those of you who have worked at the central nervous system, and especially at the complicated relations of the animal to the exterior, and who have stimulated me with observations and conclusions to undertake the detailed study of the subject which I have in hand. In these studies we have always felt to what an extent we were dependent upon the work of others, rather than upon our own initiative.

I desire to express my best thanks to our distinguished president for having given me the opportunity of speaking to such a distinguished gathering of my professional brethren on a subject to which I have devoted a good third of my scientific life; and you, gentlemen, I must also thank for your attention, which I have so long abused.

"STRUMA" AN IMPORTANT FACTOR IN DISEASE OF THE EYES.*

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THE older school of ophthalmologists recognized "struma" or "scrophula" as an important factor in many ocular affections, but when Koch showed conclusively that struma and tuberculosis were identical the term was more or less dropped and their successors ceased to employ it. The logical sequence of thought would have been—certain affections of the eye were once regarded as strumous; struma is only another name for attenuated tuberculosis, therefore these diseases are due to attenuated tuberculosis. This reasoning, however, failed to arrest the attention of ophthalmic surgeons, and consequently many of them have even now failed to appreciate the fact that attenuated tubercle plays an important rôle in many of the diseases of the eye, diseases as common and simple as phlyctenular conjunctivitis and keratitis. Dr. Koller, of New York, in a paper on recurrent tuberculous choroiditis, says that the prominent part played by tuberculosis in the causation of eye diseases was not recognized until the beginning of the present century. I would go further and say that even to-day the most recent textbooks pay little or no attention to it. Von Michel was the first to point out, many years ago, that about 50 per cent. of all diseases of the uveal tract were tuberculous in nature. His work received little notice, although Sydney Stephenson and Carpenter amply confirmed his views, mainly on clinical grounds. Dr. Windbiel, writing in *Ophthalmology* (vol. vii, 1910, which also contains Koller's paper), says that tuberculosis of the eye is a relatively frequent disease, although up to within two or three years ago it was believed that the eye was immune to the tubercle bacillus. He goes on to state that in his clinic at Amsterdam, New York, about one half of all the eye diseases were due to tuberculosis and occurred chiefly in childhood and middle life. I think this high percentage must have been associated with some peculiar local conditions. Mackay, of Edinburgh, read an interesting paper at the annual meeting of the British Medical Association in Liverpool, 1912, which showed that the activities of the *Bacillus tuberculosis* were responsible for a large number of diseases of the eye. His paper was copiously illustrated by a series of excellent lantern slides, and was founded upon a laborious and painstaking research. Many other prominent ophthalmic surgeons, both in England and abroad, are fully alive to the importance of tubercle, but others are still content to talk of diatheses and dyscrasias, and to them the word "rheumatic" is a veritable shibboleth.

Before considering the various parts of the eye and their liability to affection with tuberculosis it will be well to consider the grounds for regarding this etiology as probable or certain in any case under consideration. The most important diagnostic agent we possess is tuberculin used by subcutaneous injection. I reject Calmette's procedure at once as utterly fallacious and very dangerous. I have myself proved it to be harmful to normal eyes, but were the eye actually infected with tubercle it might quite easily lead to its total loss. It is unnecessary

to go further into this question, it is one upon which all ophthalmologists, including the originators of the test, are agreed. Von Pirquet's reaction is far too delicate; it gives a positive answer in about 90 per cent. of all adults and in a high percentage of children. A negative result would be far more valuable than a positive, especially if the test were repeated and remained negative. The subcutaneous test is made by injecting old tuberculin into the subcutaneous tissