictor action of a watery extract of the supra-renal capsule. The preparation that I used was composed thus :—

powdered supra-renal capsule, 1; distilled water, 1. This solution* is put up in aseptic *ampoules*, keeps very well, and renders great service. Since that time a day has never passed but I have used this interesting product.

I had already remarked at that time that a drop of the aqueous extract, placed upon the normal conjunctiva, provoked in two or three minutes a profound anæmia of the whole surface of the eyeball. One then fails to see, as it were, a single conjunctival vessel; the sclera becomes of a brilliant white; the eye assumes a cadaveric aspect—one might say an eye of porcelain. This anæmia lasts, according to the subject and the dose employed, from one to two hours. The more hyperæmic the eye, the shorter is the duration of this effect; but there is no congestion of so intense a character that it will not yield for some moments if the applications are repeated two or three times.

No agent hitherto known possesses in so marked a degree the power of producing anæmia.

Thanks to this potent vaso-constrictor action, I have been able in many cases to practise interventions which would otherwise have been very difficult and most troublesome. Everybody knows, in fact, that cocaine has scarcely any anæsthetic action upon markedly congested eyes, or even, according to some authors, none at all. Well, if one drops into the eye turn by turn two or three times cocaine and adrenaline, one can obtain enough anæsthesia, even in the most difficult cases. By this means I have been able, in inflammatory glaucoma, to perform iridectomies which it would have been impossible to do without chloroform.

The application of the cautery to the inflamed sclera, to the conjunctiva, or to the tarsal cartilage, is rendered relatively painless by the same means; it is the same as regards scarifications and many other operations upon the anterior segment of the eyeball.

When these procedures are likely to be bloody, hæmorrhage is much less abundant from eyes which have been submitted to the action of the supra-renal extract; indeed, it is with difficulty that one obtains a slight oozing of blood.

The vaso-constrictor action of supra-renal juice has been taken advantage of for the purpose of arresting or diminishing hæmorrhage after operations for removing chalazion, etc. This hæmostasis may render service in some cases. L. Dor, indeed, has already experimented upon the hæmostatic power of adrenaline; but as a case lately quoted by Landolt, of Strassburg, has shown, this

* Prepared by Dr. Jacquet, 269, Rue Boileau, Lyons.

hæmostasis may be followed by alarming reactionary hæmorrhage. For my part, I believe I have noticed that hæmorrhages under the conjunctiva, or into the anterior chamber, are easily produced after iridectomies.*

Supra-renal extract has not yet found a specific application, or at least, for my part I know no affection which can be cured by its exclusive use, except, perhaps, Spring Catarrh. On the other hand, its indications are numerous, and it is able to render service in a crowd of eye affections, and that is why I always have it ready during my consultations.

Certainly, I shall not say that adrenaline renders me as great service as cocaine, but I affirm that I could not spare it so easily as I could fluoresceïn.

As a diagnostic means, **adrenaline** is a valuable reagent. When an eye is extremely hyperæmic, one may be puzzled to know the cause of this intense conjunctival injection. A drop or so of adrenaline gives us in these cases rapid and precise indications. If the entire surface of the conjunctiva becomes pallid in a uniform and regular way, one has to do with a conjunctival affection. The redness having disappeared, it is simple to inform oneself with regard to the lesions of the mucous membrane. If granulations exist they take the aspect of old granulomata, allowing their characteristic contents to shine through; one may even judge well enough the depth of the lesions in the tarsal cartilages. If the case is one of conjunctival or pericorneal pustules, or of lardaceous infiltrations, as in Spring Catarrh, these lesions appear prominent, and, as it were, increased in size against the anæmic surface of the conjunctiva.

But the effect of adrenaline is still more interesting in cases of episcleritis or of incipient iritis, while it is very useful in making an early and positive diagnosis. Under these circumstances one must observe with attention and patience, so as not to allow the most favourable moment for observation to slip by. Conjunctival hyperæmia disappears the first, and then one may see for several minutes the deep hyperæmic circle surrounding the cornea, which is characteristic of iritis, persist by itself. If this profound hyperæmia, on the contrary, is localised to a point in the sclerotic, episcleritis is present; but at the end of several minutes, after a fresh instillation of adrenaline, all hyperæmia may disappear.

* Copious hæmorrhage into the anterior chamber followed four consecutive iridectomies in the Translator's practice after the combined employment of adrenaline and cocaine.

In cases of iritis, however, a characteristic violet tint persists around the cornea. If we have to deal, on the contrary, with an affection of the sclerotic, we see appear at one or several points more or less projecting spots of a greyish-yellow colour encroaching upon the bluish-white aspect of the sclerotic surface. Some deep, transparent veins of large size are sometimes present on the border of these spots, which strongly resemble tophi in gouty subjects.

These diagnostic data are certainly not of capital importance or pathognomonic. For that matter, fluoresceïn is not indispensable to the diagnosis of ulcers of the cornea, and every experienced clinician could do without it if necessary. But it is our duty to surround ourselves with every precaution possible, in order to assure a well-authenticated diagnosis, and sometimes even for demonstrating that fact.

Adrenaline, however, serves not only for diagnosis, but also for treatment. In every case where a pronounced conjunctival hyperæmia is able to clog treatment or operation, it is easy to make it disappear. That is already something gained.

In pustular conjunctivitis and keratitis, without pretending to attribute to adrenaline a specific action, I have often remarked that its employment before the application of yellow ointment shortens materially the course of the disease. I first instil a little cocaine, then a drop of adrenaline,* and, when the redness has disappeared completely, I apply yellow ointment and practise a light rotatory massage. The effect of this treatment is sometimes surprising.

In secretory affections of the eye of whatever nature—purulent, catarrhal, granular, or other form of conjunctivitis—adrenaline, if not exerting any direct action upon the pathological process itself, brings about a marked reduction in the purulent or catarrhal secretion. Thus, for some time, I have almost always instilled into the eye a drop of the coca-renaline solution mentioned above before the cauterisations I am in the habit of practising, whether with protargol, zinc sulphate, or mercury cyanide. The caustic, acting upon elements

* To avoid the delicate handling of a concentrated solution of adrenaline, I have recently employed a collyrium of coca-renaline, thus composed:

Hydrochloride of cocaine	0·10 gr.
Solution of 1 : 1000 of adrenaline	1 gr.
Solution of $Hg(CN)_2$ 1 : 2000	10 gr.

A single drop of this liquid is enough to render the whole conjunctiva anæmic and to cause all redness to disappear. This collyrium will render great service to artistes, who are obliged to play even when the eyes are red, for after its use the eye is of a brilliant white, and wider open, without the pupil being much dilated.

at once ischæmic and anæsthetic, exerts a double intensity, at the same time producing less pain.

This action of coca-renaline is very useful in the treatment of granulations by "friction-lavage" by sublimate. One is not then troubled with sanguineous oozing, which often hides the field of operation and neutralises the caustic too quickly; hæmorrhage comes on later, and by carrying away organic waste, produces a salutary flushing of the parts.

Zimmermann praises adrenaline in lacrymation. It is a palliative measure, which may be indicated in patients who are too timid to bear probing of the lacrymal passages.

For myself, I always inject with success the coca-renaline mixture into the lacrymal sac to increase the degree of anæsthesia, to diminish the swelling of the mucous membrane of the canal, and to render the passage of the probe easier, while avoiding hæmorrhages.

Adrenaline should not be employed in the treatment of ulcers of the cornea except with precautions. During the healing stage, it hinders *resorption by vascularisation*, and may provoke relapses. On the contrary, when the ulcer has cicatrised and nothing remains but a pannus, which is slow to disappear, adrenaline will play an important part in bringing about the disappearance of the vascular cluster.

This beneficial action of adrenaline upon pannus of every kind—granulous, tuberculous, and gouty—has been well spoken of by Zimmermann, who obtained remarkable cures by repeated instillations.

In Spring Catarrh, Dr. Perret, of Hartennes, has found out that the oft-repeated application of adrenaline causes not only a momentary bettering of the ailment, but a complete disappearance of the pericorneal lesions and of the inconvenient symptoms of the disease. He concludes that we possess in supra-renal extract a medicament easy to employ, not toxic, painless in instillations, and, above all, of certain action in an affection where the other treatment amounts to very little. In the event of relapse, it is always easy to begin the treatment anew. Since the appearance of Perret's communication, I have employed adrenaline with remarkable success in many cases of Spring Catarrh. I prescribe frequent instillations of the following collyrium, of which the effect is so marked that patients are apt to think themselves cured from the moment they begin to use it:

Adrenaline, 1 : 1000 . . .	2 to 3	grammes.
Cocaine hydrochloride . . .	0·10	„
Cyanide of mercury solution, 1 : 1000	8	„

The cure is so rapid that patients often discontinue the treatment too soon. When there is marked pericorneal infiltration, absorption may be hastened by daily massage with mercurial lanoline.

Lastly, I have recently had under my care a case of glaucoma, where vision continued to fall notwithstanding an iridectomy performed previously. As the intra-ocular tension was always raised, despite repeated instillations of eserine and pilocarpine, the idea occurred to me to add to the action of those two myotics that of supra-renal extract. I was surprised to see the tension fall rapidly and in a notable and prolonged fashion. The patients even stated that the vision was improved, and, above all, experienced a feeling of well-being one or two hours after the application of the collyrium. Far from me to make of adrenaline a specific for glaucoma, although I believe that its use, combined with eserine or pilocarpine, is able to render service in certain cases. I prescribe the following formula:

Hydrochloride of pilocarpine . .	0 gr. 0·5—0·10
Neutral sulphate of eserine . .	0 gr. 0·2
Adrenaline 1 : 1000	2·5 gr.
Distilled water . . .	ad 10 gr.

S.—*This collyrium should be instilled, according to the clinical indications, five or six times a day.*

The vaso-constrictor action of adrenaline can only have a favourable effect in glaucoma, especially if one admits the truth of Abadie's sympathetic theory.

In a case of subacute bilateral glaucoma, already advanced, I obtained a complete cure, which has lasted these three years. With this patient I prescribed not only the above-named collyrium, but I also administered internally pastilles of surrenaline, kindly prepared for me by Dr. Jacquet. Massage-pressure was also practised daily for more than a month, and then at longer intervals; the collyrium of adrenaline was continued for about six months. In this case it must be observed that the omission of alcohol, formerly taken to excess, was not one of the least important causes of permanent cure. In the second patient affected with chronic glaucoma with acute attacks having formerly called for iridectomy on the left eye, eserine and pilocarpine prevented well enough the glaucomatous phenomena, but the latter soon returned. During the six months that the adrenaline-eserine collyrium was applied there has been no relapse.

The third case, one of chronic glaucoma, subject to acute relapses, with one eye already completely lost, did well under this collyrium,

but I have seen the woman lately, and she was well when I last examined her.

When we study glaucoma and its treatment, I shall cite other and even more interesting observations.

As regards the last two cases, I may add I was contented with the palliative treatment mentioned above only after the patients had refused to have the second eye operated on.

Zimmermann, who, on my advice, has prescribed adrenaline a good deal in glaucoma, believes that on glaucomatous eyes the agent has not always an identical action. On one occasion we may remark a very notable reduction in tension, and on a second, nothing of the kind. In no single case has any increase in tension been observed. In the normal state this author has several times proved upon himself a very marked diminution of ocular tension, which fell almost to an alarming degree. He concludes that the combination of supra-renal extract with myotics is a praiseworthy method of treating glaucoma, not only to prepare the eye for operation, but also every time that iridectomy is contra-indicated. But the general rule must never be forgotten, namely, *that glaucoma should be operated on as promptly as possible if one wishes to preserve good visual acuity for the patient.*

It would be interesting to practise **subconjunctival injections of adrenaline**, but the marked, and as yet ill-understood, toxity of this organic product has made me recoil from this somewhat hazardous experiment. It seems to me, however, to be indicated in some cases of exophthalmos, especially in exophthalmic goitre, before proceeding to the excision of the superior cervical ganglion.

Landolt, of Strassburg, who has practised subconjunctival injections of surrenaline in the rabbit, has observed after it a marked mydriasis, but he has noted no action upon the vessels of the fundus of the eye. On account of the great toxity of the product, he has not dared to administer it to man. Bates had already observed in man, after a hypodermic injection of supra-renal extract, a disconcerting syncope. I myself, after a brushing of the nasopharynx, experienced such giddiness as to make me hesitate to employ surrenaline internally.

From the standpoint of general therapeutics, the supra-renal extract is likely to occupy before long a prominent position, not only in eye work, but still more in certain general maladies due to atony of the blood and lymph vessels. But the experiences so far acquired,

although encouraging and even very conclusive, are not sufficiently numerous to allow us to formulate precise indications or doses, or to indicate the favourable cases.

Stoelzner has administered, in the course of sixteen months, supra-renal gland to seventy-six children affected with rickets. There was a remarkable improvement—bettering of the general state, improvement of dentition, and the children soon became able to sit up and to walk. In an autopsy he was able to prove a calcification of the osseous substance more advanced than in those who had not been treated with extract of the supra-renal gland.

The opotherapy of this organ is still in its infancy, and we are not able to predict that which it may bring forth, but I shall not overstep the limits of sound logic when I say that atony of the capillaries, which characterises lymphatism, may be due, in part at least, to an insufficiency of the functions of the supra-renal capsule.

That is a pure hypothesis, I admit.

I was already imbued with this idea from my first experiences with adrenaline, and, without wishing to attribute to this substance a direct therapeutic action, I claim that in lymphatic keratitis the cure was obtained much more promptly when adrenaline was used as a collyrium before applying the yellow ointment.

But, for the moment, the main point of interest is the local action of adrenaline in therapeutics. It is remarkable in phlyctenular keratitis, episcleritis, Spring Catarrh, and in glaucoma.

Its action, from a physiological standpoint, is of great general interest. Permit me to explain how everything that the *clinique* has indicated has been confirmed by a very interesting series of experiments.

At the last Heidelberg Congress, Wessely presented a communication from the laboratory of Professor Leber. In it are related the results of numerous experiments made upon the rabbit. We are happy to say that his researches fully confirm the clinical observations and the therapeutic experiences made with adrenaline.

When injected into the veins, adrenaline provoked a contraction of all the muscles innervated by the great sympathetic—mydriasis, protrusion of the eyeball, retraction of the third eyelid, and enlargement of the palpebral fissure. This effect, which lasts only one or two minutes, may pass unnoticed. Repeated instillations of sufficient doses of adrenaline bring about also a marked mydriasis. It acts directly upon the vessels of the iris and ciliary body, which it contracts strongly. There results from that a notable slackening in the production of the aqueous humour, as the

following experience proves:—on one eye there was practised a subconjunctival injection of adrenaline, and on the other eye an injection of artificial serum. A quarter of an hour afterwards the aqueous humour was evacuated from both eyes; ten or fifteen minutes later, the anterior chamber of the serum side was re-formed, the tension had become normal or even a little raised, and the aqueous humour of that side was more albuminous than in the normal state. As regards the other side, on the contrary, the adrenaline had slackened the production of the aqueous humour to such a point that, after thirty minutes, the eye is still of low tension and the aqueous humour contained no more albumen than in the normal state. This demonstration of the slackening of the secretion and of the filtration of the aqueous humour may be shown in even a more brilliant way by the intra-venous injection of fluoresceïn. One knows, in fact, that in such cases, soon after the injection, fluoresceïn appears through the pupil as a greenish ring, which in ten minutes colours the aqueous so that the iris is no longer visible. Upon the adrenalised eye this green ring, the so-called "line of Ehrlich," appears only at the end of an hour, and it is with difficulty that the aqueous humour becomes coloured green. If we next examine the two eyes histologically, we find a few greenish striæ in the ciliary body of the eye which was injected with adrenaline, while the other eye shows the same tissues to be gorged with fluoresceïn.

Another means of submitting the action of adrenaline to the proof is the following:—By means of a stick of silver nitrate we cauterise the border of the cornea. This violent chemical irritation provokes an intense hyperæmia of the ciliary processes, which quickly betrays itself by an abundant albuminous transudation into the anterior chamber. This reaction of the ciliary body can be prevented by injecting ½ to 1 milligramme of adrenaline.

Subconjunctival injections of 5 per cent. sodium chloride solution also provoke in the rabbit an augmented amount of albumen in the aqueous humour, a thing that we can equally prevent by means of adrenaline. Clinical experience, however, has shown us that sometimes slight iritis may follow subconjunctival injections made upon man.

It is important to know that experimental irido-cyclitis may be set up in different ways.

If I allow myself to insist thus upon purely experimental facts, it is because they have a clinical and therapeutical bearing of a very important nature. In fact, quite at the beginning of an iritis, frequently repeated instillations of adrenaline may prevent or hinder

the evolution of the pathological process as regards the ciliary processes.

Experimental therapeutics have shown me, in an almost constant manner, that adrenaline lowers intra-ocular tension in an appreciable way. These facts have been confirmed by Zimmermann and others, but no manometric or tonometric research had yet been undertaken to give experimental confirmation to clinical observation.

Wessely, continuing his interesting work in Leber's laboratory upon renaline, has just demonstrated in the most precise way the lowering of intra-ocular pressure, which he found to be 3 to 4 mm. lower than on the sound side when estimated by an exact manometric measurement.

After a series of clinical and experimental facts, as varied as they are interesting, it was natural to seek to explain the intimate mode of action of surrenaline. Was it a direct excitation of the vascular walls or of the ganglia that deck them, or was it an excitation of the vaso-constrictor nerves, the terminal branches of the great sympathetic ?

The last hypothesis is not acceptable, for even when the sympathetic filaments were atrophied by an anterior extirpation of the superior cervical ganglion, adrenaline, when injected either into the veins or beneath the conjunctiva, has always the same vaso-constrictor effect (Lewandowsky, Wessely). It acts, therefore, not upon the terminations of the sympathetic, but upon the more peripheral elements still—namely, the ganglionic cells or muscular fibres.

Adrenaline, in strong doses or in subconjunctival injections, provokes a very marked dilatation of the pupil, simply by action upon the muscular or ganglionic cells of the pupillary dilatator.

The contraction of the vessels goes for nothing in the mydriasis, since that can be produced even in an iris detached from the eye. In fact, if we isolate the iris of a frog or of a rabbit, we can preserve it for several hours in artificial serum. The pupil is then rather contracted. If the iris be plunged into a solution of surrenaline, the pupil dilates *ad maximum*. There is no question of vaso-constriction, any more than we can admit an excitation of the sympathetic terminations, for we have just said that mydriasis is produced even after the extirpation of the superior cervical ganglion.

LECTURE IX.

Summary.

Agents capable of modifying the muscular tone of the iris.—Mydriatics: atropine paralyses the sphincter of the iris, and increases the contraction of the radial fibres.—Scopolamine acts in the same way, but more energetically.—Homatropine has a less durable action.—Euphthalmine dilates the pupil without paralysing the accommodation; it is the mydriatic *par excellence* for ophthalmoscopic examination.—The myosis provoked by eserine or pilocarpine is produced by a contraction of the sphincter pupillæ.—Spasm of the ciliary muscle sets up a fleeting myopia.—Agents capable of modifying the secretions or the mucous membranes: astringents, different local applications, antiseptics, etc.—The difficulty of sterilising the conjunctival sac; antiseptic properties of the tears.—The antiseptics best borne by the eye.—The salts of silver are the ones most used in conjunctivitis.—The advantages of organic combinations.—Argentamine, by its penetrating power, has shown itself superior to silver nitrate.—Argonine, largin, itrol, actol, etc.

We shall soon have finished with generalities. We have already passed in review the general and local medicaments most in vogue.

We have divided therapeutic agents into (1) modifiers of superficial sensibility (**anæsthetics**); (2) modifiers of profound sensibility (**analgesics**); (3) modifiers of vascular tone (**vaso-constrictors and vaso-dilators**).

To-day we shall rapidly review (4) modifiers of the muscular tone of the iris (**mydriatics and myotics**). They are, for the most part, so widely known that we need only linger a little upon one of them, euphthalmine, the most valuable mydriatic for ophthalmoscopic examination, and one that deserves to be widely recognised.

We shall afterwards add a few words upon (5) modifiers of the secretions (**astringents**), which will bring us to the treatment of conjunctivitis, and applied therapeutics generally.

The study we have just made of adrenaline conducts us by a natural experimental transition to an examination of the tonicity of the ciliary muscle and iris.

Atropine (known since the year 1833), when dropped into the conjunctival sac, penetrates through the eyeball as far as the aqueous

humour, where it reaches the iris, and paralyses—first, the sphincter, and, then, the ciliary body equally, thereby doing away with the power of accommodation of the eye.

It has been thought that this action was produced by way of the general circulation; but, as already seen, that cannot be so, inasmuch as the pupil of the second eye fails to dilate.

The action of atropine does not limit itself to a paralysis of the sphincter of the iris; for, if such were the case, paralysis of the oculo-motor, which innervates the sphincter, would produce the same mydriasis. That brought about with atropine, however, is much more marked, and atropine applied to an eye with paralysis of the third pair manifests its action by dilating the pupil still further. At the same time as the sphincter is paralysed, atropine therefore stimulates the dilator fibres of the pupil.

Atropine is prescribed in 0·5 per cent. solution, one drop twice or thrice a day.

Scopolamine* acts more energetically than atropine, and renders great service in cases where the latter fails to dilate the pupil. The following is the formula recommended in such cases:

Hydroiodide of scopolamine . .	0·25 gr.
Cocaine hydrochloride . . .	0·20 gr.
Distilled water	10 gr.

S.—*One drop into the affected eye four times a day.*

The addition of cocaine increases the effect of mydriatics—first, because it enhances absorption; secondly, because it provokes a contraction of the vessels of the iris; and, thirdly, because it acts directly both upon the dilating fibres of the iris and the ciliary muscle itself.

Homatropine acts upon the pupil in a way analogous to atropine, with this difference, that the action is more rapid and lasts a shorter time. A 1 per cent. solution provokes, within a few minutes, complete dilatation of the pupil with paralysis of accommodation, which disappears at the end of twenty-four hours. It is very useful when refraction has to be determined, especially in children, in whom accommodation plays an important *rôle*.

Duboisine has marked toxic properties which tend to limit its employment.

A desideratum still to be realised is the possession of a mydriatic which has an action at once rapid and short and without effect upon

* **Scopolamine** is now regarded as chemically, physiologically, and clinically identical with **Hyoscine.** It is prescribed in 0·25 per cent. solution. (*Die Neueren Augenheilmittel*, 1902, by Dr. M. Ohlemann, p. 64.)—TRANS.

the power of accommodation. Ophthalmoscopic examinations, in fact, are more complete and easier to make, especially for beginners, when the pupil is dilated.

Until recently **cocaine** was the agent most commonly used for ophthalmoscopic examination, although its action on the pupil was very uncertain, and on accommodation often very marked. Moreover, the epithelial alterations of the cornea sometimes formed a serious enough complication, not to mention the toxic effects observed in predisposed subjects.

Ephedrine, introduced some years ago into ophthalmology, produces, as a 10 per cent. solution, painful conjunctival irritation, but its mydriatic action was very marked and lasted only fourteen hours. The ciliary muscle was slightly paralysed. A drop of a 5 per cent. solution, which has no irritating action, gives rise to a powerful and temporary mydriasis, and modifies accommodation but little. The mydriasis lasts for three and a half hours only.

Merck* has quite recently discovered a new preparation of atropine, called the **methylbromide of atropine,** the action of which is more rapid and intense than that of the sulphate salt. All mydriasis and paralysis of accommodation, however, are said to disappear in four hours.

Mydrine, sold by Merck, is a mixture of homatropine 1 and ephedrine 100. It therefore unites the respective properties of those two agents.†

We have tried all these mydriatics, and the one that seems to us to combine best the qualities of a rapid and brief mydriatic, without notable affection of accommodation, is **Euphthalmine,** employed as a 5 per cent. solution. One or two drops of this solution suffice to bring about in thirty-five minutes a maximal dilatation of the pupil, which facilitates ophthalmoscopic examination, without any marked alteration of sight. Aside from a slight dazzling, caused by the diffusion of luminous rays penetrating through the dilated pupil, the patients can, as a matter of fact, read, without much difficulty, the print of an ordinary book or newspaper. The action of the drug passes away in two or three hours.

Since we have used euphthalmine before ophthalmoscopic examination, we have never experienced any of the discomforts so common

* *Wochen. f. Therapie und Hygiene,* October, 1902.

† According to observations made by the Translator, a 10 per cent. watery solution dilates the pupil in 29·35 minutes, and this effect passes away in a little more than three hours. The function of accommodation is scarcely affected. See *Lancet,* July 2, 1898.

with other mydriatics. Beyond the slight dazzling, patients have never complained of the least discomfort. The eye has always returned to its normal state by the same evening. This agent may well be used in doubtful cases where one wishes to ascertain whether iritis is or is not present. In this event, indeed, if one has really to deal with an iritis, the use of atropine presents no inconvenience. If, on the contrary, one has to do with a simple perikeratic hyperæmia, or a slight diffuse episcleritis, the employment of atropine imposes upon the patient five to eight days of paralysis of accommodation, while euphthalmine dilates the pupil rapidly, regularly, and completely, and allows us to make the diagnosis just as well without any of the inconveniences of atropine.

The name **euphthalmine** has been bestowed upon a synthetic product, which, in contemporary chemical nomenclature, bears the name of oxytoluylen-methyl-vinyl-diacetone-alkamine. This substance has close parental connections with B-eucaine, which is known as the hydrochloride of benzoyl-vinyl-diacetone-alkamine; it differs from the latter by the substitution of the radical methyl CH_3 for the hydrogen of the amide group AzH, and by the substitution of the radical amygdal for the radical benzoyl.

Pharmacological Characters and Physiological Effects.—Euphthalmine occurs as a white crystalline powder, readily soluble in water. In simple extraction of cataract the transient mydriasis produced by euphthalmine facilitates the delivery of the lens and of cortical masses, without in any way interfering with the action of the eserine indicated for ensuring perfect reduction of the iris.

From the view-point of the physiological effects, euphthalmine must essentially be distinguished from B-eucaine. While the last-named, when instilled into the eye, produces local anæsthesia without pupillary modification, the first gives rise to mydriasis without local anæsthesia. For example, according to Vossius's observations, the instillation of two or three drops of a 2 per cent. solution is followed twenty to thirty minutes later by mydriasis of medium degree, which lasts for two to three hours. During the duration of this mydriasis the accommodation is not affected.

Treutel experimented with a stronger 5 per cent. solution. He obtained a maximum dilatation of the pupil in the same period as when he used a 1 per cent. solution of homatropine. With such a solution, accommodation is less affected than when homatropine is employed. In subjects advanced in age, the effect of euphthalmine is at once less intense and slower in production. In addition to which, we do not find with euphthalmine concomitant subjective

manifestations—no prickings, pain, or alterations in the corneal epithelium. It would therefore appear that euphthalmine lends itself particularly well to ophthalmoscopic examination in place of homatropine and atropine.

Advantages of euphthalmine:

1. The dilatation of the pupil takes place not much later than with the other mydriatics.
2. The influence on accommodation is so slight as to be negligible.
3. The intra-ocular tension is not modified.
4. No toxic action has yet been observed.
5. No corneal or conjunctival irritation has been noted.
6. The mydriasis disappears rapidly.

We shall say but few words on **myotics,** of which the chief are eserine and pilocarpine. They act by provoking a continuous contraction of the sphincter of the iris and of the ciliary muscle, thus bringing about a considerable contraction of the pupil and a spasm, a contracture of accommodation.

Eserine, more energetic than pilocarpine, gives rise to headache and a sensation of painful tension. For that reason **pilocarpine** is to be preferred, except there are definite indications otherwise. Pilocarpine keeps better, and a 1 per cent. solution possesses a sufficiently energetic action.

The action of myotics is less prolonged than that of mydriatics. This is why it is possible, as a rule, to dilate with atropine a pupil contracted by eserine, while it is impossible to contract by eserine a pupil that has been just dilated by atropine.

À propos of iritis and glaucoma, we shall offer detailed indications for the use of mydriatics and myotics.

According to recent experiences, eserine is better supported as an oily collyrium. A 1 per cent. solution of eserine in sterilised olive oil keeps almost indefinitely, although in aqueous solution it quickly undergoes change. Patients intolerant to the latter bear the former solution very well. We have made comparative trials between the different solutions, watery and oily, and have proved that the oily solution of eserine presents such great advantages that we have completely abandoned the use of the watery solution.

Other myotics* have been recommended during the last few years, but they present no sufficiently marked advantages over eserine and

* **Midrol,** a synthetic compound introduced by Cattaneo, is one such myotic. It is employed as a 10 per cent. watery solution, which first produces contraction, and, later, dilatation of the pupil.—TRANS.

pilocarpine to allow them to replace the last two products. **Arecoline,** as a 1 per cent. solution, provokes a rapid contraction of the pupil, the myosis attaining its maximum in ten minutes. The more intense and rapid action of arecoline may be turned to advantage in certain cases where eserine has not given the result expected from it. The **hydrobromide of arecoline** has a slightly irritating effect upon the conjunctiva.

We now come to **agents which are capable of modifying the conjunctival secretions.** What do we mean by "modifiers of secretions"? But, first, what are the ocular secretions in the physiological state? Tears and the sebum of the Meibomian glands need not detain us long. Catarrhal or purulent secretions from the conjunctiva are oftenest provoked by the presence of infectious microorganisms transported by contact from one individual to another. The infectious element is not always the same; it is, as we shall see presently, of specific importance. Modifiers of secretion, therefore, must be, before everything, agents capable of stopping the development of these infectious elements, while at the same time they have a stimulating and tonic influence upon the cells.

The salts of silver, mercury, copper, zinc, and lead are the principal astringent and antiseptic applications.

Silver nitrate has, until recently, been recognised as the *topique de choix*, not to say specific, in almost all the secretory affections of the conjunctiva. Alum, zinc, lead, copper, are merely its substitutes having special indications; but, if we understand how to apply the salts of silver, we are able with one of them, and by judiciously varying the strength of the solutions, to obtain perfect therapeutic results in most forms of conjunctivitis.

For more than fourteen years I have obtained by cauterisation with silver nitrate alone results so constantly good that it has been with a struggle that I abandoned so valuable a remedy in order to have recourse to new salts of silver. But the latter (I ought to acknowledge the fact) have shown themselves so superior to the nitrate that, for my own part, I have nearly absolutely renounced the use of this salt for the last five years.

In weak solutions, 0·25 per cent. to 0·50 per cent., daily touchings with silver nitrate quickly cure superficial inflammations of the conjunctiva. In some infrequent cases, especially chronic diplobacillary conjunctivitis, sulphate of zinc is to be preferred, but it is not yet proved that, even in these cases, nitrate of silver, handled in a certain way, is not equal to the last agent, which, on the other hand,

has the advantage (if it be an advantage) of being applicable by the patient himself.

In severe purulent ophthalmia, no method has brought about so many cures as cauterisations with a 2 per cent. solution of silver nitrate, repeated once or twice daily. Opinions are to-day altogether unanimous on this point, and this we may rightly consider as the classical treatment of purulent ophthalmia.

Prophylactic applications of silver nitrate, after the precepts of Credé, have equally furnished their proofs, supported by many statistics.

It must accordingly appear presumptuous or even imprudent to present new products to the practitioner already possessed of a medicament of which he thoroughly understands both the advantages and the dangers. I should be one of the first to blame those who acted thus, without having studied widely and maturely all the advantages and inconveniences, and the different indications and contra-indications of the new remedies.

Silver nitrate has a powerful bactericidal action, which is due to its base silver, but it also has a violent caustic action due to its contained nitric acid. It is that fact that has incited to the search for new silver combinations, which shall possess the same antiseptic properties and be less irritant and less corrosive. The salts of mineral origin tend more and more to be replaced by organic combinations, and all the chemical laboratories pour forth so many new products — argentamine, largin, itrol, actol, nargol — that the practitioner is troubled to make their acquaintance quickly enough to be able to appreciate them at their true value.

Following a paper by Hoor upon **argentamine**, which was published in the *Klin. Monatsbl.* for July, 1896, I tried this new salt of silver—to begin with, in simple affections of the conjunctiva. Having obtained results that satisfied me fully, and recognising qualities in the new remedy that I had never found in silver nitrate, I treated also by these means more serious forms of conjunctivitis—as, for example, purulent conjunctivitis, granulous conjunctivitis, etc.

From the beginning I recognised that cauterisations practised with 3 per cent., 5 per cent., and even 10 per cent. of argentamine were much less painful than those produced by the application of 0·50 per cent. to 2 per cent. solutions of silver nitrate, solutions equivalent in strength to those of argentamine named above. The application to the conjunctiva of even a feeble solution of argentamine produced at once a milky precipitate, which proved that the product was very decomposed by the tears. This precipitate, however, re-

dissolves in an excess. It is, therefore, very important to apply the medicament more generously than one usually does the silver nitrate.

It is, perhaps, one of the drawbacks to the new salt that it decomposes with great readiness, and that its solution does not keep well.

On the other hand, even with a strong solution, I have never observed, as is almost always the case with silver nitrate, the epithelial desquamation that comes away in fine films, rolling itself into white filaments and gathering into a group at the internal angle of the eye, allowing the conjunctiva to appear of a lively red hue, deprived of its superficial epithelial layer. This exposure of the conjunctiva, after touchings with silver nitrate, is not one of the least important causes of pain as regards the patient, and it may be seen even when feeble solutions are employed. The action of silver nitrate, therefore, is too caustic, not to say too brutal; it destroys the epithelium without making its effects fully felt upon the deeper layers of the conjunctiva; while, on the contrary, this very power of penetration is the principal quality of the new salts of silver, which we shall consider at some length.

Argentamine is a solution of silver phosphate in ethylene-diamine.* This liquid, colourless and alkaline, is equivalent in strength to a 10 per cent. solution of silver nitrate, and if diluted with ten parts of water a solution corresponding to 1 per cent. of silver is obtained.

The ethylene-diamine, which enters into the composition of argentamine, is an organic base having little caustic power, and possessing the peculiar property of re-dissolving precipitates formed by salts of silver in contact with the tissues; in this way the penetration of the silver salt into the depths of the anatomical elements is favoured, where it exerts its powerful germicidal action.

Schaeffer,† working in the clinique of Professor Neisser, of Breslau, has furnished the experimental proof of the foregoing facts by employing the relatively equivalent solutions of silver nitrate and argentamine. Microscopical sections of organs treated by these salts and then steeped in sulphite of ammonium, showed a black infiltration of the sulphite of silver absolutely superficial in sections treated by the nitrate, while the zone of penetration was five times deeper in those submitted to the action of argentamine. Continuing these experiences, Schaeffer tried to determine the disinfecting and germicidal power of argentamine, comparing it with that,

* For some time the phosphate has been replaced by the nitrate of silver.

† *Zeitsch. für Hygiene und Infections-Krankheiten*, 1894.

already well-known, of silver nitrate. He found that the antiseptic action of argentamine was more pronounced than that of silver nitrate when studied with various micro-organisms; but that which touches us more closely may be given in his own words: "Argentamine kills gonococci more rapidly and certainly than nitrate of silver."

Grounding myself, therefore, on these optimistic considerations, I tried for eighteen months argentamine in all conjunctival affections where silver nitrate was indicated. In some patients argentamine was used in one eye and nitrate in the other; at other times, after several days' trial of the first-named, this was replaced by the second application, without telling the patient, and in such a way as to inform me of the effects and sensations produced. It did not take me long to arrive at the conclusion that the application of argentamine was much less painful than that of silver nitrate, the due proportions of saturation being adhered to. With regard to the therapeutic effect, that appeared to me from the first at least as marked, to say no more, in all forms of conjunctivitis of medium intensity;* but before the point could be settled in a question so important as that of the treatment of purulent ophthalmia, it was necessary to submit the agent to a long and extended trial. Accordingly, I waited eighteen months before publishing my results.

My opinion is now fixed to this extent—*i. e.*, that in my *clinique* all solutions of silver nitrate, from 0·5 per cent. to 2 per cent., have been almost completely abandoned for five years.

Other salts of silver have been equally praised in recent times, such as **argonine**, which has been vaunted as a most powerful anti-gonorrhœic agent. It is a combination of casein and silver, forming a crystalline salt, which is soluble in water, and of which fifteen parts are equivalent to one part of silver nitrate. The salt has hardly any irritating properties, and destroys gonococci very rapidly; but those who have tried it find that it has no astringent or anti-catarrhal qualities, and, hence, to complete the treatment of blennorrhœa, they employ ichthyol or other astringents. For my own part, I have never tried argonine enough in ocular therapeutics. I shall therefore abstain for the moment from all appreciation of the product, which is interesting enough from other points of view.

Zanardi has recommended the employment of **sulphophenate of**

* The Translator would add his testimony to the great efficacy of **Argentamine** in affections of the conjunctiva. Under the use of a 5 per cent. solution, he has seen cases of subacute trachoma clear up completely, a thing he has never observed with silver nitrate.

silver, which possesses all the antiseptic properties of silver salts with the other advantage of being little irritating, very soluble, and easily preserved. Zanardi has used it with success in surgery and in eye work, but he has not published in detail the results he has obtained.

Itrol, or **citrate of silver,** was introduced into therapeutics by Credé, who used it with success in the dressing of wounds. This salt has struck me as interesting, because it is not at all irritating, and is a light powder—impalpable, so to speak—easily applied by insufflation. The results I have obtained, whether in powder or in ointment form, have not encouraged me to continue my researches into the agent, which has offered me no advantages over argentamine, and, still less, over protargol.

Nénadovic, at the Moscow Congress, has praised itrol when used as powder or as a 1 per cent. to 3 per cent. solution. By these means he has obtained good results in the treatment of granular conjunctivitis. To my mind, the powder is an excellent means of obtaining perfect asepsis of wounds, but its insufflation into the conjunctival sac is not without danger to the cornea. Nascent silver developing in contact with wounds acts, according to Credé, as a most powerful antiseptic means, but the cornea does not always seem to support well the application of this agent.

Mergl, of Strassburg,* praises itrol, insufflations of which he has employed in catarrhal, purulent, and granulous conjunctivitis, prescribing at the same time sublimate lotion and iced compresses. The discharge disappears in two or three days, and definite cure was obtained in six to eighteen days. In trachoma, secretion was stopped as quickly as under treatment by silver nitrate.

In some cases of ulcerated cornea, cure can be got by a single insufflation and an occlusive dressing, while in other instances a total infiltration of the cornea followed. Hence, *there are some patients who do not tolerate itrol well.*

A product of the same kind, **actol,** or **lactate of silver,** was also recommended by Credé at the second German Congress of Surgery at Berlin in 1896. This salt is soluble in water and albuminous liquids in the proportion of 1 : 25. Its antiseptic power is extremely great; a watery solution of this salt kills in five minutes all pathogenic microbes, and a solution of 1 : 80,000 hinders the development of bacteria completely. The trials made with the salt in ocular therapeutics are not yet advanced enough to justify any definite statement

* *Aerztliche Rundschau,* p. 48.

on the subject, and so far I am not acquainted with any communications on actol in eye work. Mergl has found actol to be a more painful application than itrol.

Lastly, **Nargol,** the **nucleinate of silver,** has been praised as superior to protargol. I am not able to substantiate the claim as the result of my experiments. Protargol will be considered in the next lecture.

LECTURE X.

Summary.

Protargol is the most practicable of the salts of silver.—It is not precipitated by the ocular secretions, and its penetrating power is combined with most potent germicidal properties.—These are real advantages over silver nitrate, which it may well replace in almost all its applications.—It may be readily employed by the patients themselves.—It is the least caustic and painful of the silver salts.—It may, therefore, be applied more freely and frequently than silver nitrate.—Argyrosis may, perhaps, be prevented by washings with sublimate.—"Savonnage" of the cilia with protargol.—Insufflations with protargol.—Formulæ.—Attempted scientific classification of conjunctivitis.

Lastly, we come to **Protargol**, which appears to be the silver salt combining the greatest number of advantages with the fewest inconveniences.

Neisser, professor of dermatology in Breslau, under whose direction Schaeffer made his interesting observations on argentamine, previously spoken of, does not hesitate to consider protargol as much more active and efficacious than any of the other salts of silver of which we have spoken.

Protargol, a combination of protein and silver, takes the form of a fine powder, yellowish in colour, and readily soluble in cold water. The solutions thus obtained are of a yellow hue, but perfectly clear; they give no precipitate on the addition of alkalies, sulphates, albumens, etc. These are most important qualities when it comes to treating affections of the eye. This agent appears, therefore, likely to render signal service in ophthalmology.

If protargol is precipitated neither by sodium chloride nor by albuminoids, it must possess a power of penetration still more powerful than argentamine; and, as it does not precipitate a 2 per cent. or 3 per cent. solution of cocaine, happy combinations may be formed with that product. According to Neisser, the antiseptic

properties of protargol are superior to those of the other salts of silver; but he gives no figures on the subject.

Protargol contains 8·35 per cent. of silver. Argentamine includes 6·35 per cent. of silver. Argonine has 4 per cent. of silver.

The characteristic of protargol, however, is that its application causes scarcely any pain or irritation. In all cases its use is easily borne by patients.

For the rest, here are the words employed by Neisser in finishing his study of protargol in blennorrhœa:—"In recapitulating the observations made in the clinique, polyclinique, and private work, I should first say that never by any treatment have I obtained results as good, as rapid, and as certain as with protargol. In practice, all the brilliant hopes that one entertained theoretically have been fully realised, and I do not doubt that ulterior experience will confirm these first and striking cures."

Having read with the greatest interest in the *Dermatologischer Centralblatt* Neisser's article, I procured some protargol and proceeded to try it, in order to compare its effects with those of argentamine, with which I was already so satisfied.

At first I made a 5 per cent. solution, and thus obtained a clear brown liquid, resembling beer, with a slight opalescence, but quite transparent, and devoid of any flakiness or deposit. This solution seemed to keep without the least alteration if it was shielded from light, as should be done with all preparations of silver; in default of this precaution, the solution of protargol became of darker hue and lost some of its activity.

To begin with, I applied some of the protargol solution to the conjunctiva, previously cocainised. The patient experienced no pain either during or after the application; no reaction was appreciable even half an hour afterwards; no precipitate nor redness of the conjunctiva. I next practised these applications without instilling cocaine, and patients complained of a pain scarcely more marked than that attending the use of any collyrium.

My first therapeutic trials were conducted upon cases of simple catarrhal conjunctivitis. In the first patient there was a sufficiently intense conjunctival inflammation. For three days a daily touching with a 5 per cent. solution of protargol was practised. The cure was complete and radical; and the patient, a woman of extreme sensibility, was able after each cauterisation to attend to her business without the least difficulty. As to the pain produced by protargol, it was, said the patient, scarcely more than that caused

Encouraged by this first fact, I employed protargol and argentamine comparatively—that is to say, sometimes by treating one eye with each product, and sometimes by using the two medicaments turn by turn. I could not make out any appreciable difference between the two means of treatment in so far as concerned the rapidity of cure. Protargol therefore appears to act as well and as rapidly as argentamine, and possesses over the last agent certain advantages—namely, that its application is almost painless, and that its solution keeps perfectly when protected from light.

In my first communication on protargol I concluded:—"Protargol, by its marked powers of penetration, by its antiseptic action—similar to, but more energetic than, those of silver nitrate and argentamine—and especially on account of its perfect harmlessness and the little irritation it causes when in contact with the conjunctiva and cornea, deserves to be tried systematically in all forms of conjunctivitis in the treatment of which silver nitrate has heretofore been employed."

Von Graefe, who so well established the rules for the use of silver nitrate, himself recognised that it was a very difficult thing to ascertain the exact amount that suited each case, when one had to deal with so powerful an agent, which may do as much harm as good if it be not cleverly used. It is equally important to know when the cauterisations should be repeated, since they must be made neither too seldom nor too often. The caustic ought to be brought into contact with every part of the conjunctiva. Briefly, the employment of silver nitrate is so delicate an affair that it became really desirable to discover a new product, the application of which should be easier and less dangerous. In protargol we have a trustworthy medicament, which is able to penetrate the mucous membrane without harming the same, thus stopping the development of micro-organisms, and probably even destroying them in the depth of the tissues. This cannot be effected by silver nitrate, which destroys the superficial epithelium without penetrating deeper.

To adduce the experimental proof of the deep germicidal action of protargol, more time must elapse, but innumerable clinical observations have shown evidence of this action upon the living tissues, and that should be proof enough for the clinical observer. The action of silver nitrate is caustic and superficial—it destroys the membrane at the same time as the microbes; protargol, on the contrary, has a profound germicidal action without being so caustic. The last named, therefore, has unbounded advantages over silver nitrate.

Method of Employing Protargol.—Since the communication men-

tioned above*—the first published upon the effects of protargol in eye work—a number of works have appeared upon the same subject, almost all confirming the brilliant results that I had announced. A few writers, not yet familiar enough with the management of the new agent, have related some instances of lack of success, due most often to the employment of inadequate strengths or to applications not being repeated often enough.†

In fact, we must not forget that just as caution is needed in the use of silver nitrate, so temerity is called for in the use of protargol, the action of which is less caustic, less powerful, and also of shorter duration. While protargol contains only 8·3 per cent. of silver, the nitrate contains 65 per cent. As regards the first salt, the solution used for cauterisation must therefore be much stronger, and in the interval between the cauterisations frequent instillations must be practised, either by the patient or by his attendants, in order to prolong the antiseptic and astringent action of protargol. I affirm to-day, without fear of contradiction, that whoever will employ protargol in accordance with the principles laid down will find that it can thus advantageously replace silver nitrate.

Protargol, soluble in all proportions in water, should (as is the case with all preparations of silver) be kept from the light, since if that precaution be neglected, the solution becomes darker in colour, thicker, and less active. Therefore small quantities only should be prepared at one time, subject to their being renewed more frequently.

For instillations, the following formula may be recommended in the majority of cases:

Protargol	0·50 gr.
Distilled water	10 gr.

(Allow the protargol to dissolve spontaneously,‡ and in the cold in a yellow or blue bottle.)

S.—*To be dropped into the eye three or four times a day, or oftener if necessary.*

These instillations may be made by the patient himself or by his attendants. They are often sufficient by themselves to bring about the cure of slight conjunctivitis. Contrary to silver nitrate, which, often instilled into the conjunctival sac, is decomposed by the tears and the mucous membrane, protargol, not precipitated, becomes

* *La Clinique Ophtal.*, 10 Janvier, 1898.

† One can find in the *Clin. Ophtal.*, 1898—1900, an analysis of all works published on protargol.

‡ The solution must not be made in the presence of heat, nor must the powder be rubbed in a mortar. Solution is thus made imperfectly.

intimately mixed with the ocular secretions, penetrating to the bottom of the retro-tarsal folds and infiltrating even the depths of the epithelium. Instillations ought always to be employed even when cauterisations are practised twice a day by the surgeon, and the more serious the malady, the oftener should they be used. In cases of purulent ophthalmia they should be used, if necessary, every half-hour. Instillations of the 5 per cent. collyrium should be prescribed for home use, in addition to usual attention to cleanliness, every time the conjunctivitis reaches a certain pitch of intensity. Patients, however, should be warned that its use must not be kept up for too long, under penalty of seeing their conjunctiva take a brown colour, often very difficult to get rid of (**Argyrosis**).

For cauterisations with the brush one employs, in almost all cases, the following solution, with which the conjunctiva is painted more or less liberally:

Protargol	5 grammes.
Distilled water	10 grammes.

Cauterisation with the brush should act not only upon the everted conjunctiva, but also upon the borders of the eyelids; in this way one obtains, by rubbing with the brush steeped in protargol quickly and energetically, a kind of soaping (*savonnage*) of the lashes and border of the eyelids, which renders great service, especially when conjunctivitis is accompanied, as is so often the case, with blepharitis. Small compresses of protargol, applied during the night, are extremely useful.

In many cases of blepharitis and blepharo-conjunctivitis I have obtained rapid and permanent cures by the above means. In such cases one need not be afraid to rub the eyelids for some minutes with the brush energetically, much as a chin is soaped before it is shaved. Protargol (of albuminous composition—proteinate of silver) lathers like soap, and soaks in, penetrating the cilia as far as their roots, where it destroys the infectious germs.

Insufflation of protargol powder, which I recommend more especially in trachoma, should be carried out with one of those instruments generally used for insufflations of iodoform, but one must be careful to see that the powder is as fine as smoke.

The eyelids being everted, one insufflates the protargol so as to impregnate the entire conjunctival surface; then the lids are allowed to assume their natural position, and a rotatory massage of the eyeball is practised for one to two minutes, in order to make the powder, which dissolves at once, penetrate all the recesses of the conjunctival sac. The massage is of great importance: it renders indurated and

swollen eyelids supple, hastens the disappearance of pseudo-membranes (when such exist), facilitates the resorption of chemosis, and, lastly, provokes a copious exudation of tears and serous secretion, which cleanses the ocular surface and carries away any excess of caustic.

These insufflations, followed by massage, can, strictly speaking, replace cauterisation with the brush even in the slighter forms of conjunctivitis, and, indeed, also in blepharitis, if one takes care in the latter cases first to moisten the edge of the eyelid by means of a wet brush, with which one can, as stated above, practise a more or less energetic brushing; digital massage, again, of the border of the lid may perfectly replace *savonnage* with the brush, but one must have a very good insufflator projecting only a very light cloud of powder, in the absence of which one may provoke too deep a cauterisation.

If there be a disease where a 5 per cent., 10 per cent., or 20 per cent. solution of protargol is indispensable, it is in dacryocystitis; and it is not one of the smallest merits of protargol to have shown that suppuration of the lacrymal canal can be cured without extirpation of the sac. Injections of protargol made with an Anel's syringe —at first daily, then every other day, and then every third or fourth day—often suffice to cure long-standing suppurations. I believe I am in a position to say that if this means, combined with treatment by Vulpius' permanent styles, does not succeed, then the case can scarcely be cured, except by the destruction of the lacrymal sac.

Advantages and Inconveniences of Protargol.—The superiority of protargol is so incontestable that one may ask why it is not universally recognised. The explanation is that nothing is so difficult to root out as habit and routine. To make a truth penetrate amongst the masses, it is at first necessary to impregnate thoroughly the new generations. It is through you, Gentlemen, through youth, that the new ideas that you have proved to be good and true will eventually triumph. The practitioner, accustomed for years to the management of nitrate of silver, will renounce with difficulty the assistance of a friend so sure and faithful.

On the other hand, those who try, without conviction, any new treatment whatever, will rarely get from it any tangible benefit, unless circumstances themselves come to their help. There are, as you have seen, favourable chances in clinical work as well as in experimentation.

In applied therapeutics, as you know, scepticism is no longer fashionable; it is faith and willingness that make for good cures; it

is the conviction which often communicates itself from the doctor to the patient, acting as much upon the mind as the body, which constitutes one of the main factors in successful cures.*

How many times have we not seen purulent ophthalmia, treated by nitrate of silver, have a fatal issue in the hands of practitioners who, lacking confidence or will, have allowed themselves to be outflanked by unfavourable circumstances? It will be the same for those who employ protargol without conviction or who use bad solutions.

The fact also is well-known that so-called control experiments, conducted by those who criticise a method, always yield to those who make them negative results. Have I not furnished you with the proof at my own expense when I recounted that my first trials with dionine were almost negative? *Quantum mutatus ab illo!*

When entering into detail as regards the treatment of the various forms of conjunctivitis, we shall find many occasions for showing the superiority of protargol. Let us see here what are the intrinsic inconveniences and advantages of protargol:

1. Its solutions are easy to make and necessitate no apparatus. It suffices to place in a flask containing distilled water the required quantity of protargol; the solution is made spontaneously in the course of a few hours.

2. These solutions, shielded from light, keep very well.

3. Even in solutions of 33 per cent., protargol is less irritant than 2 per cent. silver nitrate.

4. In weak solutions of 2 per cent. or 5 per cent., protargol may without inconvenience be dropped into the eye every half-hour, if that is necessary, without the least inconvenience resulting from it.

These instillations may even in many cases replace cauterisations made by the practitioner, since we know that, thanks to its powers of penetration, protargol insinuates itself to the bottom of the *cul-de-sac*, and perhaps into the depths of the mucous membrane.

It was once thought that protargol did not provoke argyrosis as did silver nitrate; this is merely an affair of comparative dosage.

A very simple means of preventing argyrosis† is to follow the *protargolage*, of which we have spoken before, by washing the parts with sublimate or with mercury cyanide, 1 : 1000. That is a pro-

* Naturally, I do not allude to experimental therapeutics, where, on the contrary, the most absolute scepticism should direct the scientific observation of the results obtained.

† This simple plan does not, in the Translator's experience, prevent the production of **argyrosis**. Indeed, it does not even seem to delay the onset of the latter complication.

ceeding at once simple and practical, augmenting the action of protargol, and at the same time diminishing its inconveniences.

Protargol stains linen a little less than silver nitrate. But that is partly due to the fact that the colour of the solutions allows one to see the spots at the moment when they are made, so that they can be prevented from marking the linen permanently by moistening them with a solution of sublimate or, better, with potassium iodide. Stains of silver nitrate, on the contrary, do not show themselves until after several hours, when it is often too late to cause their disappearance.

Classification of Conjunctivitis.—The secreting affections of the conjunctiva seem so commonplace to the clinical observer who has had any experience, that it might appear difficult to make of them a study containing new or interesting facts.

The cause of conjunctivitis is most often the presence of infectious elements, now-a-days well enough known.

Almost always one finds upon the surface of the normal conjunctiva a number of micro-organisms, which fortunately produce no damage as long as the lacrymal secretion proceeds in a normal way. The tears, in fact, have an obvious antiseptic power. But if for any reason whatever there supervenes an arrest or a modification of that secretion—for example, under the influence of cold—a sudden multiplication of the infectious guests of the conjunctiva may take place. That is a way, at once simple and logical, of explaining the popular "draught," which we know to be commonly due to a commonplace infection.

But aside from these local infections, there are the whole series of conjunctivites by contamination, which for the most part we are able to diagnose and class according to their infectious agents.

Therapeutics, by pure empiricism, has found a local application, so to say a specific, for each kind of conjunctivitis. And yet what obscurity still reigns in the classification of that category of eye diseases!

The first ray of light was thrown by Neisser when he discovered the gonococcus. One was able from that moment to admit as quite special the grand category of **purulent ophthalmia** or conjunctivitis with Neisser's gonococci, or of Neisser.

Some rare cases of purulent ophthalmia have lately been related which were caused by other organisms (pseudo-gonococci, colon bacilli, Weeks' bacilli, pneumococci, etc.), but these facts are, after all, uncommon and exceptional; and one may even say that these forms of conjunctivitis are not really purulent by the essence of their infection, but by an individual and particular reaction of the

tissues. In fact, do we not know that a lymphatic or scrofulous person may react with extreme violence to the slightest infection?

For several years one recognised clearly only this single form of conjunctivitis due to gonococci of Neisser, while all the remaining kinds were styled acute, catarrhal, or chronic.

Some years ago, in 1883, Weeks* described clinically and experimentally a particular form of **acute contagious conjunctivitis**, characterised and caused by the presence of a specific bacillus, already found by Koch in the season conjunctivitis of Egypt; this may be called **Weeks' conjunctivitis.**

Lastly, quite recently a third morbid entity has been discovered by MM. Morax† and Axenfeld—namely, subacute **diplobacillary conjunctivitis**, once styled **angular conjunctivitis.**

A fourth class, also well outlined, is that of **diphtheritic conjunctivitis** caused by the Löffler bacillus, either pure or associated with other micro-organisms. The pneumococcus and the bacillus of Weeks, among scrofulous subjects, may produce false membranes, but such are devoid of gravity, provided they are not treated injudiciously.

With regard to **granulous conjunctivitis**—which is also certainly of infectious origin—we do not yet know the pathogenic agent, but, all the same, it does not on that account constitute a less well-characterised morbid entity.

Pneumococcal conjunctivitis manifests itself by rare epidemics, in general of a benign character; it is often unilateral, and has a symptomatology similar to that of Weeks' conjunctivitis. It may assume, according to the epidemic, all the appearances of the most violent purulent conjunctivitis; but, from the third or the fourth day, the diagnosis becomes obvious by the sudden bettering of all the symptoms. It is with cases of this kind that such good success is obtained by the most anodyne medications. We cannot, therefore, repeat it too often: one should not praise a treatment of purulent ophthalmia in the absence of conclusive bacteriological examinations.

Streptococci are found especially in dacryocystitis and in lacrymal blepharo-conjunctivitis; they are sometimes superimposed on other infections, and often give to pseudo-membranous conjunctivitis a particular gravity.

Without doubt there are many forms of conjunctivitis of which the etiology still escapes us. **Phlyctenular conjunctivitis**, of which the determinism is not yet well-established, is often set up by the

* Weeks, *Archives d'Ophtalmologie*, 1886.

† Morax, *Annales de l'Institut Pasteur*, June, 1896.

staphylococcus, sometimes by the Weeks' bacillus, and by other micro-organisms still.

Does there exist, in addition to these microbic conjunctival affections, a pure catarrhal conjunctivitis, due to a special pathological state of the conjunctival mucous membrane? Is cold or mechanical irritation capable of setting up an attack of conjunctivitis? It is difficult to decide the point. This much is certain, *viz.*, that some individuals, lymphatic subjects in particular, present quite a special irritability, susceptibility, and vulnerability of the conjunctival mucous membrane, which thus becomes a favourable breeding-ground for all infections.

It is therefore evident that we are not far distant from the day when all will agree on a scientific classification of the various forms of conjunctivitis. The diagnosis exacts from the clinical worker a certain acquaintance with the methods of the laboratory. This knowledge, at bottom, is easy enough to acquire; for from the clinical standpoint it usually suffices to smear a cover-glass with a drop of pus, to fix the film by heat, and then to stain the film with diluted fuchsine or any other basic aniline dye. The fuchsine has the advantage of being well taken by the gonococcus, the bacillus of Weeks, and by the diplobacillus of Morax, which constitute, in fact, the three microbes most often found in the ordinary run of cases of conjunctivitis, and of which the presence implies on each occasion a particular prognosis. Truly, an experienced observer will almost always recognise an ophthalmo-blennorrhœa without having seen the gonococcus, but he will be in the difficulty of not being able to adduce any scientific proof of the accuracy of his diagnosis.

In all scientific essays upon affections of the conjunctiva, it is a prime necessity to establish a bacteriological diagnosis with the microscope. The day may perhaps even come when we shall find for gonorrhœal and trachomatous ophthalmia an antitoxic serum, such as Roux and Behring have given us for diphtherial conjunctivitis. In the meanwhile, we must try to discover local applications of which the germicidal action should be the most energetic possible, and which should provoke a minimum of pain and of inflammatory reaction.

LECTURE XI.

Summary.

The scientific classification of conjunctivitis.—Treatment of conjunctivitis according to its clinical form.—Simple conjunctivitis.—Diphtheritic infection alone calls for a specific treatment.—Treatment of purulent ophthalmia; respective importance of the infectious agent and of the *terrain* upon the efficacy of treatment.—Dionine aids us in recognising lymphatic subjects.—Protargol well applied has the advantage that it never does any harm.—Its application should be frequently repeated.—When its action is not energetic enough, one may always have recourse to silver nitrate or, better, to ichtargan.—Treatment and cause of corneal complications.—Prophylaxis of purulent ophthalmia by *savonnage* with protargol of the border of the lids, the lashes, and of the brows.—Treatment of chronic conjunctivitis and of blepharitis.

We have reviewed at some length the various agents capable of modifying the ocular secretions, studying more particularly the different salts of silver called upon to replace the nitrate in most of its applications. We have tried, also, to lay down the bases of a scientific and bacteriological classification of conjunctivitis. To-day we arrive at the—

Treatment of Conjunctivitis.—From the therapeutical standpoint, the discovery of the various bacterial infections has not, so far, given us precise enough indications to impose upon us a treatment appropriate to the bacteriological classification which we have just explained. The clinical symptomatology still remains our chief therapeutical guide. Diphtheria of the conjunctiva alone is amenable to specific treatment by the antitoxic serum of Roux and Behring.

The clinical conditions of conjunctivitis are so variable that I desire to give you a few details drawn from my personal experience.

In **simple conjunctivitis, catarrhal conjunctivitis, acute contagious conjunctivitis,** which may present the same clinical symptomatology, whether caused by Weeks' bacillus, the pneumococcus, or any other common micro-organism, treatment is the same, and varies only according to the intensity of the reactionary phenomena and the individual conditions of each subject.

In principle it is necessary to trust but little to patients in respect

to local treatment; if they are very sensitive, they recoil from instillations of the collyrium which you have prescribed; in the contrary case, they abuse it.

Every time your patient is able to attend regularly at your consulting room, it is advisable to apply the remedies yourself.

In trivial forms of conjunctivitis one or two *protargolages* or *savonnages* with protargol, as indicated previously, will bring about a complete cure in two or three days. In such cases it is not necessary to apply a strong solution to the eye itself; brushing, *savonnage* with a brush of the external border of the eyelids and of the eyelashes, induces a sufficient imbibition, and the small amount of protargol which enters the eyelids brings about a rapid asepsis of the conjunctival surface.

I have often myself been surprised at the remarkable action of this simple external application of protargol. On the first occasions I practised it to spare the sensibility of certain nervous subjects.

If the conjunctivitis is more intense, you should practise *protargolages* with a brush upon the conjunctiva; at the same time, you prescribe for home use a 5 per cent. solution, to be dropped into the eye two or three times a day. You should obtain complete cure in a few days if the treatment has been carried out regularly by you and by the patient. To stop the cauterisations too soon, or to let long intervals elapse between them, before complete cure, is to invite relapses, which may allow the conjunctivitis to become chronic.

The long employment of protargol entails tolerance, and the alternate use of drugs, of which we shall speak later, is then indicated.

It is almost needless to add that it is of great importance to make your patient understand that he should exercise care in his own home. Instruct him to practise as perfect an antisepsis as the circumstances will permit.

Advise patients to abstain from using, as a means of applying lotions and irrigations, such articles as sponges, syringes, and also eye-cups. Lotions may be applied by means of a pledget of aseptic wool dipped into the solution, borated or otherwise, which preferably should be warmed. The wool and the lotion should be thrown away immediately after use.

As regards collyria, the cleanliness and the asepticity of the pipette must be looked after carefully.

Patients should wash the hands and face frequently without being

afraid to let the soap act upon the eyebrows and eyelashes. These ablutions ought always to be carried out at least twice a day—that is, on rising and retiring.

We come now to the study of **purulent conjunctivitis.** Clinically it is certain that many of the cases of acute and violent conjunctivitis, due it may be to Weeks' bacillus or to the pneumococcus or to the colon bacillus, may be considered, especially at the beginning, as purulent conjunctivitis; but at the end of a few days the evolution of the symptoms tells us what the true diagnosis is.

At the commencement, therefore, of an acute, intense conjunctivitis, if a microscopical examination has not been made, I recommend you to content yourselves for the first day with instillations of a 5 per cent. protargol solution, applications which you prescribe the more frequently the greater the violence of the inflammatory phenomena. In the interval the eye should be washed frequently, perhaps with boric lotion, perhaps with permanganate of calcium,* 1:3000. The last solution has an obvious action against suppuration; but I would not recommend irrigations with any instrument whatever. Moreover, once or twice a day you should make a *protargolage* with a brush, which cleanses and asepticises so well the border of the eyelids, while at the same time allowing a little protargol to penetrate between the palpebræ.

By these means, if you happen to be dealing with a Weeks' or a Pneumococcal Conjunctivitis, there will be a rapid amelioration in the symptoms, and in five or six days complete cure will come about.

I have already stated my views with regard to the classification of conjunctivitis. The exceptions confirm the rule; one must admit that true purulent ophthalmia is due to gonococci, and in order to acquaint one's self with the efficacy of any treatment, it is desirable experiment only upon gonococcal conjunctivitis.

Protargol has made its proofs, both in the laboratory and in clinical work. It is the *topique de choix*, but it is necessary to know how to employ it. One must also be acquainted with the *terrain* most favourable to the development of the gonococcal infection.

He who affirms that he has never experienced any disappointment with this or that alleged specific, must not be astonished some day to meet with one of the fulminating forms, which in several days entails more or less widespread corneal ulcerations, leaving behind it thick leucomata, even if it does not induce perforation or atrophy of the eyeball, etc.

* Dr. Darier informs me that calcium permanganate (**monol**) is much better for this purpose than the permanganate of potassium or of sodium.—TRANS.

What must be done in the case of a premature baby, puny and weakly, born into the world suffering from a violent ophthalmo-blennorrhœa? The child is so small, the eyelids so swollen, that it is almost impossible to evert the latter or even to open them. Often in this case cauterisation with 2 per cent. silver nitrate solution induces so violent a reaction that it is succeeded by an enormous chemosis with pseudo-membranous formations, which can only aggravate the situation.

In such cases the fight is most arduous. We must employ to the best advantage all the resources of our therapeutic arsenal, not forgetting that our primary duty is to exercise the greatest care to do no harm. The nutrition and the general state should receive the utmost solicitude from practitioner and accoucheur.

From the first, the oculist should devote his attention to a most rigorous asepsis and antisepsis; lotion (the exact liquid matters little) must be used frequently; ice must be especially avoided, since all miserable, lymphatic, and scrofulous subjects bear cold very badly, a fact well known to the public if not to the practitioner.

It is necessary, in this case, to practise cauterisations with great prudence, inasmuch as the nutrition of the cornea is already defective **(keratomalacia)**; the least traumatism or too vigorous a cauterisation provokes or facilitates the production of a corneal ulceration, which may lead to the most disastrous consequences.

Under these circumstances I recommend that the treatment be conducted in the most delicate way. If the practitioner acts too energetically, he risks doing damage; if he is not energetic enough, the evil itself makes such progress that it is no longer easy for him to regain the upper hand.

By oft-repeated instillations of protargol, no harm can be done; they accustom the mucous membrane to cauterisations, which will then be well-borne. You have also got the attendants of the patient accustomed to the delicate care that must be given.

You are aware, nevertheless, that quite a school is opposed to cauterisation during the beginning of purulent ophthalmia, above all when the inflammatory phenomena are extremely violent. I do not personally share this view, for I recommend that it is often better to begin with instillations of 5 per cent. protargol, with *protargolage* twice a day, without everting the eyelids, rather than at once begin with cauterisations which may be badly supported.

It is most desirable to separate the eyelids every half-hour, in order to allow the pus to escape, aiding the latter with a pledget of wool steeped in solution of boric acid or permanganate. The use of

any instruments that may provoke traumatism, as retractors, syringes, irrigators, etc., must be carefully avoided.

The eye once cleansed, a drop or two of 5 per cent. protargol must be dropped between the eyelids.

In repeating these washings and instillations regularly every half-hour you surely hinder the evolution of the morbid process—perhaps you even arrest it,—but in all cases you must be certain that you have not injured your patient; and, since you have gained time, your little patient may be able to gather his forces together, and become accustomed to the touchings. More energetic cauterisations may then be applied on the second or the third day, even with silver nitrate if there be need.

To excite and encourage the baby to open his eyes of his own accord is an important thing, and when this result, so simple in appearance, is obtained, cure is very near, since suppurations of the eye love neither light nor air.* It is a bad practice that applies dressings in cases of conjunctivitis when there are no corneal changes. Once the eyelids have regained their softness, the cauterisations may be practised more energetically upon the everted conjunctiva; and if then protargol does not stay the suppuration quickly enough, call to your aid either silver nitrate, 2 per cent., or ichtargan, 3 per cent.

Tolerance, as you know, is a factor which we must count with in therapeutics; and if it is needful to know how to be patient and constant in the use of certain medicaments of long usage, it is also necessary to understand that often the cauterisations must be graduated and varied. In general, after a marked bettering during the first few days, there comes about a slackening of the therapeutic action; the infectious elements of the cells of the tissues become accustomed to the medicamentous action. It is then necessary to augment the doses, to change the application, or to modify the *terrain*.

Against tolerance to silver nitrate, Dr. Bettremieux has proposed the use of very dilute lotions of nitric acid. A concentrated solution of sodium chloride will produce the same effect, as will also an energetic washing with a pledget of wool steeped in a solution of mercury cyanide, 1 : 1000. But it is quite as easy to change the remedy as to vary its mode of application. When tolerance is produced towards protargol, one may then, without danger, have recourse to silver nitrate without going beyond the 2 per cent.

* At the present time interesting experiments are being made in Russia into the action of sunlight upon suppurating affections of the eye.

strength. For my own part, I prefer a product which has given me great satisfaction, namely, **ichtargan,** a combination of ichthyol and silver; less caustic and more penetrating than the nitrate, it takes a middle place between protargol and silver nitrate. I use a 3 per cent. solution of ichtargan when protargol has lost its effect.

But generally, when protargol is well applied, it brings about so rapid a cure that there is seldom any need to resort to alternative remedies.

It is not merely in the serious cases, of which we have just spoken, that protargol is able to render great service. It is not uncommon to see, in children who look well and strong, conjunctivitis beginning with alarming symptoms, which, in reality, are benign enough, developing upon a strumous soil. The microscopic examination is important under these circumstances, for if we do not find gonococci, violent cauterisations must not be used, since they are likely to complicate and aggravate the evil. It is preferable, for the first days at least, to use merely instillations of 5 per cent. protargol every hour or every half-hour, and to reserve stronger cauterisations for the moment when the inflammatory phenomena enter upon regression.

But, you may object, it cannot be easy, especially in the newly-born, to make at first a diagnosis of struma or of lymphatism. That is true. However, I believe that to-day it will no longer be so difficult, thanks to dionine, which possesses not only the valuable therapeutical properties of which we have spoken, but which also allows us to make a diagnosis of lymphatism, even in a subject whose antecedents are unknown.

Among these lymphatic subjects (I speak of children, for in aged people arterio-sclerosis and all affections accompanied by a slackening of the circulation may bring the same effect) dionine exercises upon the eye the singular lymphagogue effect that you already know; the conjunctiva and the eyelids become swollen and produce an abundant secretion of tears and serosity. Among healthy subjects, dionine merely produces a lively redness, some watering, and a little conjunctival œdema.

One recent case strongly interested me. Its facts are as under:—A baby, aged 6 days, of good appearance, was brought to me suffering from a fairly intense conjunctivitis. I cauterised the eyelids carefully with protargol. After some minutes the eyelids were swollen and the conjunctiva covered with a thick, whitish film, taking the aspect of a false membrane. We were in presence of one of those children in whom the least cauterisation provokes the formation of these false membranes, which impress upon an attack of conjunctivitis

a particular gravity, especially when strong solutions of silver nitrate have been employed for the cauterisation. In this case I had the curiosity to make the proof with dionine, which set up a still more marked swelling of the conjunctiva and the eyelids; there escaped from the eye an abundant yellowish liquid, mixed with filaments of fibrine, and before long the whole of the membranous deposit dissolved and detached itself from the conjunctiva. The therapeutic result was as interesting as the diagnostic information. For me, the indication was precise. I stopped all cauterisation, and prescribed only frequent instillations of 5 per cent. protargol. In a week the conjunctiva was cured; and I am convinced that cauterisations with silver nitrate would in this case have brought about regrettable complications.

Since this first observation I have had occasion to observe a number of cases of the kind, where dionine showed itself to be of remarkable use,—so remarkable, in fact, that I shall not exaggerate when I say that the lymphagogue action of this curious substance is destined to render great service in the treatment of the most different kinds of conjunctivitis.

The considerable afflux of tears and of lymph provoked by the local application of dionine gives rise to a washing, an energetic cleansing, not only of the surface of the mucous membrane, but also of the depths of the tissues; from this there follows an elimination of infectious elements and toxins, and at the same time a powerful afflux of nutritive elements stimulating a renewal of the tissues and liquids. Accordingly, every time I see a conjunctivitis resist for long the action of protargol and other local remedies, I do not hesitate to instil some drops of a 5 per cent. solution of dionine. In almost every instance I thus provoke a most favourable revulsion, after which the topical applications have a more marked and rapid action.

We have yet to praise this application of dionine in granulous conjunctivitis.

We have discussed the abnormal types of ophthalmo-blennorrhœa. If we consider the classical form, we can add little to that given above. We always recommend from the first: instillations of 5 per cent. protargol repeated every half-hour, while twice a day cauterisations are practised with the strong solution of protargol, and attention is paid to cleanliness and asepticism, as mentioned above.

At the end of ten or twelve days, if suppuration has not ceased, it is often well (if application of dionine has failed to yield results) to have recourse to silver nitrate or ichtargan. Lastly, if owing to

irregularities in the treatment, suppuration passes into the chronic stage, do not hesitate to resort to alternative remedies, such as alum, zinc sulphate, lead acetate, etc.

The most serious complication of purulent ophthalmia lies, not in the suppuration, intense and prolonged though that may be, but in ulceration of the cornea, so much the more to be dreaded as it may lead to complete loss of sight. It must not be forgotten that it is by reason of its corneal complications that this form of ophthalmia is responsible for the greatest number of blind persons.

How is ulceration of the cornea produced? Is it caused by the direct action of the gonococci or of its toxins, upon the corneal epithelium? That is possible, but usually the resistance of the tissues is first lowered by some determining cause.

The first of such causes we shall find in chemosis, the abnormal swelling of the conjunctiva and eyelids, inasmuch as the lymphatic and vascular stasis resulting from it is most injurious to the nutrition of the cornea, the epithelium of which may allow itself to become infiltrated and ulcerated.

Add to the above cause another very important one—namely, the mechanical or chemical erosions produced by hasty or maladroit interference, or violent cauterisations, involving the formation of eschars of the conjunctiva or cornea.

I have even met with a case where the two eyes were lost by the zeal of an inexperienced nurse, who, under the impression that she was doing the right thing, had carefully washed with a tampon of wool the corneæ of her little patient. A large erosion of the corneal epithelium resulted, and this promptly becoming infiltrated, the entire cornea ulcerated, and two large leucomata were produced.

You will see, therefore, that babies suffering from purulent ophthalmia need as much care from the attendants as from the medical practitioner himself. The responsibility lies heavy upon us, and it is our duty to watch carefully, in order to see how our directions are carried out.

The treatment of corneal complications is difficult, especially when they appear early in the course of the disease. Under such circumstances, the suppuration being intense, the destruction of the cornea is more rapid, while cauterisations with silver nitrate are not invariably well borne, and yet they are necessary in order to dry up the purulent secretion.

For my own part, I have found the following treatment to answer well under many circumstances. Besides using lotion frequently, I instil turn by turn every half-hour a few drops of a 5 per cent.

solution of protargol and one or two drops of a collyrium, of which the formula follows :

Dionine	0·10 gr.
Chloride of pilocarpine . . .	0·03 gr.
Sol. cyanide of mercury (1 : 1500) .	10 gr.

When the ulceration has assumed serious proportions as regards extension and depth, I find slight cauterisation of the whole of the affected area with the galvano-cautery very useful. At the same time, however, I continue the use of eserine or pilocarpine, and powder the ulcerated surface with xeroform.

Iodoform ointment, also, has rendered me real service in many of these cases.

A couple of words with regard to the **prophylaxis of purulent ophthalmia.** Credé's method made its proofs at a time when silver nitrate was considered as the specific for this malady. Since then protargol has shown its superiority equally from a prophylactic standpoint. It has over silver nitrate one advantage, namely, that it does not provoke, as the latter, a catarrhal secretion that may last for ten or fifteen days.

Speaking for myself, I cannot too highly recommend accoucheurs to make a careful *protargolage* of both eyes in their newly-born infants, without trying too much to make the solution penetrate into the interior of the conjunctival sac ; for it is oftenest that the gonococci are stationed upon the border of the eyelids and the roots of the eyelashes at the moment of birth ; they scarcely penetrate during the following days into the conjunctival sac. This *savonnage* with protargol of the eyelids, the cilia, and the eyebrows is admirably adapted for the prevention of purulent ophthalmia.

That which we have just said as to the subject of purulent ophthalmia and of the slight forms of conjunctivitis which resemble it, will save us from too long a discussion on blepharo-conjunctivitis.

We have seen all the profit that can be derived from what I have called *protargolage* or *savonnage* with protargol of the cilia and the border of the eyelids. Its action should be explained by a complete destruction of the infectious elements lodged between the cilia and the internal angle of the eye, an asepsis that possesses the greatest importance, because infectious matters, lodged about the eyelashes and continually bathed by the tears, are the cause of frequent relapses or re-inoculations.

Therefore, every time that the thing is possible, you should give the preference to *savonnage* with protargol, the patient limiting him-

self at home to the use of simple boric acid lotion, or to such a solution as the following:

℞ Acidi borici	10 gr.
Boracis	10 gr.
Boiled water	300 gr.

When patients are unable to attend at your *clinique*, besides the antiseptic lotions mentioned above, prescribe, two or three times a day, instillations of a 5 per cent. solution of protargol, with or without a preliminary application of cocaine, according to the sensibility of the patient. Patients should always be warned that the use of protargol for too long may provoke argyrosis, as do all salts of silver; that is the reason why you must never prescribe protargol as a collyrium in cases of chronic conjunctivitis.

In order to bring about a rapid cessation of the secretion, the first instillations ought always to be made close enough together; then they are little by little separated by longer intervals, and suppressed altogether when all agglutination of the eyelids has ceased.

When conjunctivitis, without presenting the alarming symptoms of purulent ophthalmia, is, however, sufficiently intense, there is no need to hesitate about combining repeated instillations of a 5 per cent. collyrium with *savonnage* with protargol, of which you can hardly make any abuse.

This *protargolage* even takes, as I have already said, great importance in the treatment of conjunctivitis associated with blepharitis and intense lacrymation—that is, when the latter is not caused by obstruction of the lacrymal passages.

There is one of the foregoing kinds of blepharo-conjunctivitis which I have recently seen often among alcoholic subjects. The lacrymation was so marked that I thought I ought to practise catheterism of the nasal canal. I obtained no result by these means. The local treatment by protargol, sulphate of zinc, and acetate of lead brought about a passing improvement only; the least excess of drink induced an abundant conjunctival oozing, escaping by the internal and external angle of the eyelids, of which the border was red and eroded by this continual and abundant secretion. I did not manage to cure these patients except by forbidding all alcoholic drink.

These forms of conjunctivitis are little known, and that is why I have said a few words about them in passing. They prove that if an infectious agent has a specific importance, it is also necessary to count with the individual soil and the modifications which come to it from the surrounding circumstances.

Blepharitis complicating conjunctivitis is generally cured with remarkable rapidity by several *savonnages* with protargol. It is necessary in these cases to rub for a long time the palpebral edge with care, much as if one wished to lather a chin before shaving it. In this way the cilia are impregnated to their roots with the solution of protargol, the infectious elements lodged there are rapidly destroyed, and the eyelashes shoot out again with remarkable vigour.

I have seen cases of blepharitis where all the lashes were fallen; treatment was complete from this point of view—after two months' treatment with protargol (one or two brushings a day), the lashes had grown more beautiful and longer than ever. Dr. A. Domec, of Dijon, was one of the first to publish a case of this kind.*

The protargol *savonnage* finished, and the lids having been washed with sublimate or with cyanide of mercury (1 : 1000) in order to avoid coloration of the parts by the silver solution, you must prescribe for your patient an ointment to use at night to the eyelids. Your formula must be varied according to the indications.

When blepharitis is little marked, a little boric vaseline will suffice. Among lymphatic children, especially if there is, or has been, strumous keratitis, the yellow ointment of Pagenstecher will produce a remarkable effect, and so will the ointment of red precipitate.

An ointment that has given me very good results is the following:

Ichthyol	0·50 gr.
Zinc oxide	2 gr.
Amidon	2 gr.
Vaseline	10 gr.

In certain cases, also, compresses of ichthyol bring about a prompt reduction in the irritative phenomena:

Ichthyol	10 gr.
Water	20 gr.

S.—*Steep a small pledget of wool in this solution, and apply at night to the border of the eyelids.*

If we now begin the study of chronic conjunctivitis, we come across first **angular conjunctivitis**, or **diplo-bacillary ophthalmia.** In this affection the first *savonnages* of protargol bring about a rapid amelioration, but when you employ the cauterisations less often, the conjunctivitis relapses, and protargol seems then to have almost no action. You will do well in these cases to replace the protargol as soon as possible by sulphate of zinc:

Sulphate of zinc	0·25 gr.
Distilled water	10 gr.

S.—*The collyrium to be instilled three or four times a day.*

* *La Clin. Oph.*, 1898, p. 162.

The instillations being rather painful, it is well to precede them by an application of cocaine or, better, of coca-renaline, of which I have already given you the formula (*see* page 73).

Zimmermann has even praised in these cases a collyrium of sulphate of zinc combined with a certain quantity of supra-renal capsule extract.

But as in all treatment applied in a chronic ailment, sulphate of zinc soon loses its effect; one must then resort to other agents. Acetate of lead, alum, and ichthyol are then our most useful reserve arms.

I commend to you the following formula, which has given me in many circumstances excellent results:

Extrait de saturne	30 gr.
Glycerine pure	30 gr.

S.—*For lotions and compresses place thirty drops of this liquid into a quarter of a glass of boiled water.*

Never forget that lead must not be employed when the cornea is ulcerated, since the cornea may then become infiltrated with salts of lead, leaving behind them very thick, mother-of-pearl-like leucomata.

It would take too long to go further into details upon the innumerable forms of chronic blepharo-conjunctivitis, which often come from a narrowing of the lacrymal passages, from errors of refraction, and especially from astigmatism, from a too sedentary life, especially in an atmosphere containing dust or irritating gases, etc., a constitutional state aggravated by bad diet, excesses of all sorts,—all things which you already know and the discussion of which would carry us beyond our intended limits.

LECTURE XII.

Summary.

Treatment of granulous conjunctivitis.—Its microbic origin obvious, although the organism is not yet determined.—Treatment by chemical caustics: protargol, silver nitrate, copper sulphate.—*Lavage-frictions* with sublimate or with mercury cyanide.—The importance of mechanical or surgical treatment recognised from times of antiquity.—Surgical treatment based upon the progress of modern surgery and the infectious nature of the granulations; scarifications, scraping, and brushing.—Care after operation.—Relapses are always to be feared if the smallest granulation is left behind.

There is no disease so diverse and multiple in its forms and development as **granulous conjunctivitis.** How, then, can we imagine that one and the same treatment will be applicable with success to all cases? Here, even more than elsewhere, it is necessary to individualise and to treat the patient, while at the same time one seeks, by all means indicated by the state of the subject, to destroy the infectious element locally as completely as possible.

But this last point is the dominating one, the pivot around which all the therapeutic efforts should revolve, for trachoma is a local microbic affection similar to lupus, superficial epithelioma, and cutaneous tuberculosis.

Clinically, its infectious nature is demonstrated as much by its contagiousness and epidemicity as by its development, course, and tendency to relapse.

Anatomically, all the histological descriptions made so far, on which it was thought we could establish the bases of a differential diagnosis between the true and the false granulation, have now no more value than histological tubercle and its giant-cells have for tuberculosis.

The pathogenic microbe will alone furnish us with the elements for a scientific diagnosis, but, unfortunately, neither its morphology nor its histology is as yet made out.

Conjunctival granulations should be distinguished from follicular

elevations, so frequent in schools and among young subjects. Follicular conjunctivitis appears to furnish a favourable soil for the development of a superadded granulous infection.

This is what makes the unitarists declare that follicular conjunctivitis is merely a first stage or an attenuated form of granulous infection. Although the pathogenic agent of trachoma has yet to be found, it is prudent to keep to the principle formulated for us by Professor Kuhnt, of Königsberg, which shows good judgment and clinical acumen:

"*From the therapeutic point of view, in doubtful cases, follicular conjunctivitis must be treated as if it were of trachomatous nature; but, from the prognostic and statistical point of view, it is necessary to make of it a special malady aside.*"

Infinite would be the number of forms of trachoma if one desired to describe as types all the different manifestations of the granulous infection. From the standpoint of treatment, however, it will suffice if we divide the principal cases into two main categories, *viz.*, (1) the acute inflammatory, and (2) the chronic form, or form subject to subacute attacks.

The first may be merely the prodromal stage of the second, while the latter may manifest inflammatory paroxysms, which bring it again into line with the acute form.

It is useless to describe an affection so well known. Its diagnosis is not difficult, except in regard to follicular conjunctivitis, and then only in the period when granulous conjunctivitis may be cured very quickly with caustics; and if that which one has taken for a follicular case resists well-applied treatment for several months, one may be almost certain that one has to deal with a trachomatous affection, which must be treated as such.

It would be as foolish to desire to treat surgically all cases of granulous conjunctivitis as it would be retrograde to wish to reject all armed intervention in the case of a chronic trachoma, which had resisted all the classical medical treatment.

When in 1890 I published my first communication upon the surgical treatment of granulations, I was careful to say that this mode of treatment was especially adapted to chronic forms of trachoma, which had already resisted many applications of the most varied forms of caustic.

We will leave on one side simple follicular conjunctivitis, which shows follicles only in the lower *cul-de-sac*. This form is readily cured by applications of collyria of acetate of lead (*see* formula on page 112), and by the observance of good hygiene.

On the contrary, when you see characteristic granulations in the upper *cul-de-sac*, you may almost certainly affirm that you are dealing with a specific, contagious, granulous conjunctivitis.

Should you have before you one of the forms associated with abundant secretion, you must first, before attempting any surgical intervention, try to stop all the discharge, so as to operate upon a carefully prepared field, thereby allowing you to obtain the *maximum* result with the *minimum* of operative traumatism.

In order to dry up the secretion, we have seen that the most reliance is to be placed upon **the salts of silver.** We have studied the advantages and the inconveniences respectively of these different salts. Protargol, owing to its penetrative power and the little pain it causes, is to be recommended above all others. You make every day, or every other day, insufflations as explained before (page 95). At the end of about ten days, if you find that the action of protargol becomes less efficacious, by tolerance, you may pass on to cauterisations with silver nitrate, which is more caustic, more mordant, and more capable of breaking through the fibrous envelope of the granulations. Another salt of silver is also to be recommended in trachoma—namely, ichtargan, a happy combination uniting the calmative and resolutive qualities of ichthyol with the astringent and antiseptic ones of silver (*see* page 106).

I cannot pass by **sulphate of copper** in silence, for it has rendered such immense services in the treatment of trachoma that it has been long considered as a specific against granulations.* It can be employed as a crayon, a crystal, or even as a solution in glycerine, 1 : 10.

The more and more **surgical treatment of trachoma,** of which we were one of the first to trace the path, has caused sulphate of copper to lose much of its ground. Sublimate and cyanide of mercury are the agents that tend to supplant it; and the treatment by rubbing the granulations with a piece of wool steeped in a solution of sublimate, 1 : 500 or 1 : 1000, which, to begin with, was only the complement of surgical intervention, is to-day recommended by many authors as the best treatment for trachoma.

We repeat the fact, however, that clinical indications show us that all cases are not amenable to the same treatment.

We have just spoken of cases of acute granulous conjunctivitis successfully treated by the salts of silver; by these cauterisations,

* The Translator has recently shown that the long-continued use of copper sulphate is liable to produce an opacity of the cornea of a very characteristic kind (see *Ophthalmological Society*, December 11th, 1902).

the purulent secretion often so far disappeared as to lead the patients to believe that they were cured, so that they did not return until several months later, when they were suffering from the chronic form and pannous attacks. It is then that your patients should be prepared for a radical cure of their affection; and while you thus prepare them morally, you should do all you can to place the operative field in the best conditions possible.

You will derive here great advantages from washings with cyanide of mercury, which are practised as follows:—(1) You instil during several minutes cocaine and adrenaline (*see* p. 73), to render the field of operation as insensitive and bloodless as possible, so as to see better where your efforts should be placed, without being blinded by the blood. You then energetically rub all the granulous surface with the tampon of wool dipped in the solution of cyanide of mercury, 1 : 500. When the sanguineous oozing becomes too abundant you cease rubbing, and let your patient wash his eyes for a long time in a solution of sodium chloride, physiological and aseptic, which facilitates the escape of the blood. These interventions are often very painful, but they should be repeated daily or every other day.

In the interval you will derive real benefit from the use of the following collyrium, which is to be instilled every hour or half-hour into the diseased eye:

Mercury cyanide	0·01 gr.
Cocaine hydrochloride . . .	0·10 gr.
Dionine	0·10 gr.
Distilled water	10 gr.

We have seen in one of the former Lectures what can be derived from the lymphagogue and analgesic action of dionine; combined with 1 : 1000 solution of cyanide its effect upon granulations and pannus is remarkable. The first drops of this collyrium provoke lively enough smarting, and at the same time redness and slight swelling of the conjunctiva are set up.

In favourable conditions this treatment ought to bring about the complete and definite cure of certain forms of trachoma. But do not forget this fact, that so long as you leave in any corner of the conjunctiva the smallest granulous deposit, you will have many chances to see, after a certain lapse of time, the evil born again, as it were, from its ashes.

In the presence of two or three isolated granulations, one should certainly hesitate to propose to the patient any surgical intervention; but our arsenal is rich enough to-day to give us a choice between

many ways of operating, from the submucous injection of cyanide of mercury to the galvano-cautery, electrolysis, scarifications followed by scraping or even by brushing, expression, etc.

The importance of the **mechanical** or **surgical treatment of trachoma** was recognised from antiquity. Hippocrates and his followers rubbed and even excised the granulations, and then cauterised them, sometimes with the red-hot iron and sometimes with different caustics.

Not until 1821 do we find in our era an acceptable conception with regard to the disease. J. B. Muller laid down the principle that relapses were to be feared and contagion was possible so long as there remained the least conjunctival granulation. Van Lil in 1849 also remarked that granulations hidden in the superior *cul-de-sac* were able not only to escape the action of medicaments but also the observation of the surgeon, and afforded the explanation of relapses of which up to then the cause was not known.

The fact once clearly established that the granulation constituted the truly specific element, it was quite natural to think of obtaining a rapid and radical cure by removing all the diseased tissue. Piltz, of Prague, in 1854, was the first to put this idea into practice. He incised the granulations with a cataract needle, in order to expel the contents. If he had to do with a diffuse, gelatinous infiltration, he practised scarifications in the infiltrated tissue, and expressed the contents by squeezing. The treatment was ended by a course of sulphate of copper. The results obtained by Piltz were astonishing, but he found few imitators, because at the epoch when his communication made its appearance the medical world was entirely dominated by the ideas of A. von Graefe, so that sulphate of copper held the field. In 1857 Borelli recommended a kind of brush; Anagnostakis and Fadda a metallic rasp. Quite recently Schroeder and others have again had recourse to brushing.

The galvano-cautery and the thermo-cautery also have found many partisans; electrolysis has been praised by Lindsay Johnson, and more lately still by H. Coppez; but the operative procedures most frequently resorted to are—the removal of a larger or smaller piece of diseased conjunctiva (Galezowski, Heisrath, Schneller, Eversbusch, Schwab, Stephenson), or expression (Knapp, Kuhnt), or scraping of the follicles. The conjunctival excision should be followed by medical treatment until there are no more granulations, in default of which relapses are frequent.

The aim of the rational treatment of trachoma should be the destruction, as promptly and completely as possible, of the granulous

infiltrations, while sparing, as much as may be, the sound tissues. Piltz had already done that very well, and so had the partisans of the galvano-cautery and of the expression of the contents of the granulations. Wolfe, of Glasgow, practised expression after having scarified the whole of the granulous surface. Bardenheuer was the first to use a sharp curette.

After having tried all these means, Sattler (to whom we owe the above historical study) adopted the following method as the most convenient and efficacious:—Scarifications of the envelope of the granulations by means of a cataract needle, followed by expulsion of their contents with a fine and cutting curette. The thing is easy as regards the tarsal conjunctiva; it is, on the contrary, very difficult to reach the bottom of the superior *cul-de-sac*, so that a special forceps is necessary to turn the lid out completely. In slight and recent cases, coming on in patients who are but little sensitive, local anæsthesia by cocaine is quite enough. Otherwise, chloroform is preferable, because one must conduct this operation very much at one's ease, so as to miss not a single granulation, no matter where hidden; "for I consider," says Sattler, "as one of the most important advantages of the proceeding, to destroy at a single sitting everything that should be destroyed, according to the indications given above." The eyelid is turned twice upon itself by aid of a forceps—*à double fixation*—in such a way as to show the bottom of the *cul-de-sac*, and allow one easily to scrape and curette all the granulations. After that a copious washing with sublimate, 1 : 1000, is necessary, to be followed by cold compresses.

After some days the raw surface is covered with epithelium; instead of granulations one sees small white cicatrices. And while the prominent granulations before operation allowed scarcely a trace to be seen of healthy conjunctiva, one sees after their destruction that the remainder of the conjunctiva is capable of reconstructing itself.

After the operation it is advisable to keep up for several weeks—at first, applications of sublimate; then, of sulphate of copper; and, lastly, of tannin.

By this treatment one generally obtains a cure in as many days as it would have taken months by other means.

I have never seen cicatricial deformities. Relapses are rare, especially if the patients are watched, and if one is careful, as soon as one finds that some granulations have escaped the curette, to destroy them without delay.

This method is equally applicable to the slightest and to the most

severe cases; the only contra-indication is the existence of great hyperæmia.

There is, accordingly, in the outline given by Sattler, a method of operation which has considerable advantages so far as we have gone.

The following is a description of the surgical proceeding that we have ourselves practised:

Before deciding upon the operation, one must carefully examine all the nooks and corners of the conjunctival surface for the purpose of acquainting one's self well with the distribution of the granulations, so as to know, as much as possible, where to direct one's surgical efforts, for, the operation once begun, the bleeding, often abundant enough, will conceal some of the growths. At all price it is necessary not to leave behind so redoubtable an enemy as the infectious agent of trachoma. During the chloroform anæsthesia, with which one may combine the action of cocaine, I cut with scissors the external angle of the eyelids whenever their complete eversion cannot be readily carried out. This removal of constriction is called for in about 30 per cent. of the cases; but it is rarely necessary to apply sutures to maintain the opening patent. That is needed only in cases where atresia of the palpebral fissure is very marked and accompanied by entropion. In cases where the caruncle is infiltrated, or where granulations are present on the bulbar conjunctiva or at the sclero-corneal limbus, or where there is pannus, one should apply the speculum used in cataract or in any other operation on the cornea. By separating it to the utmost, one brings into view the whole of the bulbar conjunctiva, and by seizing the eye with fixation forceps one can move it at will, in such a way that one can readily incise, scrape, or brush every spot where the smallest granulation is visible. If the caruncle is much infiltrated, it is more simple to excise it with a snip of the scissors; if there is a pronounced corneal pannus, we need not fear cautiously to scrape it with the curette from the centre towards the periphery, avoiding the sound tissue. A very light stroke of the brush, followed by a careful washing with sublimate, ends this delicate phase of the operation, which is called for only in about 15 per cent. of the cases. Then, if the above-mentioned act is not necessary, one proceeds to *brossage* of the eyelids. It is always well to begin with the lower lid, so as not to be inconvenienced by the bleeding which comes from the upper lid if the latter is attacked before the former. The eversion of the lower lid is very difficult with Sattler's forceps; with the instrument I employ, which acts by rolling up, one obtains, on the contrary, a perfect

reversal of the eyelid, at the same time as a support for the conjunctiva, which is usually flabby and folded. The forceps, in sum, are a pair of forcipressure forceps. In order to avoid tearing the tissues, it is necessary to seize the eyelid 2 mm. away from the marginal border; the forceps placed thus parallel to the palpebral border, one rotates the instrument around its axis in such a way as to expose the conjunctiva completely without tearing the latter. When the granulations are succulent, they rupture during this traction.

The scarifications are then made with caution, so as to divide every granulation. If the latter are rare and discrete, a simple bistoury or a discission-needle will suffice. On the contrary, if all the conjunctiva and the tarsal cartilage are infiltrated, one employs by preference a bistoury armed with three blades, which allows one to make the incisions parallel and quicker, a point that must not be despised in an operation already somewhat prolonged. The depth of the incisions should be proportionate to the depth of the granulous infiltration, the end aimed at being the exposure of the contents of the granulations, while husbanding, as much as possible, the conjunctiva. The scarifications make the gelatinous contents of the granulations run upon the raw conjunctival surface. Care must be taken not to leave them on the wound. The pledget of wool which stanches the blood does not remove very well this infectious material, whereby the brush would become uselessly infected. It is preferable to remove it carefully by means of the curette, or rather of the cutting spoon, which is larger, more convenient, and easier to empty and to wash.

The *curettage* is rapidly performed, and does not constitute the main point of the operation, as in Sattler's plan.

The most important point, after the complete reversal of the eyelid, is *brossage*, practised with a simple tooth-brush,—small, and provided with short and hard bristles. This brush should be carefully disinfected before the operation by prolonged immersion first in alcohol-formol, and then in a warm solution of sublimate or of cyanide of mercury, 1 : 100.

The *brossage* should be done with the brush steeped as often as possible in a 1 : 500 solution of cyanide. It must be performed vigorously to cleanse all the infiltrated tissue without dragging away and tearing the tongues of conjunctiva which have been left between the scarifications.

When one is convinced that all the affected parts have been scarified, scraped, and brushed, the forceps are removed. But before placing them on the upper lid, it must not be forgotten that the

forceps themselves, although so narrow, have covered and concealed some diseased points, which are easy enough to destroy, since they all lie near the border of the eyelid.

The chief focus of disease in trachoma is always in the superior *cul-de-sac*; that spot, therefore, ought to receive the maximum attention.

The complete reversal of the upper lid is much more difficult. A certain amount of practice is therefore needed in order to expose the conjunctival surface fully. That once accomplished, the operation is carried out in the same way as already described in the case of the lower lid.

It should be noted that, the eyelid being fully everted, the scarifications and *brossage* should be commenced at the parts most distant from the palpebral border; because the conjunctiva, once scarified, retracts, and some parts drawn back may thus remain hidden. The scarifications of the upper lid should, in general, be larger and deeper, inasmuch as the evil itself is seated more deeply, while the tarsal cartilage is often infiltrated in its whole thickness.

Once the eyelids are well scarified, scraped, and brushed, all the raw surface is carefully washed with a pledget of wool steeped in a 1 : 500 solution of cyanide of mercury.

As a dressing, simple compresses of wool moistened with cyanide of mercury, 1 : 2000, are applied, and kept in place by a bandage. The parents are recommended to remove the bandage at home, and to wash the eyes frequently with the 1 : 2000 solution, at the same time opening the lids, if possible, to allow the blood to escape. In the interval iced compresses are applied.

The following day, after the instillation of coca-renaline, an attempt is made to evert the eyelids. The lower lids are readily reversed, and freed from secretion with a piece of wool steeped in a 1 : 500 solution of cyanide of mercury. The upper eyelid, if it can be everted, should be washed gently, so as to avoid bleeding and destruction of any conjunctival tissue that may have been re-formed. If the lid cannot be everted, a sound must be passed very gently between the globe and the eyelid, to prevent adhesions between the parts.

The patient is advised to keep his eyes open as much as he is able, and to move them as well as he can in all directions, raising from time to time the eyelid with his fingers. The same lotions and compresses are to be continued.

The patient can easily enough half open his eyes; and on the

following days the same lotions must be used to the everted eyelids. Cure is complete at the end of several days.

The results obtained by the foregoing operation cannot be compared with those yielded by the classical treatments of trachoma. A week or fortnight after the operation the patient may look upon himself as cured, on condition that he remains under attention and maintains a perfect antisepsis. Lotions of sublimate or, rather, of cyanide of mercury ought nevertheless to be used for a month; they are then replaced by light touchings with glycerole of lead once a week. This treatment is carried out as a measure of precaution and in order to keep the patient under observation, rather than for any other motive.

Conclusions.—If we consider the main types of the great family of granulous conjunctivitis, we shall see that subacute trachoma is the one which benefits most rapidly from surgical intervention, from the form characterised by few and discrete granulations, which can be evacuated one by one at several sittings, up to the form associated with abundant granulous infiltration, succulent, with large granulations filled with gelatinous contents. All these forms receive especial benefit from surgical intervention, whereas the classical treatment by cauterisations is quite inadequate to bring about a definite cure.

The therapeutic indications are quite otherwise in the acute purulent form of trachoma, where the conjunctiva is red, turgid, tomentose, and papillary. In presence of cases of this kind the first indication is to dry up as quickly as possible the conjunctival secretion and to induce a prompt depletion of the blood-vessels. The application of leeches to the temple, and scarifications of the conjunctiva can bring about a rapid diminution of the venous congestion, which is so unfavourable to the nutrition of the cornea. Supra-renal extract, by its intense vaso-constrictor powers, is able to induce an extraordinary devascularisation of the cornea and conjunctiva, which become pale and cadaveric, and allow true granulations, up to then hidden by the vascular conjunctiva, to come into view. We have already spoken of this local vaso-constriction, while combining it with depletion by leeches.

There are cases of acute granulous conjunctivitis of exceptional gravity where one's hands may be forced by circumstances; for example, an extensive ulceration of the cornea or an intolerance of the subject to all kinds of treatment. Under such conditions it may be necessary to act surgically. I have seen cases of this kind operated on with great success by M. Abadie. Patients in a desperate state, having been submitted without benefit to all kinds of treatment,

found their martyrdom cease after the performance of the operation. It is doubtless that which has made our master claim that even cases of extremely acute conjunctivitis were amenable to surgical treatment.

This fact is incontestable; but, for my part, unless my hand is forced by circumstances, I prefer, before intervening surgically, to bring the very acute affection to a relatively calm state.

Then the after-treatment, so long and so painful in patients who have been operated on in the extremely acute period, is almost *nil*, with the wounds united, as it were, by first intention.*

Cuprol has recently been much praised as a substitute for sulphate of copper. It possesses one quality of the highest importance—namely, that it is really painless. For my own part, I have been much surprised to find that, after having cauterised the conjunctiva with a 20 per cent. solution of cuprol, patients experienced not the least inconvenience. The therapeutic action of cuprol, however, is incomparably feebler than that of copper sulphate, but, then, how much less painful!

Cuprol appears to me likely to be of service in certain forms of subacute or chronic conjunctivitis, in diplobacillary conjunctivitis, and also in the simple follicular conjunctivitis of school children. It should prove valuable as an alternative method of treatment in certain cases of conjunctivitis that have proved rebellious to the salts of silver, zinc, lead, etc.

With respect to **jequiritol**, it was with real enthusiasm that I welcomed its introduction, because I had long sought an energetic means of modifying the nutrition of the cornea.

The singular lymphagogue action of dionine had given me a glimpse of what might be expected in trachomatous pannus from an agent of the same kind, but having a profounder and more powerful action.

We all know jequirity, but its use demands an experience and dexterity which it may cost much to acquire. Speaking for myself, I have seen jequirity produce an ulcer, followed by a dense and widely-spread leucoma of the cornea.

Jequiritol has the advantage of being easily dosable, and, given the necessary patience, one is able to provoke exactly the reaction that is needed. This reaction, further, may be set up on several occasions until the desired therapeutic result is obtained.

* X-rays and the high-frequency current appear likely to effect a revolution in the treatment of trachoma (see *Lancet*, January 24th, 1903).—TRANS.

If the dose has been too strong, so that the ophthalmia induced by the remedy seems likely to cause corneal complications, one may, thanks to jequirity-serum, set bounds, almost at will, to the inflammatory process.

So far I have had the opportunity of observing only four cases of long-standing pannus or leucomata treated by jequiritol. Two of these yielded me satisfactory results; the other two stole away from my care on account of the pain produced by the treatment, a pain that, in point of fact, is very severe. The patient often experiences intense orbital and hemicranial pain; the eyelids, cheek, and temple are swollen; the preauricular gland is enlarged and tender; the nights are sleepless; and sometimes there is marked fever. The cornea becomes dull, glassy, and œdematous; the vessels of the limbus are markedly dilated. There is an intense chemosis, bulbar and palpebral, and often the formation of pseudo-membranous exudations at the level of the inferior *cul-de-sac*. All these symptoms improve rapidly if a few instillations of jequiritol-serum are then made, although there is no need to employ the latter means unless it is feared that the therapeutic end proposed to one's self has been exceeded.

Most of the authors who have used jequiritol have obtained brilliant results, which thus far I have not myself been able to emulate.

In brief, this product may advantageously replace jequirity, but, like the last-named, it has only rare and special indications.* It may perhaps be recommended in all cases where, the cornea being very opaque, no risks are run by trying to clear that membrane by a violent inflammation of artificial production.

Jequirity, like jequiritol, is of no use in acute trachoma; it is only in chronic trachoma, associated with thick pannus of the cornea, that the ophthalmia set up by the agent is likely to render service.

* Jequiritol, like jequirity, is likely to set up dacryocystitis, a thing that happened in three of twelve patients recently treated by its means.—TRANS.

LECTURE XIII.

Summary.

Diseases of the cornea.—Keratitis is generally of infectious origin, endogenous or ectogenous.—A traumatism or erosion of the cornea is usually the primary cause of an infectious ulcer.—Treatment of corneal infections: prophylaxis, antisepsis, asepsis.—Slight infections treated by collyria of cyanide of mercury and of dionine.—Subconjunctival injections of chloride of sodium or of cyanide of mercury.—Galvano-cautery.—Local applications, as methylene blue, iodoform, xeroform, etc.

We have up to now, so to say, been occupied with generalities, and have studied external diseases of the eye only. To-day we must consider the affections of the eyeball itself.

We shall begin with diseases of the cornea and sclerotic, and, after that, pass on to the deeper membranes and the intra-ocular media.

The important idea of infections, ectogenous and endogenous, dominates to-day the whole of ophthalmological pathology. It is therefore logical to study especially the simplest ocular infection, the ectogenous or traumatic infection, which will explain to us many pathological conditions until now very obscure in their pathogeny.

We have already studied the superficial, or conjunctival ocular infections. They have no direct influence upon the interior of the eyeball—that is to say, so long as there has been no perforation of the external membranes.

On the other hand, certain of them may entail a general infection, as diphtheritic conjunctivitis, upon which there is no need to insist; gonorrhœal infection of the eye, also, may bring in its train blennorrhœal arthritis, resembling that produced by a common gonorrhœa. That complication, however, is much rarer, as the result of ocular infection. Speaking for myself, I have encountered only two or three such cases in twenty years of practice.

In a *mémoire* published on this subject,* I remarked that this generalisation of gonococcal infection was most frequently due to scarifications of the conjunctiva practised conjointly with cauterisations with silver nitrate. Since I have ceased from performing scarifications, I have never observed an instance of gonorrhœal arthritis.

By the similitude of the evolution of the morbid phenomena with those produced by blennorrhagic arthritis, I concluded as to the gonorrhœal origin of these arthrites generalised in the newly-born. To obtain proof absolute, it is necessary to find gonococci in the articular effusion, researches from which we have recoiled as too experimental. Somewhat later, however, Professor Deutschmann, of Hamburg, made such researches, and he demonstrated microscopically the existence of gonococci in the liquid withdrawn by aspiration from the affected joints of one or two infants. We are therefore now in possession of the proof that a purulent conjunctivitis may entail as its sequel an infection of the whole organism. Are we not also aware that a wound of the conjunctiva may be the initial cause of a fatal attack of tetanus ?

Let us begin by studying the superficial traumatic infections of the cornea.

The simplest type is a **corneal erosion,** or any other superficial wound of the ocular tunics, which has allowed of the penetration of infectious germs. Under these conditions, we must consider all the clinical indications that may present themselves before us.

The first thing to ascertain is the nature of the infection itself, the biology and the virulence of the infectious agent, a desideratum most difficult to attain. Ought we to await, before intervening, the results of a bacteriological examination ? Assuredly not. To begin with, the state of our knowledge does not yet allow us to affirm, in a positive manner, the degree of virulence of a given micro-organism. As an example, take diphtheria. A pseudo-membranous conjunctivitis, clinically benign, may furnish very virulent cultures of the specific bacillus. On the contrary, another case, associated with bacilli of little virulence, may run a fulminating course, perhaps because antitoxin was injected too late, or perhaps because the infection was complicated with streptococci.

In point of fact, it is not only a question of germs, but also of soil, and of the chances of therapeutic intervention. We shall some day

* *Annales d'Oculistique*, 1888.

certainly arrive at a better knowledge of the infectious possibilities and of the way to combat or to attenuate them.

But to-day, even with the modest amount of actual knowledge in our possession, we can do much, if we so wish. We must never forget that the will (I cannot repeat the fact too often) has an enormous influence in treatment, and a pessimist never makes a practical medical man; he may be a good physiologist, but he will always be a bad therapist.

How many diseases of the cornea, of the most varied kind, originate from the superficial infection of a simple epithelial erosion, perhaps of traumatic origin, perhaps the result of a primary neurotrophic lesion!

How often, after an almost imperceptible wound by a foreign body, do we see produced all round a greyish aureole, which may now and then invade the greater part of the cornea, and bring about the complete loss of the latter by suppuration!

Then, we have to deal with the **serpiginous ulcer**, often met with amongst harvestmen, and frequently, also, amongst workmen. The initial traumatism is not always easy to make out; but by experience we know that that which is called an abscess of the cornea is, as a rule, merely a local infection, of which the infectious origin has escaped recognition. If one searches carefully, it is surprising to find how often a keratitis that was thought to be due to a state of general malnutrition comes from a local inoculation that has remained latent during a certain length of time.

You have perhaps heard of the "dry abscess" of the cornea (Fuchs, Arlt),—that is to say, infiltrations of the cornea, more or less central and more or less circumscribed, able to persist for months without terminating in suppuration, and ending in leucomata. Fuchs* now recognises that these are local traumatic infections, of slight virulence. I have for long shared this view, and experimental therapeutics have almost given me the proof by the remarkable action of subconjunctival injections, and, more recently still, of dionine.

As for arborescent keratitis (**keratitis dendritica**) and stellate keratitis (**keratitis stellata**), do they not, both by their form and development, show that they are of parasitic nature?

Have you not often seen a phlyctenular keratitis follow a very slight injury to the conjunctiva or cornea?

However, we shall study the treatment of these infections along

* *Klin. Monatsbl. f. Augenheilk.*, July, 1901.

with the other forms of keratitis. To-day we wish to glance generally at injuries of the eyeball—first, of the cornea; then, of the sclera; and, lastly, of the ciliary body and the deeper membranes.

In presence of an infected wound of the eye, the first and chief indication is to destroy as fully as possible the infectious agent *in situ*.

There is no better means of attaining this end than by a proper application of the galvano-cautery. The thermo-cautery—a gross and terrifying instrument, useful in large destructive processes, ocular abscesses, etc.—should be excluded from the instrumentarium applicable to the living eye, and especially to the cornea.

In some desperate cases of suppuration or of traumatic infection of the vitreous body, Van Millingen,* by means of deep galvano-cauterisations, succeeded in bringing about a prompt and complete cure.

That fact had been known for long; and before the introduction of subconjunctival injections, cauterisation with the galvano-cautery represented the only efficacious means at our disposal for stopping suppuration following the operation for cataract.

M. Abadie published numerous articles on this subject during the time I acted as his *chef de clinique*. Lately, several authors† have recommended this method as a novelty.

But in cases where there exists a central corneal infection, too deep or too extensive a cauterisation may be followed by a leucoma interfering much with the sight of the eye.

It is then that subconjunctival injections often suffice of themselves to stop the morbid process. They possess the advantage not only of having a powerful antiseptic action, but also of stimulating the nutritive activity of the corneal elements, thus often provoking a reconstitution of the tissues, without leaving behind cicatrix or leucoma.

This fact, which I was one of the first to bring to light, has been confirmed by many authors, particularly by Mellinger and Marty.

That is certainly a valuable point in favour of subconjunctival injections, for, proceeding from the idea of a simple antiseptic, we prove that these injections have, in addition to their antiseptic action, an eutrophic action of a marked kind, with which we shall occupy ourselves further when dealing with troubles of the vitreous humour, profound infiltrations of the cornea, hæmorrhages, retinal exudations, etc.

* *Central. f. Augenheilkunde*, June, 1899.

† Bäumler, Peters.

In our third Lecture we have already studied at some length the general indications for subconjunctival injections.

We now enter into the details of their therapeutic applications. But do not imagine that we shall occupy ourselves with this kind of medication exclusively. Far from that, we shall regard it as an exceptional measure, as an energetic intervention, as a last resource, when all the classical treatments have proved themselves to be inadequate.

In seeking to give detailed indications, we shall find occasion to pass in review the principal modes of treatment applicable to each affection, always taking up, I warn you, a somewhat partial point of view; but it is better, I believe, to give advice based upon a long experience than to offer learned considerations or criticisms upon the views of other people.

We have already seen that, speaking generally, the chief indications for subconjunctival injections may be formulated in the following way:—When one must combat an infection, acute or chronic, primary or secondary, arising from the outside by an erosion of the cornea or a serious traumatism, or from the interior by a reflected or metastatic infection (syphilis, rheumatism, tubercle, etc.), subconjunctival injections of cyanide of mercury furnish us with the most rapid and active means of stopping the morbid local process, often even after general treatment has failed or acted too slowly. Anyhow, this local treatment does not interfere with general treatment, but seconds the latter in every sense.

Infectious ulcers of the cornea may be classed among the number of infectious traumatisms, since their starting-point is almost invariably a more or less traumatic erosion of the corneal epithelium followed by an infection, of greater or less virulence.

Some suppurated phlyctenulæ, and certain abscesses of the cornea, when treated in the same way as infectious ulcers, benefit greatly by subconjunctival injections.

Faced, therefore, by a traumatic infection or an infectious ulcer of the cornea, the clinical observer, having already acquired a certain experience of subconjunctival injections, should weigh well the indications for and against this mode of treatment, and decide whether he should have recourse to strongly antiseptic injections, eutrophic injections of sodium chloride, or whether the action of one or the other must be combined with the actual cautery, which is always called for when the infectious process is very violent.

According to my personal experience, the following is the line to

adopt in cases of this kind. We will glance at three classes of cases:

1. Infection not yet obvious, but to be feared.

2. Infection already exists, but is not accompanied by very violent phenomena.

3. Infection is serious, and threatens to compromise sight or to lead to complete loss of the eye.

1. **A very benign case.**—A workman has got a foreign body, as a particle of metal, stone, or wood, into his eye, and this has produced a superficial wound of the cornea not yet manifestly infected.

After anæsthesia by cocaine and removal of the foreign body (if it be still there), one must make an exact estimate of the extent of the loss of substance and of the epithelial desquamation by the aid of fluoresceïn.* We next wash, as carefully as possible, the whole conjunctival sac in general and the corneal wound in particular, not forgetting to inspect closely the lacrymal passages and to irrigate them should we find the least trace of suppuration, or even of lacrymal stasis. For these washings I like the 1 : 2000 solution of cyanide of mercury, for the same reasons that make me prefer this salt to sublimate, more caustic and more painful. The antiseptic powers of the two salts are otherwise about equal.

When the eyelids and the cilia are agglutinated by suspicious secretions, *brossage* of the palpebral borders may be employed by means of a brush steeped in a solution of—

Protargol	5 gr.
Distilled water	10 gr.

(*See* Lecture X, p. 95.)

If there is no suppuration and no pain, after the insufflation of xeroform,† I apply a simple antiseptic and occlusive dressing to protect the corneal wound against all ulterior infection, and at the same time to procure more repose and security for the patient.

At other times, according to circumstances—for example, when there is for any reason whatever a contra-indication to the use of a bandage—I simply prescribe antiseptic lotions, or, better still, the collyrium of dionine and cyanide of mercury.

* **Fluorescein** is a colouring matter which possesses great diffusibility and intense penetration. It stains a clear green colour all parts of the bulbus which have lost their epithelial covering. The solution to employ is as follows:—Fluoresceïn, 0 gr. 20; bicarbonate of soda, 0 gr. 20; distilled water, 10 gr.

† **Xeroform** (much preferable to iodoform in these cases) is composed of tribromophenol and bismuth oxide, the base to which its drying and cicatrising action is owing. Further, xeroform has hardly any odour, and is not irritating.

By these means cure is generally brought about rapidly, and I have often prevented infections that might have assumed the gravest proportions.

2. **The more serious cases.**—The corneal wound is of greater extent, or already infiltrated; or perhaps it is the same patient whom we have dressed as above one or several days ago, who now returns with the eye painful and discharging; the signs of corneal infiltration show that infection is already present. The partisans of subconjunctival injections of saline water would, in such cases, still be able to obtain perfectly good results, a fact we have ourselves confirmed on many occasions. But in other cases, on the contrary, we have proved that after a temporary bettering, recourse has had to be made, in despair, to cyanide injections.

For my own part, I never hesitate in presence of an infiltrated corneal wound, or even one merely suspected to be infiltrated, to inject beneath the conjunctiva* a quarter, a half, or a full syringe, according to the gravity of the case, of the 1 : 5000 solution of cyanide of mercury dissolved in chloride of sodium solution, since I have convinced myself of the eutrophic action of the last-named salt. Here is the formula that I recommend in these cases:

Cyanide of mercury	0·01 gr.
Chloride of sodium	1·00 gr.
Distilled water	50·00 gr.

After insufflation of xeroform, I apply an occlusive bandage, and the patient, on presenting himself two days afterwards, is found to be almost cured. The artificial chemosis produced by the liquid injected is usually resorbed after the first day, but if that is not the case, the bandage is replaced until the next day. In this prodromal stage of infection, a second or third injection has rarely to be practised.

The pain set up by the injection varies with the sensitiveness of the subject. Some complain of very violent pain, and others merely of an uneasy sensation and smarting that can readily be tolerated. The intensity of the pain varies not only according to individual sensitiveness, but also, and above all, as to whether the puncture has or has not involved a sensory nerve. A patient who has borne, almost without suffering, one or several strong injections, may experience violent pain as the result of an even weaker injection. That fact should be fully recognised. It happens occasionally, also, that a very marked swelling of the eyelids is produced, which may be explained by the compression of a large lymphatic trunk;

* *See* Lecture III, p. 21.

ptosis (which is sometimes seen) may be attributed to a direct action on the terminations of the nerve which supplies the elevator of the upper eyelid.

Cocaine added to the solution for injection renders pain imperceptible for about half an hour; but it then makes its appearance, and is more marked than ever. But we are now able, as we have seen before, to render both subconjunctival and subcutaneous injections completely painless, thanks to acoine, which I was the first to introduce into the therapeutics of the human eye. "Human" is the word, since having perused a work by Trolldenier, of the Dresden Veterinary School, in which he concluded that acoine had on animals an anæsthetic action of much longer duration than that of cocaine, I asked the makers of the product to let me have a few grammes to try upon man. The reply was that the product was useless; that acoine, very active as regards the conjunctiva of dogs, and especially of rabbits, was absolutely devoid of effect on the human conjunctiva. I had searched too many years for the ideal agent that would permit us to make subconjunctival injections almost without pain, and so help to bring about a prompt generalisation of this valuable therapeutic method, and I could not but believe that acoine, properly applied, would be just as active in man as in animals. Upon my repeated solicitations, therefore, the firm von Heyden, of Radebeul, was good enough to forward a sample of acoine; and it was a great joy for me to see one of my dearest hopes fully realised—namely, that of rendering subconjunctival injections almost painless. But this is not the place to enter more fully into details concerning acoine, which has already formed the subject of one of the preceding Lectures.

Whenever, therefore, one has to deal with a slight traumatic infection or an early ulcer of the cornea, one may halt between a subconjunctival injection of chloride of sodium, on the one hand, and of a weak solution of cyanide of mercury, on the other.

When dealing with a wounded man, who has come from a distance, or who can present himself with difficulty at the consultation, one should not hesitate to give a liberal injection of cyanide of mercury, with an occlusive dressing that will keep its place for two or three days. If the cure is not then complete, the patient must return.

On the other hand, if one has to deal with an in-patient, or a patient who can attend regularly at hospital, the surgeon may choose between the different methods mentioned. Sometimes he may even get a good result with no other intervention beyond simple

It will be the same

for nervous subjects, who dread the least approach to an operation. Moreover, the frequent use of a collyrium of sublimate may, under certain circumstances, replace subconjunctival injections, seconding the effect or diminishing the number and frequency of the latter.

Recently, in a case of panophthalmitis, where enucleation has been definitely refused by the patient or his friends, and where intense chemosis absolutely contra-indicated subconjunctival injections, I obtained good results from instillations, day and night, as often as possible, of the following lotion:

Cyanide of mercury . . .	0·01 gr.
Hydrochloride of cocaine . .	0·10 gr.
Dionine	0·10 gr.
Sterilised water	10 gr.

The violent pains associated with panophthalmitis disappeared completely soon after the first application of the solution, and sleep returned to the patient. A rapid diminution took place in the purulent secretion, which came from the depths of the vitreous humour, and which was discharged through a large ulcer of the cornea; and the eye atrophied little by little without the patient complaining of the least suffering since the beginning of the treatment, while he was affected with atrocious pain before the use of the lotion.

Some authors would make of sublimate instillations an exclusive method of treating the infectious complications of wounds of the eyeball. There are certainly good points about this method of applying antiseptics; to begin with, the simplicity and even the harmlessness of the proceeding place it at everybody's disposal; but, like all therapeutic measures the application of which is left to the patient or to those around him, it may lose all its most valuable qualities by the least negligence on the part of him who is charged to apply it.

But, I repeat, there are cases, and I have met with many such, where simple instillations yield very good results. Unhappily, the state of our bacteriological knowledge does not yet allow us to appreciate exactly the virulence of this or that infection; clinical observation only is able to guide us in the use of one or other method of treatment.

The case just mentioned does not form an isolated fact; I have proved it many times; when, for one reason or another, treatment has been interrupted, it is often impossible to seize again a favourable moment for its application. To-day it is the galvano-cautery that will not work; to-morrow it is the patient who refuses an in-

jection; on another occasion it is a delay that has entailed the loss of a cornea.

In a word, one can say of subconjunctival injections in infected wounds that it is better to do too much and perceive it than to do too little and repent of it.

In fact, all the harm they can do is to cause considerable pain if repeated too often, and to bring about some unimportant adhesions between the conjunctiva and the episclera. Abstention from them may lead to loss of the cornea or of the eye. Here, as always, treatment should be prompted by clinical acumen and conscience, which should never be a sectary with preconceived ideas and routine fancies. There is no single treatment for each disease; the individual reactions of the patient are as multiple as the different modalities of the same infectious element, more or less virulent, more or less toxic.

In the treatment of infectious ulcers one must know how to select the best available weapon placed at our disposal by our therapeutic arsenal, already so poverty-stricken: lotions, collyria, and antiseptic powders as protargol, iodoform, xeroform, etc., the caustic disinfectants as tincture of iodine, phenic acid, etc., have their indications, as have the galvano-cautery, subconjunctival injections, and Saemisch's operation of transfixation.

LECTURE XIV.

Summary.

The treatment of the most serious forms of infectious ulcers with hypopyon.—Some practical examples.—The galvano-cautery and subconjunctival injections form the basis of treatment, and many other therapeutic agents, moreover, ought to be laid under contribution.—Infected wounds of the cornea: their gravity when they are complicated with traumatic cataract; antiseptic treatment, protection of the wound by conjunctival autoplasty; infectious complications; sympathetic ophthalmitis; causes of the particular gravity of wounds of the ciliary region.

3. We have just studied the relatively benign forms of ulceration of the cornea of various kinds. If we now look at the third category, that of the **severe corneal infections,** where not only is sight seriously menaced by destruction or opacity of the corneal tissue, but the eye itself may be lost in consequence of profound suppuration, we shall see that the clinical observer is no longer permitted to renounce, on principle, any of the therapeutic measures placed at his disposal by our arsenal, already too poor. I can only repeat what I have said many times with regard to this subject.

When we understand the nature of the infection and of the micro-organism that causes it, we shall discover a serum or an antitoxin capable of checking the morbid process, as is now the case in diphtheria and in pneumococcal infections.

All our efforts must tend towards finding the exact elements of differential diagnosis between the various forms of infectious keratitis, so as to give us a solid basis of judgment to guide us in the use of the different therapeutic remedies we employ.

In the meanwhile, to act in accordance with the logic of existing pathogenic notions, here follows the treatment of all grave infectious ulcerations of the cornea:

1. Asepsis of the orbital region, *savonnage* of the eyebrows, cilia, and skin, followed by washing of the conjunctival *culs-de-sac,* the lacrymal passages, and the cornea itself with a 1 : 2000 solution of cyanide of mercury.

2. Impregnation of the ulcerated surface with fluoresceïn, methyl blue, or methyl violet, in order to penetrate the deepest portions of the ulcer and thereby delimit with sufficient exactitude the whole extent of the infectious infiltration which has to be eliminated.

3. By curettage, or, rather, by the galvano-cautery, destroy as completely as possible all the morbid tissue, which should be annihilated as far as the limits of the sound tissues. In case of necessity, the sharp spoon (curette) may replace the galvano-cautery, but it presents the inconvenience of being able to inoculate infectious germs into sound tissue, when a slight scratch of the epithelium is accidentally produced. The galvano-cautery is not exposed to this danger; but the point must, I recognise, be very fine, not too incandescent, and managed with a delicacy—a therapeutic fingering—to be attained only after a long clinical experience.

4. If pus be present in the anterior chamber in sufficiently large amount, and if the tension of the eye be raised, the pus must be evacuated. This may be effected with the galvano-cautery if the whole depth of the cornea is ulcerated or infiltrated, or by a peripheral incision with a keratome, which is preferable in most cases.

5. Lastly, the infection almost invariably invades the regions which are beyond the attack of the therapeutic means just enumerated.

As proof of this statement I need merely point to the iritis and the synechiæ which nearly always complicate grave ulcerations of the cornea.

Well, it is in such cases that subconjunctival injections are indicated. It is there, in fact, that they yield marvellous results, as Secondi was the first to remark. His observations have since been confirmed by many other authors.

In short, as long as bacteriology does not give us a precise diagnostic between benign and malignant ulcers of the cornea, we should behave towards the latter as if they contained the most virulent kind of germ. It goes almost without saying that in this place we deal only with the most serious clinical varieties, and not with herpetic, lymphatic, arthritic keratitis, etc., which, although often persistent, are devoid of gravity.

Therefore, I say, asepticise the surroundings, and especially the lacrymal passages, the cilia, and the conjunctiva; destroy the morbid tissue with the galvano-cautery; asepticise the media of the eye by means of a subconjunctival injection; impregnate the ulcerated surface with methylene blue, iodoform, or, better, xeroform.

The cure, at the end of some days, will be making good progress. The surgeon will then judge if he should leave the case alone or

again interfere. He should also ascertain whether the general condition requires special indications—depletions of blood, antipyretics, analgesics, tonics, etc.,—those trivialities which there is no need to recapitulate to the practitioner.

We are not altogether decided as to the respective value of the different methods—subconjunctival injections, galvano-cauterisations, paracentesis, washings, etc.—in corneal ulcerations, only when in regard to each clinical observation we possess the exact results of a bacteriological investigation of that particular case.

If it is now and then a matter of urgency to burn deeply and at white heat a serpiginous ulcer of rapid progress (**ulcus serpens**), in order to preserve the yet transparent parts of the cornea, it is at other times indicated to practise lighter, punctiform cauterisations, in order not to entail very opaque leucomata.

Such was the following case, which I have recently seen. It presents us with a very interesting example of the partial regeneration of a cornea, which had been almost completely destroyed.

There came to me an old man, who had been ill for ten days, suffering from an ulcer that had destroyed the entire cornea and left no trace of transparent tissue. The ulcerated and flattened surface was overhung at the level of the limbus by a hyperæmic pad or cushion. The anterior chamber existed no longer; towards the centre of the ulcer there was a fungous excrescence, and a yellowish-white magma appeared to be an hypopyon escaped through a spontaneous perforation of the cornea. I did not hide from the patient the gravity of his condition. However, at all hazards, after cleansing as carefully as possible the eyelids, the lacrymal passages, etc., I touched the ulcer with the galvano-cautery brought to scarcely red heat, in close spots, and so as to respect as much as possible what remained of the corneal tissue. I next made a subconjunctival injection of a syringeful of a 1 : 5000 solution of mercury cyanide as far as possible from the cornea; lastly, I applied two leeches to the temple. The dressing was left in place for two days, after which I was immensely surprised to find that a zone of transparent tissue had formed all around the cornea; the ulcer had assumed a less yellow and more transparent colour. A new intervention, as above, was practised with the addition of an insufflation of protargol over the entire ulcerated surface. In short, after three or four applications, there formed, at the end of a month, a leucoma occupying the centre of the cornea, whilst above a transparent zone allowed me to make, a month later, an iridectomy, as the result of which the patient could count fingers.

Permit me briefly to relate another instructive case, which affords us a striking example of the importance of subconjunctival injections when dealing with a really serious infection.

A workman came to my *clinique* with an infectious ulcer of the cornea as large as the head of a pin; the foreign body, a fragment from a hammer, had not remained in the wound. Although the anterior chamber had not been penetrated, the wound, which was round, with well-defined edges, sunken like a white nail, extended almost as far as the membrane of Descemet. There was neither hypopyon nor chemosis; a little photophobia and pain were present. I touched all the white, infiltrated parts with the galvano-cautery; but I did not deem the condition serious enough to make a subconjunctival injection, so I simply prescribed half-hourly instillations of the collyrium of 1 : 1000 cyanide of mercury and dionine mentioned below. The next day there was a marked aggravation of the symptoms; the patient presented himself with a serpiginous ulcer, larger than a lentil seed, of a greyish-white colour, associated with hypopyon, chemosis, and severe pain. All the ulcerated surface was cauterised anew with the galvano-cautery, and a syringeful of 1 : 1500 of cyanide of mercury with acoine (*see* page 48) was injected deeply beneath the conjunctiva behind the eyeball. Two leeches were applied to the temple for the purpose of diminishing the chemosis set up by the injection. Two days later all was changed: the patient had experienced no further pain after the subconjunctival injection. The ulcer had changed completely in appearance; it no longer had the greyish-white, pseudo-membranous aspect, and its edges were cicatrising. There was no hypopyon. The eyelids were still a little swollen. The instillations of cyanide of mercury were continued. All went well for five days; but two fête days having prevented the patient from attending at the *clinique*, we saw him again with a greyish infiltration of ominous aspect, accompanied by violent pain and redness of the eye. The infective process was stopped by a new galvano-cauterisation and subconjunctival injection; but this time the iris was agglutinated to the posterior surface of the cornea. Briefly, the same treatment was renewed four or five times, and the patient was eventually cured, with a leucoma the size of a small lentil. Six weeks afterwards an optical iridectomy gave him good sight.

It is scarcely possible to find a more convincing example to demonstrate the superiority of subconjunctival injections of cyanide of mercury as compared with simple instillations.

Upon the other hand, subconjunctival injection is not always

sufficient of itself to stop a grave suppurative process. Thus, in a case of ulcer with hypopyon, already advanced, complicated with suppuration of the lacrymal passages, a subconjunctival injection of 1 : 5000 cyanide of mercury, made by a colleague, produced no result beyond a temporary disappearance of the sufferings of the patient. When I saw him, the ulcer occupied two-thirds of the cornea, hypopyon reached the border of the pupil, and a very marked pericorneal chemosis contra-indicated a second subconjunctival injection. To begin with, the lacrymal passages, which were full of pus, were carefully washed, and then the whole of the ulcerated surface, previously coloured green by fluoresceïn, was touched with the galvano-cautery at a low red heat. The corneal tissue, for a diameter of 6 mm., was destroyed as far as the membrane of Descemet, and, despite the delicacy with which the cauterisation had been performed, the aqueous humour leaked out little by little. Hæmorrhagic extravasations appeared on the iris, accompanied by ciliary pain of a sufficiently marked kind. Since the anterior chamber was effaced without the pus escaping, I did not dare to perform a paracentesis. I contented myself, for the moment, with touching the ulcerated surface with tincture of iodine and insufflating xeroform as above, prescribing for home use frequent instillations, day and night, of the following solution :

Cyanide of mercury	0·01 gr.
Dionine	0·10 gr.
Hydrochloride of cocaine . . .	0·10 gr.
Distilled water	10 gr.

On the following day there was a notable improvement: the ulcer had not progressed; it had lost its greyish-white aspect and thickened and infiltrated borders; it was covered with a faint pellicle of a greyish-brown colour (the remains of iodine and xeroform), which could be readily detached, exposing the tissue of the cornea, which, although ulcerated, was almost transparent. Towards the centre a slightly raised yellowish spot showed that hypopyon, pointing at this place, simply demanded exit. I seized it with iris forceps, and extracted a good deal of the pus. Renewed application of the galvano-cautery to the edge of the ulcer, followed by touching with tincture of iodine and xeroform. On the third day there was still amelioration; the patient experienced no pain, and slept well (? dionine). A large morsel of pus was removed with forceps from the anterior chamber. The same dressings and the same frequent instillations with cyanide of mercury (1 : 1000) and dionine were continued. The bulbar chemosis had almost disappeared.

Two or three days later, all chemosis having gone and infection appearing to have been stopped, subconjunctival injections of sodium chloride brought about a kind of regeneration of the borders of the corneal ulceration, and the consecutive leucoma was much smaller than had been the surface originally ulcerated.

The first injection of mercury cyanide had certainly exercised a favourable but insufficient influence, and if electric cauterisations and antiseptic applications of various kinds had not been used, it is much to be feared that the sight of the eye would have been seriously compromised.

We have not, as you see, even with all our most varied weapons, one too many to cure certain grave forms of infectious ulcer of the cornea.

It is not by the galvano-cautery alone, or by subconjunctival injections, or by paracentesis of the anterior chamber, or by cauterisations with this or that more or less specific agent, that you are able to cure the varied forms of corneal infections. This series of cases may react favourably to this or that therapeutic method, while another series may resist it. So long as we do not know the nature of the pathogenic microbe and the degree of virulence of each infection, we must leave ourselves to be guided by sound clinical observation, summoning to our aid all the various means culled from the experience of other observers. And, despite these efforts, still we shall not be absolutely certain to cure all the cases that come to us; for there are pathological conditions so grave that unhappily they still resist all our therapeutic measures. In fact, there are forms of corneal ulcer which, in spite of all interference, destroy fatally in a few days the whole cornea, unless a desperate and intelligent treatment is opposed to them from the very outset.

Other extremely grave forms of infectious ulceration of the cornea are furnished by the corneal complications consecutive to purulent ophthalmia, to diphtheritic conjunctivitis, and even to some deep scrofulous keratites in much debilitated subjects. These complications exact special indications; but the treatment first recommended for ulcers in general applies equally to the last-named.

Another grave form of corneal ulceration is **ulcus rodens.** This slowly and progressively invades the whole anterior surface of the cornea, from the periphery to the centre of that structure. Perforation or hypopyon is rare. The superficial ulceration, however, leads to a more or less complete opacification of the cornea. The means described above should always be applied in these cases, but they are inadequate unless Saemisch's section of the whole of the

ulcerated surface is added to them. Quinine, locally and internally, is also recommended.

That which we have just said with regard to infective ulcers of the cornea applies also to infected wounds from traumatism, accidental or operative, but the situation may be more seriously complicated by various circumstances.

Thus, the suppurations consecutive to the operation for cataract borrow from the presence of crystalline masses in the aqueous humour quite a special gravity; it is the same, moreover, in the infections that may be produced by injury of the crystalline lens. The gravity becomes still greater if the posterior capsule of the lens has been torn, inasmuch as that permits a rapid spread of the suppuration to the vitreous body and the deep membranes of the eye.

We have made a detailed study of injuries to the eye in a general review published in the *Gazette des Hôpitaux*.* This we may briefly epitomise.

We then said, "The gravity of a wound of the eyeball, whatever be its position, is quite subordinate to the degree of asepsis in which the wound remains until its complete cicatrisation."

It is consequently of the greatest importance to render aseptic, as speedily as may be, the wound and its surroundings. This is followed by cauterisation with the galvano-cautery of all parts that are infiltrated, greyish, or yellowish; when necessary, one need not fear to plunge the point of the cautery into the depths of the cataractous crystalline lens or into the vitreous body itself, if the latter is already menaced by profound suppuration.

If the cauterisation has been performed carefully, the state as to asepsis of the wound and of the infectious focus is thereby almost complete; but, in order to render the work of disinfection more efficacious, one need not hesitate to practise forthwith a subconjunctival injection of cyanide of mercury, so much the stronger and more copious the more advanced the infectious process. A full syringe or a half-syringe, according to the case, of a 1:1500 solution should be injected deeply behind the eyeball, so as to avoid too marked a chemosis.

This asepticism well carried out, we next recommend, in all cases where the thing is possible, that the wound shall be covered with a conjunctival flap, for the purpose of protecting it against any new infection. This shielding of the wound had already been recommended by Abadie and E. Meyer, but later it was warmly praised

* *Gaz. des Hôpitaux*, 10 octobre, 1891.

by Kuhnt,* who made of conjunctival protection a method of treating all losses of substance of the cornea, ulcers, traumatisms, etc.

For wounds made in the performance of cataract extraction the exact covering with conjunctiva is difficult, so I ask permission, in passing, to describe the method which has given me the best results.

It is to be recommended under many circumstances:—(1) to cover and protect a wound that has just been disinfected; (2) in cataract extraction, when the wound remains half open, it may then advantageously replace the corneal suture, its performance being easier and less dangerous; (3) in secondary herniæ of the iris following "simple" extraction of cataract. In these cases the removal of a piece of the herniated iris, which is most frequently done some days after the cataract extraction, leaves a semi-open wound in a quite peculiar state of infectious receptivity (traumatic irritation and iris or capsular traction). For a long time I have not performed these secondary excisions without also protecting the wound by the above proceeding.

One need not hesitate to cover a good third or even the upper half of the cornea, since retraction soon coming into play, there remains no more than a very small conjunctival encroachment upon the corneal limbus.

This autoplasty prevents the formation of cystoid and pervious cicatrices, of which the ulterior infection is always so formidable an event.

The operation, which I perform in the following way, must be done with much care, if the best results are to be obtained:

An injection of cocaine (1 per cent.) and acoine (1 per cent.) is made beneath the conjunctiva above the level of the wound which it is intended to cover. The injection should be abundant enough to detach the mucous membrane of the episcleral tissue, and to prepare, as it were, the graft in its entire extent. The dissection is then made very easily with strabismus scissors. One need not fear to detach the conjunctiva as far as possible towards the bottom of the *culs-de-sac*, from the internal to the external rectus, passing above the insertion of the superior rectus muscle. Before bringing down the conjunctival flap from above the wound, it is necessary to vivify the latter with minute care, either with a cutting instrument (knife, scissors, curette, etc.), or with touchings with silver nitrate, tincture of iodine, or the galvano-cautery. The former plan is

* Kuhnt, *De l'utilisation de la conjonctive dans la pratique et de la chirurgie* ... of Wiesbaden, 1898

always preferable. That done, it only remains to lower from above the conjunctival flap, assuring one's self that it can without traction cover one-third or, better, one-half of the cornea. The flap is kept firmly in position by a silk suture drawn from each side of the horizontal diameter of the cornea.

At the end of four or five days the sutures are removed—that is to say, if they have not come away of themselves in the meantime. The conjunctiva remains adherent only at the freshened parts, and owing to the contraction that occurs, there is no need to fear too large a cicatricial swelling.

In my hands, this is the proceeding that has succeeded best in all ocular traumatisms trenching upon the periphery of the cornea; it is infinitely superior to the *suture en bourse* and to coverings with fillets or detached flaps of conjunctiva.

With a wound thus protected, however, it is not right to think that all is finished, and that nothing remains except to fold one's hands. Far from that, the case must be watched constantly until cure is complete.

A somewhat violent reaction comes on the same day or the day after the operation. The dressing must then be removed, two, three, or four leeches be applied to the temple, and the following collyrium be used frequently to the eye:

Cyanide of mercury	0·01 gr.
Hydrochloride of cocaine . . .	0·10 gr.
Dionine	0·10 gr.
Distilled water	10 gr.

S.—*Two or three drops of the collyrium to be instilled into the affected eye every half-hour.* (According to the indications furnished by the state of the pupil, one may add 0·05 gr. of atropine or of eserine.)

The inflammatory reaction passed, one must ascertain whether it is necessary to practise more subconjunctival injections. In cases of doubt, however, abstention will be unwise; many cases have turned out badly because of waiting too long; it is better to give one or two injections too many than not enough. Here, as always, clinical acumen is our only tutor. Cure is often attained only by a desperate strife continued from day to day.

We do not pretend that absolutely favourable results can always be obtained. We recognise how easy it is to make an error or commit a fault in the difficult battle between therapeutic measures and infectious elements; it is thought that the progress of the mischief has been stopped, and some days afterwards infection is

born again, so to say, from its ashes. It is therefore necessary never to disarm, and to keep the patient under observation for a lengthened period, so as to interfere each time the clinical indications are precise. That is what we ourselves have had to do in most of the cases we have observed. With some two or three exceptions, it has been necessary to renew on several occasions the cauterisations and the subconjunctival injections, and sometimes even to adopt intra-ocular injections.

The more surgery advances, the more conservative it becomes, a rule to which eye work is no exception.

As to the indications for removing the eye, for us they are already too frequent and sufficiently exact. Enucleation should be performed whenever the wound is too serious to allow us to hope to preserve the eye—it may be for sight, or it may be only for form,—and also every time that the globe contains a foreign body that we are unable to extract.

Wounds of the ciliary region have always been regarded as injuries of the greatest possible gravity.

Has not experience, in fact, shown that a penetrating wound of this part of the eye (apart from immediate complications) often entails as a sequel acute suppurative irido-choroiditis terminating perhaps in an abscess of the eye, perhaps by a progressive atrophy of the globe, and very frequently being complicated by a secondary irido-choroiditis of the other eye (sympathetic ophthalmitis)? Complete blindness, therefore, is often the consequence of a simple wound of the ciliary region.

Until the recent discoveries of microbiology, the primary cause of this gravity of a relatively slight traumatism was obscure. Up to then what could be more natural than to seek the explanation of the serious nature of wounds of the ciliary body in the anatomical or physiological importance of the injured parts? But it has long been established that the iris and the ciliary processes play a capital *rôle* in the nutrition of the eye. From this fact it naturally follows that a profound alteration of this part of the eye may have grave consequences in the future.

Where one formerly saw a purely mechanical action, we now see an infectious, parasitic process, destroying the ocular tissues progressively and more and more deeply, and even spreading, by the optic nerve, to the opposite eye.

Do we not already know that simple wounds of the cornea are also able to bring about a panophthalmitis, a progressive phthisis of the eyeball, and even sympathetic ophthalmitis? The same is true

of wounds limited to the sclera, even although neither the iris nor the ciliary body has been involved. We can therefore say as regards wounds of the ciliary body, as well as the preceding, *the gravity of a penetrating wound of the eyeball, whatever its situation, is altogether subordinate to the degree of asepsis in which the wound is kept until its complete cicatrisation.*

All that can now be conceded to the anatomical theory is that, according to the region involved, the wound may offer a greater or less receptivity to the infective germs. A wound of the ocular tunics, regarded by itself, offers almost the same resistance to infectious micro-organisms, whether it involves the ciliary region or some other part. But the eyeball once penetrated, the microbic elements find a culture medium and ways of propagation absolutely different according to the region involved. From the cornea, in order to spread to the posterior segment of the eyeball, the infection must traverse the anterior chamber, invade first the iris, and then the ciliary processes. On the contrary, an infected wound of the ciliary region allows of the immediate propagation of the inflammatory process, at one and the same time, to the anterior chamber and to the whole of the uveal tract.

One peculiarity of wounds of the ciliary region also is the difficulty experienced, in some cases, of knowing whether infection has or has not taken place ; inasmuch as infection may make its way backwards in a slow and insidious way, and little by little invade the entire ciliary circle without producing marked reactionary phenomena until one perceives that the eye is on the point of atrophying, or a sympathetic ophthalmitis suddenly breaks out.

As regards wounds of the cornea, on the contrary, most goes on openly, so that an opportune intervention may avert threatened danger. That is all the difference that anatomically we are compelled to admit, both by experience and by reason. The general laws of infectivity remain unshaken.

LECTURE XV.

Summary.

Diseases of the cornea (*continued*).—Superficial and deep keratitis.—Phlyctenular or pustular keratitis.—General treatment: quinine, tannin, iron, iodine, arsenic.—Local treatment: yellow ointment always, atropine sometimes.—Fascicular keratitis.—Marginal ulcer, arthritic ulcer; general treatment: salicylate, quinine, lithium.—Local treatment: dionine and occlusive dressing.—Arborescent keratitis.—Herpes corneæ febrilis.—Zona.—Bullous keratitis.—Macular keratitis.—Circumscribed parenchymatous keratitis from contusion.—Keratitis *en grillage*.—Keratitis striata.—Syphilitic parenchymatous keratitis.—Hutchinson's teeth.

By dividing **keratitis** clinically into the two great classes, superficial and deep, we shall the more readily establish the principal therapeutic indications of the diseases of the cornea.

For superficial keratitis, bordering on almost every ulceration of the cornea, more or less extended, more or less profound, we shall have to keep count of all the relative indications for the aseptic cleansing of the morbid focus, which, necessarily in contact with the air and the ocular secretions, never fails to be infected, however aseptic may be the tears. Almost always, also, there is a concomitant conjunctivitis and sometimes a blepharitis.

In all these cases, therefore, as perfect a sterilisation as possible should be got of the conjunctival *culs-de-sac* and the edges of the eyelids by frequent washings and especially by *savonnage* of the eyelids with protargol, which gives, as we have already seen, excellent results (*see* p. 95).

We have spoken on several occasions (*see* pp. 32, 73, 77) of **lymphatic, phlyctenular, or pustular keratitis.** This affection, in which the general state plays the principal part, as a rule is rapidly cured by yellow ointment (*see* p. 32) and by general treatment, of which we shall speak immediately. But there are grave cases with profound infiltration and corneal abscess where there is no better remedy than subconjunctival injections of sublimate. Secondi and many others after him have demonstrated the bene-

ficent action of this local intervention, which has not only the advantage of stopping the pathological process, but also provokes a rapid absorption of the pathological infiltrations and augments the transparency of the corneal tissue involved. Mellinger has observed the same facts after the injection of saline water, in which we recognise a stimulating action upon the circulation of the nutritive lymph of the eye, giving to that humour greater fluidity and a more pronounced solvent and resorbent power.

We have already had occasion to occupy ourselves with this so-called lymphagogue action in studying the new and extremely curious remedy dionine (*see* Lecture VI).

Leber, by a series of very interesting anatomical and experimental researches, has quite recently shown that phlyctenulæ of the cornea or conjunctiva may be caused by an endogenous infection, of which the primary peripheral localisation may be found in the internal coat of the small vessels. The numerous giant-cells and the obviously tuberculoid aspect of a phlyctenule would make us think of a tuberculous infection, without, however, our being able to find either bacilli or caseous degeneration. Scrofula and tuberculosis are members of the same family. It is therefore natural, as practice has long taught us, to insist particularly upon general treatment whenever we have to do with children affected with pustular keratitis.

A 1 per cent. solution of dionine, by its lymphagogue and analgesic properties, often exercises a salutary action in phlyctenular keratitis. By its use photophobia is notably diminished, while sleep becomes deeper and quieter. Almost always the prescription is as under:

Dionine	0·10 gr.
Cocaine hydrochloride . . .	0·10 gr.
Solution of mercury cyanide, 1 : 2000 .	10 gr.

S.—*One drop into the affected eye every hour.* In cases where atropine is indicated, one introduces into the above formula 2 or 3 centigrammes of that mydriatic; and when perforation of the cornea has occurred, eserine is added to the liquid. In very vascular forms of keratitis it is good practice to finish the treatment by adrenaline:

Cocaine hydrochloride	0·10 gr.
Adrenaline, 1 : 1000	2 gr.
Solution of cyanide of mercury, 1 : 1500 .	8 gr.

S.—*One drop to be used every two hours.**

* However, the yellow oxide of mercury must always be the mainstay of treatment.

A good hygiene and diet, iron, quinine, and arsenic, are the first things to be recommended; cod-liver oil and the iodotannic preparations* also give good results. In some rebellious forms, benefit may be got from almost homœopathic doses of sublimate, as in the following formula:

Iodide of potassium . . .	5 gr.
Bichloride of mercury . . .	0·05 gr.
Cognac and syr. aur. . . .	30 gr.
Water	120 gr.

S.—*One to four teaspoonfuls a day, according to the age of the patient.*

In passing, we have enunciated the theory that lymphatism may be due to an insufficiency of the tone of the capillary vessels (blood and lymphatic), perhaps caused by an inadequacy of the function of the supra-renal capsules. Opotherapy by these glands may one day come to possess a certain importance in the treatment of scrofula and rickets. We have enumerated the advantages of adrenaline in vascular keratitis, pannus, spring catarrh, etc. (*see* p. 77). In all cases we shall in the meantime be able to use powerful vaso-constrictors, as quinine, ergotine, and tannin, which form the basis of almost all the popular preparations of rhatany, radishes, and walnuts.

Fascicular keratitis is in reality only a form of strumous or lymphatic keratitis, and calls for similar treatment. In these cases, as in those that are accompanied by a central ulcer of the cornea, atropine is indicated. On the other hand, the use of atropine is to be rejected completely in all phlyctenulæ of the periphery of the cornea and of the limbus, since they may be readily cured without its aid (*see* page 7).

The **marginal ulcer**—called also the "**arthritic ulcer,**" because it is usually seen in aged people who suffer more or less from rheumatism—is often accompanied by violent irritation, but it generally heals without the production of a leucoma. It is, however, liable to relapse.

Irritating collyria or violent caustics must not be employed in dealing with these ulcers. The general condition should be the object of particular care. In dealing with a rheumatic or a gouty subject, one prescribes the preparations of salicine, and especially

* In France the iodotannic preparations enjoy a great reputation as tonic remedies, although in England they are scarcely known. One of the best is Naline's *Elixir iodotannique*, which contains iodine, tannin, phosphate of lime, and arsenic, mixed with syrup of orange and Malaga wine.—TRANS.

aspirine, of which the antineuralgic action is most valuable when administered in moderate doses of two or three grammes a day. The benzoate of soda or the salts of lithia are useful in gouty persons, but if their action is not enough, colchicine,* one to three milligrammes daily, will be found very useful. In those suffering from arterio-sclerosis, iodide of soda, 0·50 cent. daily, combined with a milk diet, gives good results. As local applications, Abadie recommends simple alkaline lotions of Vichy water or a 4 per cent. solution of bicarbonate of soda. Asepsis of the palpebral borders may readily be secured by *protargolage* of the eyelashes. If pain be violent, the following collyrium should be prescribed :

Dionine	0·10 gr.
Hydrochl. cocaine	0·10 gr.
Bicarb. soda	0·20 gr.
Distilled water	10 gr.

S.—*One drop in the affected eye five or six times a day.*

I have seen marginal ulcers of the cornea, which had resisted treatment and were accompanied by violent pain, cured in a few days by these simple instillations. The latter always bring about a definitive cessation of pain from the first moment they are applied.

All cases, however, do not resemble one another, nor are they influenced in the same way by our therapeutic agents. We must, accordingly, possess many reserves. When pain does not yield to the use of dionine, salicylate of soda, aspirine, alone or combined with quinine, we may employ, following the recommendation of Abadie, tincture of rhus toxicodendron (Tinctura Rhois), in five-drop doses three or four times a day in a little sweetened water. The occlusive dressing now and then yields signal service in these cases.

As to infectious ulcers of the cornea, we have discussed them at the same time as traumatic ulcerations of the cornea. We only wish to say a few words, in passing, on a particular form of disease, the **superficial arborescent keratitis**, which, although not very grave, is often rebellious to all treatment, especially when occurring in aged or decrepit persons. All the general medications have proved useless in these cases, while the number of the local applications recommended proves that no single one of them possesses any specific action.

This is what I myself do under the circumstances. After having marked out with fluoresceïn the extent and topography of the lesion, I proceed to render the cornea, conjunctiva, and lacrymal passages

* Darier, *Bulletin de la Société d'Ophtalmologie de Paris*, 1889.

as aseptic as possible. Next, having lightly grazed the affected parts of the cornea with the galvano-cautery brought to a feeble red heat, I practise a subconjunctival injection of 1 : 5000 cyanide of mercury, half a syringe, with acoine (*see* page 48). Xeroform is then applied, and the eye covered for two or three days with an occlusive dressing. If, after that, fluoresceïn be still found to stain a notable portion of the old ulceration, I repeat the intervention described above—even, if necessary, two or three times to obtain complete cure.

We cannot enlarge upon **vesicular keratitis**, the primary cause of which is generally connected with neurotrophic action.

Herpes corneæ febrilis, well studied by Horner, is generally a syndrome of the febrile affections accompanied by herpes of the lips or skin. The therapeutics of this disease are limited to cleanliness, to asepsis of course, and to a general treatment indicated by the disease. Cure is thus obtained rapidly, with or without the application of yellow ointment.

Much more serious are the vesicles of corneal herpes in **herpes zoster.** One has to deal in these cases with a disease of the trifacial, as everybody knows, arising, according to Abadie, from a lesion of the sympathetic, of which the trophic branches accompany the great nervous trunks. In these cases the cornea is usually insensitive, although that does not sometimes prevent the patient from suffering cruelly. One endeavours to calm the pain by the local application of a 1 per cent. collyrium of dionine in a 1 : 1000 solution of cyanide of mercury, so as to keep the ulcerated cornea as aseptic as possible. Ointments of iodoform or xeroform are useful, and the cornea must be protected against external irritants by an occlusive bandage. Quinine and electricity (constant current) form the basis of the general treatment.

Vesicular or **bullous keratitis** manifests itself on corneæ which have already undergone trophic changes. In absolute glaucoma, for example, one sometimes sees the epithelium of the cornea raised over a considerable area by transparent fluid; but such cases present only a secondary therapeutic interest, the eye being already lost. Nevertheless, enucleation being supremely a last resource, it is well to know how to cure or prevent corneal vesicles.

There are also cases where small, transparent vesicles appear on healthy corneæ, without known cause.

These vesicular keratites are almost always liable to frequent relapses, leaving, after the shedding of the pellicle which covers the bullæ, an ulcer, which is doubtless the form commonly called "relapsing ulcer."

The nervous element is in these cases one of the principal causes of the affection. The reflex may be provoked by a peripheral irritation or by errors of refraction and, in particular, by astigmatism. The general treatment must be guided by the causal indications. Locally, we employ ocular analgesics and a protective bandage.

Macular keratitis or **keratitis punctata superficialis** is characterised by the presence of numerous little grey spots lying in the anterior layers of the corneal tissue, a kind of eruption of foci of parenchymatous infiltrate, clearly of an infective origin. The treatment of this disease is the same as that of circumscribed parenchymatous keratitis.

With regard to the condition known as **keratitis punctata,** marked by a more or less pronounced stippling upon the membrane of Descemet, that is far from being a morbid entity. It is a physical sign denoting the existence of a so-called **serous iritis,** due to the most heterogeneous causes, as syphilis, rheumatism, tuberculosis, and even sympathetic ophthalmitis. In such cases the treatment depends upon the diagnosis, and we shall discuss the matter when speaking of the treatment of diseases of the iris.

In the Lecture on adrenaline a few words were said about Spring Catarrh, an affection that has been studied more particularly by Saemisch and by Horner. It is a malady of slow evolution (four to five years), the recrudescences of which are most pronounced in spring and summer, especially in dry seasons. It gives rise to characteristic changes in both the limbus and the tarsal cartilages, but scarcely affects that part of the conjunctiva which is not adherent to a firm base, as the cartilage or the sclero-corneal junction.

The disease is certainly of parasitic nature, but the microbe, although described, is not yet generally accepted as the cause.

Spring catarrh usually assumes the episcleral type; a waxy, gelatinous, yellowish roll develops on the inner and the outer side of the cornea. It may even encircle the cornea, and induce the formation of an opaque zone in the limbus, resembling an arcus senilis. This form is often confused with a corneal phlyctenule; but it is much more persistent, and pustules or ulcerations are never seen.

The conjunctiva of the tarsus, especially that of the upper lid, is also usually involved. The surface of the conjunctiva is covered with large papillæ, flattened and pressed against one another in such a way as to form a polygonal pavement, sometimes of admirable regularity. The entire surface is lustrous, as if coated with oil or milk.

Until recently the treatment of this curious affection amounted to very little. All the irritant, antiseptic collyria had an action that was unfavourable rather than the reverse.

The episcleral form, however, benefited from massage with yellow ointment, or, rather, with mercurial lanoline. As to the tarsal form, it was rebellious to all treatment, now becoming cured spontaneously, after lasting for years, and again undergoing cure, absolute or relative, after surgical removal of the granulations.

We now have in adrenaline a specific treatment, as it were, which, if it is not absolutely curative in these cases, is such an efficacious palliative that patients often think they are cured. The future is alone able to tell us if this treatment is truly efficacious, because, as the affection tends to return every year, a certain lapse of time is necessary to judge the remote effect of any remedy.

We now come to the most important class of the deep forms of keratitis—namely, **parenchymatous** or **interstitial keratitis.**

One must guard against making a single class of all forms of corneal infiltration, more or less profound, diffuse, extended, etc. There exist corneal infiltrations (*mesokeratites*) which have a very different origin.

There are forms of parenchymatous keratitis of benign character and circumscribed form, and there are others of very grave significance, capable of persisting for years, and sometimes of entailing blindness in consequence of various complications.

Kératite quadrillée or **kératite en grillage** (*gitterförmige keratitis*),* which has been recently described, is probably due to a leucocytic infiltration into the corneal spaces, of which one sees with the naked eye the larger lines, simulating canals, crossing and cutting one another at different angles. This form of corneal infiltration often improves very rapidly under the influence of subconjunctival injections of sodium chloride, and, indeed, even under the sole influence of instillations of dionine.†

This striated keratitis, as yet, has been met with only in slight form. But, for my part, I have observed in rheumatic subjects two cases that assumed a type of remarkable intensity. At first the cornea took a greyish aspect that, to an attentive examination with the naked eye, looked like an intense infiltration of all the lymphatic spaces intersecting almost at right angles, and giving an appearance of checkered hatchings. In a month the cornea had become in this

* Haab, Deutschmann's *Beiträge*, 1899.

† Darier and Dulnoy, *La clinique ophtal.*, No. 6, 1900.

way completely white; it was only secondarily that there ensued a pericorneal hyperæmia associated with deep vascularisation of the cornea. Resorption took place at the end of several months.

Should we regard these cases as special forms of parenchymatous keratitis to which we might give the name of rheumatic parenchymatous keratitis? I shall not banish this clinical conception, so much the more as the cases to which I allude are benefited only by an antirheumatic treatment—salicylate, warm compresses, ocular massage, etc. Subconjunctival injections, badly borne at first, towards the period of resolution brought about a rapid clearing of the cornea.

Another uncommon form of disease, **keratitis striata**, is now and then observed after the operation for cataract. It is due most frequently to a folding of Descemet's membrane. Cure is slow to come about, whatever the treatment adopted.

After the penetration of a foreign body into the cornea, a zone of parenchymatous infiltration around the injured spot is often observed. This generally disappears spontaneously after the removal of the foreign substance. Nevertheless, since these infiltrations may entail small opacities of the cornea, it is advisable to make repeated instillations of a collyrium of dionine, or to practise several subconjunctival injections of 2 per cent. or 4 per cent. solution of sodium chloride.

In certain corneal troubles consecutive to violent contusions of the cornea (**traumatic mesokeratitis**) similar treatment is to be adopted. These now and then simulate parenchymatous keratitis, and may be mistaken for the latter, especially when the accident is sustained by a more or less predisposed subject, as was the case in a young mechanic after a violent blow upon the cornea by a bulky foreign body—a splinter of metal.

The patient came for advice on the following day. The cornea was not ulcerated, but it had a dull, depolished aspect, with a slight, cloudy, greyish infiltration occupying its centre and veiling completely the pupillary orifice. The iris reacted normally, and atropine produced marked dilatation of the pupil.

The young man manifested all the signs of syphilis, he had even the Hutchinsonian face, and that was why, despite the affirmation that he had never suffered from any affection of the eye, I made a mental reservation in diagnosing contusion of the cornea. In fact, a traumatism, or even the presence of a foreign body, is often the determining or occasional cause of an outbreak of true parenchymatous keratitis when one has to deal with predisposed subjects.

After using a collyrium of dionine* for several days, a notable clearing of the cornea took place. I believed the disease definitely cured, when suddenly the corneal infiltration assumed such considerable proportions that almost the entire cornea was invaded; marked photophobia, accompanied by pain, made me fear the onset of an attack of acute true parenchymatous keratitis. I then subjected the patient to subconjunctival injections of 1 : 5000 cyanide of mercury, and made mercurial inunctions all around the orbit. Cure was so rapid, that I was unable to bring myself to believe that this was an example of true parenchymatous keratitis. In fact, one month after the accident, the wounded man resumed his work again with an almost completely transparent cornea.

This case, regarded as one of parenchymatous keratitis due to hereditary syphilis, would show how powerful is the action of subconjunctival injection when applied at an opportune moment—it may be quite at the beginning or it may be towards the end of the disease.

Who can assert, indeed, that the malady, without this energetic intervention, would not have progressed as a veritable parenchymatous keratitis? I present the observation to you as it stands; you may profit from it when you find yourself in analogous circumstances. We must, however, return to this subject in a few moments.

Parenchymatous or **interstitial keratitis** does not always assume one and the same form.

We shall study it more particularly because it is the best known, the parenchymatous keratitis so well described by Jonathan Hutchinson. In most cases it is met with in the children of parents who have had syphilis, as one of the multiple manifestations of that melancholy heritage.

In hereditary syphilis premature births and great mortality are found amongst the newly-born, who are puny, weakly, and much predisposed to meningitis. The cranial sutures present in these infants a peculiar aspect; the frontal bosses are prominent and asymmetrical; the jaws meet imperfectly; the internal ear suffers in its development, so that more or less pronounced deafness is often the result. The bones of the limbs, especially the tibiæ, present nodosities, following thickening of the periosteum. The knee-joint

* Dionine, 0·10; cocaine hydrochloride, 0·10; atropine sulphate, 0·02; cyanide of mercury solution (1 : 2000), 10 gr. S.—*One or two drops to be put into the affected eye every two hours.*

is often affected. Dentition proceeds slowly and badly. The first or milk teeth are small, spaced-out, and often insufficient in number. It is, however, especially the second dentition that may show stigmata almost characteristic of hereditary syphilis.

Hutchinson's teeth* are marked by a kind of arrest in the development of the enamel. This bears upon the summit of the tooth, of which the tubercles, almost deprived of this protecting envelope, come out as irregular, more or less hypertrophic points, constituted only of dentine, the bony substance of the tooth, of great fragility when not covered by its protecting cuirass of enamel, a substance, so to say, which is practically unalterable. From these facts comes the peculiar shape of the Hutchinson teeth, which, separated from one another, are small to the point that their dwarfishness often by itself constitutes a presumption of hereditary syphilis.

The incisors, instead of having a rectangular form, are larger towards their base, while their cutting edge is narrow, and presents a notch. This notch is due to the loss or the wearing away of that portion of dentine deprived of enamel observed when the patient is examined soon after the eruption of the tooth.

The canines terminate in a single point instead of in the three little indentations observed in sound incisors, showing when erupted a small and often very sharp point, below which a collar of enamel juts out. This point of dentine breaks up or is soon used up, and leaves behind it a notch smaller than that seen in the incisors.

Although the fact, so far as I know, has not yet been mentioned by any observer, yet the first permanent molars present the same arrest of development, which is easily explained by the fact that the enamel for these three classes of teeth—incisors, canines, and first molars—is formed towards the fifteenth or sixteenth week of embryonic life, while the dental follicles of the remaining permanent teeth develop much later (three months after birth). This leads us to think that it is during the first weeks of intra-uterine life that the syphilitic taint makes its inhibitory influence felt upon the development of the different fœtal tissues.

The first permanent molars, to the number of four (one above and one below on each side), are each provided with four tubercles. As in the case of the other teeth described above, the normal formation of enamel is arrested or proceeds imperfectly at the summit of the tooth. The osseous substance, or dentine, not being compressed and

* Hutchinson, Jonathan, *Syphilitic Diseases of the Eye and Ear*, London, 1863.

enclosed within its enamel cuirass, proliferates and grows rapidly and irregularly; the four tubercles, instead of being rounded, smooth, and white with enamel, are pointed, yellowish, and often extremely anfractuous. These osseous spines are very fragile, and since they are subjected to two simultaneous actions of a deleterious kind, they are soon affected with caries, which destroys them quickly: first, the permanent molars, in fact, suffer the greatest pressure during mastication; second, their jagged tubercles give asylum to particles of food, which during the night undergo chemical changes or fermentations, and these attack the dentine and render it friable. The dentine breaks and becomes exhausted, and soon there remains nothing beyond the crown of the tooth with a large carious cavity towards its centre.

In order to study these particular changes in the first permanent molars, it is necessary to examine many children of different ages, so as to seize the moment when the tooth is, as it were, born, and then to follow its evolution. Often, in fact, at the end of some months, one sees merely four carious teeth presenting nothing characteristic. But for the careful observer these four carious symmetrical teeth should possess a meaning; for my own part, after twenty years of attentive clinical observation of this minute pathological detail, I have arrived at this conclusion: that the first permanent molars making their embryological evolution at the same time as the canines and incisors, may suffer from the influence of specific heredity those arrests of development so well studied and described by Hutchinson.

It often happens that one meets with proven hereditary syphilitics who have teeth almost beyond reproach. However, if one looks carefully, one notes that the teeth are somewhat spaced-out, and smaller than fits in with the bony structure of the face. When the patient smiles one does not see the jaw, while the mouth is often enlarged by old rhagades of the labial commissures. These cases, however, without being very rare, are the exception, and if one searches carefully among many who are the subject of hereditary syphilis, with all the front teeth sound and almost pretty, one will find that the first great molars present the signs described above, or, if age is already a little advanced, the four teeth are carious and several of them have completely disappeared, while those that remain allow us still to recognise a crown of sound enamel with one or two tubercles pointed and covered incompletely with enamel.

I have never heard the permanent molars spoken of as being able to

show the stigmata of Hutchinson, not even by this eminent authority, whose teaching I had much pleasure in following at the London Hospital. It is in verifying their typical alterations among many subjects having the true Hutchinsonian teeth, and perhaps other signs of the diathesis, that I have reached the conclusion that the first permanent molars are able to yield us valuable indications in the diagnosis of hereditary syphilis.

LECTURE XVI.

Summary.

Parenchymatous keratitis (*continued*).—Oftenest due to hereditary syphilis.—Sometimes of tuberculous or scrofulous nature.—Importance of general treatment by hypodermic or intra-venous injections of soluble salts of mercury.—Local applications: atropine, dionine, warm compresses, mercurial poultices.—Subconjunctival injections of sodium chloride, sea water, cyanide of mercury, etc.—Massage with mercurial lanoline.—Diseases of the sclera.—Episcleritis, rheumatic or gouty in nature.—Salicylate of sodium, aspirine, colchicine.—Episcleritis of tuberculous nature.—Massage with mercurial lanoline.—Cauterisations with the galvano-cautery.—Subconjunctival injections, etc.

Until the last few years it was almost generally admitted that **parenchymatous keratitis** represented one of the chief manifestations of "Hutchinson's triad," characteristic of hereditary syphilis.

Recently, however, interesting works * have been published which tend to show that many cases of parenchymatous keratitis have a tuberculous cause and origin. The bacillus of Koch may be found in the different organs primarily affected, or only in the eye itself, or sometimes in the corneal infiltration alone.

Certain authors have accordingly concluded that, in addition to syphilis, tuberculous as well as all dyscrasic affections of long standing are able to engender not only the corneal alterations, but all the trophic troubles characteristic of "Hutchinson's triad," so that the grouping of those signs ought not to be considered as a proof of hereditary syphilis.

We are not of this opinion. We think that clinical observation and therapeutic observation are in accord in showing us that, if parenchymatous keratitis may occur in subjects who are simply scrofulous or debilitated, like a manifestation of local or general tuberculosis, the fact is exceptional. Before long, we hope that clinical observation, aided by experiment and pathological anatomy,

* E. von Hippel, von Graefe's *Archives*, xlii.

will give us the signs of the differential diagnosis between these different forms of parenchymatous keratitis.

From the foregoing remarks flow the indications for the general, and perhaps also for the local, treatment of the condition. Faced by a grave parenchymatous keratitis, associated with the more or less complete loss of the transparency of the cornea, one must not hesitate to adopt general treatment, which in every form of this redoubtable affection (even when of tuberculous essence) has yielded us such constant results that we are able to say that it cures almost with certainty. We speak of hypodermic or intra-venous injections of soluble salts of mercury. This plan of treatment we have pursued for some considerable time in common with our master, Abadie, to whom belongs the merit of having popularised the plan.

The analogy of form and of evolution shown by some tuberculous affections—notably those affecting the bones, the joints, the lymphatic glands, and the skin—with syphilitic lesions, has naturally suggested the idea of employing in these local tuberculoses the means used against the manifestations of syphilis, namely, iodine and mercury.

Iodine has figured for years in the treatment of chronic adenitis. During more recent times it has been often used for the cure of surgical tuberculoses under the form of hypodermic injections according to the method of Durante.

With respect to the employment of mercury in tuberculosis, it must suffice to mention in this place the subcutaneous injections of calomel in warty tuberculosis of the skin and lupus, and injections of sublimate in Pott's disease, to say nothing of the mercurial treatment of tuberculosis, facts concerning which have been published from time to time.

That said, it is interesting to note that quite recently an Italian medical man, T. Silvestri, of Nonantola, has obtained encouraging results in various forms of tuberculosis by mercurial treatment. The observations of Silvestri include examples of large glandular tumours of the neck, scrofulosis with multiple manifestations, Pott's disease, white swelling of the knee, coxalgia, tuberculous ostitis of the sternum, and a case of pulmonary lesion with tubercle bacilli in the sputum, associated with ascites and hydropericardium. Our *confrère* administered to these patients sublimate, sometimes by subcutaneous injection (0 gr. 005 milligr.), and sometimes by the mouth (0 gr. 005 milligr. to 0 gr. 02 centigr., according to age). He now and then also prescribed mercurial inunctions. In all the cases treated in this way Silvestri obtained a considerable improvement, and, indeed, in the less pronounced, often a cure.

In one of our former Lectures we have given the indications for, and the technique of, mercurial injections (*see* page 16, *et seq.*). Here we shall merely add that in parenchymatous keratitis, which is chiefly met with in children, we give the preference to hypodermic injections. The intra-venous injections, which are more difficult to perform in children, should be reserved for older and more docile patients.

General treatment by mercurials has for long been recognised as efficacious. Locally, during the acute period, which may last for several months, irritating applications must be avoided, and we must be contented with repeated instillations of atropine and the frequent use of warm compresses. A very good application under these circumstances is what may be called the "mercurial poultice:" the contents of an *ampoule* of 2 grammes of mercurial lanoline are spread by gentle friction around one or both orbits, and over all a thick linseed-meal poultice, as hot as the patient can bear it, is placed. During this painful acute period of the disease, however, it is general treatment which almost exclusively relieves true parenchymatous keratitis.

Later, subconjunctival injections, made at an opportune moment, are capable of exerting a capital influence upon the evolution of the morbid process. The authors are already numerous who have confirmed our original assertions with regard to this particular. We need only repeat that which we have written many times, *viz.:*

In benign and atonic parenchymatous keratitis, often merely the first stage of a grave form, although the infiltration is circumscribed and the reaction is trifling or absent, subconjunctival injections give excellent and sometimes even marvellous results.

One now and then observes, after each injection, the corneal infiltration pushed back from the periphery towards the centre, every injection sweeping out, so to say, the corresponding segment of the cornea; and one may thus go around the cornea so thoroughly that in several days the infiltration is no longer visible except in the most central parts of the cornea. It would therefore appear that the liquid injected beneath the conjunctiva does not penetrate farther than the lymphatic spaces most distant from the sclero-corneal limbus.

At this time, massage with mercurial lanoline, of which we spoke several years ago, renders good service. After cocainisation, a piece of the medicament as large as a grain of wheat is introduced between the eyelids, and gentle and prolonged rotatory massage is then practised. This may be repeated by the patient once or twice

a day. These frictions may be alternated with warm compresses, vapour douches, and "mercurial poultices."

It would take too long to enumerate the results obtained by all the authors who have written on this subject.

Marti,* working under the direction of Mellinger, of Basle, has published a very authoritative thesis on the therapeutic action of subconjunctival injections of saline water in affections of the cornea. He recognises that sublimate injections have a favourable action in infectious or destructive processes of the cornea; but he reproaches sublimate with bringing about an adhesive inflammation, leading to an obliteration of the subconjunctival lymphatic spaces.

To this we have already replied that adhesive inflammation is produced only when an unduly concentrated solution is employed, or when the injection is made too near the sclero-corneal limbus or into the capsule of Tenon. Moreover, we have for several years completely abandoned sublimate, as too irritating, in favour of the cyanide of mercury.

Marti, like his master, therefore concluded that subconjunctival injections of chloride of sodium, while energetically stimulating the lymphatic changes, have a very favourable action on the absorption and elimination of the noxious elements infiltrated into the corneal tissues.

Moreover, injections of sodium chloride have the important quality of causing little pain. In these circumstances we can recommend their employment in most of the more or less parenchymatous infiltrations. In the hands of Dianoux, of Nantes, sea water has given equally good results. Nitrate of sodium, according to Demicheri, has an extremely potent exciting action on the circulation of the blood and lymph.

Other agents furnished by the incessant progress of chemistry will soon enrich the arsenal, still precarious enough, of subconjunctival therapeutics.

It can scarcely be repeated too often that during the acute, violent, and vascular period of parenchymatous keratitis all local treatment of an irritating nature is absolutely contra-indicated; but when the period of decline is reached, when the ocular conjunctiva has resumed its normal aspect, when vascularisation is no longer apparent, then subconjunctival injections exert the same favourable influence as in the initial stage or in the atonic and circumscribed forms mentioned above. It has often happened to us to witness in

* Marti, *Des injections sous-conjonctivales d'eau salée dans les maladies de la cornée*, Basle, 1894.

the course of a few days, under the influence of this local treatment, corneæ which had been opaque for several months clear rapidly and in a remarkable way.

Here, as everywhere, it must be clinical acumen which should guide the practitioner in the appreciation of the opportune moment when the therapeutic intervention will yield the maximum advantages with the minimum inconveniences. That fact explains why some authors have renounced subconjunctival injections in parenchymatous keratitis, while many others are their warm partisans. Applied haphazard, the method gives only eventual results, even if it does not carry with it other inconveniences.

Lastly, to return to practice, this is how we advise you to proceed in the treatment of parenchymatous keratitis.

1. The first indication is general treatment. It must be grounded upon the etiology of the disease, and on the constitutional state of the patient. It will generally take the form of hypodermic or intra-venous injections of cyanide of mercury, which give the best results. When injections cannot be used—for example, in very young subjects—one has recourse to inunctions or to the administration of sublimate by the mouth.

2. To commence with, the only local applications should be collyria of atropine and of dionine, hot compresses, and such cleanliness and antisepsis as may be indicated by any intercurrent affections of the eyelids and conjunctiva.

3. When after this period of expectation, armed with general treatment, one sees that the conditions are favourable to local intervention—that is to say, when there is no marked conjunctival hyperæmia—and when one has to deal with a subject of a certain age and docility, one proceeds to subconjunctival injections, beginning with half a syringeful of a 2 per cent. solution of chloride of sodium at a temperature of about 32° C.

If the first injection is completely resorbed by the following day, a second should be made, but inasmuch as the evolution of the malady is very gradual, it is better to be in no hurry and to practise the injections at the most once every two or three days.

The injections, commenced with half a syringeful of a 2 per cent. solution, should be progressively increased both in volume and strength until a syringeful of 4 per cent. solution is employed.

When some ten injections have been made, the patient is given a period of rest, during which general treatment and warm applications and atropine should be continued, with or without interruption.

If one has to deal with a patient who is manifestly the subject of

hereditary syphilis, and even in many cases where other treatment has failed, we must not hesitate to use subconjunctival injections of mercurial salts. In these conditions the most active solution and that best borne by the patient is the following, which represents a 1 : 5000 solution of cyanide of mercury with 2 per cent. of chloride of sodium :

Cyanide of mercury . .	0·01	centig.
Chloride of sodium . .	10	grammes.
Distilled water . .	50	grammes.

At first half a syringeful is injected every two or three days, and the doses are gradually augmented until a syringeful is reached. The injection is better borne, more quickly absorbed, and more efficacious when the solution is used warm (about 32° C.), and when a hot dressing is afterwards applied. We have already said that there is scarcely any pain if a few drops of a 1 per cent. solution of acoine be added to the contents of the syringe.

But it is useless to be so infatuated as to practise many injections when the latter are not followed by a good result, and especially when they are not well tolerated. As soon as one sees that they set up any marked irritation, longer intervals must be allowed to elapse between them, or they must even be suspended for a time, insisting upon the general treatment and hygienic care of the case. Saline baths with marine salt or with the sea water of Salies-de-Bearn * render real service in many cases of the kind.

Parenchymatous keratitis is nearly always complicated with iritis, and often with choroiditis also. The treatment of these complications will be studied in the chapter specially devoted to the therapy of those affections.

Episcleritis and **scleritis** are affections which have been benefited relatively little from local treatment by subconjunctival injections. It is true that diseases of the sclera are rare and imperfectly understood, which makes the therapeutic indications more difficult.

Van Moll was among the first in publishing three cases of episcleritis cured by the subconjunctival injection of salicylate of sodium.

For our own part, we have never had occasion to employ subconjunctival injections in affections of this kind. The latter we have always treated by the internal administration of salicylate of

* A watering-place in the Basses Pyrénées, about two hours by rail from Bayonne, noted for its strong saline waters.—TRANS.

sodium or of colchicine,* and locally by adrenaline and punctate cauterisations with the galvano-cautery. But the observations on this subject by several authors do not lack an interest worthy of arresting the attention of the practitioner.

Unable to relate the results of our personal experience, we shall, we think, do well to quote here *in extenso* the extremely interesting observation that we owe to Terson, of Toulouse.

Mrs. B—, a very rheumatic subject, had been affected for four months with typical episcleritis. This ailment was very painful, although not complicated with iritis. There was a slight sclerosis of the cornea in the part corresponding to the infiltrated scleral zone. Warm applications, all kinds of sedatives, salicylate of sodium, and iodide of potassium, had not influenced the course of the disease, despite the fact that the treatment had been assiduously pursued. No sooner had the inflammation ceased at one spot than it appeared at another, and was always accompanied by lively pain. There existed a sclerotic *plaque* of some size, owing to two relapses within a brief period of time, when I made a first injection of two drops of a solution of sublimate into its immediate neighbourhood a little behind the most inflamed part. A moderate reaction followed the injection, and this lasted several hours. But next day the pain had disappeared, as well as the vascularisation of that part of the episcleritic patch into which the injection had been able to penetrate. A second injection was practised after a week, this time into the opposite part of the *plaque*, and this brought about further improvement. A third injection, after a week's interval, suppressed definitely all redness of the affected region and completed the cure. The last-named has been maintained for more than three months, as the patient comes from time to time to let us assure ourselves. The eye presents merely a slight trace of sclerosis at the periphery of the cornea, and this does not affect sight.

Let us discuss together the therapeutic indications.

There are forms of scleritis, of sclero-keratitis, of keratitis and marginal ulcers of the cornea arising from the so-called arthritic or rheumatic diathesis.

These affections are often promptly improved by the salicylic preparations, if the last-named are employed in adequate doses.

The following is the way we proceed in the various manifestations of rheumatism:—(1) When there is simple episcleritis—that is, localised infiltration in the episclera and the subconjunctival tissue

* Darier, *Société d'Ophtalmologie de Paris*, 1889.

(the *subconjunctivitis* of Inouye), without corneal complications—the differential diagnosis of this affection from conjunctivitis in general is much facilitated by instilling one or two drops of suprarenal gland extract or, better, adrenaline into the eye. This agent provokes a very marked anæmia of all the conjunctival surface, leaving at the level of the focus of episcleritis only a profound hyperæmia with a prominent infiltration.

In these conditions, if little pain is present, or there is merely the sensation of a foreign body, you will find adrenaline, applied six or eight times a day, of great service. Each application gives rise to a marked anæmia, of which one takes advantage to practise a gentle and prolonged rotatory massage, in order to hasten the resolution, resorption, of the subconjunctival infiltration. The massage may be applied with various ointments, among others mercurial lanoline, of which we all recognise the potent resolutive action, and which has given us excellent results in many cases of scleritis and episcleritis.

If the episcleritis of which we have just spoken is accompanied by lively pain, we must endeavour at first to calm the same by the use of a collyrium of dionine. This generally succeeds in dulling the pain if the instillations are repeated six or eight times a day.

At the same time, and from the first consultation, the patient must take salicylate of sodium in the dose of two to three grammes a day. Even during the first days, if the patient suffer much and dionine remains without effect, it is well to prescribe, in addition to the salicylate, one of the following cachets to be taken at the time when the violent crises of pain supervene:

Antipyrine	0·50
Phenacetine	0·30
Citrate of caffein	0·20

S.—*Make one cachet.*

Salicylate of sodium is often tolerated badly; it provokes buzzing in the ears, and cerebral and stomachic trouble, which makes many patients desirous of discontinuing the remedy. Patients who have suffered from rheumatism and experienced the effects of the salicylate, frequently even warn us that they cannot take the medicament, as they are unable to bear it, or they do a simple thing and change their medical man.

For about a year a new product, a salicylic combination called aspirine, has been vaunted as possessing all the qualities and none of the defects of salicylate of sodium.

Insoluble in acid menstrua, aspirine passes through the stomach

unchanged, and is absorbed only in the alkaline fluids of the intestinal canal.

We prescribe aspirine daily in almost all the cases where the preparations of salicine are indicated, and so far we have nothing but praise for the product. With this new and interesting agent we have never observed any of the inconveniences charged against salicylate of sodium. We have, it is true, never employed large doses—3 to 4 grammes daily is the maximum we have prescribed.

However, if the preparations of salicine are relatively sovereign remedies in all cases where rheumatism is more or less acute, it is no longer the same in the manifestations of chronic or gouty rheumatism. But there are numerous forms of episcleritis or of scleritis which arise from this organic defect, often of an hereditary nature.

In such cases, after having employed for fifteen or twenty days or longer the preparations of salicine, alkalies, and lithia, without result, one often obtains prompt and brilliant results from colchicine, as we were the first to point out.

℞ Granules of colchicine of . 0 gr. 001 milligr.

S.—*Take* 1, *then* 2, *then* 3, 4, 5, *or* 6 *a day at equal intervals.*

Do not forget to advise the patient to stop the granules the moment he feels the least colic or cramp in the stomach (sometimes very violent), for such constitutes the valuable indication that the therapeutic effect has been produced.

Therefore, when one has reached the dose that sets up colic, the colchicine is discontinued for a day, commencing it again the following day at the initial dose of one milligramme. This amount is augmented daily until the onset of another attack of colic, and so on for a month or so.

If no therapeutic effect is produced, it is because we are not dealing with a truly gouty affection, or because the patient is not sensitive to the treatment. We must then search for other means that will allow us to cure the case.

Punctate cauterisation with the galvano-cautery of the scleral nodules may be employed in these cases with advantage. Electrolysis, also, has yielded good results, as well as subconjunctival injections. The galvano-cautery, however, if it is very fine and brought to a dull red heat, acts more rapidly and is much simpler as regards its manipulation.

These cauterisations have a powerful revulsive action, and at the same time they provoke a development of connective tissue which leads to rapid cicatrisation.

The potent resolutive action of light but frequently repeated

cauterisations is sustained in a remarkable manner by the continued use of the supra-renal extract or adrenaline (*see* page 73).

Sclerosing keratitis is not a morbid entity, but rather a nutritional trouble of the cornea due to an obstacle bearing perhaps upon the vessels or perhaps upon the nerves of the sclero-corneal limbus.

It is generally a nodule of scleritis which implicates the organs essential to the nutrition of a sector of the cornea, which at this level becomes more or less opaque, opalescent, and mirror-like.

If the sclerotic alteration be not quickly stopped, the corneal mischief may become indelible. On the contrary, if the treatment indicated above be applied in time, the corneal infiltration may recede under the influence of subconjunctival injections of sodium chloride and the other means which you know.

Episcleral nodosities, such as the case of "button-like scleritis" described by me in the *Archives d'Ophtal.* for 1889, are now and then of tuberculous nature. The best results are obtained in such cases from cauterisations, local massage with lanoline and iodoform, and the use of iodoform internally.

LECTURE XVII.

Summary.

Diseases of the iris and ciliary body.—The infectious origin, endogenous or exogenous, of most cases of iritis or irido-cyclitis.—Variable symptomatology according to the intensity of the morbid process.—Therapeutic indications: (1) calm pain; (2) dilate the pupil; (3) treat the cause.—Adjuvants: depletion, leeches, cupping, conjunctival blood-letting, intestinal or cutaneous derivatives.—Concerning dionine as an analgesic and lymphagogue hastening the resorption of pupillary exudations.—Of paracentesis of the anterior chamber.—Of syphilitic, rheumatic, and blennorrhagic iritis.—Importance of general treatment.

We open to-day the interesting chapter of diseases of the uveal tract, commencing with **iritis** and **irido-cyclitis**, which are clinically and therapeutically almost inseparable from one another. In fact, it is very rare for an inflammatory or infectious process to attack the iris without spreading by continuity to the entire ciliary body.

Irido-choroiditis and choroiditis attack the deepest part of the vascular membranes of the eye; we shall therefore study separately these two affections.

Iritis is generally due to an infection. The last-named may come from outside by an injury or erosion of the conjunctiva or cornea; it may be propagated by contiguity from some infection in the neighbourhood, as keratitis, infectious ulcers, episcleritis, scleritis, etc.; or, lastly, it may be the outcome of a localisation of a general infection, such as syphilis, rheumatism, gonorrhœa, tuberculosis, and other acute infectious diseases.

Must we consider strumous or scrofulous iritis and irido-choroiditis as being of infectious nature or as dyscrasic troubles of trophic character? For my own part, I incline rather to an infection of an hereditary kind, such as that we have studied in parenchymatous keratitis proceeding from hereditary syphilis.

Scrofula is an hereditary taint, the nature of which is not yet exactly worked out. It is, however, associated at one and the same time with tuberculosis, syphilis, alcoholism, etc.

In this place we cannot dwell longer upon the etiology of iritis; we shall consider the question while occupying ourselves with the different means of treatment, general and local.

The pathological evolution of the different clinical varieties of iritis and irido-cyclitis is, if we except the degree of intensity, identical as regards the various clinical forms, namely, hyperæmia, cellular infiltration, exudations, synechiæ of the iris, occlusion or seclusion of the pupil able to cause the gravest complications, such as glaucomatous degeneration or atrophy of the eyeball.

The acuteness of the inflammatory phenomena depends upon the virulence of the infection, the resistance of the individual, and a crowd of surrounding circumstances. It is difficult, even nowadays, to assign a well-defined clinical form of inflammation to each of the various infections. Further, it is, as a rule, impossible to diagnose rheumatic or syphilitic iritis without examining the patient generally and inquiring into his antecedents, rather than by the particular, specific form assumed by the morbid ocular process.

We will at first speak only of classical iritis, and not of the more special forms accompanied by gummata, condylomata, or tubercles, which bear upon their face stigmata more or less pathognomonic of their origin. Still, in many such cases the diagnosis is open to question, for there exist bastard forms of iritis in which the opinion of the most competent authorities may differ widely.

Plastic, exudative, parenchymatous, and suppurative iritis may represent nothing more than the different grades of an identical pathological process. But it is to be hoped that we shall some day arrive at more precise means of diagnosis, and that the degree of virulence of the different infectious agents may be easily determined, thanks to more rapid and exact means of investigation.

But that which should interest us the most from the therapeutic point of view is the symptomatology of iritis, because in this malady more than in any other it is of the greatest importance to act with promptitude and energy, in order to prevent complications, which may be most serious when affecting an organ so delicate and invaluable as the organ of sight.

You know too well the cardinal symptoms of a **simple, acute iritis** for it to be necessary to insist upon their description. The general symptoms include redness, pain, and photophobia, while the special symptoms are contracted pupil with a dull, glaucous aspect of the iris, the colour of which changes little by little.

If the iritis is extremely acute, the various symptoms break out with great suddenness, and are accompanied by violent pain and

abundant exudation, leading to large synechiæ of the iris, more or less adherent, and often taking a long time to get rid of.

On the other hand, one may observe **insidious iritis,** the evolution of which is so slow that the patient at first experiences scarcely any pain, until the moment when more or less numerous synechiæ sometimes necessitate surgical interference.

A crowd of intermediate grades intervene between these two extreme forms, including, among others, the so-called **serous iritis,** which depends rather upon an inflammation of the ciliary body than of the iris itself.

Let us study somewhat in detail the therapeutics of this important group of eye diseases, since the least mistake in treatment may entail the gravest consequences.

The application of atropine, although so trivial, demands a certain experience.

How many cases of glaucoma, mistaken for iritis, have led to loss of the eye by the untimely use of atropine? How many synechiæ have been the consequence of an inadequate mydriasis?

Every time iritis begins with violent symptoms, accompanied with a lively reaction, with photophobia, marked pericorneal injection, etc., the first indication is to follow, in the words of our forefathers, an antiphlogistic treatment. In fact, it is necessary for us, and still more so for the patient, to bring about as promptly as possible a diminution of the inflammatory phenomena at the same time that one dilates the pupil and calms the pain.

To attain the last aim, we have at our disposal the entire series of anæsthetics, narcotics, analgesics, etc. Antipyrine, phenacetine, quinine, and the preparations of salicine are the anæsthetics most to be recommended for calming the ciliary pains and the violent headaches produced by iritis; but they are not invariably successful.

Opiates induce sleep but depress the nervous system, as do also bromide of potassium, bromidia, paraldehyde, etc.

Injections of morphia are our supreme and heroic resource when pain is intolerable.

But to calm the pangs of an iritis or irido-cyclitis is it always necessary to have recourse to such energetic sedatives, which depress all the faculties of the organism, the cerebral as much as the digestive functions? The heart and the circulation in general are often also affected by the abuse of narcotics and of general analgesics.

Since the discovery of cocaine one had hoped that the local anæsthesia produced by that valuable agent would prove itself capable of diminishing ocular pain of any sort. When congestion—

conjunctival hyperæmia—is not too violent, cocaine calms pain, diminishes photophobia, and facilitates examination of the affected eye; but this lull lasts for a few minutes only, and the pain then returns with redoubled violence.

The substitutes for cocaine, such as tropococaine, eucaine, holocaine, etc., have not given the best results in permanently calming ciliary pain.

To-day, as I have already pointed out to you in one of my former Lectures, we possess an ocular analgesic, the action of which is profound and of long duration. It allows us to calm the pains of iritis and irido-cyclitis, and sometimes even causes them to disappear permanently. We speak, of course, of dionine (the hydrochloride of ethyl-morphine), of which the rapid and profound analgesic qualities were discovered by chance alone.*

By instilling into the conjunctival sac several drops of a 5 per cent. solution of dionine, the ciliary pain may in many cases be quieted. These applications give rise to chemosis, often very marked, and one or two hours later pain is much reduced and, indeed, often disappears completely and permanently.

In some rare circumstances the analgesic action of dionine is *nil;* at other times the suffering reappears at the end of twelve or twenty-four hours, when the instillations must be repeated. In some cases, tolerance towards the medicament is induced in two or three days, and the pains then become more difficult to calm locally, because up to now dionine is the only local analgesic of really efficacious action, although it is very probable that chemists will presently furnish us with new and powerful remedies of that kind.

At the same time, and even before relieving pain, it is necessary *to safeguard or re-establish the freedom of the pupillary sphincter provoking as marked a mydriasis as possible.*

For that purpose we have a classical agent, which retains an incontestable reputation, namely, atropine, the most trustworthy and widely used mydriatic. But if atropine does not suffice, we have recourse to a still more powerful agent, scopolamine, which you will prescribe in the way you have learnt in the lecture upon collyria (*see* Lecture V):

Hydrobromide of scopolamine . .	0·025 gr.
Hydrochloride of cocaine . . .	0·25 gr.
Distilled water	10 gr.

S.—*One drop three or four times a day into the affected eye.*

In cases where dilatation of the pupil can be obtained by no other

* *See* page 51 *et seq.* for the mode of action and of application of dionine.

means, Fuchs recommends the introduction into the conjunctival sac of a morsel of atropine the size of the head of a pin. As yet we have not put this method to a test, but the interesting results which we have ourselves obtained by the direct application of powdered dionine into the conjunctival cul-de-sac, lead us to believe in the efficacy of this dry collyrium under certain particular conditions. We shall try it on the first convenient occasion.

Since we have learnt from our own personal experience that dionine augments the mydriatic action of atropine, at the same time that it brings about a diminution or cessation of ciliary pain, a more rapid resorption of pupillary exudations, and a diminution of intra-ocular tension, we prescribe in iritis associated with pain the following collyrium in preference to all others:

Dionine	0·10 gr.
Cocaine hydrochloride . . .	0·10 gr.
Atropine sulphate	0·05 gr.
Distilled water	10 gr.

S.—*One drop of this collyrium to be placed in the affected eye six to eight times a day.*

This collyrium, perhaps, provokes a little more smarting than the ordinary collyrium of atropine. It presents, however, such great advantages over the latter that it is not allowable to hesitate between the two.

Moreover, dionine has the advantage of lowering the intra-ocular tension. As we have just said, it thus prevents the dangers of hyper-distension so often provoked by atropine.

When one has to deal with a slight iritis, marked by little pain, it is better not to prescribe dionine at the first, reserving this invaluable but delicate agent for cases where pain supervenes. For if the latter come on, after a fortuitous aggravation, when the eye is already accustomed to dionine, it is often impossible to obtain local analgesia with that agent, of which the action has been weakened by a premature tolerance.

When iritis or irido-cyclitis is accompanied with violent inflammatory phenomena, as circumcorneal hyperæmia, with chemosis and swelling of the eyelids, radiating pains, and intense photophobia, one must not hesitate to have recourse to the local depletion of blood, decried though it has lately been, especially by a certain school.

All impartial clinical observers who have witnessed the change undergone by a very acute iritis after the application of two to four leeches to the temple, or even of a single one near the inner angle of the eyelids, will be no longer tempted to deny the efficacy of this

ancient and empirical medication, even if the physiological explanation of the process appears to him to be most improbable.

However, what is more natural than to think that organs as vascular as the iris and ciliary body, soaked with blood like a sponge, are not able in these conditions to permit a mydriatic to act properly, whilst, after the local abstraction of blood, the action of atropine manifests itself with rapidity and intensity ?

With this end in view, bleeding from the conjunctiva has recently been praised; but, in my opinion, leeches present a practical advantage over all other means, as wet cuppings of all kinds, bleedings, etc., namely, that their application is painless, and that, under all circumstances, they are readily applied by the patient or his attendants.

This much is certain, that after an adequate abstraction of blood, the patient often opens his eye more readily, bears light better, and finds that his pupil, which at first did not dilate to atropine, undergoes mydriasis, sometimes *ad maximum*, after one or two fresh applications of the agent. The orbital pains and the headache are notably diminished under the influence of the abstraction of blood.

There remain, however, cases where, despite all the means enumerated above, the patient cannot be freed from violent pain, and these occur especially where the tension of the eyeball is notably raised. Under such circumstances one must often resort to puncture.

This paracentesis of the anterior chamber is very painful in spite of cocaine and adrenaline. Narcosis by chloroform or ether lasts too long, but ethyl-chloride gives an easy and rapid anæsthesia, and leaves behind it no *malaise*.

The means of which we have just spoken—mydriatics, dionine, and leeches—enhanced by the general treatment indicated by the etiology of the disease, usually bring about a prompt retrocession of the inflammatory process, and one is able to foresee an approaching cure without further effort.

Indeed, I have often seen patients return to me with serious relapses, because the subjective state, under the influence of dionine and the other medicaments passed in review, had improved to such a point that, believing themselves quite cured, they stopped all treatment completely, and came to consult me no longer. That is the reason why I invariably caution clients against being proud of apparent cures, due only to the disappearance of the painful symptoms, and warn them that general treatment should be kept up until the complete disappearance of all changes in the iris.

There exist cases where therapeutic means of secondary importance may render real service. For example, it is not uncommon to meet with cases of grave iritis which have resisted the above-described treatment, and which are influenced very favourably by an energetic intestinal derivation. A purgative that cannot be recommended too highly in such circumstances is the following:

Calomel	1 gramme.
Scammony	1 gramme.*

S.—*Divide into two cachets, taking one at night for two successive nights, provided the purgation has not been too intense the first day, in which case the administration of the second cachet is to be suspended.*

Besides having a powerful purgative and cholagogue action, calomel possesses a marked antiseptic and resolutive power. It is of great benefit when the iritis is due to syphilis.

Cutaneous revulsives, as blisters, setons, the cautery, and mustard pediluvia, are still recommended by many practitioners. We must admit that we have employed them so rarely that we must decline expressing any opinion with respect to their value. To deny all efficacy to them, however, because our physiological or pathological knowledge does not as yet allow us to explain their mode of action, would be as unscientific as the abuse which many authors shower on these empirical measures.

We must not forget that in some forms of iritis, rebellious to all treatment, it is advisable to understand how to graduate our means of action, so that we are never taken unawares by the incessant, offensive, and multitudinous relapses of an evil which is born again, so to speak, from its ashes.

We have already seen how quickly the organism becomes accustomed to the most different medications. It is, therefore, always necessary to have at one's disposal new means of action.

There is, perhaps, no eye affection the evolution of which is so irregular as that of iritis or irido-cyclitis, principally those forms which appertain to the rheumatic diathesis. How often do we not see a relatively slight iritis, which seems subdued on the tenth day, reappearing with startling suddenness under some influence, such as cold, strong light, work, or any other cause that eludes only too often our powers of observation.

The etiological diagnosis of diseases of the iris, as pointed out, is

* The addition of a drastic purgative prevents the calomel provoking any mercurialism when the purgative effect comes on too slowly.

far from being always exact, while the indications that are drawn from it often lack clearness.

When **syphilis**, of comparatively recent date, is admitted, the odds are that this infectious disorder is the true cause of the iritis, even although the exciting cause may be a chill, a traumatism, or some other irritating local agency.

Syphilis is certainly the most frequent cause of iritis. Syphilitic iritis, however, can be diagnosed but rarely by the aspect of the eye lesions alone—at least, as we have said, not unless we have to do with a gummatous iritis, in which case the gumma, or rather the condyloma, can scarcely be confounded, except with a tuberculous product.

The diagnosis, therefore, may now and then present real difficulties. The anamnesis gives us the key to the mystery, but there are many cases where syphilis may be overlooked, especially in women.

Finally, when one has made a diagnosis of syphilitic iritis, general treatment must be adopted from the first day, from the first tentative trials of local treatment; for, it cannot be repeated too often, whatever importance local therapeutics may possess, it should always be preceded, accompanied, and followed by general treatment.

From our second Lecture it has been seen that, in our opinion, the best treatment for the ocular manifestations of syphilis is the administration of mercury by subcutaneous or, preferably, by intra-venous injection of one centigramme doses of the cyanide of mercury.

Personally, we repeat these intra-venous injections at first daily, then, if colic comes on, every alternate day (*see* page 16), and according as they are more or less well borne, to the extent of thirty to fifty injections.

By this means I have seen extremely grave iritis, even in senile and cachectic subjects, cured in a short space of time.

Mercurial inunctions around the orbit, followed by the application of poultices (*see* page 160), are frequently valuable adjuncts, on account of their special action upon the infected lymphatic territory.

Too much has been asked of potassium iodide in the treatment of iritis, and all the affections of the uveal tract, where, as Abadie has often remarked, its action is rather harmful than useful.

It is indicated only when the iritis is almost cured; it has scarcely any curative action except in gummatous iritis; on the other hand, its prolonged use may consolidate cure and prevent relapses, especially if one is careful to alternate its employment with a more or less prolonged series of mercurial injections.

When the injection of soluble salts cannot be practised, recourse must be had to mercurial frictions, pills, solutions, etc., but these means are irregular in their action, the patients in general following with difficulty the directions given them on the subject. We shall see further on that subconjunctival injections of cyanide of mercury have in certain subacute forms of iritis a remarkable therapeutic action.

Of inunctions, which are equally active, we have already studied the chief indications and contra-indications.

Rheumatism is much more difficult to affirm categorically, as it is an unknown quantity of such elasticity that it is able to accommodate itself to everything. Nevertheless, it is recognised that many cases of iritis are of rheumatic origin.

Gonorrhœa, if it is synchronous with iritis, or precedes it by a short time, is still rather easy to incriminate. But when it manifests itself only by an endometritis or a "morning drop," one does not always think of its being the cause; and yet!

Rheumatic and gonorrhœal iritis are united by ties of relationship, especially in the acute form sometimes distinguishing itself by a fibrinous exudation so abundant that, when it begins to contract, it may be mistaken for the crystalline lens luxated into the anterior chamber. This phenomenon, indeed, cannot be regarded as belonging exclusively to gonorrhœal iritis, inasmuch as many other infectious maladies, especially rheumatism, may give rise to abundant exudations into the anterior chamber.

Salicylate of soda (two to four grammes daily) should form the basis of the general treatment of these forms of iritis. Even when a gonorrhœal origin is manifest, the salicylate yields very good results; it goes without saying that the urethral discharge must at the same time be treated energetically.

The acute forms, of sudden onset, which are often the characteristic of rheumatic iritis, may, as a rule, be cured readily and rapidly. More than ever, local and antiphlogistic treatment should go hand in hand with general treatment; and more than ever, also, treatment should be kept up for a long time, and great precautions should be taken to avoid those relapses which are so common in all affections caused by rheumatic infection. This is why one may term relapsing iritis "rheumatic iritis."

There are periods when the practitioner is consulted, so to say, at the same time, by all his patients liable to rheumatic iritis. This is owing to sudden changes of temperature, in cold and damp seasons.

When rheumatic iritis becomes chronic, its treatment is more difficult, and the practitioner should summon to his aid all the means indicated by the special features of the rheumatism, such as hygienic care, special *régime,* warm dwelling-places sheltered from damp; sun, fresh air, physical exercises, dry rubbings, vapour baths, massage, etc.

With regard to the general treatment of **tuberculous iritis,** we have little to say. Good hygiene and life in the open air are recommended. As internal treatment, iodoform has given good enough results; the local application of that agent—perhaps into the anterior chamber, perhaps beneath the conjunctiva—is a subject of study at this moment. Several years ago Abadie recommended in tuberculous iritis massage of the cornea with equal parts of iodoform and lanoline. The results thus obtained were encouraging.

Farther on we shall see that subconjunctival injections have now and then a rapid and salutary action upon miliary tubercles of the iris.

LECTURE XVIII.

Summary.

Diseases of the iris and ciliary body (*continued*).—Recapitulation of general indications for the treatment of iritis.—Subconjunctival injections are rarely indicated in acute iritis.—They succeed well in gummatous iritis and in chronic irido-choroiditis, where all other treatment has failed.—They have, when combined with paracentesis of the anterior chamber, a powerful action.—Traumatic irido-choroiditis and sympathetic ophthalmitis.—Enucleation of the wounded eye.—Mercurial inunctions and strong and oft-repeated subconjunctival injections.—Relapses of sympathetic ophthalmitis, their gravity.

From all the preceding considerations it will be evident how delicate are the indications for the **general treatment of iritis.** That is the reason why our greatest confidence must be placed in local applications.

When, by the means enumerated in the last Lecture, we have succeeded in (1) calming pain, (2) obtaining a dilatation of the pupil, absolute or relative, and (3) extinguishing or diminishing the violence of the inflammatory process, nothing remains except for us to make the disease and its cause disappear. If this is not possible, we must follow the precise indications furnished by the etiology, when the last-named can be clearly determined.

In addition to the fact that this determination, as we have said, is often very difficult, the effects of local treatment are sometimes extremely tardy. It is, therefore, our duty to have recourse at first to all the local means which lead, in the least possible time, to a more speedy and surer cure.

Local applications, as collyria, responding to the general indications, have so far been little used. However, according to the case, ointments or collyria of sublimate, iodide of potassium, salicylate of soda. etc., have been recommended, followed or not by the application

of electrolytic currents. These local interventions, however, have proved themselves to be of lengthened application and of little effect.

A measure that should not be neglected is the use of mercurial friction around the orbit, especially when applied as "mercurial poultices," such as were recommended in the treatment of parenchymatous keratitis (*see* page 160). These applications have the advantage of acting through the warmth and the resolutive action of mercury absorbed by the skin, small though the quantity may be. They are, in short, the first step towards local therapeutics.

In acute iritis, irido-cyclitis, and irido-choroiditis, the indications for the use of subconjunctival injections are more difficult to establish. Indeed, we do not hesitate to affirm that the method is able to render service in the minority of cases only. But rare though its applications be, it constitutes all the same one of our most potent weapons in affections of the uveal tract.

It is almost impossible to repeat too often that mercury is not an antisyphilitic merely, but that it is also a resolutive and a most powerful lymphagogue, to say nothing of its valuable antiseptic properties. Therefore, whenever we want to induce a prompt resorption of pupillary exudations, we must begin with peri-orbital mercurial inunctions, followed by subconjunctival injections—at first, of chloride of sodium, and, later, of cyanide of mercury.

The indications for recognising the timely moment for beginning subconjunctival injections are almost the same as those we laid down for parenchymatous keratitis.

It goes without saying that in avowed syphilis one need never hesitate about the choice of the solution for injection—it is a salt of mercury which should be employed every time that circumstances give us indications for subconjunctival injections.

General treatment, it must never be forgotten, should invariably precede, accompany, and support local treatment, even although the obvious lesions have disappeared after two or three subconjunctival injections. For in the treatment of syphilis we must remember that our duty is to cure, not only current accidents, but also to prevent, as much as lies in our power, ulterior attacks of this redoubtable affection.

In **syphilitic iritis**, when the first assault upon the morbid process has been delivered by means of general treatment and mydriatics, attenuating its violence and preparing the ground for more energetic local intervention, subconjunctival injections of cyanide of mercury may yield very brilliant results.

I have seen cases where, after a fortnight's general treatment, along with the use of atropine, the pupil, having kept its irregular shape owing to posterior synechiæ, has dilated fully after a single injection, perhaps of two or three divisions of 1 : 1000 cyanide of mercury, or perhaps of a half or a syringeful of a 1 : 5000 solution. To arrive at this result, more injections are now and then needed.

Many observations of this kind have already been related by different authors. To obtain the result, the eye must be in a state of receptivity, and the ciliary injection not too marked. In the contrary event, the injections are contra-indicated.

The cases most favourable to the action of the injections are certainly those of **gummatous iritis**, where a yellowish elevation, of oval shape, appears at some point, distorting the pupil, but not associated with very marked hyperæmia. In such cases I have seen large gummata melt away before my very eyes, as it were, after two or three subconjunctival injections. Patients should be warned, however, to submit themselves to prolonged general treatment for fear of relapses, which may be worse than the original disease.

It is not alone in syphilitic subjects that the resolutive action of the injections manifests itself. I can recall to mind an interesting case, where small granulomata of the iris disappeared so quickly under the influence of three or four injections that I concluded that what I had at first taken for tubercles were simply atypical syphilomata of the iris. The patient, nevertheless, died a year after from tuberculosis. I am quite aware that a syphilitic person may succumb to tuberculosis; but it must also be admitted, in the absence of more precise *data*, that in the case of this patient, tuberculosis had commenced with a slight granuloma of the iris. But, whether gummata or tubercles, the activity of the injections is none the less manifest, and nothing could demonstrate better the remarkable power of this method of local treatment.

Every form of iritis or of irido-choroiditis does not benefit in the same measure from subconjunctival injections. Side by side with cases that are improved, sometimes in a surprising way, there are others that are not in the least modified by the treatment. I do not allude to cases where an untimely interference provokes the appearance of an acute outbreak, nor to cases where a badly-performed injection gives rise to so much pain that the patient refuses further injections.

This subject is still shrouded in a certain obscurity. It is sometimes an element of luck that brings success in cases where injections

were tried in despair of anything better. At other times, where we had counted upon a good effect, the results are *nil.*

We must not, therefore, everywhere and always, systematically use subconjunctival injections, since most cases of acute iritis may be cured without them. Such energetic means must be reserved for particular cases, the nature of which has been explained earlier.

If it was once wise to experiment with this new therapeutic measure, in order to acquaint ourselves with its properties, it is now the more natural to avoid its abuse. For our own part, as we have maintained for several years, the use of injections in simple acute iritis ought to be the exception and not the rule. That is to-day the opinion of all those who have had a prolonged experience of the plan.

In **chronic iritis, serous iritis, irido-cyclitis, and irido-choroiditis of slow evolution,** subconjunctival injections have more numerous and important indications. Many such affections have been greatly benefited by the local application of an antiseptic possessing the resolutive properties of mercury.

In some particular case, treated for long by the usual means, the injections may have made a prompt and salutary impression upon the morbid process, so that cure has speedily followed. All cases, however, are not so happy. Very often, after the amelioration produced by local treatment, a relapse comes on sooner or later, and it may then happen that fresh treatment under the same conditions produces nothing more than a mere temporary effect.

Nevertheless, speaking generally, the practitioner will find in subconjunctival injections a valuable adjuvant to general treatment, or even a substitute for the latter, allowing the over-treated organism a wholesome rest. These alternations of local and general treatment can only be very favourable to the eventual cure of the case.

In some **extremely grave forms of irido-choroiditis,** associated with violent inflammatory attacks and glaucomatous tension, where energetic interference is urgent and cannot be delayed without fear of the most serious consequences, there can be no question of practising iridectomy under the circumstances. Well, subconjunctival injections often then render great service, provided they are combined with paracentesis of the anterior chamber, which we have spoken of in the preceding Lecture.

This operation allows the altered fluid of the anterior chamber to escape, and provokes a useful change of the whole ocular circulation. A subconjunctival injection, even when abundant, is then absorbed rapidly, and contributes powerfully to the disinfection and renewal of the intra-ocular fluids.

Truly remarkable results may be obtained by the combination (repeated more or less frequently) of the evacuation of the aqueous humour, and of subconjunctival injections.* One employs in these cases more or less concentrated liquids, according as one foresees that they will be well borne. In general, it is advisable to inject a syringeful of the following solution:

Cyanide of mercury	0·01 gr.
Chloride of sodium	0·10 gr.
Distilled water	50 gr.

There are, on the contrary, cases of irido-choroiditis with raised tension—cases which often terminate in atrophy of the eyeball—where subconjunctival injections have induced such a transformation that more or less complete cure was obtained when the eye was thought to be lost.

A case that I shall never forget was that of a young woman affected for several years with a scrofulous irido-choroiditis, against which treatment, including mercurial frictions, hypodermic injections, and tonics of all kinds, seemed to be powerless. Despite a well-made iridectomy, the eye became more and more cloudy, and its tension fell. Two subconjunctival injections of half a syringeful of 1:3000 cyanide of mercury induced a notable rise in the tension, and, after several other injections, the eye was completely metamorphosed. General treatment and fresh air did the rest, and sight has now remained relatively good for six years. It may be added that two or three relapses, each milder than its predecessor, were cured in the same way.

There are doubtless circumstances where subconjunctival injections fail more or less completely; but in the majority of cases, if the injection is made at the right moment, one almost always obtains, if not a great improvement, at least some amelioration. At all events, one seldom has occasion to regret having had recourse to the little operation, especially since now the latter can be performed altogether without pain, thanks to acoine.

Chronic iritis generally terminates, especially in aged persons or in scrofulous children, in more or less complete loss of vision. It may, in fact, produce an atrophy of the iris, followed by an atrophy of the ciliary processes, which causes a softening of the eye from inadequate secretion of the aqueous humour. This may go on to complete **phthisis bulbi**. The trophic mischief may betray its existence by a gradual opacification of the crystalline lens, thus bringing about a complicated cataract of evil omen.

* See *La Clinique Ophtal.*, 1896, p. 102.

At other times, on the contrary, frequently repeated attacks of iritis leave more or less marked synechiæ, and the entire pupillary border ends by becoming soldered to the anterior capsule of the crystalline lens, when "exclusion of the pupil" is said to be present. The aqueous humour secreted by the ciliary processes can no longer make its way into the anterior chamber. It accordingly accumulates behind the iris, which is little by little pushed forwards until it lies in contact with the posterior surface of the cornea. The iris then forms a pad, in the centre of which the pupil appears as a crater. The usual consequence of this condition is an increase in tension, associated with glaucomatous phenomena, against which it is necessary to act as quickly as possible by performing an iridectomy.

Under these circumstances, the operation is so difficult and delicate that I may recall to your mind the procedure that I recommended some years ago for obtaining a good iridectomy in cases of exclusion of the pupil associated with complete abolition of the anterior chamber.

The iris being completely applied to the cornea, you will perceive how difficult, or, indeed, impossible it is to perform keratotomy without wounding the iris. Many operators do not hesitate to penetrate both the cornea and the iris simultaneously, so as to be enabled to seize the iris from behind, draw it out, and excise it. The apparent simplicity of this operation, however, is likely to be more than counterbalanced by two great drawbacks: first, the cutting of the iris may be followed by hæmorrhage, which at once obscures the entire field of operation, and renders the excision of the iris difficult or imperfect; secondly, the crystalline lens may be wounded, perhaps by the knife, or perhaps by the forceps introduced to seize the iris from behind. That the ultimate result of the operation may be seriously compromised by these complications, you will readily understand.

I was thus led to seek another plan which at first sight appeared more difficult and complicated, but of which the results, to my mind, are better. Its details are as follows:—The eyeball being fixed by an assistant, I take a lance-shaped knife in each hand and penetrate simultaneously the corneal limbus at two opposite points, distant one from the other 6 to 7 mm. The point of each knife should pass through the cornea, and push back the iris without wounding the latter. The two instruments are then withdrawn. Next, by means of a fine, blunt-pointed knife, passed from one incision into the other, the corneal bridge that separates the two incisions is cut.

One has thus an incision of 7 or 8 mm., which opens the anterior chamber widely, without the least bleeding having occurred. The iridectomy may then be practised with great facility under the best conditions possible.

The operation described above may render service under many other conditions—as, for example, in certain cases of glaucoma, complicated cataracts, corneal staphyloma, and, in short, wherever the effacement of the anterior chamber renders incision of the cornea difficult or impossible.

We now come to that form of irido-choroiditis which is in the highest possible degree amenable to local therapeutics and to rigorous antisepsis, namely, **sympathetic ophthalmitis.**

We desire in this place to consider only sympathetic irido-choroiditis, whether the infection arises by direct migration or whether it is merely of endogenous origin by auto-infection favoured by a vaso-motor ciliary irritation, as certain authors have lately claimed.

Simple **sympathetic irritation,** set up by a painful stump, we leave on one side. We mean the simple reflex irritation which at once disappears after removal of the exciting eye.

In our experience, true sympathetic ophthalmitis evolves along the following lines :—an eye has suffered an accidental or operative injury, as the sequel of which a more or less intense infection is brought about. The eye undergoes apparent cure, for if it suppurates completely, sympathetic mischief is never set up. The infection, therefore, remains, as it were, latent in the wounded eye; it invades the ciliary body and afterwards the choroid and optic nerve to make a way through the chiasma to the other eye, where it sets up a typical infectious irido-choroiditis, beginning sometimes in the optic nerve, but not manifesting its existence very clearly until it has involved the ciliary body and the iris.

The difficulty of finding in anatomical preparations the way taken by the infection through the chiasma makes us inquire even now how the passage of sympathetic ophthalmitis from one eye to the other occurs. This question need not be discussed here. One thing is certain, *viz.*, that true sympathetic irido-choroiditis is recognised by everybody as a process of infectious origin.

What must be the treatment of sympathetic ophthalmitis ?

Here we have to do with experimental human pathology; the cause of the malady is known—that is to say, we are aware that it is due to a microbic infection, having its place of origin in the eye

wounded.

The primary indication, therefore, should be to remove that eye as the original source of infection, without concerning ourselves unduly about any sight it may chance to retain.

The eye once removed, and the optic nerve cut as far back as possible, a syringeful of a 1 : 500 solution of cyanide of mercury is injected into the bottom of the orbit as far as the optic foramen, or even, if possible, into the nerve or its sheath. Afterwards, taking advantage of the narcosis needed for the enucleation of the eye, a syringeful of a 1:1000 solution of cyanide of mercury is injected deeply under the conjunctiva behind the globe of the sympathising eye.

Both orbits are covered with a dressing. On the following day the patient is submitted to an energetic mercurial course by the daily inunction of four grammes of mercurial lanoline. As soon as the injection is absorbed and all chemosis has disappeared (on the average on the fourth day) one must not hesitate to practise a second injection, the effects of which are kept up by the application of two or three leeches to the temple. The abstraction of blood will diminish the ciliary congestion and the chemosis produced by the injected fluid.

In the interval between the injections, some drops of the following solution must be instilled every hour or half-hour:

Sulphate of atropine	0·05 gr.
Dionine	0·10 gr.
Hydrochloride of cocaine . . .	0·10 gr.
Cyanide of mercury, 1 : 1000 . .	10 gr.

In proportion as improvement manifests itself by a fuller dilatation of the pupil, a diminution of the exudation upon the posterior surface of the cornea, and the disappearance of photophobia and circumcorneal hyperæmia, the number and strength of the injections are diminished. Care must nevertheless be taken not to stop all treatment prematurely, inasmuch as relapses of sympathetic irido-choroiditis, more than any others, are pernicious to the last degree. Indeed, one risks the power of remaining master of the situation if one has allowed relapses to make insidious progress by having failed to push the treatment far enough to extinguish every trace of infection.

That the task is difficult cannot be disguised, and it needs all the help of the patient and all the tenacity of the practitioner to bring to an end an established sympathetic irido-choroiditis. Relapses may, in fact, be seen even after years of apparent cure.

Quite recently Dr. Abadie has related a very curious and interesting case. It was that of a young lady, from whom, twelve to fifteen

years ago, we had together enucleated an eye, on account of sympathetic ophthalmitis. After an intensive cure by mercurial frictions (we did not then know of subconjunctival injections) the disease was cured, but the patient nearly died from a most acute nephritis caused by hydrargyrism.

Briefly, the patient (now a governess), after twelve to fifteen years of perfect sight, was seized several months ago with grave irido-choroiditis of her remaining eye. A transient improvement was brought about by several subconjunctival injections combined with inunction, but it was not maintained, and soon the eye became much worse and was threatened with atrophy. The idea then occurred to Abadie of injecting into the orbit of the enucleated eye, at the level of the stump of the optic nerve, as deeply as the apex of the orbital cone, a 1 per cent. solution of cyanide of mercury. In the course of several days he thus obtained an almost complete cure.

At almost the same time there returned to me a young woman whom I had cured of sympathetic ophthalmitis three years before by enucleation, subconjunctival injections, and inunctions. She came with a fresh attack of irido-choroiditis, with complete seclusion of the pupil and obliteration of the anterior chamber. An iridectomy having failed to stop the inflammatory attacks, I made on two occasions an injection of a syringeful of a 1 : 500 solution of cyanide of mercury into the apex of that orbit from which the eye had been taken out. The very violent pain was calmed by the application of three leeches to the temple, and at the end of some days, several injections having been made in the meantime, the patient was completely cured. Two years have passed, and the patient, who has resumed her work, has not experienced the least trouble as regards her sight. She returned to me three weeks ago with vision of $\frac{1}{2}$.

Abadie, to explain these facts, believes that the infectious process, which originally affected the enucleated eye, had already, at the moment of the operation, passed the limits of the eyeball and invaded the optic nerve. It remained fortified, as it were, at this point for a longer or shorter time, and then (under the influence of causes yet unknown) the virulence of the infectious germs was exalted, and invasion of neighbouring parts and of the other eye took place anew. The sole means of arresting this process is to inject *in situ*, in the vicinity of the infectious focus, some drops of a strong solution of cyanide of mercury. Apart from the foregoing explanation, might one not also maintain that the orbital injection acted by contiguity of tissue in producing an antiseptic irrigation of all the lymphatic spaces in which the morbid process was in train of evolving?

My long experience of subconjunctival injections has shown me that an injection made on one side often manifests its therapeutic action equally upon the second eye.

In some circumstances it is possible to stop sympathetic ophthalmitis, and yet to preserve both eyes. Since the introduction of subconjunctival injections into ocular therapeutics, several such cases have been published, and I know more than one observer who can quote instances of the kind from his own personal experience. But the risks to be run are so great (as both eyes may be lost as the result of a delayed enucleation) that if one wished to lay down a general rule for the guidance of young practitioners, it must be that which gives the maximum security.

Enucleation, therefore, should remain the rule in the majority of cases, and, indeed, the absolute rule when the exciting eye does not lend itself to any hope of the restoration of useful sight.

On the contrary, when the mischief is only beginning and both eyes retain relatively good sight, it is natural to adopt a conservative treatment before resorting to enucleation. This is how we understand that requirement. We have already, in the lecture on injuries of the eye (*see* page 142, *et seq.*), described the way of stopping traumatic infections:—(1) Cauterising with the galvano-cautery all infected parts of the wound, penetrating with the wire at a white heat into the crystalline lens, or even into the vitreous body; (2) covering the wound, after cleansing and perfect freshening of its edges, with a conjunctival flap, kept in place by several sutures; (3) injecting a syringeful of 1 : 1000 cyanide of mercury solution deeply into the orbital tissues.

Thanks to this energetic treatment, I believe that I have saved many grievously wounded eyes amongst the workmen of the numerous factories at Saint-Denis, and I do not exaggerate when I say that by this means I have avoided sympathetic complications.

But when this formidable complication has just declared itself, when the wounded eye shows relatively slight anatomical lesions, one is justified, at least for the first few days, in trying to extinguish on the spot the first indications of sympathetic infection. In order to accomplish that, we must act with an energy that might appear excessive to any one who has not had often to fight against such a terrible enemy as sympathetic ophthalmitis.

It is usually necessary to anæsthetise the patient. The wou[illegible] which the infection has penetrated, must be reopened, the[illegible] seared with the galvano-cautery, carefully cleansed, an[illegible]ered with a conjunctival flap; a syringeful of 1 : 500 or 1 : 1000 solution

of cyanide of mercury must, lastly, be injected beneath the conjunctiva. As regards the sympathising eye, which must be kept deeply under the influence of atropine, one makes equally an injection of cyanide of mercury, 1 : 1000, deeply behind the eyeball towards the apex of the orbit, and, after that, three leeches are applied to the temple.

Beginning from the next day, the patient is submitted to an intensive cure by mercurial inunction, accompanied by instillations every hour or half-hour of the collyrium of 1 : 1000 cyanide of mercury, dionine, and atropine. Since one cannot be certain that all infection is extinguished, the subconjunctival injections are repeated as soon as the absorption of the last injection is complete.

The first few injections, which cannot be made in such strong doses as when the patient was under the influence of chloroform, take three or four days to be resorbed. It is at this moment only that improvement shows itself. This is frequently so striking that one may allow one's self to remain inactive, but that is often a great mistake. So redoubtable an affection as sympathetic ophthalmitis must be felled to the ground. In these cases it is better to err on the side of excess rather than lack of care.

Many cases of sympathetic ophthalmitis have been cured without operation. But the greatest prudence must be exercised, and in truly serious cases, we repeat, we must not hesitate to enucleate.

Where it is feasible to introduce into the anterior chamber a morsel of iodoform, as recommended by Haab, it is perhaps a valuable adjuvant, but one of which I have as yet no personal experience. It goes without saying that no foreign body has been left in the wounded eye. Haab's proposal represents a very interesting application of local therapeutics, and as such deserves to be studied seriously.

Roemer, at the last Heidelberg Congress, concluded from his observations that iodoform acts only against ordinary pyococci, as staphylococci, and this conforms to the experiences of Ostwald.

LECTURE XIX.

Summary.

The treatment of glaucoma: iridectomy is the sole treatment that can really be recommended; medicamentous treatment should rarely be applied.—The latter is merely palliative, and often causes valuable time to be lost, and compromises the final results of an iridectomy.—Sclerotomy also is but a palliative, or at most an adjuvant, useful only when one apprehends complications with iridectomy.—Detailed indications for methods of treating the various forms of glaucoma: acute and chronic glaucoma, chronic irritative glaucoma, chronic simple glaucoma or glaucomatous atrophy.

To continue our study of the treatment of diseases of the uveal tract, we shall to-day occupy ourselves with **glaucoma**, a most malignant malady, and one considered to be incurable not so very many years ago.

Since the remarkable work of von Graefe, the treatment of glaucoma has been well established, and iridectomy remains the best treatment in the great majority of cases, not to say in all cases, of acute glaucoma, since we can never say what the future will bring. Who knows that it may not be reserved for one of us to find a cure for glaucoma without operation? In fact, will it always be necessary to operate in every case?

May it not come about that slight attacks of glaucoma may relapse two or three times and then disappear, perhaps under the influence of some medicinal treatment or perhaps spontaneously, the occasional cause having vanished and the predisposing constitutional state having been improved?

I always remember a case of acute glaucoma with cloudy cornea, tension + 2, fundus of the eye unexplorable, and violent pain. I advised an iridectomy, which was to be performed on the following day. In the meanwhile I prescribed a collyrium of eserine; three grammes of salicylate of soda a day; and 0·50 of quinine at night.

Next day the patient felt so much better that he did not return for the operation, and a week later he was completely cured. This cure was maintained for several years, during which period he suffered from no fresh attack. Fifteen years have now elapsed. This patient was still young, 38 years, which is doubtless an important factor in the case.

In many other cases, attacks—slight, it is true—disappear spontaneously, a fact that has given them the name of **prodromal glaucoma**. However, these attacks are rarely arrested, despite eserine and pilocarpine, despite the best devised general treatment, and in the end the patient is compelled to resign himself to operation.

Rheumatism and gout have a very marked influence upon the pathogeny of chronic irritative glaucoma, as observers have noted for long.

Czermak has established a theory of glaucoma based upon a pathological alteration of the vessels consecutive to rheumatism, gout, atheroma, arterio-sclerosis, senility, etc.*

Wagenmann,† by means of a suitable anti-gouty treatment, has obtained good results in certain forms of glaucoma, with or without iridectomy.

Walter ‡ praises the anti-gouty properties of piperazine in preventing attacks of glaucoma and in aiding the operative treatment. He relates cases cured for the time being without iridectomy.

Many cases of glaucoma have been reported as cured in the most various ways. The greater number has been by myotics, employed persistently in feeble and frequently repeated doses. Pilocarpine is better supported than eserine, which readily provokes ciliary pain; sometimes these pains are even accompanied by a state of nausea, which tends to render the application of the agent less regular, because the patient dreads its employment.

Pilocarpine should be prescribed in weak and oft-repeated doses.

We have seen in the eighth Lecture, devoted to the study of the most powerful vaso-constrictor known, the part that supra-renal extract may play in the treatment of glaucoma. We were the first to note the action possessed by adrenaline of reducing tension in glaucoma.

Zimmermann has confirmed clinically by several interesting observations the very marked diminution of intra-ocular tension in the glaucomatous, and even in the normal eye.

* *Prag. med. Woch.*, 1897.

† *Archiv für Oph.*, xliii.

The interesting observations made by Wessely in Leber's laboratory have, as we have seen, given us a complete explanation of the clinically observed facts.

Adrenaline, combined with myotics, as eserine or pilocarpine, is able, then, to render real service in the medical treatment of glaucoma (*see* Lecture VIII for the dose).

In one of the forthcoming Lectures we shall study the marked action of **massage** upon the intra-ocular tension. It is a surprising thing to see, after massage for several minutes, the eye become soft, both in healthy persons and in those suffering from glaucoma.

If one tries to explain this particular effect of massage in reducing tension, one must suppose that stronger and stronger pressure, applied perpendicularly to the cornea, flows back in obedience to the law of the incompressibility of liquids, and the iris and the crystalline lens, dilating mechanically the angle of the anterior chamber, and expressing, so to speak, the aqueous humour, which then escapes by the natural channels of excretion.

You may see all the practical advantages that may be derived from this mechanical action, which, under all circumstances, is within anybody's reach.

At the present time I have several glaucomatous patients, iridectomised or not, who derive real benefit from massage.

Domec, of Dijon, to whom we are indebted for several excellent works on the action of massage, has published some observations of attacks of acute glaucoma rapidly stemmed by frequently repeated massage.*

Certain cardiac medicaments have also a favourable action on glaucoma owing to their vaso-constrictor properties. In the first place we quote quinine, then digitalis and the remaining cardiosthenics, as convallaria majalis, strophanthus hispidus, bromide of potassium, etc.

Allow me to quote an example of glaucoma kept in check for more than three years without operation. It is of real therapeutic interest. It may perhaps serve to give you the indications respecting cases that may be cured by simple medicinal treatment.

A young man, 32 years of age, of corpulent habit, loving wine and good cheer, consulted me on May 13th, 1898, complaining of a notable reduction of sight in both eyes.

The eyes were large, projecting, hyperæmic, and hard. R.V. = $\frac{1}{3}$, T. + 1·5; L.V. = $\frac{1}{2}$, T. + 1. No hypermetropia or astigmatism.

* *La Clinique Ophtal.*, 1899.

The discomfort experienced by the patient is greater than the defect of sight as measured on the types,—that is a phenomenon seen often enough in glaucoma; where we find patients who have been operated on retaining sight of $\frac{1}{2}$ or $\frac{2}{3}$, we say that they see very badly. The visual field, in the left eye a little contracted on the nasal side, presented in the right eye an infero-internal scotoma, especially well-marked as regards colours, green scarcely passing the median line; no central scotoma.

I gave the patient a glimpse of the necessity of an approaching operation, and in the meantime prescribed a very severe *régime*, including abstention from tobacco and alcohol, and a calm and regular life, and repeated instillations of a collyrium of pilocarpine and eserine, along with one gramme of bromide of potassium and 0·30 of quinine daily internally.

Four days later the sight was much better (R.V. = $\frac{2}{3}$; L.V. = 1); the visual field was enlarged, but the intra-ocular tension remained above normal. The patient was very satisfied, and wished to hear no more about any operation. I then prescribed Jacquet's extract of supra-renal capsule with pilocarpine and eserine.

The rigid *régime* was followed regularly, and corneal massage was practised as often as possible. The latter invariably reduced the intra-ocular tension markedly. In brief, on July 1st the patient was able to look upon himself as cured, at all events relatively, and for the time being. R.V. = 1; L.V. = 1. The visual field of the right eye still presented a well-defined infero-internal scotoma for colours only. The optic disc manifested an obvious excavation, especially as regards the right eye. The tension of both eyes remained a little above normal. The patient, who has been seen frequently during the last three years, has not had the slightest return of glaucoma.

With regard to the foregoing case we may remark that the first signs came on in a rheumatic subject, still young, after excesses of all kinds. The hygienic conditions having modified profoundly the constitutional state, and treatment by myotics, adrenaline, and massage having brought about a complete cessation of the glaucomatous troubles, the patient may perhaps consider himself as cured.

Certainly the above is a well-marked case of glaucoma apparently cured for three years. Will the cure be permanent? Who can affirm that fresh excesses will not be followed by new attacks? Should new attacks come on, we shall perhaps regret not having operated earlier. But we cannot, lastly, compel patients to submit

cataract, able to guarantee that surgical interference will almost certainly restore sight.

Without wishing to go deeply into the pathology of the affection (which is still known but imperfectly), we may say that glaucoma is due to a sudden increase of the intra-ocular tension, provoked probably by a reflex vaso-dilator action, which upsets the balance of the nutritive intra-ocular exchanges.

It must now be admitted that the "soldering" of Knies—that is, obliteration of the paths of elimination by the irido-corneal angle—is a lesion associated with, rather than the cause of, glaucoma.

On the other hand, obliteration of the angle and the reduction of the surfaces of resorption are states predisposing to glaucoma; they are often seen in senile persons and in those suffering from arterio-sclerosis, gout, etc. The vitreous body, in a state of hyper-distension, pushes forward the crystalline lens and applies it to the iris, and, according to some, closes the pupillary valve, through which the surplusage of the posterior chamber can no longer pass.

In order to cure glaucoma, it should therefore suffice, according to the last theory, to make an artificial pupil, so as to allow of the posterior liquids passing into the anterior chamber, thence to escape from the eye by the natural channels of elimination, namely, the irido-corneal angle and the anterior surface of the iris.

This explanation of the action of iridectomy in glaucoma is seductive by reason of its simplicity; but, as it has failed to satisfy all the critics, others have been sought.

The nervous theory—that of the action of the great sympathetic—has recently commanded many and important suffrages.

According to Abadie, to whom we owe the sympathetic theory of glaucoma, the disease is due to an excitation of the vaso-dilator nerves, which, in traversing the superior cervical ganglion, go to the uveal tract by different paths, and reach the eye by following the principal nerves.

In acute and subacute glaucoma, the irritation of the vaso-dilator centre by the superior cervical ganglion should be produced by a reflex starting from the iris, and, above all, from its sphincter.

According to this theory, in order to stop the attack of glaucoma, it should therefore suffice to interrupt the reflex arc by practising an iridectomy, or even, perhaps, a simple section of the iris embracing the sphincter.

Simple chronic glaucoma may be assigned to a primary and

chronic affection of the great sympathetic. The only treatment likely to benefit it, therefore, would be sympathectomy.

Hydrophthalmos or buphthalmos—which is, in sum, a simple chronic glaucoma in infancy—should be amenable to the same treatment.

If we wish to get an exact idea of the therapeutic action of the different means employed in the treatment of glaucoma, we must know something of the chief theories by which the pathogeny of that formidable affection has been explained.

Let us pass them quickly in review.

We have seen that glaucoma is characterised by an increase of the intra-ocular pressure, and this may be due either to hypersecretion or to a retention of fluid. Von Graefe admitted a hypersecretion the result of a species of serous choroiditis.

Donders attributed the hypersecretion of fluid to a vaso-motor reflex through the ciliary nerves, a kind of secretory neurosis in which Dr. A. Terson believes to-day.

Stellwag believed that it was connected with a simple increase of blood-pressure in the vessels of the eye. That view is also shared by Abadie, who assigns to the sympathetic the chief *rôle* in the production of the dilatation.

Knies and Weber, as we have seen, explain the increased intra-ocular pressure by a venous stasis, which causes the ciliary processes to swell so much as to push the iris against the cornea and to obliterate completely the irido-corneal angle and the excretory channels of the aqueous humour.

All these theories only half satisfy one's curiosity.

At the last Congress of the French Ophthalmological Society (May, 1902), Dr. Zimmermann, of Stuttgart, propounded a new theory, seductive and complete enough to explain all the pathological conditions found in the various forms of glaucoma.

According to Zimmermann, glaucoma is due to a disturbance of the equilibrium which should normally always exist between blood-pressure and intra-ocular tension. This equilibrium may be disturbed (1) by excess of primary intra-ocular tension (iritis, synechiæ, swelling of cortical remains, etc.); (2) by diminution of the blood-pressure, such as may be brought about by an acute or chronic affection of the heart or vessels, or under the influence of a physical or moral shock. Briefly, in one way or another, the blood-pressure being lower than the ocular tension, the blood-wave conveyed by the retinal artery has no longer the force necessary to overcome the resistance opposed to it, and this is especially the case because of the angle formed

by the artery on entering the retina. It is then that one sees an arterial pulse in glaucoma on examining the eye with an ophthalmoscope.

Retinal ischæmia is thus induced, the nutrition of the capillaries suffers, lymphocytes transude, and the exudation of serum brings about a kind of œdematous infiltration, which helps in its turn to raise the intra-ocular pressure. As regards the ciliary processes, the infiltration is the more marked as the long ciliary arteries traverse the sclerotic without making angles; the blood-supply would take place more easily than for the retinal arteries. On the other hand, the ciliary veins with their fine walls are compressed by the excess of intra-ocular tension. From all this there comes about a ciliary hypersecretion, and then a swelling of the entire ciliary body, which compresses the irido-corneal angle, etc.

This theory appears satisfactorily to explain all the facts, from a simple chronic glaucoma, due to a chronic, as it were, arterial hypodistension, to an attack of acute glaucoma provoked by violent emotion, passing through all the intermediate forms of acute and chronic irritative glaucoma. Before the theory, however, can be generally adopted, it must first be examined in the light of clinical observation, and tested by experimental therapeutics.

Zimmermann has already brought together forty cases which, from his point of view, are conclusive; when they have all been published, we shall be in a position to discuss the theory with a better knowledge of the facts.

The therapeutic results that may follow this novel conception of the pathogeny of glaucoma have important bearings, especially from a preventive point of view, and even as regards the treatment of certain forms of the disease. But we shall always regard iridectomy as the best treatment of confirmed glaucoma.

According to Zimmermann's views, an attack of glaucoma could easily be aborted by giving to the patient a cardio-vascular tonic capable of re-establishing the equilibrium between the ocular tension, on the one hand, and the blood-pressure, on the other.

From the practical point of view, let us review the treatment of the various forms of glaucoma that may come before us.

1. A patient consults us with a slight attack of **acute glaucoma.** The cornea is somewhat dull; the tension is raised; the pupil a little dilated; the eye more or less reddened; the visual field is sometimes contracted as regards the nasal side; and there is moderate headache.

The patient, who has never had an attack before, is clearly rheumatic, and attributes the trouble to a chill.

In such a case, before practising an iridectomy, we may calm the pain with dionine, prescribe a collyrium of eserine and pilocarpine,* and at the same time administer 3 or 4 grammes of salicylate of soda in the day, and 0·30 to 0·50 centigramme of quinine at night.

The first applications of the myotics should be made by yourself. The effect of the remedy may be kept up or increased by corneal massage, which favours the elimination of the aqueous humour, and notably reduces the intra-ocular pressure. Zimmermann, in these cases, recommends cardiac tonics, especially tincture of strophanthus in eight-drop doses three times a day. He thus obtains a rapid augmentation of arterial tension, the lowering of which, as we have just seen, is, according to Zimmermann's views, the primary cause of the glaucoma.

If, however, under treatment a marked improvement is not apparent after two or three days, one must hesitate no longer about doing an iridectomy, the performance of which will have been facilitated by the adoption of the means described above.

Indeed, under such circumstances the patient must not be lost sight of for a single instant, and we must not wait even until the next day if the glaucomatous process shows the least tendency to become worse rather than better under the influence of the treatment applied. In the contrary case, if a manifest improvement is produced in the sense that sight returns and tension is reduced, we may wait and seize the most favourable moment for surgical intervention.

If the attack passes away completely, and the patient is young, with his vascular system in good condition, and if he resides near the oculist, a fresh attack may be awaited before operating. In the meantime one prescribes a good *régime* and hygiene and treatment appropriate to the supposed cause of the trouble. On the contrary, if we have to do with an aged subject or one who suffers from arterio-sclerosis, an operation should be performed even when the attack has passed away. The operation will then only be easier, and present a very good chance of success.

2. We are faced with a case of **hyperacute glaucoma**, associated with violent pain, leading sometimes to nausea and vomiting. The

* Collyrium of adrenaline:

Hydrochloride of pilocarpine	0·05
Salicylate of eserine	0·02
Solution of adrenaline, 1 : 5000	10 gr.

S.—*One drop to be used every hour.*

eye looks green, and is hard as a marble; the pupil, of oval shape, is dilated; and the iris is applied to the posterior surface of the almost insensitive cornea.

Iridectomy should be done as quickly as possible; but still it is necessary to be able to perform the operation in conditions that assure a good result. Many authors, under these circumstances, recommend that an **equatorial puncture** be first practised, so as to lead to a cessation of the pressure and of all the self-styled inflammatory phenomena. Iridectomy is performed several hours later, or even next day; the cornea is then often markedly clearer, and the anterior chamber is sufficiently re-formed to allow of the incision in the cornea being made by the usual method.

Equatorial sclerotomy is a very good operation in the condition just described. It is, however, not devoid of danger. For example, it may provoke a retinal or choroidal hæmorrhage, which may readily compromise the final result of an iridectomy. If one can dispense with it, therefore, so much the better.

One should endeavour to bring the affected eye into a more favourable state for operation by attempting in the first instance to calm pain with dionine. The latter is prescribed, combined with myotics, in the following form:

Dionine	0·10 gr.
Hydrochloride of pilocarpine . . .	0·05 gr.
Salicylate of eserine	0·02 gr.
Distilled water	10 gr.

S.—*One drop to be placed into the eyes every half-hour until the following day.*

The first instillations smart somewhat, and often set up a pronounced chemosis with intense watering of the eye, after which there is a notable decrease in tension and a complete disappearance of pain. The operation may often then be performed.

The application of leeches to the temple and the administration of cachets of antipyrine and phenacetine (*see* page 165) second the effect of the dionine drops, if the latter do not suffice to rid the patient of pain.

Massage, applied very lightly at first and then more and more energetically, in proportion as it is well-borne, now and then brings about a marked reduction in tension, and aids in re-establishing the anterior chamber.

As already pointed out, salicylate and quinine have also valuable indications in some cases.

The next day, or even the same day, a relative lull will be pro-

duced; the pupil will be a little contracted, and the anterior chamber deeper. No more is needed, and we hasten to perform iridectomy.

Chloroform should be used in most of the cases of hyperacute glaucoma, for one can rarely obtain with cocaine sufficient anæsthesia of the eye, on account of its congested state.

Nevertheless, in many cases one is obliged, perhaps by circumstances or perhaps by the desire of the patient, to practise iridectomy without narcosis. In order to obtain as deep an anæsthesia as possible, it is advisable to employ adrenaline combined with cocaine and eserine.*

By these means, the keratotomy is rendered practically painless. The incision should always be made with the knife, and not with the keratome, which is liable to wound the crystalline lens, lying in close contact with the iris, in consequence of the intra-ocular pressure. If the point of the knife touches the iris in passing, the patient complains of a lively pain, or makes a sudden movement, which may possibly cause a traumatic cataract. The greatest possible care should be exercised in performing this operation. The cornea once incised, it is necessary to take care not to introduce the forceps at once into the anterior chamber; it is better at first to instil, perhaps over the open wound, or perhaps even into the anterior chamber, one or two drops of an aseptic solution of cocaine. The few moments' rest allows the patient better to bear the section of the iris, the most delicate and painful step in this perilous operation, which it is of the greatest consequence to perform correctly, since upon this point depends the final result.

An imperfect section of the iris may be the cause of synechiæ, which are frequently obnoxious to cure. On the other hand, if the lens has been touched with the forceps or knife, a cataract may follow, and this will annihilate sight for a longer or shorter period. An injection of morphia into the temple, a quarter of an hour before the operation, is always of signal assistance.

3. We have to deal with a patient who at various times has suffered from **glaucomatous attacks of a more or less acute nature and duration.**

We find in time all the classical signs of chronic irritative glaucoma.

The patient complains of seeing coloured aureoles around lights; his sight is dim; and he sometimes experiences a more or less pronounced headache. With the perimeter we find a marked scotoma in the nasal half of the visual field. The cornea, which is little or

* *See* Lecture VIII, Extract of Supra-renal Capsule.

not at all cloudy, allows us to recognise at the fundus of the eye an excavation of the optic disc. The eyeball is manifestly hard.

In such cases one should not hesitate, but proceed to operation as promptly as possible; and, generally speaking, the result will be very good. After the operation, sight returns almost to what it was before the last attack.

4. Lastly, we have to do with **chronic simple glaucoma**—*i. e.*, with one of the forms of glaucoma that lacks, as it were, all the cardinal symptoms of that malady. There is never the least dulness of the cornea; the pupil is not dilated; the eye is scarcely hard; and there is no pain. However, these patients often suffer from migraine.

Sight becomes progressively worse, and the visual field gets more and more contracted, although the nasal scotoma, which is almost pathognomonic of irritative glaucoma, is not invariably present.

Were it not for the retention of the colour-perception, the visual field might be mistaken for that of optic atrophy. As a matter of fact, the optic disc is atrophied and deeply excavated. Moreover, von Graefe himself, in his earlier publications, placed the affection outside the glaucomatous group, and regarded it as "an atrophy with excavation of the papilla." Later, he changed his opinion, and classified the disease as chronic simple glaucoma.

The characteristic feature of glaucoma is a rise in intra-ocular pressure, the anatomical stigma of which is cupping of the optic disc. The fact that augmentation of tension can rarely be demonstrated in simple chronic glaucoma is no proof that such does not exist. It may be intermittent, showing itself only in the night or during certain physiological acts, efforts of accommodation, or during activity, physical or psychical, and then only at rare intervals. But all these moments, added one to another for years, are enough at length to cause cupping of the optic discs.

For myself, I am a believer in the unity of glaucoma, since one may meet amongst the different members of a single family with all forms of the disease, with an individual evolution for each one—an affair of temperament or of circumstances.

As regards treatment, therefore, one must admit that an iridectomy is still the best thing we can offer to patients. It is unfortunate that generally they do not consult us until the optic disc is profoundly atrophied.

The operation done at the commencement gives good results, but much inferior to those obtained in the other forms of glaucoma. Lack of success, we must recognise, is common. That is what makes

many practitioners deny that iridectomy has any action in glaucomatous atrophy.

Indeed, the question of surgical intervention is most delicate in an affection of progressive and almost fatal progress. Accordingly, the practitioner must surround himself with all possible precautions and reservations.

The surgeon must not employ myotics for too long in this disease, for that is to expose one's self to the risk of operating too late. He should also bear in mind that the various kinds of sclerotomies lately praised have merely a passing and often illusory action. They serve to feel the ground in view of an approaching iridectomy, the only operation worthy of our confidence; and yet, alas! we are often betrayed even by it.

As to **sympathectomy**, that operation must be studied more fully before it can be recommended to the practitioner. It belongs, in point of fact, rather to the domain of general surgery. Nevertheless, it has already rendered service in cases where all other treatment had failed.

LECTURE XX.

Summary.

The treatment of glaucoma (*continued*): example of the inadequacy of medical treatment.—Iridectomy should be performed as near the beginning of the disease as possible.—It is the most delicate operation in eye surgery.—Operative faults are often credited to the account of malignant glaucoma.—Hæmorrhagic glaucoma; glaucoma by sympathy.—Results obtained from iridectomy in the different forms of glaucoma.—The treatment of diseases of the choroid and retina: the importance of rapid and intense treatment in macular choroiditis.—Subconjunctival injections alone respond well to this desideratum by their selective action, so to say, on the choroid in direct communication with the subconjunctival spaces.

In our last Lecture we studied the indications for **iridectomy** in the different forms of glaucoma. But the question is so important and interesting that I shall quote one more observation, which will show you that, in spite of the great benefit that may be obtained from medicinal treatment, it is almost always necessary in the end to resort to iridectomy, especially in persons of a certain age, with more or less arterio-sclerosis.

The analgesic and lymphagogue action of dionine favours the rapid and powerful action of myotics; reduction of tension by massage and surrenaline; counter-proof by means of mydriatics; complete restitution of the sight and visual field, pallor of the optic disc, scarcely appreciable excavation; new attack; iridectomy; cure.

M. H—, aged 65 years, jeweller, had always suffered from a little dulness of sight as regards his right eye, which he attributed to work with his jeweller's magnifying glass. Lately, he had often remarked that with this eye he saw coloured nimbuses around lights.

On March 10th, after a violent emotion, M. H— experienced a lively pain in the right eye and brow; the sight became quickly blurred; and pain invaded the whole of the right side of his head. On March 17th the patient came to me with all the symptoms of

a grave attack of hyperacute glaucoma. The eye was extremely red and watery; the iris was almost fastened to the cornea, so much was the anterior chamber obliterated; the oval pupil was little dilated, although it is true that on the other side there was very marked myosis; the tension was *plus* 2 or 3; sight was reduced to perceiving movements of the hand at 0·30 centimètre; and the patient, who was in a state of marked prostration, complained of a violent headache allowing him repose neither by night nor by day.

In view of the violence of the symptoms, I dared not perform an iridectomy then and there. At first, therefore, I tried to calm pain by repeated instillations of 5 per cent. dionine. The latter produced a very marked chemosis, with swelling of the eyelids, watering of the eyes, and sneezing. At the end of an hour, the patient felt himself relieved; notwithstanding the swelling of the eyelids, he could expose his eye more readily to light, the cornea was more brilliant and transparent, and the sight was so much improved that he could not only count fingers at one mètre, but was able also to read the first rows of Snellen's optotypes at 0 m. 50. The tension seemed to be clearly reduced: T. + 1·5.

With the intention of performing iridectomy under the best conditions, I made an appointment with the patient for the following day.

Meanwhile I prescribed—

Dionine	0·10 gr.
Hydrochloride of pilocarpine . .	0·05 gr.
Distilled water	10 gr.

S.—*A drop of this collyrium to be instilled into the inflamed eye every half-hour.*

The following day, to my great surprise, the condition had undergone a profound change. The patient said that he had slept well and had no pain. The eye was still very red, and its tension was + 2, but the sight was almost equal to that of the other eye. R. V. + 1·25 = $\frac{2}{3}$. L. V. + 1·5 = 1. The visual field was normal on both sides. With the ophthalmoscope, nothing tangible was seen as regards the papilla, examined with difficulty through the narrow pupil. The pupillary border of the iris was slightly adherent to the crystalline lens.

Several *séances* of pressure-massage practised during the course of the afternoon, caused all excess of tension to disappear. Massage and the same collyrium were continued daily. After each application of the first-named, it was noticed that the tension, at first elevated, became normal or almost so.

On March 20th the patient was very well. He had no more pain,

but sight was slightly reduced (R. V. + 2·0 = $\frac{1}{2}$), and the visual field was clearly contracted with an infero-internal scotoma.

The patient, who regarded himself as free from the prospect of any operation, was distressed when I gave him to understand that, despite all efforts, an iridectomy would be necessary. Nevertheless, moved by his entreaties, I promised him I would try other measures, and while keeping up the massage, the following collyrium was prescribed:

Hydrochloride of pilocarpine . .	0·05 gr.
Sulphate of eserine	0·02 gr.
Adrenaline 1 : 4000	10 gr.

S.—*One drop of this collyrium to be dropped into the affected eye every hour.*

Two leeches were also applied to the temple, and a calomel purgative administered. After this treatment had been followed for three days, on March 23rd, the visual fields had become normal, while the sight (with + 1·25 lens) was $\frac{3}{5}$ normal. Although the tension was still a little elevated (+ 1), it always fell to normal after massage, which was practised three or four times during the course of the consultation. On April 17th—that is, one month after the first visit—the patient was cured.

Two months later there was a violent enough relapse, less influenced by the foregoing treatment. Iridectomy was performed on the third day, without chloroform or much pain. The patient was now completely cured, although, to obtain passable vision, he needs astigmatic glasses.

Some authors have obtained good results in glaucoma by **subconjunctival injections of saline water.** Speaking for myself, I have never cared to adopt them in the presence of an affection so grave as idiopathic acute glaucoma, since I feared to set up too much irritation in an eye, the tension of which was already raised.

However, this would be an interesting study to follow out, as in glaucoma secondary to a grave iritis or irido-cyclitis, very brilliant results have been obtained by the combination of subconjunctival injections and paracentesis of the cornea (page 173).

Puncture, by evacuation of the infectious fluid contained in the anterior chamber, and by lowering the intra-ocular tension, places the eye, primarily unfavourable to the action of medicamentous agents, in better conditions, so that one is right to try subconjunctival injections. The injected liquid then acts at once as an antiseptic, stimulant, renovator of the nutrition of the tissues, and as

a cleanser of the paths of elimination obstructed by inflammatory exudations.

Upon this subject you may refer to a very instructive observation published in 1896.*

It is quite likely that in subinflammatory glaucoma subconjunctival injection of saline water, combined or not with paracentesis or sclerotomy, is able to yield a favourable result, especially if to this treatment one adds massage and the collyria of which we have already spoken.

A remarkable phenomenon, and one that is seen often enough, is what one may call **glaucoma by sympathy.** We allude to those cases where, after the performance of an iridectomy on one eye, the second eye is seized with an attack of acute glaucoma the next day or two or three days after the first operation. The eye has often been until then quite healthy, but at other times several minor attacks of prodromal glaucoma have occurred in it.

To prevent this serious complication, it is always indicated, when operating upon the first eye, to place the other under the influence of myotics, particularly when premonitory signs, as aureoles, have already been noticed in the latter.

Most authors recognise this provocative influence of iridectomy in bringing about that which we have just described as glaucoma by sympathy, and all advise that it be operated on as speedily as possible. It is thus that we ourselves have acted until the last few years; but we now think that by temporisation with the therapeutic means enumerated above, one may succeed in curing the attack of glaucoma and those which are liable to follow it. In this way we may obtain a definite result as good as that got from iridectomy.

Must not one admit that in such cases an iridectomy having provoked a violent initial reaction afterwards exerts an inhibitory action, which allows us to succeed in curing the second eye without an iridectomy?

That is a question that deserves careful study with numerous observations in its support. The treatment that has given us the best result is massage, combined with the alternate use of the two following collyria, applied turn by turn for three days:

Hydrochloride of pilocarpine . .	0·05 gr.
Salicylate of eserine	0·02 gr.
Adrenaline, 1 : 5000 (*see* page 75) . .	10 gr.

S.—*One drop to be instilled four times a day; during the three*

* Darier, *La Clin. Ophtal.*, No. 8, 1896.

following days instil a drop of the following collyrium five or six times a day :

Chloride of pilocarpine . . .	0·05 gr.
Dionine	0·10 gr.
Distilled water	10 gr.

It goes without saying that if serious attacks come on, recourse must be had to iridectomy.

The operation for glaucoma is one of the most beautiful discoveries of modern therapeutics; but it does not lack difficulties, and in many cases its brilliant results leave something to be desired. Alas! there is no medal without its reverse.

Malignant glaucoma, as its name indicates, is the gravest form of the disease, on account of its constant and progressive march towards blindness, with or without operation. Indeed, it would seem in these cases as if iridectomy gave a fillip to the morbid process, thus provoking a more rapid loss of vision with or without hæmorrhages. It is therefore recommended, when one suspects a malignant glaucoma, first to operate upon the worse eye, since usually both eyes are involved.

In these cases **sclerotomy** is able to render great service. It may even yield valuable indications, since if sclerotomy (by preference the anterior sclerotomy of De Wecker) gives no improvement even of a momentary character, it is to be feared that iridectomy will do no more. Sclerotomy generally produces an improvement or an arrest of the disease.

It should, however, be clearly recognised that a result due to a therapeutic or operative mistake may be put down to the agency of malignant glaucoma.

At other times, an iridectomy performed with a perfect surgical result as regards the first eye almost completely lost, gives as regards the second eye a disastrous result on account of an expulsive hæmorrhage, as happened to me six months ago. This last complication, which occurs quite independently of the surgeon, is not very rare, and should be included amongst the most important causes of loss of sight consecutive to iridectomy.

On the other hand, losses caused by surgical complications or accidents are much more numerous, inasmuch as iridectomy in acute glaucoma is certainly the most delicate operation in eye-work, and many instances of lack of success are due to operations performed under bad conditions. Accordingly, one cannot agree with von Graefe, who, in his enthusiasm for this beautiful operation, wished that the technique of iridectomy might be taught to every practitioner, so that

the latter might be able to operate on urgent cases even in the most out-of-the-way country districts. One cannot protest too strongly against any such idea. The bulk of the discredit thrown upon iridectomy has certainly arisen from the fact that the operation has been done badly, or performed too late. The practitioner should understand that he should apply to a specialist as quickly as possible every time he comes across a serious disease of the eye, limiting himself to the prescribing of those medicines that will allow of the necessary delay with the least possible danger.

Iridectomy cures glaucoma. But all of those who have been operated on do not share this opinion, and, upon the whole, few of them are quite satisfied. We must take care to make them understand this, namely, that the defect is often due to the fact that the operation has been delayed too long.

Almost all of those who have been operated on complain of dazzling in broad daylight or at certain times of the day. This is attributable not only to the iridectomy but also to the glaucoma itself, owing to defects of the visual field and to a rapid exhaustibility of the functions of the retina. Indeed, it is remarkable to hear those who have been operated on for glaucoma complain of the great difficulty with which they see, with or without correcting glasses, when by our means of investigation we are unable to demonstrate a reduction of the visual acuity to correspond with the trouble experienced by the patients.

The results of iridectomy, on the whole, are not always brilliant, except when performed in a first attack of acute glaucoma. The patients often experience no pain after the operation, and the earlier the iridectomy is done the better is the sight obtained.

In **glaucoma of subacute or slow evolution** the diagnosis is often not made until the visual field has become contracted and the visual acuity markedly lowered. Even then the operation is frequently not decided upon until after many tergiversations, complicated with consultations and various kinds of treatment, all of which entail a loss of precious time. The results are then less good the longer one has waited.

Now, in the present state of things one must not depart from the general rule, namely, **that all cases of acute or subacute glaucoma should be operated on as soon as the diagnosis is clearly made.** I say subacute rather than chronic glaucoma, because the use of the latter expression may lead to confusion with simple chronic glaucoma, as regards which disease opinions are still very much divided as to its treatment by iridectomy.

Iridectomy, broadly speaking, is really efficacious only when tension is manifestly raised. In short, iridectomy gives good results in about 70 per cent. of the cases of acute or subacute glaucoma. In chronic simple glaucoma, however, an arrest of the morbid process can be affirmed in scarcely a quarter of the cases, while often one observes, if not an actual aggravation, at least a continuation in the reduction of sight, which almost always ends in its complete loss.

How difficult, therefore, is the conduct even of the most experienced specialist when faced by a case of glaucoma! He may promise a cure, yet he has always unhappy risks to dread, which are altogether independent of his will. For we are as yet unable at once to recognise the cases where iridectomy, instead of bringing about cure, precipitates complete loss of sight.

We now come to the study of diseases of the fundus of the eye itself. We shall first discuss affections of the choroid and retina, and afterwards those of the optic nerve.

The pathogeny of **choroiditis** is even nowadays still imperfectly understood, in spite of fifty years' observation with so valuable an instrument as the ophthalmoscope.

It may be divided into suppurative and exudative choroiditis. In the latter there are no inflammatory symptoms, and the disease betrays its existence only by visual defects and ophthalmoscopic lesions.

The fundus changes manifest themselves as foci, first of yellowish and then of white infiltrations, generally surrounded by pigment. When the inflammatory process has run its course, there remains an atrophic patch, which allows the white colour of the sclera to show through.

The retina in contact with the morbid focus takes an obvious part in the inflammation. If this participation is very marked, one speaks of a **choroido-retinitis.**

The progress of choroiditis is essentially chronic. The disease may invade almost the entire periphery of the fundus of the eye without setting up marked visual disturbances (disseminated choroiditis). But when a scarcely visible focus lies in the macula, sight is involved in direct proportion to the extent of the lesion.

An extremely small spot provokes metamorphopsia, and if it increases in size, may entail a positive scotoma, whereby central vision may be permanently injured (central choroiditis).

Aside from myopia and syphilis, we understand but imperfectly the etiology of diseases of the choroid. It is, however, evident that

these means are merely so many labels. But certain instances of chroiditis assume a character so peculiar that a relatively exact diagnosis may be made when one possesses enough personal experience, although the systematic treatises say little with regard to this subject.

The choroid most frequently is not alone involved in the morbid process; the ciliary body, the retina, and the vitreous humour suffer the reactions of pathological troubles in the choroid.

Until the last few years the treatment of changes in the deep membranes of the eye was, so to speak, *nil* as regards the local condition, and the only indications were those furnished by the general affection to which the local lesion could be etiologically traced. As to the medicaments used, they have almost all been tried in vain with the same lack of success, so much so that abstention has become the rule with many practitioners. Alterative treatment by mercurials has alone yielded some results, not only in specific choroiditis, but even in the choroidal changes so frequently met with in myopia.

In May, 1891,* when, after more than a year of experimentation, I communicated the results I had obtained with subconjunctival injections in macular choroiditis, the scepticism manifested by most members of the Congress convinced me more than any arguments what was the compass of this new and intrepid treatment. I had been able to collect only five observations, all, it is true, very conclusive to one who had been able to see the lesions with the ophthalmoscope and to demonstrate the great and rapid improvement in sight.

It was that which led me to claim that we were in possession, if not of a specific method, at least of a rapid and potent means of treatment.

A year later, in order to confirm the original results, I published in a *mémoire* presented to the same Society † a fresh series of observations (with drawings) of alterations in the fundus of the eye, *viz.*, seven cases of macular choroiditis, three cases of myopic choroiditis, and five cases of disseminated choroiditis. Lastly, I have since then exhibited several patients affected with macular choroiditis to the Ophthalmological Society of Paris.

Rare are the cases, as I recognise, in which one can speak of complete cure in diseases of the choroid or retina, because it is

* Darier, *Archives d'Ophtalmologie*, No. 5, 1891.

† Darier, *Société Française d'Ophtal.*, 1892.

seldom that one is called upon to treat these affections until there has been time to allow of destruction of some of the anatomical elements. Of this, an indelible cicatrix is the result. But there are, on the other hand, many cases where the evil may be arrested soon enough to preserve sight without too much havoc.

In no malady of the fundus of the eye more than in those of the macula is it important to act with celerity and intensity.

In most of these cases the effects are appreciable after the first or second injection; at other times only after a larger number of injections.

In macular choroiditis, when central vision is not already irretrievably lost, one can obtain, if not normal sight, at all events a considerable improvement of the visual acuity, and that in so short a time that it is impossible not to believe in the relation between cause and effect. It goes without saying that these results can be obtained only when one has to deal with cases where the pathological changes have not destroyed function along with the anatomical element.

In all acute or relapsing cases local treatment is indicated.

In very long-standing cases it should always de tried, because one has often seen lesions disappear which seemed to be indelible. This has been the case in many of the observations related by me.

Speaking generally, in most of the examples of choroiditis that I have treated by subconjunctival injections, alone or combined with general treatment by hypodermic injections, I have obtained favourable results in at least 25 per cent., and in 10 per cent. results that I call surprising.

The foregoing statistics are apparently not very brilliant. However, if we consider the gravity of the pathological process, and especially the physiological importance of the anatomical elements implicated (in central choroiditis the retina is always affected), and the results obtained by the old treatment—results looked upon by most authors as almost *nil*—we are constrained to admit that ophthalmology owes something to local therapy by subconjunctival injections.

The action of the injections upon diseases of the choroid is particularly striking, a fact that has led some writers to claim that the injections have, so to speak, a selective action upon the choroid.

The true explanation, as we have seen, is furnished by the communication between the choroidal and the subconjunctival lymph-spaces, through the intermediation of the perivascular sheaths of the venæ vorticosæ.

A substance injected beneath the conjunctiva acts not only by

osmosis, but also by continuity of liquids, with chemical exchanges and biophysical excitations (phagocytosis, chemotaxis, etc.).

In recent and not too profound choroiditis or central chorio-retinitis one may study, almost mathematically, the truly remarkable action of subconjunctival injections.

That subconjunctival injections are a panacea nobody claims. They are not more so than mercury itself, of which remedy they are only a scientific and practical application, and that explains the multiplicity of their indications. They have merely underlined the importance and the mode of action of mercury, and, on that account, have already deserved well of science.

As regards myself, I encountered, when I published my first communication on the subject, a scepticism that was the reverse of encouraging.

The preliminary gropings were long, because in employing so irritating and active an agent as corrosive sublimate great perseverance was needed to attain the end, and also because of the pusillanimity of the patients, and the complications that always arise at the beginning of a novel form of treatment. Especially were difficulties caused by inducing in relatively painless diseases a lively suffering, and a notable tumefaction of the conjunctiva, and sometimes even of the eyelid.

That I was too enthusiastic was possible. But I can affirm that in no instance have I been misled with regard to the therapeutic results that I have observed with the greatest care, distrusting myself and, still more, my patients, who are very easily deceived, and always desire to make you share their delusions.

Nevertheless, this enthusiasm was speedily shared by others, who had obtained good results—that is to say, by all those who had conducted a long series of observations, and had looked at things with an impartial eye.

As to the influence of suggestion on the patients, that may have existed, but it is not easy to prove, at all events in the beginning, with a treatment whose nature is little suggestive, and whose application is so painful that one does not resort to it except when absolutely necessary.

When the management of a medication is not understood, one should always at first apply it with the greatest prudence and in favourable cases, until its indications and contra-indications are thoroughly grasped; for despite the most exact determinism guiding the prescription of a new treatment, the experience of others can never wholly replace personal experience, especially in so complex a

science as medicine, where each patient presents variable and infinite reactions, according to the intensity of the morbid process, the temperament of the subject, the influence of the media, etc.

These generalities once admitted, we shall in the next Lecture enter into the details of applying the treatment suitable for the different forms of choroiditis, and adduce cases in support of our views.

LECTURE XXI.

Summary.

Treatment of diseases of the choroid (*continued*).—Observations on macular choroiditis, cured by the rapid and intense action of subconjunctival injections of chloride of sodium and cyanide of mercury.—However infinitesimal the quantity of mercury resorbed, its action is twenty times more intense than when injected hypodermically.—The lesions must naturally be treated, if possible, at the beginning.—So-called congenital lesions.—The choroidal alterations of myopia are much improved by subconjunctival injections of sodium chloride, mercury cyanide, iodine, etc.—Great improvement as regards sight.

For the purpose of illustrating this study of the treatment of **Macular Choroido-retinitis**, allow me to quote a case (one of the first I treated), the facts of which are as follows :

M. X—, aged 38 years, without syphilitic antecedents, but a frequent sufferer from gout, consulted me on account of a marked deterioration of sight, especially for near objects. The latter appeared to be deformed and were seen in a diffuse way, and this, with fluctuations, had lasted for more than a year. With the ophthalmoscope, I found in the left eye a seed-plot of small white spots in the macula. There were in the right eye three or four similar spots above and below the macula. Such lesions, I may say in parenthesis, I have several times encountered in gouty subjects.

All treatment having been futile, I persuaded the patient to try subconjunctival injections of sublimate. One division of the Pravaz syringe filled with 1 : 1000 sublimate solution was injected after the eye had been cocainised.

On the following day the patient returned furious, said that he had suffered atrocious pain, and that he would not submit to such treatment. Upon examining sight I found L. V. = $\frac{1}{2}$, and No. 1 at 30 cent. Neither dulness nor metamorphopsia. The day before V. = $\frac{1}{3}$, and No. 4 (scarcely).

When the patient appreciated the rapid change in sight he became very grateful and demanded a continuation of the treatment. After

six injections similar to that first given, the patient returned, so to say, cured.

Upon this subject you may consult the numerous observations I have published upon the treatment of choroiditis in the *Bulletins and Mémoires of the French Ophthalmological Society*, 1892, pp. 269—290. The cases quoted show the efficacy of local treatment when all general treatment has failed or lost its effect.

Let us now see upon what profoundly scientific theory rest those who deny to subconjunctival injections the possession of any true therapeutic action.

To begin with, the possibility of any mercury reaching the interior of the eye has been disputed.

Sublimate, when in contact with the albuminous liquids of the organism, is transformed into a barely soluble albuminate. That fact is widely recognised as regards the strong solutions employed for hypodermic injections, but it is not proved to be true in regard to such diluted solutions as those used for subconjunctival injections, and besides, the same therapeutic effects are obtained by cyanide of mercury, which, in more or less diluted solutions, is absorbed and does not coagulate albumen.

Now let us admit that mercury penetrates the eye in infinitesimal quantities only. How, then, can we explain the therapeutic action which even the most sceptical have been compelled to admit? Does the water injected act, as claimed by certain authors, like a purifying stream (*courant laveur*)? This is very probable in cases where a syringeful of liquid is injected, but, on the other hand, how can we explain the cases where the therapeutic action is produced after the injection of a single drop of liquid?

I have made many control experiments by employing different liquids, such as distilled water, artificial serum, etc. I have never obtained results comparable with those given by injections of sublimate or cyanide of mercury.

According to another explanation the injections act by the revulsion they give rise to. There is a little truth in this hypothesis, but how little!

Why seek such an out-of-the-way explanation instead of agreeing with the sensible and simple clinical facts?

Can one possibly pretend that the injected sublimate has no action—chemical, antiseptic, or alterant,—or that it simply modifies nutrition? For the liquid which gives rise to conjunctival chemosis, constituted by the sublimate solution injected and the albuminous liquids extravasated, is finally absorbed; it enters the general circulation and the

lymphatic spaces of the eye, perhaps in a state of nature, perhaps as redissolved albuminates, perhaps even, if you like, in the state of insoluble particles transported by the leucocytes, like morsels of Indian ink injected beneath the conjunctiva.

Accordingly, whatever theory one adopts, it is not possible to deny scientifically, on the strength of mere theory, all therapeutic action to subconjunctival injections of mercurial salts.

Experimentally the controversy remains open. In any case, however, experiments made on the rabbit can never invalidate the numerous clinical results obtained by so many distinguished practitioners.

Another objection currently made is to the effect that the amount of mercury injected is so minute that it is impossible to attribute to it any therapeutic action whatever.

To deny a well-observed fact is not to reason. The fact being granted, it becomes necessary to explain it, although that is not always an easy matter.

A single drop of a 1 : 1000 solution of mercury cyanide injected beneath the conjunctiva contains $\frac{1}{20}$ milligramme of mercury, of which one part, probably considerable enough, will be swept away in the general circulation and be lost as regards the eye. Very little, therefore, penetrates into the interior of the eye; let us admit $\frac{1}{60}$ of a milligramme. One sixtieth of a milligramme reaches the interior of the eye; that is very little, but who can say how such a feeble dose acts? If not as a simple bactericide, is it perhaps as a stimulant of the anatomical elements charged with the defence of the organism, as serum, cells, phagocytes, etc? How can we tell? The objection, however, has no value except as concerns the infectious traumatic accidents, and in such cases the dose injected is ordinarily ten or twenty times stronger.

Let us put on one side this question, which, however simple in practice, is very difficult to settle by theory, and consider a very easy case—a macular focus of syphilitic choroiditis. According to my experience and that of many others, local treatment acts more rapidly than general treatment. May this not be explained in the following way? One twentieth of a milligramme injected beneath the conjunctiva, admitting a loss of $\frac{2}{3}$, allows of the penetration into the eye of $\frac{1}{60}$ of a milligramme. A hypodermic injection of the ordinary dose of 1 centigramme, if one estimates the average weight of the body at 60 kilogrammes, allows of the penetration into the globe only of $\frac{1}{1000}$ of a milligramme, taking the weight of the eye at 6 grammes. There penetrates, therefore, more than twenty times as much mercury

when the latter is employed subconjunctivally than when it is employed hypodermically.

It may be objected that hypodermic injections can be repeated daily, and can be combined with a cure by intensive frictions. But I have never attempted to supersede general treatment. I have merely said that local treatment by subconjunctival injections is a rapid and powerful method, which may render great service, and in some cases give a fillip, as it were, to the pathological process, and which may be used alone or concurrently with general treatment.

Whenever one finds a choroidal lesion of recent origin situated in the macula or its immediate neighbourhood, it is not general treatment that is the first indication but local treatment instead, and the only efficacious means that we yet possess—we are bound to confess the fact—is that by subconjunctival injections.

It cannot be too often repeated that it is necessary to act as quickly and as energetically as possible in cases where central vision may be definitely extinguished by a lesion of the macula.

All the same, it goes without saying that general treatment must not be neglected.

Permit me to quote a recent observation which will bring before you all the details of the pathological evolution of the process and the efficacy of treatment in cases of small macular deposits, which, for my part, I regard as isolated tubercles of the choroid.

Miss Z—, aged 21 years, apparently in good health, had formerly been treated for slight anæmia. Her mother and her uncle had died from tubercle. She had suffered for more than a year from a localised pain under the instep at the level of the scaphoid bone, possibly due to an osseous tuberculous lesion.

Miss Z— came to me on January 6th, 1900, complaining of a cloud before her left eye. R. V. = $\frac{2}{3}$, No. 1. L. V. = $\frac{1}{3}$ to $\frac{1}{2}$, No. 1 with difficulty. With the ophthalmoscope, one saw above the macula a choroidal focus—whitish, prominent, and rounded,—with a vessel passing over its surface. The vessel appeared displaced and raised by the exudation. There was a difference in height of 2 D. between the summit of the exudation and the surface of the retina.

A subconjunctival injection was made of half a syringeful of 1 : 1000 of cyanide of mercury with acoine, and a dressing was applied to the eye. A second injection was made on January 8th.

On January 10th the exudation had disappeared, and was represented by a zone of greyish infiltration. The twisted vessel had almost regained its rectilinear direction. The scotoma had vanished. V. = $\frac{1}{2}$ to $\frac{2}{3}$. A third injection was practised.

On January 13th the patient again complained of a black spot. With the ophthalmoscope, one saw the greyish zone in place of the old infiltration, but below the macula existed a second deposit, and this also was crossed by a vessel raised 1·5 D. to 2 D. The spot was whitish, and appeared to be clearly conical. On January 20th sight had fallen to $\frac{1}{3}$. As the patient had been indisposed, she had not been able to come for a week. There was, with the ophthalmoscope, much the same aspect with, in addition, a third punctiform deposit, white and quite like a tubercle, lying between the macula and the second deposit. It also was situated along a small vessel. On January 23rd a fourth subconjunctival injection of 1 : 1500 was made. But precious time having been lost, it was feared that the effect of the injections would not be so marked as at first, a surmise borne out by the further course of the case, which I shall not weary you by quoting at length.

It is important to note that the primary focus, which was treated from the first, disappeared in four or five days without any treatment, except three subconjunctival injections of cyanide of mercury. The second deposit, treated somewhat late, was cured but slowly, and left an indelible choroidal cicatrix. The third and smallest deposit, taken almost at its inception, disappeared, like the first, in five or six days.

The evolution of the three deposits show well the great importance of local treatment in such affections, even when there are no specific antecedents, and when everything leads one to believe in the tuberculous nature of the changes.

The sooner injections are made so much the more active and rapid is their action, because the anatomical elements have not had time to be completely destroyed. As is proved by the facts quoted, there is no other treatment capable of acting with such intensity and rapidity.

However, it is not always necessary to enter the scene at the beginning in order to obtain good results; it is needful only to come before the rods and cones are completely atrophied or destroyed by the morbid process.

In fact, I have seen instances of foci of central choroiditis (mistaken for congenital changes) benefit markedly from general treatment by subcutaneous injections to begin with, and then from local treatment by subconjunctival injections.

I have further seen disseminated choroido-retinitis which had for long invaded the macula largely improved by subconjunctival injections when general treatment had remained without effect or

had ceased to act. Several such observations are related, with drawings to support them, in the *Bulletins de la Société Française d'Ophtalmologie* for the year 1892. Since then I have met with other cases, many of which were improved by the same means.

In pigmentary choroiditis, and even now and then in pigmentary retinitis, surprising results are sometimes obtained by local treatment, even although specific treatment has been useless. It cannot be too often repeated that *subconjunctival injections have a specific action, so to say, in diseases of the choroid.*

We now come to the **Choroidal Lesions of Myopia.**

Only a short time ago I was struck by the following case:—A Sister of Mercy consulted me, complaining that the sight of her right eye had been very dim for more than six months. The practitioner by whom she was sent suspected a retinal hæmorrhage. There was high myopia, especially of the right eye, and in spite of correcting glasses, sight was equal only to the counting of fingers at 30 centimètres. Upon ophthalmoscopic examination, a large myopic staphyloma, with marked macular lesions, was found, but no hæmorrhage.

Without expecting any great result, I practised injections of chloride of sodium, at first of a 2 per cent. and then of a 4 per cent. solution, and afterwards of 1 : 5000 cyanide of mercury. In all, six injections were made in a fortnight, and the patient left me charmed with the result. She was able to read with the eye No. 6 of Wecker's type, and had, with the aid of a — 16 D. lens, vision equal to $\frac{1}{8}$. The patient, who formerly complained of seeing all objects covered with a large black spot, now perceived only a light fog, through which things could be recognised clearly enough.

I could quote many fresh observations in support of those I have already published, but a general agreement will soon be reached, for almost every serious experimenter is unanimous in recognising that the best treatment for the choroidal changes of myopia is by subconjunctival injections.

But in a paper published in the first number of the *Zeitschrift für Augenheilkunde*, Burri, of Basle, in relating the favourable effects of injecting saline water in macular choroiditis, could find only the case I related in 1893 to quote. Professor Mellinger, however, who is familiar with everything that has been written about subconjunctival injections, might very well have shown to his

pupil my two former communications, by far more important than the third. He is also acquainted with the numerous successes obtained by Marc Dufour, of Lausanne, recounted in the thesis of Auguste Dufour (1896). In this thesis are reported numerous cases of myopic choroiditis, of which twenty-one were treated successfully by subconjunctival injections of sublimate. Professor Pfluger, of Berne, also has expressed himself as more satisfied in affections of the choroid with subconjunctival injections than with any other treatment.

Mellinger wishes everywhere and always to replace sublimate by chloride of sodium, under the fallacious pretext that the first-named, being too irritating, gives rise to adhesions between the conjunctiva and the episclera in the eyes of rabbits. I have shown that such adhesions are observed in man only when the injection has been made too near the cornea or too deeply under the capsule of Tenon. Moreover, I have replied to Mellinger's objections; and, whilst recognising the great value of his communications upon subconjunctival injections of sodium chloride, I may point out that I have related before (*see* p. 22) a very interesting observation of bilateral macular choroido-retinitis, in which injections of cyanide of mercury were made beneath the conjunctiva of the worse eye, and of sodium chloride beneath that of the other eye. Sight remained impaired in the latter, while it became normal in the second eye after three injections of cyanide. A fact still more interesting was that the patient, who gave a specific history, had employed during the course of the affection hypodermic injections of cyanide of mercury as a general treatment.

I have been charged with abusing the subconjunctival injection of mercurial salts to the detriment of many other agents capable of being used in the same way. It is not in default of having searched for these other agents; I had abandoned sodium chloride, as it was less active, doubtless because I did not employ the large doses recommended by Mellinger (2 to 4 per cent., a syringeful every day or every other day).

Trichloride of iodine, iodide of potassium, salicylate of sodium, etc., have not given me results superior, or even equal, to those obtained with sublimate or cyanide of mercury.* Only cyanide of gold, in a case of retro-bulbar neuritis, yielded a striking result, after three injections of cyanide of mercury and of chloride of sodium had remained without effect.

* For more than eight years I have exclusively used this salt, which is less caustic than sublimate.

Sourdille,* of Nantes, has recently praised the good results of iodised injections in macular choroiditis due to myopia, disseminated choroiditis, etc. Every second day he injects beneath the conjunctiva four or five drops of the following solution:

Metallic iodine . .	0·01 to 0·02 gr.
Iodide of potassium . .	1 gr.
Distilled water . .	30 „

The pain lasts scarcely for a quarter of an hour. My friend, Dr. de Spéville, has also informed me that in three cases of macular choroiditis (myopic) he has obtained very good results, but that the injections were extremely painful. I at once tried the method, as indeed I have tried all those proposed as superior to mercurial injections.

But I should say, to begin with, that the first case in which I tried the injections was one of long-standing macular choroiditis,† which had withstood twenty intravenous injections of cyanide of mercury and twelve subconjunctival injections of the same salt. One thing was obvious, namely, that these injections were incomparably more painful than those of cyanide of mercury. As to the better results, I still await them. But if the iodised injections have not succeeded in this case I do not on that account regard them as inactive. I have stated in my first communication:—"One cannot obtain results in macular choroiditis except when the lesion is neither too deep nor too ancient—when it has not stifled or irremediably destroyed the sensory elements of the retina."

It is often impossible to determine, even after the most minute ophthalmoscopic examination, whether a macular lesion is curable or not. At the same time it is permissible to say that if subconjunctival injections have not been tried, the lesion has no right to be classed as incurable. In fact, I have seen a case, where a macular focus had been mistaken for a congenital coloboma, undergo a surprising improvement under subconjunctival injections.

What is the respective value of injections of sublimate, saline water, iodine, etc.? That would be interesting to establish in a really exact way.

As long as this study has not been made, I shall myself adhere to the injections which I have practised since the appearance of Mellinger's communications, and which have demonstrated the lymphagogue action of chloride of sodium. A 2 per cent. solution of this salt (the medium strength employed by Mellinger) serves me

* *La Clinique Ophtal.*, Nos. 4 and 6, 1896.

† *La Clin. Ophtal.*, No. 20, 1898.

as the vehicle of cyanide of mercury, 1 : 5000. I have come to employ these diluted injections because, as in hypodermic or intravenous injections, the quantity of the liquid acts by its mass. Indeed, I inject the same quantity of cyanide with one division of the Pravaz syringe with 1 : 1000 as I do with five divisions of the 1 : 5000 solution thus prepared; and, moreover, I inject the same saline solution as is praised by the Basle school :

Cyanide of mercury . . .	0·01 gr.
Chloride of sodium . . .	1 gr.
Water, sterilised and distilled .	50 „

The dose of this liquid for injection varies from ½ to a syringeful; the place of election is the equator of the eye, far from the cornea and preferably above and external to that structure.

But on that account there is no need to renounce the 1 : 1000 solution. The latter alone is capable of stopping a grave traumatic or operative infection, in which I do not hesitate to inject a half or a syringeful of the strong solution every second or third day to cure a panophthalmitis or a sympathetic ophthalmitis. It is owing to the difficulty of fitting the dosage to the intensity of the morbid process that many authors have reported negative results.*

Finally, Senn,† of Saint-Gall, in a recent work based upon the experience of five years, shows us that, even in Switzerland, whence sets the stream of injections of chloride of sodium, they are beginning to render justice to subconjunctival injections of cyanide of mercury. In order to obtain good results in the operative treatment of high myopia, he states that it is always necessary at first to improve the central vision, which is usually much affected by the choroidal changes. To arrive at this end, Senn knows no better plan than by subconjunctival injections of cyanide of mercury 1 : 5000, or even 1 : 2500, injections of chloride of sodium having shown themselves to be too inactive, or having promptly lost their effect. In pursuance of this plan Senn submits all his cases with high myopia to a six weeks' treatment by means of subconjunctival injections. He then performs extraction or discission of the crystalline lens, and thereby gets infinitely better acuity of vision.

But let us return to the treatment of choroiditis.

Subconjunctival injections undoubtedly have their drawbacks. For example, they are sometimes accepted with difficulty by the patients, and they are more or less painful. If an easier and more active treatment could be found that would be a great advantage.

* For the technique of the injections, see pp. 28 and 48.

† *Archiv f. Augenheilk.*, 1901.

Of late Sucker* has narrated two cases of choroiditis much improved by the employment of **Thiosinamine.** I hastened to submit to proof this therapeutic agent, which possesses properties resembling those of iodide of potassium. I have used it in pills, and in hypodermic and subconjunctival injections, but up to now, among twenty cases, I have failed to find any of a very encouraging nature.

Wolffberg believed that he had found in **Dionine** a substitute for subconjunctival injections. But the lymphagogue action of dionine, energetic though it be, is too fleeting to yield appreciable results in the treatment of choroiditis. Until more ample information reaches me, I can only repeat what I stated in 1893 to the Ophthalmological Society of Paris.†

It is exactly in affections of the macula that it becomes of the greatest importance to intervene with rapidity and intensity. No means possess these two qualities more than local treatment by subconjunctival injections. The latter have been tested with good results in such cases, and, apart from any theory, speak for themselves and should accordingly be employed.

However, it cannot be claimed that they are able to cure every affection of the macula. In a lesion that has induced complete destruction of the anatomical elements in so important an area as the macula or optic nerve, I hardly imagine that the idea of resuscitating them will occur to anybody. Where I spoke of several cases where I had improved the sight in patients suffering from macular choroiditis of myopic origin, somebody replied that it was impossible to cure such lesions, which were of a purely mechanical nature. The fact is true. But it is also true that acute relapses of a different nature often arise in the myope, and these one has never been able to improve except by mercurial treatment. It is in cases of this kind that I have obtained excellent results by subconjunctival injections of sublimate, starting always from the principle that in an acute local process it is advisable to act as energetically, as quickly, and as topically as possible.

What should constitute our ideal in medicine? It is to make surgery of it, if I may say so. It is, in other words, to attack the evil locally, and not to delay by attempting to circumvent it by those indirect measures to which we are too often reduced.

Even in such general affections as syphilis, tuberculosis, and rheumatism, therapeutics tends more and more to localise its means of action.

* *La Clin. Ophtalmologique*, No. 18, 1898.

† *Bull. de la Soc. d'Ophtal. de Paris*, 1893.

In an organ as delicate as the eye it is not always possible to attack the seat of the mischief by fire and sword; but we must always try, as far as may be, to bring the medicament into immediate contact with the lesion.

In the following Lecture we shall occupy ourselves with diseases of the retina itself, affections which generally proceed from general ailments by changes in the state of the blood. We shall have little to say with respect to the local treatment of these maladies, which belong rather to the province of the physician. At most we are asked to express an opinion as to the ophthalmoscopic lesions and the disturbances in vision produced by albuminuric, diabetic, and leukæmic retinitis.

Atheroma and arterio-sclerosis have equally and very often an echo upon the retinal vessels, and these cases of hæmorrhagic retinitis possess for the clinical observer great diagnostic importance. We shall not stay to deliver a course of lectures upon general pathology, but we shall soon open the interesting chapter of detachments of the retina, where we shall have occasion to study the remarkable action of subconjunctival injections, electrolysis, etc.

LECTURE XXII.

Summary.

Diseases of the retina: anæmia and hyperæmia of the retina.—Vascular spasm-arterio-sclerosis.—Embolism of the central artery of the retina.—Retinal thrombosis.—Hæmorrhagic retinitis.—Retinitis proliferans.—Albuminuric retinitis.—Diabetic retinitis.—Uræmic amblyopia or amaurosis.—Pigmentary retinitis.—Essential hemeralopia.—Electric ophthalmia and retinal electrocution.

We pass to-day to the study of the **Diseases of the Retina.** *A propos* of choroiditis, we have already seen that there may be an implication of the retina by contiguity, so that we have generally to deal with a choroido-retinitis.

There are, however, diseases peculiar to the retina, and first of all by its peculiar **vascular system** (terminal arteries) the retina is exposed to the gravest circulatory disturbances.

An inadequate supply of blood provokes sudden but temporary defects of sight. A momentary stoppage of the retinal circulation may entail an amblyopia, which may go on to complete and definitive blindness, as in retinal ischæmia due to cardiac insufficiency, serious hæmorrhage, hæmatemesis, hæmoptysis, etc. Lastly, in embolism of the central artery of the retina the loss of sight is usually irremediable.

The possibility of examining the fine vascular ramifications of the fundus oculi with the ophthalmoscope allows us to study in the living retina the vascular lesions, which once could be studied only in anatomical preparations. The indications furnished by the ophthalmoscope to general pathology, as you know, are numerous and important. We are able to observe retinal anæmia and hyperæmia, vascular sinuosities, and anomalies of the vessel-walls. Even the quality of the blood is revealed in leukæmia by the light hue of the fundus of the eye.

The various retinal exudations—brilliant and star-shaped—indicate

to us almost infallibly the presence of nephritis, even when the latter has not been discovered by the chemical tests for albumin in the urine. We can go even further and foretell, almost with certainty, a fatal termination of the case generally within a year, because albuminuric retinitis is always a grave sign.

Diabetes, also, may imprint stigmata upon the retina. They are, however, less characteristic than those of albuminuric retinitis. In fact, it often happens that the reniform spots of retinal exudation observed in diabetes are complicated with hæmorrhages, and even with the star-like and nacreous designs so common in albuminuric retinitis. Besides, serious diabetes is often complicated with albuminuria.

We do not purpose in this place to enter into details of the treatment of diabetes or albuminuria. Diet and general treatment deserve, however, the first place in this connection. Naturally, we are able to exert little local action upon a pathological process dependent upon alterations in the state of the blood.

Between these two well-defined forms of retinal disease we must place what has been called **Hæmorrhagic Retinitis**, a condition that may complicate either of the two preceding affections.

Under the name hæmorrhagic retinitis are grouped the different forms of retinitis which are accompanied by numerous hæmorrhages, and which indicate an alteration of the retinal vessels. This form of retinitis is often observed as the precursor of hæmorrhagic glaucoma.

The therapeutic indications in this event are clearer than in diabetes and albuminuria. Every time that you see retinal hæmorrhages at their beginning remember that the best way to hasten their resorption is by the repeated application of leeches to the mastoid process. The local abstraction of blood (however much it is decried by certain authors) exerts a really favourable action, and since we have not yet found any means that are more scientific and surer in their action, it is our duty as practitioners to summon to our aid these ancient means. If abstraction of blood has no action upon the pathological process itself, it assuredly brings about in the shortest time a marked functional amelioration and often even an obvious resorption of the hæmorrhagic exudations.

It is very certain that the true therapeutic indications will be furnished to us by a more profound knowledge of the pathogeny of hæmorrhagic retinitis.

We know that the causes of hæmorrhages are: (1) a peculiar fragility of the vessel walls, sometimes congenital, but oftener it is

atheroma or arterial sclerosis that predispose to the retinal or cerebral hæmorrhages observed almost exclusively in aged persons.

The treatment in such cases should be directed towards giving more elasticity to the arteries, as by prescribing sodium iodide, the injection of Trumseck, and by forbidding the abuse of alcohol and, in general, all excesses, as sudden emotion and violent efforts. You will take care that the intestinal functions are performed with regularity, and will inquire into the condition of the heart, lungs, and kidneys.

The overloading of the vessels in consequence of local or general disturbance of the circulation also predisposes to hæmorrhages, as seen in thrombosis of the central artery, embolism, etc.

(2) Retinal hæmorrhages may be caused by a more or less profound change in the blood-state. Of such an origin are the hæmorrhages observed in pernicious anæmia, leukæmia, purpura, scurvy, albuminuria, diabetes, etc.

In these cases our plan of action is quite clear. It is to modify the state of the blood itself by all the agents placed at our disposal by general medicine, and, above all, to try to get rid of the primary cause of the mischief. We shall say no more on this subject.

Some words may, however, be added with respect to a treatment much praised during the last few years. According to certain authors, gelatine has the property of facilitating coagulation of the blood, whether applied as a powder or as an antiseptic solution to a bleeding wound, or whether allowed to enter the circulation by hypodermic injection or by internal administration.

In eye work gelatine has been lauded by de Wecker and Prioux in the treatment of profuse hæmorrhage into the vitreous body. By practising subconjunctival injections of a 2 per cent. sterilised solution of gelatine these authors have been able not only to arrest the hæmorrhagic process, but also to bring about the rapid resorption of the sanguineous effusion.*

Similar subconjunctival injections have been equally praised by de Wecker in the treatment of detached retina.

For our part, we have up to now been unable to convince ourselves that gelatine injections possess any marked advantage over those of sodium chloride. For a long time, it is true, we have not met with those diffuse vitreous hæmorrhages which are seen in young persons, and which often abolish sight completely. For that

* One may fairly inquire whether the same result might not have been obtained by injections of sodium chloride.

formidable affection we are, in general, satisfied with the treatment recommended by Abadie, which comprises (1) sulphuric lemonade, (2) extract of quinine, 1 to 2 grammes a day, and (3) perchloride of iron, in 20- to 30-drop doses. Of all these remedies that which has undoubtedly the greatest action is the extract of quinine. The latter in large doses has powerful vaso-constrictor properties, like quinine itself.

Abadie also highly recommends wet-cupping, as well as hypodermic injections of ergotinine (Tauret) in the dose of a half or full syringe daily.

Hypodermic and subconjunctival injections of gelatine should certainly be tried in these cases, concurrently with the preparations mentioned above.

It must not be forgotten, however, that intra-ocular hæmorrhages, whether of the vitreous humour or of the retina, become absorbed very slowly, and that in these cases there is no chance of obtaining a lasting effect by instillations of dionine, as certain authors have maintained.

The hæmorrhages often leave behind them connective-tissue or cicatricial bands. These may now and again become vascularised, thus giving rise to the condition known as **Retinitis proliferans**, against which all our medicaments up to now have failed to act.

Anæmia of the Retina may be observed in many different conditions. It may, for instance, arise from insufficiency of the blood-supply in cases where the ocular tension is suddenly raised, in diseases of the heart, after profuse hæmorrhages, and so forth. Spasm of the retinal arteries may be produced, nervous spasms, or provoked by the powerful vaso-constrictor action of certain drugs, as quinine in large doses. In such cases anæmia may be so profound that definite blindness results; but more frequently a more or less complete cure comes about, accompanied by permanent defects, such as contraction of the visual field, marked pallor of the optic disc, and slenderness of the retinal arteries.

Arterial atheroma is also a cause of arterial anæmia, but this form is speedily accompanied with retinal hæmorrhages, as we have learnt a moment ago.

In some of the sudden amblyopias following copious hæmorrhage (epistaxis, hæmatemesis, bleedings, etc.) one is tempted to believe that the abolition of sight is due to a sudden anæmia of the retina. Certainly there is a lessened afflux of blood to the retina, but with the ophthalmoscope it can be proved that the circulation of the fundus of the eye is going on normally; the pupillary reflexes are

always present. In these cases, then, the blindness comes from above—that is to say, the cerebral cortex itself is involved.

The same applies to **Uræmic Amaurosis**, a condition liable to supervene suddenly in albuminuric persons; it entails the loss of sight without any ophthalmoscopic changes. The blindness may be temporary or permanent; there are usually several successive attacks.

In this place we are unable to discuss the treatment of uræmia and of eclampsia.

Embolism of the Central Artery of the Retina.—This condition allows us to study with the ophthalmoscope all the phases of an absolute anæmia of the retina.

The patient often consults us on the very day that he has been smitten with a sudden blindness of one eye. We then see that the retinal arteries are empty of blood, and resemble threads, while the retinal veins show but little alteration. The retina loses its transparency. It assumes a cloudy aspect, which becomes intensified around the macula lutea, so that the latter itself looks like a bright red spot. At a later stage the infiltration of the retina disappears. The membrane becomes transparent and completely atrophic, and when the central artery itself has been obstructed sight is always lost. On the other hand, if a lateral branch only has been blocked, a corresponding section of the visual field persists.

From the therapeutic standpoint, embolism of the retina offers little interest, inasmuch as treatment is usually without effect.

What are we able to do? How can we cause the emboli which obstruct the artery to disappear? That is beyond our powers. At the most we must try to mobilise the embolus in such a way towards the periphery that it may involve a vascular territory of less importance and extent. With this end in view, massage of the eyeball has been praised. The plan, as we shall learn in the Lecture on massage, has yielded definite results in some cases. Puncture of the anterior chamber provokes, by the abrupt evacuation of the aqueous humour, a marked and sudden lowering of the intra-ocular pressure, and as the blood then flows with great violence, the embolus may be pushed onwards.

Other remedies have also been recommended, as, for example, inhalations of nitrite of amyl, instillations of dionine, subconjunctival injections of saline solution, etc., but we possess in these means merely adjuvants of little importance.

All the means of treatment enumerated have a *raison d'être* only on the condition that they are used during the first few days or

even hours after the embolism has occurred, inasmuch as atrophy of the retina supervenes quickly, and then all efforts are useless to restore the least sight.

The blindness may not be complete; a little central vision may persist, because a small macular artery comes off before the central artery breaks up into its retinal expansion. But more often the embolus becomes arrested astride a bifurcation of the artery. The blood, then, continues to reach by this arteriole the part of the retina lying between the papilla and the macula.

We shall not say much about **Thrombosis of the Retinal Veins.** Opposed to this rare affection our means of action are as uncertain as those we have enumerated *à propos* of embolism of the central artery. The first step in all cases lies in the local abstraction of blood, of which it is needless to exaggerate the importance. If we have to do with a mechanical compression by an orbital tumour, the therapeutic indication is clear, namely, to remove by surgical means the obstruction to the venous circulation. But we generally have to deal with a chronic alteration of the vascular walls amongst aged persons who are suffering from atheroma or cardiac disease, and, as you will readily understand, our *rôle* is then clearly thrown into the shade.

Thrombosis may begin in the deep veins, and be propagated thence to the orbit and the eye. Death is the most frequent end of such cases.

A few words may next be said with respect to **Retinitis Pigmentosa,** which constitutes a well-marked morbid entity, both by its symptomology (hemeralopia and concentric contraction of the visual field) and by its ophthalmoscopic stigmata (pigmentary spots, about the fundus of the eye, having the appearance of bone corpuscles).

It is due to a progressive degeneration of the retina with migration of the pigment from the pigmented epithelium. The degeneration begins at the periphery, towards the end of the finest retinal arterioles, a fact that explains the contraction of the field of vision.

Retinitis pigmentosa, as a rule, is an hereditary and family affection. Consanguinity has been noted in the parents; and other congenital anomalies, as deafness, idiocy, hare-lip, polydactylism, posterior polar cataract, etc., may co-exist with the retinitis.

Certain forms of pigmentary retinitis are said to be "without pigmentation" because one finds the full clinical picture of the disease without any pigmentary deposits being visible in the retina. From the point of view of treatment, our impotency is complete in face of this congenital and characteristic affection. Nevertheless,

as certain forms of retinitis resembling retinitis pigmentosa have benefited greatly by hypodermic or intra-venous injections of cyanide of mercury, I adopted this treatment in several cases of retinitis pigmentosa, with results favourable enough to allow me to recommend the method to your notice. In spring and autumn I made some twenty intra-venous injections of 0·01 per cent. at the rate of two a week.

I had little recourse in these cases to subconjunctival injections of sodium chloride or mercury cyanide, because their very real efficacy is not lasting, and they cannot be repeated frequently enough.

In **Essential Hemeralopia,** which is found in persons who enjoy good health and who are free from pigmentary retinitis, you should always try the method of treatment which has been so highly praised * during recent years, *viz.*, the administration every day for a week or two of 200 to 300 grammes of grilled lamb's liver.

The more general use during the last few years of electric currents of high voltage has tended to produce eye mischief of various kinds.

We shall not speak in this place of conjunctivitis, the ocular irritation attributed to the intense brightness of the electric light,—there is much there to take and to leave.

Symptoms of retinitis may also be caused by fixing an intense luminous *foyer* for too long. The sun looked at during an eclipse without very dark protective glasses may entail, as you know, a retinal dazzling, which may be followed by a persistent central scotoma.

It is not, however, of retinitis by dazzling that I wish to speak to you. It is of that form which I shall call **Retinal Electrocution,** in preference to the most unsuitable name **Electric Ophthalmia**—the term commonly and indefinitely employed both for the dazzling mentioned above and also for the cerebral and retinal shock provoked by the passage of a short circuit through the upper part of the body and the head.

The light of the current produces not only dazzling, but also sideration of the whole central nervous system. The persons thus injured are sometimes rendered unconscious, while at other times that is not the case, according to the intensity of the current and the part of the body affected. In every case the patient at first complains of a loss, more or less complete, of sight, with intense photophobia, generally accompanied by marked blepharospasm. At this stage the photophobia is so marked that for the first few days

* Trantas, *La Clinique Ophtalmologique*, 1900.

accident it is impossible to examine the fundus of the eye or to study the action of the pupil. The least light, especially electric light, sets up spasmodic contractions of the eyelids and marked pains in the eyes and head.

It sometimes happens that the electrocuted patient is for several days unable to open his eyes to light, and when at last they are opened he maintains that he cannot see clearly or can see for a moment only. His sight soon wearies, and the headache returns with intensity.

On account of the photophobia and of the prompt exhaustion of the retina, the exact determination of the visual acuity is at this moment difficult or impossible. The retinal exhaustion causes the characters read at first soon to become dulled or to disappear.

The field of vision is extremely difficult to take, as the patients get exhausted so rapidly. But in all the cases where I have succeeded in mapping it out, there was found a characteristic and very marked contraction for white, while colours were seen so imperfectly that they could not be registered on the chart of the perimeter.

The pupil has a medium size, and the pupillary reaction is generally normal. An examination of the fundus of the eye reveals no alteration, apart from a certain degree of hyperæmia of the papilla and retina.

It must not be forgotten that simulation may enter a good deal into the troubles complained of by injured persons. The latter know quite well that we can control their statements only with difficulty, more especially when they complain of a reduction in sight affecting both eyes; they often supply each other with the indications to deceive us, in order to obtain from their employers an indemnity as high as possible. Add to this that, combined with visual troubles, there may be nervous disturbances dependent upon traumatic neurosis. You perceive, then, how difficult is the *rôle* of the medical man in these cases of retinal electrocution. The practitioner desires to make a report satisfactory both to science and to conscience, and at the same time he wishes to try to cure a patient with whom he is scarcely as yet acquainted. The annals of medicine so far do not include many records of this affection, which for that matter is quite modern.

The treatment of retinal electrocution exacts, at first, absolute rest and hot and prolonged baths, and then as soon as a little light can be borne by the patient, the latter should be provided with large, dark glasses with black silk around their edges (automobilists' spectacles). Bromide of potassium, 2 grammes a day, and quinine in doses of 0·10 centigramme, five or six times a day, reduce the photo-

phobia rapidly. Collyria of cocaine, dionine, and adrenaline yield only very remote results.

Antipyrine soon relieves the headache, and when its effect has become weakened, it may be replaced by phenacetine, administered according to the formula already given several times in the course of this book.

A treatment (paradoxical though it may seem) that in my hands has more than once yielded good results is electricity applied to the eyeballs by means of a constant current of feeble intensity (2 to 4 elements of Gaiffe), the negative pole being placed indifferently upon any part of the body. These electrisations act not only by the calmative effect of the positive pole, but they also permit us to exercise suggestion without inducing sleep, a suggestion of which the value should not be neglected in an affection which is essentially of nervous origin and which is so often combined with hystero-traumatism.

LECTURE XXIII.

Summary.

The treatment of Detachment of the Retina: the first trials of subconjunctival injections.—Intra-ocular injections of tincture of iodine.—Simple puncture of the sclerotic.—Electrolytic puncture.—Intra-ocular injections of artificial serum, aqueous humour, and of the vitreous body of the rabbit.—Clinical forms of retinal detachment; their particular therapeutic indications.—Is the complete cure of detachment impossible?—Subconjunctival injections, electrolytic puncture, and the dorsal decubitus constitute our most powerful weapons.

At the time of my first communications on subconjunctival injections of sublimate I had occasion to treat some uncommon cases of **Detachment of the Retina**, in which I tested, without too much conviction, the value of this novel therapeutic method.

I have still under observation one of the first patients treated in this way. He is a man, aged about fifty years, extremely myopic, who consulted me for the first time in 1892 for a marked dulness of the only eye that remained to him, the other having been lost from detachment of the retina twelve years before. Sight was markedly reduced, and a scotoma—very clearly confined to the upper part of the visual field—corresponded to a detachment of the retina. The latter, slight but evident, occupied the inferior equatorial region of the fundus. The papilla was encircled by a zone of myopic choroidal atrophy, while a transverse streak of choroiditis ran across the fundus of the eye. The choroidal changes made me think that subconjunctival injections of sublimate might exercise a salutary effect upon the detachment itself. The truth of this surmise was borne out by the sequel of the case: the patient was quickly cured of the detachment.

At about the same time I observed two other similar cases. I have, however, never dared to publish them, inasmuch as I might have been looked upon as a madman for thinking that several drops of sublimate injected beneath the conjunctiva were able of themselves

to bring about the cure of a retinal detachment, a disease reputed to be almost incurable.

Further, at that time my teacher, Abadie, was treating retinal detachments by **Intra-ocular Injections of Tincture of Iodine**, which was soon advantageously replaced by electrolytic puncture.

To-day the tide has turned. From every quarter we hear of cures by subconjunctival injections of sodium chloride, sulphate of soda, gelatine, etc. In every case, if this treatment is not better than others, it is at least quite harmless, and, thanks to acoine, scarcely painful.

At the present moment I have under my care a girl of twenty years, who was brought to me almost blind. She had lost her right eye four years ago from detachment of the retina. Now suddenly, four days before seeing me, her left eye became clouded as if covered with a bandage, which interfered so much with vision that Miss M— could scarcely distinguish hand movements at some centimètres distance. With the ophthalmoscope, one could demonstrate the existence of retinal detachments above and below; lying between two of them the papilla could be distinguished encircled by a large myopic staphyloma. It was decided to perform electrolytic puncture on the following day. In the meanwhile I made a subconjunctival injection of a syringeful of a 4 per cent. solution of sodium chloride with acoine. A compressive bandage was applied and absolute rest enjoined.

Next day, everything being in readiness for electrolysis, I removed the bandage from the patient, who could not contain herself for joy at seeing the world around her. The sight, with a − 26 D. lens, was equal to $\frac{1}{8}$; she could read the smallest letters very close by. The visual field was almost normal, except as regards colours, which were imperfectly recognised above. With the ophthalmoscope, no trace of the detachment was visible; all the vessels were in close apposition with the fundus of the eye. Towards the inferior equatorial region there was a dull greyish aspect of the parts, but no detachment.

A series of subconjunctival injections of the same strength were practised, and strict confinement to bed maintained.

The patient is still under treatment. What will be the outcome of the case?

Nevertheless, that was a very encouraging result, although it is difficult to draw definite conclusions from a single case, because the *post hoc* is not always the *propter hoc*, and many instances of the spontaneous cure of retinal detachment have been related during

recent years. One must not make any mistake with regard to the importance of spontaneous reattachment of the retina. Speaking for myself, I have never seen a case, and the fact alone that so much stir is made about one of these cures proves that they are extremely uncommon.

Then we must never forget that there is no more baneful principle in therapeutics than the expectant one of *laissez-faire*. One should wish to cure, and to that end one should employ all methods and all available energy.

Subconjunctival Injections in the treatment of detachment of the retina have been alternately used and given up. De Wecker, who formerly employed injections of saline water, resorts nowadays to injections of gelatine, having abandoned punctures, drainage, etc.

A most interesting thesis was published last year under the auspices of Professor Mellinger, of Basle. As the outcome of twenty-three observations, Dr. Staerkele reached the following conclusions:

1. That subconjunctival injections of sodium chloride are devoid of danger and almost painless; they materially aid in quickening the resorption of intra-ocular pathological products.

2. This resolutive action is the greater the more concentrated the solution of sodium chloride.

3. In retinal detachment the injections bring about a prolonged improvement, and in some cases even a permanent cure.

4. Subconjunctival injections of saline solution are capable of improving partial detachments of recent date, rather than total and long-standing detachments.

Mazzoli, Vinselmann, Haitz, Senn, and others have also reported instances of cure, or of more or less marked improvement, by the subconjunctival injection of feeble solutions (2 to 4 per cent.) of chloride of sodium.

Dor, Bourgeois, and, lastly, Jocqs, basing their remarks upon recent work dealing with the laws of isotony and of osmotic pressure, have recommended strong and even saturated solutions in order to provoke the resorption of the subretinal fluid by exosmosis. It is difficult to imagine how even a saturated solution is able to exert an osmotic action through a membrane so dense as the sclerotic, although the fact cannot be denied. In the following case I had an example at once too troublesome and conclusive.

In a myope of 48 years, in whom I had practised removal of the crystalline lens, I succeeded in obtaining an extraordinary visual acuity. She enjoyed this great boon for three or four months,

when a localised detachment of the macula suddenly made its appearance, with the consequence that sight was almost completely annihilated. The intra-ocular pressure was scarcely lowered. What was to be done? One could not think of puncture, simple or electrolytic, any more than one could of the cautery. In fact, how could one reach the macula of an eyeball affected with twenty to twenty-three dioptres of myopia? Indeed, nothing remained except to try to provoke the resorption of the subretinal fluid by subconjunctival injections, periorbital inunctions of mercurial lanoline, and especially by the dorsal decubitus. An injection of a syringeful of 10 per cent. solution of sodium chloride with acoine was made as deeply as possible behind the eyeball. A compressive dressing was applied over an application of mercurial lanoline.

Five days later the patient came to me desperate, saying that as her eye was lost it was not worth the trouble of keeping her in bed, more particularly as there was no chance of curing her. I found, in fact, that the eyeball had diminished considerably in volume, the eyelid covering more than one half of the sunken globe. The cornea collapsed under the pressure of the finger. Sight was almost *nil*. No wound was anywhere visible; the corneal cicatrix, through which the crystalline lens had been extracted, was scarcely recognisable. The intra-ocular fluids had evidently escaped by the usual channels of elimination through the sound membranes. It is possible that the exodus of the fluid had been favoured by the compressive bandage, which, however, was not very tight, but chemosis must have been very considerable in order to augment notably this compression. A few subconjunctival injections of artificial serum soon restored the eye to its normal volume, although the tension always remained lower than normal, because the detachment persisted.

Deutschmann, in two consecutive works based upon numerous observations, praises **Incision of the Fibrous Tract** provoking the shrunken state of the vitreous humour, which, according to Leber's theory, is the real cause of detachment of the retina; and then, to give a new vitality to the altered vitreous, he injects into the eyeball a solution of the vitreous humour of a rabbit. That therapeutical measure is as logical as it is daring. But is Leber's interesting theory true of all cases? It is not, because in young subjects the vitreous body is really little altered, although more fluid than in the normal state.

Following up the same idea I have made the following experiments upon eyes affected with long-standing detachments. By

means of a hollow needle, of lanceolate shape and constructed of iridised platinum, I make a puncture at the level of the detachment, and aspirate the subretinal fluid. Then, without withdrawing the needle, I push it more deeply into the vitreous body, beyond the detached retina, and adapting to the needle another syringe filled with physiological serum at a temperature of 32° C., I inject this liquid into the vitreous, until the globe has assumed an almost normal consistence. The needle is next slowly withdrawn until nothing beyond its point remains in the wound. Then, placing the platinum needle in communication with the positive pole of a battery prepared for the purpose, I allow a current of 4 to 5 milliampères to pass for three minutes. After this operation subconjunctival injections are made, at two or three days' interval, for three or four weeks.

That also is a rational treatment, but, like Deutschmann's plan, it has the inconvenience of being somewhat complicated. Instead of serum, I have injected the aqueous humour from cats and rabbits and also an extract of the vitreous humour of the rabbit.

I must, however, admit that my results have not been more brilliant than with simpler procedures. Nevertheless, I believe that this method is possibly called upon to render service where other measures have failed.

I have lately seen **Electrolysis** applied by Abadie in many cases of detached retina with a fair amount of success. That is why I have myself practised the method, as simple as it is active.

Professor Terson,* of Toulouse, has reported the cure of many cases of detachment by electrolysis, and more recently still, Maraval,† of Oran, has published the results of his practice, from which he concludes that—

1. Electrolysis gives, in recent cases of detachment of the retina, a real and constant improvement, and by it a definite cure may be now and then obtained.

2. Its application offers no danger, and a current of five milliampères rather favourably influences the general nutrition of the eye.

3. The operation may, without inconvenience, be repeated several times at a few days' interval.

It is of great importance to employ for electrolysis blades of silver, or rather of iridised platinum only, because the needle is corroded by the powerful chemical action of the current, so that when the knife is withdrawn it is notched, comes out with difficulty,

* *Bulletin de la Société Franç. d'Ophtal.*, 1896.

† *La Clinique Ophtalmologique*, No. 17, 1901.

and may provoke vascular lesions, bringing about the loss of the eye from intra-ocular hæmorrhage, as I have once had occasion to see.

In few words these are the various methods at our disposal for the cure of detachment of the retina.

We ought to add to them **Simple Punctures**, which have yielded good results in the hands of many writers.

The **Cautery**, which has been equally praised, may be applied concurrently with other methods. In certain special circumstances the application of leeches to the temple may render service.

Copious **Diaphoresis**, induced by sodium salicylate and especially by pilocarpine, is a valuable adjunct.

But, let us admit the fact, one of the most important points in the treatment of retinal detachment is, beyond doubt, the **Dorsal Decubitus** maintained for a month or six weeks. To wish to keep in bed for two, three, or even six months persons in good health appears to me to be a remedy several degrees worse than the disease, and the abuse of decubitus that I have witnessed made me from the very first a declared enemy; but experience has convinced me that to permit patients to get up under a month is usually to commit a great imprudence.

Quite recently I cured a myopic detachment of some size by electrolysis followed by subconjunctival injections. On the ninth day the patient, against my wishes, desired to get up and to return to his house. On the day of his departure no trace of detachment could be found; his sight was $\frac{1}{2}$; his visual field was normal. A month later the patient returned to me with a total detachment.

If the foregoing were an isolated case I should draw no conclusions from it, but unhappily I have always found that the patients who could not be cured were precisely those who would not stay in bed long enough.

Now that we have passed in review the main methods of treating detachment, let us study the best means in the different clinical varieties of this affection.

The simplest and in general the most benign form of detachment of the retina is certainly that caused by a contusion of the eyeball. Naturally it is not necessary for the injury to be violent enough to cause multiple and profound lesions, great ruptures of the choroid, with copious hæmorrhages into the vitreous humour, luxation of the lens, and tears of the iris, with or without ruptures of the sclera. No! We speak only of cases where a more or less violent shock upon a globe previously healthy and not strongly myopic has pro-

voked a detachment of the retina without further complication than a slight subretinal hæmorrhage.

In these conditions, if the patient attends soon after the accident, cure should result from several days' rest in bed with a simple compressive bandage after the application of two or three leeches, if there has been retinal hæmorrhage. If reattachment has not taken place in five or six days one should have recourse to subconjunctival injections of sodium chloride, of which a syringe filled with 2 or 4 per cent., or, if necessary, 10 or even 20 per cent., should be employed. Rare will be the cases that resist this treatment, if it is applied seriously, and especially if dorsal decubitus has been kept up from the first.

There are cases of traumatic detachment which, by reason of the negligence of the patients, have become chronic; it is then necessary to employ the most energetic means, of which we shall speak presently when treating of grave myopic detachments.

There are a crowd of circumstances which complicate the prognosis of retinal detachments. First, there is the age and condition of the patient; then the pathological antecedents of the eye itself, which may have been affected with iritis, iridochoroiditis, etc., or even be simply myopic, with or without choroidal lesions. Lastly, the detachment may be so old that the retina and the choroid have undergone changes which practically preclude even a relative cure.

With respect to cure, some authors claim that they have never seen a detachment of the retina absolutely cured. Let us come to a right understanding: a lesion so serious as detachment of the retina cannot be cured without leaving traces—that is evident. However, in traumatic detachment cure may be got with *restitutio ad integrum*.

In myopic detachment the retina may become completely reapplied, and vision again become as good as or better than it was before, but the visual field now and then retains scotomata corresponding to the part formerly detached. These scotomata may sometimes be as widely spread as they were prior to the reattachment. I have two cases of this kind, which for five or six years have the retina perfectly reattached with a notable contraction of the visual field. There is no longer any tendency to detachment, but it is evident that these are instances of relative cure only.

Certainly, examples of the complete cure of myopic detachment are extremely rare; but they do exist, more rarely, perhaps, than glaucoma cured by iridectomy. Indeed, where is the glaucomatous patient on whom iridectomy has been performed who can call him-

self absolutely cured, and who can see well without the aid of any glass? And the coloboma of the iris, is that not in itself a pathological remnant of a very troublesome character?

Amongst the traumatic detachments we must classify those which follow an abundant loss of vitreous humour during the operation for cataract. The prognosis in these cases should be carefully guarded.

We now come to the class of detachments secondary to pathological intra-ocular changes.

In tumours of the choroid the diagnosis is sometimes very difficult at the beginning. Postero-lateral illumination, under these circumstances, often affords valuable indications. With regard to treatment, if mercury and potassium iodide, in large doses, remain without effect, enucleation must be practised without hesitation.

Detachment may be consecutive to a choroidal hæmorrhage. In such a case we must endeavour to induce as quickly as possible the resorption of the effused blood. When the hæmorrhage is recent leeches are indicated; puncture in the early stage may provoke a fresh hæmorrhage. Subconjunctival injections and massage may hasten resorption of the extravasation.

Exudative choroiditis, when abundant, may also produce detachment of the retina, the treatment of which is indicated by the nature and cause of the exudation. In cases of syphilis, mercury, intravenously or subconjunctivally, will often yield brilliant results. Even in the absence of syphilis I have seen cases rapidly cured by subconjunctival injections of cyanide of mercury. For example, in a young soldier affected with retinal detachment due to exudative choroiditis extending as far as the macula, I succeeded in causing the detachment to disappear completely, bringing about normal sight, although a scotoma of the visual field persisted for a long time.

Detachments consecutive to chronic iridochoroiditis exact a bad prognosis, because all the tissues of the eye are in a state of trophic decay, and this allows of little hope; but there are cases of the kind which have retained some sight for years, it is true, thanks to prolonged treatment by hypodermic or intra-venous injections of cyanide of mercury.

Finally, as we have seen above, certain cases of atrophic choroiditis, especially when widely spread, may cause retinal detachment. In cases of this kind, unless occurring in myopes, subconjunctival injections give the best results. I have even quoted one of my first observations, where, despite a myopia of 7 D., cure was rapidly obtained by these means, and was permanent for ten years.

We now come to the gravest form of all, namely, to the detachment, so to say, idiopathic, so often met with in high myopia. The progressive distension of the eyeball, still sufficiently elastic in young subjects, may attain considerable proportions, but the retina and the choroid, being less elastic, may be torn or detached.

It can be readily understood that in such conditions even a relative cure may be obtained with difficulty. Ought we on that account to abstain from all intervention? Certainly not. On the contrary, we should try by all means in our power to obtain, if not an actual cure, at least an arrest of the mischief.

The following represents, according to my opinion, what should be done in the different cases that come before us.

First: a myope (of more than 6 or 7 D.) consults us with a partial detachment, involving a quarter or a third of the retina, of a few days' duration. Our first duty is immediately to prescribe the dorsal decubitus and to practise several subconjunctival injections of sodium chloride, 2 per cent. to 4 per cent., and then of 10 per cent. If at the end of a month the retina is reattached, we allow the patient to get up for an hour and then for two hours daily, watching carefully in the meantime the fundus of the eye, and especially the visual field for blue.* During the whole of this period of observation, subconjunctival injections are continued. They are of cyanide of mercury, 1 : 5000, then 1 : 3000 and 1 : 2000. The mercurial salts have a manifest salutary action on the choroidal alterations of myopia, which at bottom are the cause of the detachment.

The application of leeches, of wet cups, of the cautery to the sclerotic are valuable adjuvants, often capable of rendering real service, a remark that applies also to diaphoresis by pilocarpine, etc.

I have never observed any favourable effects from the use of myotics. With regard to the compressive bandage, it is of service, but it should not be too tight for fear of unpleasant complications.

Second: we have just considered a case where cure was obtained by the means indicated above. But it often happens that no result is obtained after a week's delay; or even after an immediate reattachment the retina again becomes detached from the third to the fifteenth day.

Precious time must not then be lost in useless experiments. We must have immediate recourse to more energetic means. The

* The visual field for white shows no deformities in very slight detachments, while a scotoma for blue gives us exactly the limits of the detached portions of the retina.

indications are clear enough: a liquid, more or less abundant and changed, is effused between the choroid and the retina; the fluid is not absorbed under the influence of saline injections, and it becomes necessary to evacuate it by puncture.

Simple Puncture has given good results in many circumstances; but, for my own part, always fearing a too rapid reaccumulation of the evacuated fluid, I prefer to combine puncture with a strong subconjunctival injection, which, by its osmotic power, will perhaps prevent a new subretinal effusion.

Electrolytic Puncture has the great advantage over simple puncture that after the evacuation of the subretinal fluid the electric current, passing through the choroid, retina, and the intra-ocular liquids, may provoke an adhesive inflammation, which in some instances may keep the retina fastened to the tunics of the eyeball. This is how I proceed in the cases which we have just considered.

Third: those where the detachment already dates back a certain time, and those where the lesion is too gross to allow of a definite result being obtained by the parasurgical means enumerated above.

The patient lying horizontally on his bed, the eye is rendered aseptic, and well anæsthetised with cocaine. A constant current of nine small Gaiffe's elements, provided with a rheostat and galvanometer, is placed upon a firm table. In performing electrolytic puncture, I use the blade with a double-cutting edge, recommended by Abadie. It is connected by an insulated wire with the positive pole of the battery, the negative pole being applied to the patient's arm. The eye being luxated as far as possible with fixation-forceps so as to expose that part of the sclera corresponding to the detachment, the blade is introduced far back in order to avoid the ciliary processes. The blade penetrates 2 mm. or 3 mm., and the subretinal fluid is evacuated by giving the knife a half turn. The current is then passed softly and progressively in such a way as not to provoke any shocks; when it has reached four or five milliampères it is allowed to act for two or three minutes. During the last minute the needle is very slowly withdrawn, so that at the moment of withdrawal nothing beyond the fine point is in contact with the wound. As the needle is taken out the current is equally diminished *decrescendo*.

The electrolysis finished, a subconjunctival injection of a syringeful of the following solution is made a centimètre from the puncture:

Chloride of sodium . . .	1 gramme.
Cyanide of mercury . . .	0 gramme 005.
Distilled water	10 grammes.

Since acoine, very necessary to render this injection as little pain-

ful as possible, is precipitated by strong solutions of sodium chloride, it may, with advantage, be injected beforehand, and, the cannula remaining in place, the saline solution may be injected over and above without pain. Should there be marked chemosis or sharp pain, two or three leeches are applied to the temple. Dorsal decubitus must be rigidly observed. The dressing is removed on the fourth day, when one is often surprised to find a perfect reattachment of the retina. There may be some reaction—a little iritis and cloudiness of the vitreous. Atropine and mercurial frictions around the orbit must be used, and when the redness has diminished, subconjunctival injections must again be employed, at first diluted.

In some cases a partial reattachment only is obtained. New electrolyses must then be made when the inflammatory phenomena have subsided. The cautery, leeches, and sweating by pilocarpine, alternated with subconjunctival injections, sometimes complete the cure.

Lastly, if after a month or six weeks devoted to vain endeavours, the detachment is always reproduced, one may try the **Intra-vitreous Injections** mentioned elsewhere.

We have, finally, the whole series—alas! too numerous—of chronic retinal detachments which resist all treatment, and which terminate in complete disorganisation of the eye. A cataract first forms, and the eyeball then undergoes more or less complete atrophy.

All interference is contra-indicated under these conditions, apart from special indications, as dislocation of the cataractous crystalline lens, and inflammatory glaucomatous accidents; but then we go beyond the treatment of retinal detachment.

LECTURE XXIV.

Summary.

The treatment of diseases of the optic nerve.—Our impotence in atrophy of medullary or cerebral origin.—In retro-bulbar neuritis we have a potent means of action in subconjunctival injections, especially when the process depends upon an infectious malady, and when the neuritis is treated quite at the beginning or at the decline of the acute period.—Examples of these different clinical forms.—Neuritis due to chill.—Toxic neuritis due to alcohol, tobacco, etc., cured by the suppression of the toxic agent.—Leber's hereditary retro-bulbar neuritis cannot be cured, but seldom terminates in complete blindness.

To-day we will study the treatment of **Diseases of the Optic Nerve.** One alone amongst these maladies appears accessible to our remedies, namely, retro-bulbar neuritis.

We have seen, *à propos* of sympathetic ophthalmitis, that in subconjunctival injections we have a powerful means of acting upon the optic nerve itself, and we are about to have of that fact a new proof.

When the optic nerve has been seriously affected, as we all recognise, it is extremely rare to obtain a cure with *restitutio ad integrum;* indeed, we see it only in retro-bulbar neuritis, which, despite all treatment, too often ends in a partial atrophy of the optic nerve.

Therefore we should seek the therapeutic indication given by the pathogeny of the disease such as we conceive it to be in the light of the discoveries made by modern medicine. Certainly the pathogeny of neuritis of the trunk of the optic nerve is still far from being very clear. Nevertheless, we know that in the majority of cases these inflammations are of infectious origin.

We shall regard as **Retro-bulbar Neuritis** those cases where a pathological alteration of the axial fibres of the optic nerve has brought about a more or less marked atrophy of the nervous

filaments that go to the macula. As regards the papilla, all inflammatory phenomena may be completely absent, and it is with difficulty, in some cases, that one can recognise a partial pallor with excavation of the optic nerve. The primordial symptom is the presence of a more or less absolute central scotoma with a relative integrity of the periphery of the visual field.

Neuritis is usually bilateral from the first, but in some rare cases the eyes are affected one after the other. It is even possible that one eye alone is involved if by a happy treatment we have managed to stop the evil in time and to destroy its cause.

In theory the limits of retro-bulbar neuritis are well defined, but practically many cases present peculiarities that render their classification difficult. To our mind, the atypical forms are more common than the others. If one does not wish to consider the latter as instances of retro-bulbar neuritis, they may be termed cases of central amblyopia, in order to distinguish them from papillitis and neuro-retinitis.

The first observation that I shall quote is the following:

Retro-bulbar neuritis with contraction of the visual field and relative central scotoma; almost complete cure after subconjunctival injections.

M. T—, 40 years, had never had syphilis, but suffered from pains in the extremities when exposed to cold. No acute rheumatism, alcoholism, or abuse of tobacco.

After having been exposed to cold whilst perspiring, he was seized with shivers and heaviness of his head. He did not keep his bed. On the following day he was astonished not to be able to distinguish the people who passed in the street. He tried to read, but could not do so. All of this he attributed to the chill, and did not let it engross his mind. This state of things continuing, his medical man advised the patient to give up the use of tobacco and of alcohol. It may be noted, in passing, that the patient drank one litre of wine daily, and smoked a few pipes of tobacco only.

The patient, obtaining no improvement, came to Paris, where he was subjected to injections of strychnine and to electricity without result. We saw him on June 4th, 1891, six months after the trouble began. With the ophthalmoscope, the papillæ were very pale, with deep physiological cups. The visual fields were contracted, with a relative central scotoma: eccentrically all the colours were well seen. R. V. $= \frac{1}{20}$; L. V. $= \frac{1}{15}$; read No. 8. The patient was subjected to subconjunctival injections of $\frac{1}{20}$ of a milligramme of sublimate, one a week to each eye, without other treatment.

After six subconjunctival injections, the visual field was double its former size. R. V. = $\frac{1}{10}$; L. V. = $\frac{1}{8}$; read No. 4. Able to read his newspaper. After fifteen injections the visual field became almost normal, except for the central scotoma, which persisted in an attenuated form. R. V. = $\frac{1}{8}$; L. V. = $\frac{1}{6}$. Treatment was discontinued from this date. This relative cure was maintained. Six months later V. = $\frac{1}{8}$ and No. 2. A very slight central scotoma persisted.

In the foregoing case we had, therefore, a sudden reduction of sight in both eyes, with concentric contraction of the visual field, and a central scotoma, absolute for colours and relative for white. Despite four months' treatment with pilocarpine, followed by strychnine and electricity, the vision failed to improve in the least, although the use of tobacco and of alcohol had been stopped. In my opinion, the amblyopia was due neither to tobacco nor to alcohol, but to an inflammatory process affecting the posterior part of the optic nerve, a retro-bulbar neuritis of an acute infectious origin, or one due to cold. There was no infiltration of the papilla when the patient was examined six months after the beginning of the disease. But that sign is usually absent, or of so fleeting a character that it is no longer to be recognised when the patient consults us. A sign which, on the contrary, is almost constant is pallor of the temporal segment of the papilla and a more or less deep excavation of the last-named structure. But it is not at all characteristic, and has a relative value only.

I recognise that the above observation is not very convincing, but here is a second of a more conclusive nature.

Central amblyopia, non-toxic; rheumatism; rapid cure by subconjunctival injections.

M. H—, 36 years, a rheumatic subject, has kept his bed for six weeks on account of an attack of acute articular rheumatism. The heart has been affected. The patient has often complained of pain in his jaws and ears. There has not been the least abuse of tobacco or alcohol. The sight had been failing for a year, so that the patient experienced great difficulty in doing his work as a notary's clerk. Since September 1st he had been compelled to give up all work, as he was not able to read: a cloud came between his eyes and the letters he looked at. When we saw the patient we thought at first of a toxic amblyopia, but for several months M. H— had given up smoking, while he had never taken too much to drink. Nevertheless his sight continued to fail. With the ophthalmoscope, the fundus of the eye was normal, but there was a tolerably well-

marked physiological excavation, with pallor of the temporal half of the papilla.

October 15th, 1891.—R. V. = $\frac{1}{6}$ and No. 8 Wecker at 20 cm., L. V. = $\frac{1}{6}$ and No. 7 Wecker at 20 cm. The periphery of the visual field was normal, but there was a relative central scotoma, especially for colours, none of which could be recognised centrally. 29th.—After four subconjunctival injections, R. V. = $\frac{1}{2}$ and No. 3, L. V. = $\frac{2}{3}$ and No. 2. No other treatment had been adopted beyond the subconjunctival injections of sublimate. The cure being, so to say, complete, nothing more was done except to administer one subconjunctival injection a week for two months. Sight did not become altogether normal, but finally the patient was very pleased to be able to read and write, things that he had been unable to do for more than a year. Under extremely feeble illumination, a central scotoma for dull-green could still be demonstrated.

How can we explain in this case the instantaneous, as it were, improvement of sight produced by the subconjunctival injections of sublimate? That is difficult. If we had had to do with an alcoholic or tobacco amblyopia the cessation of the use of tobacco and of alcohol should have improved the sight, but not in so short a time. Moreover, the patient had not smoked for two months, and had always been very temperate. Is it not simpler to think that we had to deal with an amblyopia of an infectious nature, of which we do not yet know the exact cause? In this case the antiseptic action of the sublimate would explain the rapid disappearance of almost all the morbid symptoms. The patient, we may repeat, was a rheumatic subject.

It would occupy too much time to relate here all the observations that I have collected of retro-bulbar neuritis improved or cured by subconjunctival injections.

The two cases given above may not appear to be very conclusive, but it must not be forgotten that in the first case the disease was not treated until it had lasted for six months, so that a partial atrophy of the optic fibres had already taken place.

Retro-bulbar neuritis, however, taken at the commencement, may sometimes recede or be completely cured, it may be spontaneously, or it may be under the influence of an appropriate treatment.

In the April number of *La Clinique Ophtalmologique*, 1896, I related a case of unilateral retro-bulbar neuritis, which, in the absence of other ætiological factors, I attributed to the action of cold. Here in a few words are the salient facts of the history:

The patient, a conductor on the electric railway, had been

exposed for the whole of one day to a glacial wind, which struck the left side of his face. After two or three days, he noticed that his forehead was benumbed, and that the sight of his left eye was obscured as if by a cloud. When I examined the patient, I found an amblyopia of his left eye so complete that he could scarcely distinguish fingers at some centimètres. The fundus of the eye presented no alterations whatever. I thought of a retro-bulbar neuritis and examined the visual field with care. The existence of a large absolute central scotoma confirmed this supposition.

But the optic nerve was not alone affected, inasmuch as the branch of the trigeminal, which emerges from the infra-orbital foramen, was itself paralysed, and all the parts of the face and eyebrow supplied by it were quite insensitive. A slight prominence of the eyeball seemed equally to indicate that the tissues lying at the bottom of the orbit were involved in the inflammatory process.

With three retro-bulbar injections of cyanide of mercury I succeeded in producing in a few days a *restitutio ad integrum* of the sensibility, the acuity of vision, and of the visual field of the patient.

I wish yet to mention a case which presented a great likeness to the preceding.

Mrs. A—, 24 years, a very robust woman, received five months ago a violent blow from the shaft of a carriage upon the external orbital border of the right eye, an injury that was not followed by any further symptom as regards the eye. It was not until six weeks or two months had elapsed that Mrs. A—, who had nursed a baby for six months, found the sight of the right eye failing; the things she looked at were covered with a light fog. The cloud became progressively thicker and thicker, until at the end of several weeks the patient found, on April 28th, that she could distinguish nothing with the eye; it was with great difficulty that she could see hand-movements at a few centimètres.

Upon ophthalmoscopic examination, no appreciable alteration in the fundus of the eye, aside from a redness of the papilla, somewhat more marked than that of the other eye. No cloudiness of the media could explain so pronounced an amblyopia. To exclude the hypothesis of hysteria, the cutaneous sensibility was carefully tested and found to be normal; no anæsthesia of the pharynx; no stigmata of hysteria; no trouble of accommodation; emmetropia. The visual field—taken with difficulty but great care—involved a positive diagnosis which placed hysteria out of the question as a cause. The marked amblyopia, accounted for so little by the results of ophthal-

moscopic examination, had as its cause a large absolute central scotoma, in which neither white nor colours could be perceived. The peripheral boundary of the field, however, was scarcely diminished.

That was a special form of amblyopia not so rare as one might believe, and one that would be observed oftener if the visual field were taken in many of the cases where it is thought to be impossible. Had the prolonged nursing anything to do with the development of the amblyopia? In any event, I told the patient to wean the infant.

Recalling the former case, which was almost identical, I applied the same treatment to the present patient.

After three injections of cyanide of mercury, 1 : 5000, there was no change in sight. Was the solution too weak? A final trial was made, this time with a stronger solution, not of cyanide of mercury, but of cyanide of gold and potassium (1 : 1500), half a syringeful being injected. Pain was violent from the start; chemosis was notable. Three leeches were applied the same evening. Three days afterwards I saw the patient again. Her conjunctiva was still much swollen, but she could half-open her eye, and I found with surprise that she could count fingers at 2 mètres, and had a measurable acuity of vision equal to $\frac{1}{10}$. With the perimeter, the central scotoma could no longer be demonstrated except for red and green. May 15th.—V. = $\frac{1}{2}$. 18th.—V. = $\frac{2}{3}$. 22nd.—V. = 1. The field of vision had become normal, aside from a tiny central scotoma for green and a slight contraction of the field for that colour, a fact almost constantly observed in true retro-bulbar neuritis.

What a strange and rapid metamorphosis! Had I seen a single case only of this kind I should not have hesitated to diagnose hysteria, despite the altogether unusual nature of the visual trouble. In fact, everything is possible in that curious and capricious neurosis.

The miraculous effects of **Metallotherapy** might explain this cure, since the first injections of mercurial salts remained without effect, while a single injection of a salt of gold had, in nine days, brought about normal vision. But is it not simpler to assume that the injection of cyanide of gold was more active because its strength was so much greater, 1 : 1500, as compared with the cyanide of mercury, 1 : 5000; that, moreover, it was helped by a ground already prepared by the three preceding injections, the cyanide of gold having thus a therapeutic action more energetic than that of

mercury? For my own part, I am convinced that the same result would have been obtained by injecting 1 : 1000 cyanide of mercury; and that this was not an instance of hysteria, because there is too close a connection between this and the first observation which presented anatomical stigmata, precluding all idea either of hysteria or of simulation. Then the sequel of the case fully confirmed the diagnosis of retro-bulbar neuritis. Upon ophthalmoscopic examination, the papilla of the affected eye, which had at first shown only a little ill-marked redness, now presented an obvious pallor of its temporal segment, corresponding to the region occupied by the macular fibres.

A certain number of cases consecutive to lactation * have already been published, but they do not in the least resemble the case just related. All of these amblyopias, in fact, came on about the seventh week after confinement; in no instance was the existence noted of an absolute central scotoma. On the other hand, all the pathological lesions could be explained by enfeeblement of sight; an intra-ocular optic neuritis of a marked kind was always found with the ophthalmoscope; the cure was almost always relative, accompanied by slight atrophy of the optic nerve. In my own case there had never been papillitis, but, on the other hand, all the symptoms indicative of a characteristic retro-bulbar neuritis.

Retro-bulbar neuritis has now become almost a morbid entity by its cardinal symptom—central scotoma.

Von Graefe was the first to suggest that a disease of the optic nerve might occur behind the eyeball, and produce a serious effect on vision without betraying its existence by any ophthalmoscopic alterations.

Leber studied retro-bulbar neuritis more in detail, insisting upon the absence of intra-ocular lesions, and upon the fact that intoxications are its only cause. He brought forward the importance of heredity, and created a type based upon numerous observations, namely, **hereditary retro-bulbar neuritis.**

To Sammelsohn belongs the honour of having furnished the irrefutable anatomical proof of its localisation. It is at the level of the optic foramen, in the osseous canal, and in the axis of the optic nerve that one finds the chief focus of the inflammatory lesion—interstitial neuritis, partial, central, with multiplication of the nuclei. As it gets farther away from the chief focus the lesion goes *decrescendo*, upwards and downwards, and one soon finds only

* Heinzel, Deutschmann's *Beiträge z. Augen.*, xxi, 1895, with bibliography.

an atrophy of the nervous fibres. The latter, which occupy the centre or axis of the optic nerve at its entrance into the orbit, end by occupying, at the point of penetration of the retinal vessels, the external sector of the optic nerve in order to reach the macula. The atrophy of these macular fibres, which have become external at the level of the papilla, explains the atrophic temporal excavation that is almost always found after a retro-bulbar neuritis.

How can the genesis of the pathological process be explained? Why should the optic nerve suffer more as regards its axial fibres than as regards those which lie in immediate contact with the sheath, and which are accordingly more exposed to neighbouring lesions?

An inflammation of the sheath should *a priori* affect specially the subjacent fibres. That is true in some cases, but inflammation of the sheath or of the osseous canal would be able also to cause compression of the whole optic tube. Now in that case the part which would suffer the most would be that receiving its nutritive blood-supply with the greatest difficulty. This would be the centre, since at that level, before the entrance of the central vessels, the finest capillaries are those which nourish the axial part of the nerve. Accordingly, it is at this spot that a trophic and then an inflammatory disturbance will be set up.

As regards the ætiology of retro-bulbar neuritis, we have, to begin with, all the inflammatory lesions of the bone, periosteum, and sheath at the level of the optic foramen, whether due to a chill, syphilis, tubercle, or a neighbouring affection, such as sinusitis, etc.

Next, we have the whole series of chronic or infectious intoxications. In the last category, how can we explain the fact that the centre of the nerve suffers most? It is, without doubt, for the same reason that the axial fibres are poorer in vessels, and that this part of the optic nerve somehow forms its *locus minoris resistentiæ*. According to Nuel, toxic retro-bulbar neuritis is secondary to an alteration of the retinal elements themselves. The observation is true as regards animals poisoned by quinine (Druault).

One fact is important and should not be lost sight of, namely, that the entire pathological process may evolve without betraying its existence by a single ophthalmoscopic sign, although central amblyopia may already be definite and irremediable. It is not until later that partial atrophy and temporal excavation of the optic papilla are noted.

It is not so much the size of the scotoma as its intensity that

renders the prognosis serious. The gravest result of the disease, in any case, is the persistence of an absolute scotoma.

Retro-bulbar neuritis due to a chill, taken at first, is, as a rule, favourably influenced and even cured by local abstraction of blood, iodide of potassium, and local mercurial inunctions.

We are now in a position to claim that intensive subconjunctival injections yield rapid and brilliant results. Similar treatment is applicable to the neuritis of syphilis, tubercle, or any other infection.

As to retro-bulbar neuritis set up by intoxication by tobacco, alcohol, or different medicamentous agents, when the cause is recognised, before there has been time for atrophy to supervene, they are, as a rule, cured spontaneously *sublata causa*.

Hereditary retro-bulbar neuritis, so well described by Leber, exacts amongst all the forms of the disease the worst prognosis. Nevertheless, even in these cases it is necessary to follow the treatment unswervingly and without despair for long months, since improvement has been seen, and blindness never becomes absolute.

Allow me to quote a case very interesting both as regards its evolution, and especially the way in which subconjunctival injections manifested a remarkable action.

Mrs. P—, 19 years, came on April 19th, 1901, complaining of very marked trouble of her sight. For almost two months her left eye had been affected. This followed pain diffused over her whole body, which she attributed to rheumatism, a malady from which she had often suffered (two years before she was confined to bed for a fortnight with rheumatism). However, the illness appeared rather to have been of the nature of the lumbago which characterises an attack of influenza. There had been neither pain nor neuralgia of the head or eyes. It was eight or ten days after this attack that the patient found the sight of her left eye so poor that it disappeared almost completely after the lapse of another week. The sight of the right eye gradually became affected, but to a slighter degree. On March 4th she consulted an oculist, who made the following diagnosis:—R. E.: incipient retro-bulbar neuritis. L. E.: complete loss of sight; retro-bulbar neuritis with very marked central scotoma. A month later the diagnosis was thus modified:—R. E.: retro-bulbar neuritis in full evolution. L. E.: atrophy of the papilla following retro-bulbar neuritis. No treatment beyond potassium iodide.

Actual condition.—Externally, the eyes showed no particular changes. For several days past the sight has been so bad that the patient has had to be led about. R. V. = $\frac{1}{50}$; L. V. = $\frac{1}{40}$. A very marked central scotoma, both for white and colours. As

regards the right eye, the periphery of the visual field on the temporal side was contracted. With the ophthalmoscope the papilla of the right eye is slightly dull, with diffuse edges and somewhat dilated vessels. In the left eye, on the contrary, the optic papilla is white, and manifestly atrophic on the temporal side.

The diagnosis, therefore, was obvious—*retro-bulbar neuritis, evolving in the right and receding in the left eye.*

On April 11th a syringeful of cyanide of mercury, 1 : 1500, was injected behind the globe. The injections, numbering seven in all, were repeated turn by turn to the two eyes. In the left eye sight improved quickly, but in the right eye the neuritis continued to evolve. May 15th.—R. V. = $\frac{1}{60}$; L. V. = $\frac{1}{4}$.

After a fortnight's rest, a new series of subconjunctival, or, rather, retro-bulbar, injections were practised—about ten all told. June 1st.—R. V. = $\frac{1}{15}$; L. V. = $\frac{1}{3}$. 7th.—R. V. = $\frac{1}{8}$; L. V. = $\frac{2}{3}$. July 8th.—R. V. = $\frac{2}{3}$; L. V. = 1. With the ophthalmoscope, it was found that the neuritis had disappeared from the right eye, while it could no longer be said that atrophy existed in the left eye. Visual fields normal; no trace of a scotoma for white or colours.

The foregoing observation is most instructive, and shows us—

1st. That subconjunctival injections exert a powerful action upon neuritis of infectious origin.

2nd. That the timely moment for therapeutic intervention is quite at the beginning, or when the inflammatory process begins to recede.

In point of fact, the eyes in our case were treated at altogether different stages. The left eye, already on the way to atrophy, or rather to regression of the inflammatory process, improved rapidly, while the right eye, in the full development of optic neuritis, at first obtained no benefit from the treatment. One had to wait a fortnight, and the injections then brought about a rapid cure.

At the *acme* of retro-bulbar neuritis the therapeutic action is scarcely appreciable, whereas at its commencing or regressive stage treatment exerts a remarkable action. There is nothing in that that need surprise us; it is almost the same in all morbid processes, and we have in it a simple question of therapeutic opportunism taught by experience to every clinical observer. Many diseases can be aborted at the beginning; at the climax it is better to wait, and to resume the offensive only when the malady has reached the end of its evolution.

Apart from Leber's hereditary form and from tobacco and alcohol amblyopia, we therefore conclude that in acute retro-bulbar neuritis

due to infection or to cold, as well as in the form coming from neighbouring lesions, as sinusitis, periostitis of the optic foramen, etc., the influence of subconjunctival injections is undeniable and potent when the latter are well understood and applied before the central fibres have undergone complete atrophy.

This local therapy should not be allowed to interfere with general treatment by mercurial inunctions, which constitute, in fact, the only really efficacious means at our disposal up to now. Hock * maintains that mercurial inunctions applied to the brow and temple every two hours constitute so sovereign a means as to allow one to affirm that cure will surely come about in a few weeks. The method combines local and general treatment.

* *Beiträge zur Lehre von Neuritis retro-bulbaris*, Wien, 1883.

LECTURE XXV.

Summary.

Diseases of the optic nerve (*continued*): intra-ocular optic neuritis, specific neuritis or neuro-retinitis: its gravity.—The importance in these cases of intensive and prolonged treatment.—Papillitis or neuritis from stasis (*Stauungspapille*).—Neuritis from cerebral tumours.—Trephining, lumbar puncture, etc.—White atrophy of the optic nerve, grey atrophy, and tabes.—Specific treatment: electricity, strychnine, phosphorus, etc.

We have seen in the last Lecture that however precarious may be our means of action in the treatment of disease of the optic nerve, it is yet sometimes possible to stop the morbid process at its commencement or to hasten resolution towards its decline, and in that way to reach a cure that will be relative or complete according to the particular case. Such results have been obtained, especially in retro-bulbar neuritis due to infection or to cold.

These cures are, unfortunately, exceptional, and despite all our efforts we generally find that a neuritis follows its course and ends in a partial **Atrophy of the Optic Nerve**, which entails the loss of the greater or less part of the visual field (*central or peripheral scotoma*).

But is this really because we are completely disarmed against a morbid process that develops in the depths of the tissues, and because we find it difficult to make our remedies reach so far? Is it not rather that we still know too little about the pathogeny and evolution of the pathological processes that are going on in the optic nerve itself? Is it not also because we are taught to believe too implicitly in the fatal issue of the disease—because we lack that wish to cure which makes the force of true therapy?

Recognising the few weapons with which we are armed, let us know how to seize the propitious moment for bringing them into

action; let us know how to profit cleverly on the least occasion offered by nature for successful intervention.

Clinical observation will give us the bases of therapeutic opportunism. The most potent and specific medication, if I may say so, involves not only a risk of failure, but may also give bad results if it is not applied at the proper moment.

A striking example of the truth of this statement is afforded by our first case, one of bilateral retro-bulbar neuritis of infectious origin. The eye first affected, which was certainly the more seriously compromised, and which appeared to be on the road to atrophy, improved with remarkable rapidity because it was at the period of regression of the morbid process. The other eye, on the contrary, which was in the full evolution of the pathological process, was scarcely influenced by our therapeutic efforts. We were forced to wait almost a month before resuming the subconjunctival injections, which then yielded a prompt result.

Have we not already demonstrated the same thing in central choroido-retinitis? I have just repeated the experience in three cases of myopic choroiditis. The first two, after some injections, first of sodium chloride and then of mercury cyanide, experienced so much improvement, that in less than a fortnight, reading became possible, although that had been out of the question for a long time previously. The third case, on the other hand, became worse and worse despite the treatment, and fresh foci of choroiditis and small hæmorrhages could be found around the papilla and the macula, along with a marked congestion of the fundus of the eye. For several days the injections were replaced by the application of leeches. The injections were then resumed, being followed each time by the application of leeches. The result soon showed that we had been right to temporise in order to secure the best conditions for opportune therapeutic action.

À propos of iritis and parenchymatous keratitis, we have already remarked that the therapeutic results obtained by the most active measures were denied by some and affirmed by others. All of this goes to show that different observers do not always find themselves under equally favourable conditions, although all are treating the same affection by identical means.

So far we have studied only neuritis affecting the trunk of the optic nerve; we have seen that this form has generally but little effect upon the intra-ocular portion of the optic nerve—that is, the papilla.

Optic Neuritis or **Papillitis** is rarely a local malady. It generally proceeds from a deeper affection.

Syphilis, infectious ailments, toxæmias due to troubles of nutrition (diabetes, albuminuria, serious forms of anæmia, etc.), or intoxications (plumbism, etc.), as we have already seen, usually entail simultaneous changes in the retina, choroid, and papilla. Heredity (Leber) appears to be the cause of certain cases of neuritis. But we shall not dwell on this form, especially as in it our therapeutic efforts are next to useless.

Diseases of the orbit and of neighbouring cavities, tumours, or inflammations are the only cases where one can look upon optic neuritis as a local affection. It is then almost invariably unilateral. The treatment of such cases is obvious: the cause of the mischief must be got rid of as quickly as possible. If we have to do with a sinusitis, it becomes necessary, at the earliest possible moment, to evacuate the pus by surgical means through a large opening. Operable tumours of the orbit must be removed. Periostitis of the walls of the orbit must be treated according to its ætiology and its particular surgical indications. The most prompt and the surest results will generally be obtained by making frequent applications of what have been called "mercurial cataplasms." The heat and the local action of the mercurial lanoline induce a rapid resolution of the inflammatory process. Further, it will be advisable to aid this local action by the administration of potassium iodide in ascending doses of two to ten grammes a day.

An interesting form of disease is that known as **Specific Neuritis.** We are in the habit of looking upon all diseases which depend on syphilis as having a relatively favourable prognosis. Well, Gentlemen, that is not so as regards the form of specific neuritis we are about to study. There are, nevertheless, cases of papillitis consecutive to syphilitic lesions of the orbit which yield very quickly to the classical treatment; but it is not of that purely neuritic form that I am going to speak, but rather of that form in which the optic nerve, the retina, the choroid, and the vitreous body itself are implicated in the morbid process at one and the same time.

We have, in fact, not to deal, strictly speaking, with a true neuritis, inasmuch as the papilla is hardly swollen, and the veins are scarcely more turgescent and tortuous than usual. The striking feature is a dulness and a dirty aspect of the papilla, which is due, in the main, to a slight infiltration of the retina, and to the fact that the layers of the vitreous body lying in immediate contact

with the papilla have lost their normal limpidity, and present a highly characteristic dusty state.

As a rule, this specific neuritis is merely the first stage of multiple alterations in the retina and choroid. In fact, finally one sees appear, perhaps at the periphery, or perhaps around the macula and papilla, deposits of choroido-retinitis, with all the ultimate complications belonging to those affections, such as choroidal atrophy, hæmorrhages, retinitis proliferans, etc.

You will understand, then, that when faced by so redoubtable an affection your treatment should be rapid and energetic, and maintained for a long time, naturally with intervals of rest. You at once submit your patient, therefore, to an intensive mercurial cure. This is done by means of periorbital mercurial frictions, and by daily intra-venous injections in doses progressively rising from 0·008 to 0·020, or even 0·030. The care of the mouth must be attended to, and a look-out be kept for the first signs of reaction in the shape of the abdominal symptoms already mentioned. The patient must be asked each day whether he has suffered from diarrhœa or colic. When this reaction is produced, the doses must be reduced. They are then brought back to the limit dose. The latter may later be exceeded, on account of the tolerance that is soon acquired as well by the patient as by the infectious elements, to which time must not be given to regain their virulence.

Thanks to this plan of action, I have obtained cures in cases that I at first regarded as hopeless, inasmuch as I had never been able to get a cure before, since I had confined myself exclusively to the classical indications of syphilitic treatment.

In these rare cases it is, I repeat, necessary to understand thoroughly the limits of the toxic reaction of the cure by intra-venous or hypodermic injections—that reaction upon the intestinal canal you seldom if ever observe in treatment by inunction, which entails a stomatitis more rapidly. This may be of so intense a nature that you are obliged to suspend mercurial treatment before the latter has had time to stop the morbid process completely.

It must not be forgotten that you cannot get a permanent cure in specific neuritis by any treatment which lasts for a few days only. Distrust the rapid ameliorations that are sometimes observed after an intensive cure. If the patient stops treatment too soon, manifestations may come on later which are more serious than the original ones, and against which our weapons find themselves more or less blunted.

This is the reason why alternations of treatment should never be

neglected. I should add that after you have first made thirty or forty intensive intra-venous injections, it becomes necessary to change for a time the method of treatment. For example, you may make a series of subconjunctival injections (two or three a week) in each eye, turn by turn. The patient is then left alone for a fortnight's repose, after which you may make a cure by pilocarpine, or prescribe a sojourn of three weeks in a spa provided with warm sulphurous waters.

Iodide of potassium given by itself yields results in specific neuritis that are more than mediocre. It may, nevertheless, render service if only in the sense that it compels the patient to look after himself, and that it relieves the mercurial treatment.

By these various means you manage to keep your patients under continuous observation for almost four months. Then, even if the patient seems to be cured (which is rarely the case), you will still find the papilla dull and dirty, and small choroidal deposits in the fundus of the eye. The latter show clearly that the morbid process is not extinguished, and furnish you with a formal indication for a fresh series of injections.

If the patient is observed with care you can easily find indications for continuing the treatment, naturally with intervals of rest, during two or three years or even longer. You are indeed fortunate if by your therapeutic obstinacy you manage to preserve the sight of all your patients affected with specific neuritis, because the cure of this malady is to be looked upon as constituting an important victory.

The following is a fact that I have often observed. During the whole period that you are making intra-venous injections, you see no improvement. But you must not stop on that account, for you will often be surprised to see improvement manifest itself a fortnight or a month after the last injection has been made. You will then be inclined to attribute the improvement to the remedy last administered, while it is really due to the delayed effect of the first medication, which manifests itself in this way, as I have often convinced myself, as much in choroiditis and in interstitial keratitis as in specific neuritis.

True Optic Neuritis, Neuritis by Stasis (*Stauungspapille*), is always a sign of intra-cranial mischief, as cerebral or cerebellar tumour, meningitis, or hydrocephalus, invariably associated with an increase in the intra-cranial pressure.

The patient, generally speaking, consults the oculist only when

it is too late—when the process is already so advanced that sight is seriously affected, and sometimes even completely extinguished.

The scene is usually opened by headache, accompanied by nausea and vomiting, symptoms that sometimes lead the medical man to think that he has to deal with a case of gastric disturbance or of migraine. At other times there is no disturbance of the general health, but the patient, finding his sight lowered, comes to consult us with a double optic neuritis, which has already lasted for several weeks. The papilla, enlarged in all senses, is very swollen, and its edges are indeterminate; an œdematous infiltration, striated with flame-like hæmorrhages, accompanies the tortuous and turgescent vessels, which are sometimes hidden by the exudation and the œdematous tissue of the papilla.

At other times you observe the same clinical picture in patients who do not complain of their sight in the least, but who are sent to you by a perspicacious colleague wishful of confirming a diagnosis of cerebral tumour by ophthalmoscopic examination.

The visual acuity is normal; colours are well seen; the visual field presents no peculiarities beyond an enlargement of the blind spot. Sight, however, soon sinks; and if you cannot suppress the cause of the mischief, complete blindness ensues from white atrophy of the optic nerves.

The disease is very difficult to cure, because its precise diagnosis is generally impossible.

Should you learn that the patient has suffered from a disease of the ear accompanied by suppuration, to which you assign the seat of the morbid process, you may suppose a meningitis due to caries of the temporal bone. A surgical operation done in time may, by evacuating the purulent focus, give complete cure. Further, if by a certain grouping of symptoms you can make a precise and well-localised diagnosis of cerebral tumour, then a timely trephining may have chances of success.

But it is necessary to recognise that these are exceptional cases. Much more frequently we find a double optic neuritis not associated with any symptoms precise enough to allow an exact diagnosis to be made. We are fortunate when the patient's history indicates a specific or even a tuberculous origin for the eye malady.

Under such circumstances you will have recourse to intensive mercurial frictions and to the administration of iodide of potassium in large doses. Sometimes you thereby obtain a more or less complete cure. Iodide of potassium has a powerful and rapid

action upon gummata or osseous lesions. Its effect is not at all the same as in lesions of the uveal tract.

The intra-cranial process may terminate either spontaneously or under the influence of treatment, and life be saved; but generally sight does not return, or returns to a very incomplete extent, and white atrophy of the optic nerves is often the inevitable consequence of the neuritis.

During the last few years various **Surgical Procedures** have been tried in the treatment of optic neuritis.

Trephining has been attended with some success, although usually the morbid focus has not been reached by its aid. It would seem, therefore, that diminution of the intra-cranial pressure exerts a direct action upon stasis neuritis.

A diminution in the pressure of the cerebro-spinal fluid may equally be brought about by the operation of lumbar puncture. In one case I observed a notable but transitory improvement in sight after lumbar puncture, but the patient then passed away from my observation.

These procedures, which belong to major surgery, have not yet been studied enough to allow us to lay down the indications for their performance.

Hitherto all surgical interference with the optic nerve itself—as incision of the nerve-sheath, elongation of the optic nerve, etc.—have yielded inconstant results of so imperfect a nature that they cannot be recommended. Possibly in the future, by adopting the method of Krönlein, which allows the depths of the orbit to be seen, these operations may be performed with more precision.

You will see, then, that in optic neuritis of cerebral origin our means of treatment are still very uncertain. They are even more so in essential atrophy of the optic nerve supervening in affections of the spinal cord.

White Atrophy following neuritis is, relatively speaking, under the influence of certain methods of treatment, particularly when the original cause of the neuritis is undergoing retrogression. Certain fibres of the optic nerve, not yet altogether atrophied, may then be recalled to life. Of these clinical indications I have spoken above, and have pointed out how important it becomes not to allow them to escape us, for they are not likely to occur again.

For **Grey Atrophy**, which often constitutes one of the first symptoms of tabes and of several other affections of the spinal cord, the prognosis is extremely bad. Indeed, the diagnosis, once well established by ophthalmoscopic examination, the visual field, per-

ception of colours, etc., blindness of a more or less complete description is only a question of time.

The evolution of the atrophy is very irregular. Blindness is often complete in one or two years, although it now and then happens that one eye is alone lost, and that the other, more or less affected, retains some sight for several years. At other times the process evolves with great rapidity, but some central fibres remain intact, and thereby preserve to the patient a glimmer of sight for the remainder of his days.

How many of these stoppages in the full course of the disease can be put down to the treatment adopted? That is very difficult to say; it is also equally difficult to explain the action of any medicament in a degenerative process, pure and simple, of the nerve-fibres.

Most of the remedies used in optic atrophy are merely stimulants —as, for example, strychnine, brucine; or eutrophics—as phosphorus, arsenic, etc.

Electricity applied to the optic nerve, or, rather, to the eyeballs, acts suggestively rather than scientifically; it is a good means to adopt in every case, because it can never do the least harm.

As to mercurial treatment, it is indicated in certain cases of tabes when the history of syphilis is clear. However, even under such conditions, the treatment is followed by poor results. Is this because it is commenced too late, or because it is pursued with too little energy? The opinions of writers differ completely on this point: the one school admits that specific treatment will bring about, if not actual cure, at least a slackening of the morbid process; another school (the adherents of which are numerous) believe that there is often a rapid lowering of sight under the influence of mercurial treatment.

I have often convinced myself of the truth of the last-mentioned observation. Until the last few years I was little in favour of the treatment of medullary atrophy of the optic nerve by inunctions and mercurial injections. But on two successive occasions I have observed the following fact:—after about a dozen intra-venous injections the sight of the more affected eye diminished rapidly, and the other eye, not yet involved, was seized in its turn. The injections, nevertheless, were continued, and I was happy at the end of the twentieth injection to be able to prove that sight remained stationary, and had even improved somewhat. Starting from this moment, there was in these cases a complete arrest of atrophy, a

fact that I was able to prove during the two years the patient remained under my observation.

A second case of the same kind (still under observation) has given me almost the same result. Are these pure coincidences? Who can ever tell?

LECTURE XXVI.

Summary.

Ocular massage employed from very ancient times in the treatment of trachoma and keratitis.—Rotatory massage—radial massage—vibratory massage—pressure massage.—Mechanical action upon the cornea, conjunctiva, crystalline system, and intraocular fluids; physiological action upon the ciliary muscle and the nutrition of the tissues.—Applications: accommodative asthenopia, amblyopia ex anopsia, myopia, hypermetropia, glaucoma, ophthalmic migraine, etc.

From the most ancient times **Massage** has been used in certain ocular affections, a practice continued to the present day in an absolutely empirical manner. Conjunctival massage has been lauded in various diseases of the conjunctiva, especially in trachoma. It would occupy too much space to enumerate all the procedures that have been followed from the times of Hippocrates to the present day.

Corneal massage, simple or medicamentous, has been employed particularly in the treatment of leucomata, diffuse corneal infiltrations, receding parenchymatous keratitis, and even in episcleritis and spring catarrh.

In some forms of tuberculosis affecting the cornea and the iris Dr. Abadie has suggested that direct massage of the cornea should be carried out by means of iodoform and lanolin.

Personally, I have obtained good results from massage with mercurial lanolin in diffuse corneal infiltrations, in slight forms of parenchymatous keratitis, and, above all, in spring catarrh with pericorneal growths.

Massage with calomel, sugar, etc., has furnished its proofs for a long time in the treatment of leucomata of the cornea.

If we see what modern literature has said about massage we find at the London Congress in 1872 * a communication by Donders, who

* *Klinische Monatsblatter*, 1872.

praises massage in affections of the cornea. Heiberg * has obtained good results from the method in faceted leucomata.

Junger, Chodin, and Becker recommend massage as a means of hastening the absorption of the crystalline masses left after discission of the lens.

Pedraglia, Klein, Schenkel, and Czapodi have also published communications very favourable to massage. Mauthner and Hirschberg have seen emboli of the central artery dissipated under the influence of massage. Pagenstecher,† in a preliminary communication, was especially struck by the fact that in one instance the intra-ocular tension was markedly reduced by massage; and he also had occasion to observe the extremely favourable action of massage in a case of relapsing episcleritis. In a later communication ‡ he returns with more details and many facts to massage, circular and radial, which favours the lymphatic circulation of the cornea and conjunctiva. Before practising massage he introduces a little yellow ointment (1—10 per cent.) between the eyelids, more particularly in cases of leucomata, phlyctenulæ, and spring catarrh. In cases where the ciliary muscle was affected, Pagenstecher remarked a favourable influence upon accommodative asthenopia.

Gradenigo, Schenker, Wickerkievicz, and Schnabel have found a diminution of the tension in glaucoma, but this result was fleeting.

Gradenigo § praises the effects of massage in accommodative asthenopia, and has also observed a case of paralysis of accommodation completely cured by this simple means. He further quotes a case of bilateral detachment of the retina, which was quite cured on one side and much improved on the other by massage, repeated thrice a day, without any other treatment, not even rest in bed. Gradenigo attributes to massage a powerful action upon the circulation of the blood and lymph in the eye, even the retina undergoing a marked trophic excitation.

Dantziger,‖ after having reviewed all former communications, simply relates ten observations of diseases of the cornea treated by massage with yellow ointment, conjunctival abrasion being now and then added to that.

In recent times purely mechanical massage—**Vibratory Massage**—has been practised and studied seriously by Maklakow.¶ For this

* *Nagel's Jahresbericht*, 1874.
† *Centralbl. f. Augenheilkunde*, 1878.
‡ *Archiv f. Ophthal.*, 1881.
§ *Congrès Internat. de Rome*, 1894.
‖ *Graefe's Archiv*, 1895.
¶ *Archives d'Ophtal.*, Sept., 1893.

purpose he employed Edison's pen, which is capable of giving 9000 vibrations a minute. The needle, armed with an ivory button, when applied to the ciliary region, provokes a partial contraction of the pupil on the corresponding side, and sets the aqueous humour in movement. If there is hypopyon the latter fluid becomes cloudy, or filled with crystalline masses if there is traumatic cataract. It should be a most efficacious way of hastening the absorption of the masses. The vibrations are transmitted into the depths of the eyeball, and in the course of a few minutes, in glaucomatous eyes, the intra-ocular tension becomes sensibly and progressively reduced. Chronic irido-choroiditis and punctate keratitis have been much improved by this form of massage, which exerts its action by hastening the lymphatic circulation and facilitating the intra-ocular exchanges. Deposits on Descemet's membrane are said to disappear after three applications of massage (?).

Sneguirew,* in thirty-six instances of leucoma, obtained pronounced improvement in sight, especially after the first eight applications.† The same phenomenon has equally been observed in parenchymatous keratitis, which improved rapidly from the beginning and sometimes even from the first sitting.

In serous iritis (four cases) the retro-corneal exudation disappeared after three or four massages, the iris looked brighter, while the synechiæ became detached.

In traumatic cataract, and in discission of the lens in high myopia, massage separates the crystalline masses and notably accelerates their absorption.

In eight cases of scleritis and episcleritis vibratory massage gave remarkable results. In sixteen cases of glaucoma the intra-ocular tension became reduced after the first *séance*, although it often rose in the twenty-four hours, so that it was necessary to repeat the operation several times a day.

Piesberger,‡ of Stuttgart, has recently published his results with vibratory massage.

In paralysis of the muscles of the eye the motility was markedly augmented after each application of massage. Piesberger has obtained very brilliant successes in cases of episcleritis, on the condition that the massage was continued until the latter failed to cause the least hyperæmia. In very acute cases it is best to wait until the extreme

* *Congrès international de Moscou*, 1898.

† For the explanation of this fact see the end of the work, on the action of massage upon the accommodation.

‡ *Centralbl. f. prakt. Augenheilk.*, February, 1899.

irritability of the eye has passed away. In corneal opacities, sclerosing keratitis, etc., the results are good, although slow; in parenchymatous keratitis massage should not be applied until the inflammatory phenomena have disappeared. The same remark applies to iritis, irido-choroiditis, and chorio-retinitis, where massage, applied at the proper moment, now and then yields surprising results.

More striking still are the results obtained in long-standing choroiditis. There one saw scotomata diminish, acuteness of sight increase, and at the same time the fundus of the eye clear.

Retinal hæmorrhages are absorbed more readily under the influence of massage. Amongst the other therapeutic effects manifested by vibratory massage are the reduction of tension in glaucoma, and the more rapid absorption of the needled crystalline lens.

Finally, with the **Pressure Massage** introduced by Dr. Domec, of Dijon, we enter upon a new phase, rich in the promise of being able to apply massage to errors of refraction. Domec describes his method as follows:—"The end of each thumb, acting as a plug, is applied to the centre of the cornea through the upper eyelid, the fingers being extended flatwise upon each temple. One soon acquires the delicacy of touch sufficient to feel if the cornea shifts about under the thumb, and at the same time the lightness of hand necessary to make the pressures successive and not continuous. The duration of each massage is about five minutes, with one or two intervals of rest according to the individual sensibility. The pressures may be practised quickly or slowly. Eventually 500 pressures are made in the sitting. It is necessary, in asthenopia, scarcely to touch the eye at first, or the patient may give up the treatment after the third or fourth day."

By means of these pressure massages my friend and pupil, Dr. Domec, has obtained in hypermetropes an apparent reduction in the hypermetropia, together with an augmentation (sometimes very marked) of the visual acuity, especially in eyes with amblyopia, such as are often met with in hypermetropic squints. Thus, in an instance of this kind, the hypermetropia fell from 5 D. to 1·5 D., and the sight rose from $\frac{1}{20}$ to $\frac{1}{6}$, while the finest types could be read with relatively weak glasses.

The facts, according to Domec,* may be thus explained:—"Pressure exercised upon the flexible cornea is transmitted through the liquids of the ocular media. The crystalline lens, therefore, shares in the see-saw movements of the cornea. The fibres of the zonule of Zinn

* See Darier, *La Clin. Ophtal.*, 1899, No. 8.

are stretched by each pressure brought to bear upon the cornea, and that so much the more the stronger and more sudden the pressure applied. This series of pullings finally induce a lengthening of the zonule. The action of the ciliary muscle being increased, the power of accommodation is rapidly augmented. At the end of a certain number of massages the fibres of the zonule permanently remain more or less distended, which accounts for the diminution of the hypermetropia." This persistent elongation of the zonule is so much the easier to obtain the younger the subject and the less the accommodation has been exercised (amblyopic eye). There is scarcely any need to add that this theory is plausible only on condition that the hypothesis of Helmholtz with respect to the mechanism of accommodation is admitted.

From all this it follows that by pressure massage hypermetropia may apparently be considerably diminished; that the visual acuity is sometimes so much improved that an eye almost useless from amblyopia ex anopsia, as the result of high hypermetropia, may become serviceable for work; and that some squinting eyes may thus recover sight enough for the strabismus to be cured with the recovery of binocular vision.

Different accommodative asthenopsias are also susceptible of great improvement, and a hypermetrope who had been unable to work without glasses (+ 1·5) has been able to put them aside.* The treatment acts so much the better and more quickly the younger the patient, since the elasticity of the crystalline lens is greater and the action of the ciliary muscle stronger. It gives remarkable results when applied to an eye at once hypermetropic and amblyopic of which the congener has good sight; when the two eyes are amblyopic the improvement is less marked. Amelioration is meagre enough in aged subjects. Nevertheless, in presbyopes the wearing of glasses may be equally postponed by massage.

Some myopes gain notably in distant vision as well as in vision near by without the short-sight diminishing in any way,—that is to say, it is the acuteness of vision only that improves. In progressive myopia in young subjects, whose defect yearly augments by 3 to 6 D., Domec, by successive series of massage, has obtained an arrest of the increase. Such are the very interesting results obtained by Dr. Domec.

Since August, 1899, I have conducted a series of clinical observa-

* Such was the case with Dr. Domec himself, who has abandoned his glasses for three years. When he feels tired, he employs massage for a few seconds, and is then able to take up his work again.

tions upon the action of the various kinds of massage. To begin with, I took up Maklakow's **Vibratory Massage**, and afterwards Domec's **Pressure Massage**. At the beginning I was fortunate enough to fall in with a case of so-called congenital amblyopia in a squinter upon whom I had operated ten years previously. Despite a perfect surgical result he had relapsed two years later, because, even with proper glasses, binocular vision had not been regained. The case is worth relating.

M. G—, 19 years, convergent strabismus of the left eye 15° R. V. = $\frac{2}{3}$; L. V. = $\frac{1}{8}$. Although by retinoscopy there was in each eye 3 D. of hypermetropia with a little astigmatism, yet sight was not improved by glasses. After five applications of massage the sight of the left eye $\frac{1}{3}$. In order to compel this eye to work by itself, atropine was applied to the other. After five further applications of massage L. V. $\frac{2}{3}$. No. 2 could be read very well without glasses, whereas previously with this eye the patient had been unable to decipher even large characters. The squint was corrected by means of a very slight tenotomy; binocular vision was induced by stereoscopic exercises; and now sight is good in both eyes, and there is no strabismus.

Starting from this fact, brilliant as it was, I did not scruple to submit to massage all my patients suffering from squint, amblyopia, and asthenopia. As might be expected, all did not benefit in so great a measure from the good offices of pressure massage.

It would occupy too much space to enumerate here all the cases treated in this way. I shall merely say that in many cases of strabismus, where one eye was amblyopic, I succeeded by repeated massage, combined with stereoscopic exercises, etc., in diminishing the amblyopia or in causing it to disappear, and then in establishing binocular vision by bar-reading (*la lecture contrôlée*).

It was especially in hypermetropic convergent squint, in patients between ten and twenty years, that the results were brilliant, sometimes even astonishing, when one eye was good and the other amblyopic.

This is how I proceed in such cases. The refraction is, of course, estimated objectively and subjectively with the greatest care, and the visual acuity noted, with and without correction. The amblyopic eye is then submitted to massage for ten consecutive days. Now and then the improvement of sight as regards this eye shows itself after the first day—a very good augury. At other times vision is bettered only after some ten sittings. As soon as the sight is a little improved, I prescribe glasses which correct the ametropia

of the amblyopic eye, so that the latter is rendered capable of seeing without the aid of the sound eye. The last-named is then treated with atropine for some ten days.

It is curious to note how rapidly the sight of the amblyopic eye then improves. An eye, previously only useful enough to allow the patient to guide himself by its aid, can, with proper glasses, some applications of massage, and a little exercise, read and suffice for ordinary work.

If the squint be well marked a perfect correction is obtained by means of a tenotomy or muscular advancement, especially if the operation be followed by a series of stereoscopic exercises.

In cases where operation is declined one may (if the patients are young and the parents unusually painstaking) arrive, if necessary, at a result after months or years devoted to stereoscopic exercises and the wearing of well-chosen correcting glasses; from time to time (a week in the month) atropine is to be applied to the sound eye.

In accommodative asthenopia I have obtained many successes, particularly when sight was $\frac{1}{2}$ to $\frac{2}{3}$ of the normal. In these cases, after four to eight applications of massage, V. = 1, and there was no trace of asthenopia.

In hypermetropes one must distinguish clearly between the old and the young. Amongst the latter the effect of massage is sometimes surprising. In children of ten to fifteen years I have seen hypermetropia of 2 D. and 3 D. completely compensated under the influence of pressure massage; that is to say, the sight for near and distant objects has become as good without glasses as it was previously with the correcting lenses.

The more advanced the age of the patient, the less the action of massage and the reduction in the hypermetropia. After fifty years, massage even becomes painful, and on that account should be carried out with gentleness and circumspection. In some cases it renders service, but in others it may accelerate the development of pre-existing opacities of the crystalline lens.

Starting from the hypothesis that the diminution of the hypermetropia is caused by distension of the zonule, I endeavoured to render the pressures so violent and sudden as to provoke a traumatic myopia in a single *séance* of massage. I have succeeded in almost every case able to bear the energetic compression of the eyeball that is necessary. I have seen hypermetropes in whom the visual acuity without glasses rose at once from $\frac{1}{25}$ to $\frac{1}{10}$ to $\frac{1}{6}$, from $\frac{1}{6}$ to $\frac{1}{3}$, from $\frac{1}{3}$ to $\frac{2}{3}$, etc., while the powers of reading gained in the same proportion.

In hypermetropic amblyopia the improvements as regards sight are yet more marked; and—a curious thing—I have noted almost immediate bettering of vision in many different diseases where the vision had for long been reduced by alterations in the fundus of the eye, dulness of the cornea, etc., and that in proportion as the amblyopia was of long standing. In these facts we shall perhaps find an explanation of the remarkable cures, quoted by so many authors, by simple as well as by vibratory massage. These eyes had abandoned any attempt to see, so that there has resulted a kind of idleness of the ciliary muscle and an amblyopia from disuse that may be readily dissipated by massage.

The explanation of the effects of massage, however, is not so simple as it might appear, since not only emmetropes but myopes also find the visual acuity raised under its influence. It even happens that in certain myopes the visual acuity augments as the myopia is itself augmented.

In young subjects affected with slight myopia I have often seen the visual acuity without a glass improve to such a point that the glasses became less useful. At other times sight simply improved from $\frac{1}{2}$ to $\frac{2}{3}$ normal, or 1 with the same glasses.

In high myopia visual acuity is also much bettered by massage. According to Domec, progressive myopia may often be stopped by this means. For that to occur it is necessary that the *séances* be numerous and repeated for two or three months in the course of the year.

There are, therefore, several causes at work in the amelioration of sight by massage:

1. Mechanical action as regards the zonule and the crystalline lens.

2. Tonic action upon the ciliary muscle and the accommodation.

3. Trophic action (circulatory, secretory, and excretory) upon all the intra-ocular tissues and liquids, ciliary glands, chorio-capillaris, retina, etc.

In many different pathological conditions I have made a comparative study between the pressure massage of Domec and the vibratory massage by means of Edison's pen. It has seemed to me that the two methods yield almost identical results. To my mind, to explain the action of the various kinds of massage in old leucomata, parenchymatous keratitis, and other chronic pathological conditions, besides the trophic action, great attention must be paid to the mechanical action of massage on the crystalline system and accommodation. In fact, I have seen cases where a single *séance* of massage produced so rapid an improvement that one could only

explain it by a direct action upon the accommodation, inasmuch as a leucoma of the cornea could not clear up in a few hours. We have there quite a new path to explore.

The following is one of the more striking instances that I have come across of improvement in sight by pressure massage.

M. D—, 67 years, once affected with trachoma, but cured for thirty years, has never been able to gain a livelihood since that time on account of his defective sight. His corneæ are very dull as the result of many relapses of granulous keratitis. They now present the aspect of slightly clouded glass. R. V. = $\frac{1}{10}$ No. 10 Wecker at 0·15 c. L. V. = $\frac{1}{15}$ No. 11 Wecker at 0·15 c.

After a *séance* of pressure massage (three massages of two minutes each at five minutes' interval)—R. V. = $\frac{1}{7}$ No. 6 Wecker at 0·15 c. L. V. = $\frac{1}{15}$ No. 10 Wecker at 0·15 c.

After ten massages in a fortnight—R. V. = $\frac{1}{4}$ No. 6 Wecker at 0·15 c. L. V. = $\frac{1}{10}$ No. 8 Wecker at 0·15 c. With + 2·5 D. glasses the patient could then read ordinary characters (No. 4 Wecker). He was out of himself for joy, because for thirty years he had been unable to read a newspaper. Now, on examining the patient's corneæ, it was impossible to make out that they were clear enough to account for the improvement in sight. To my mind, the action of massage in this case bore at first upon the crystalline and accommodative system, and afterwards upon the general nutrition of the eye, recalling to its duty an organ left without exercise for a long period. It is possible that prolonged massage may clear the corneæ and thus improve the visual acuity.

Finally, I desire to state the fact that in some cases of prodromal glaucoma I have obtained a prompt cure by massage, which has not been negatived up to the present time. In these cases there is an immediate action upon the intra-ocular tension, which is lowered in a few minutes. The pressure exercised upon the cornea compresses the iris and the lens, frees the irido-corneal angle, and hastens the exit of the intra-ocular fluids; and at the same time there is a direct action upon the ciliary muscle and the accommodation.

In the chapter dealing with glaucoma we have already seen what can be obtained from massage in that redoubtable malady. An intelligent patient affected with prodromal glaucoma may perhaps prevent slight attacks or hasten their departure by practising massage upon himself as soon as premonitory symptoms, such as aureoles, show themselves. Domec has several patients who are able in this way to keep their glaucoma, as it were, in check. Certainly massage cannot replace iridectomy, although, when well applied, it may render real service. All who have taken it up

seriously are unanimous in recognising that massage has a potent action upon the intra-ocular pressure. This action, it is true, is transitory only, but it is so easy to repeat massage that the method is really a very practical one, particularly in educated and intelligent people capable of carrying out massage themselves. In peasants, old persons, and those who are clumsy with their fingers, auto-massage cannot be recommended. Massage as performed by the practitioner is a palliative measure only, and cannot be regarded as a real means of treatment. Iridectomy should stand above all other treatment.

Massage gives very brilliant results in heightened intra-ocular pressure induced by the too rapid swelling of crystalline masses after discission or injury. Under its influence the tension diminishes and the fragments become rapidly absorbed—points that obviate the numerous paracenteses which used to be necessary. Further, massage allows atropine to be employed, especially if dionine, of which we have already studied the marked anti-glaucomatous action, be combined with it.

The improvement in sight is due, in many instances, to the fact that massage ensures the better nutrition of the eye. With regard to the increase in accommodative power, that is explained by a stretching of the zonular fibres, as well as by an increase in the intrinsic force of the ciliary muscle itself. But exact researches are necessary to establish on a scientific basis the mechanism by which the foregoing clinical facts are brought about.

Practically Domec advises that, to begin with, massage should be applied very gently, especially in asthenopes. Ten applications should be made with the least possible interruption (every day, or at least every other day, one *séance* of 300 to 500 pressures). A month's rest is then prescribed, and after that one begins anew, according to need, one, or even two series of ten massages, separated by a fresh interval of a month.

Dr. Capauner, of Mulhausen, in a recent communication to the *Annales d'Oculistique* (October, 1902), has related several cases of ophthalmic migraine, with scintillating scotoma, definitely cured by several *séances* of vibratory massage of the eyeballs. From these observations he draws the following conclusions:—That ophthalmic migraine is not an affection of the cortical centres, as has been admitted since Charcot's work; that in all cases the action of massage upon the eyeball tends to prove that the seat of the evil lies not in the psycho-optical centre, but rather in those parts of the visual apparatus dependent upon the internal carotid artery.

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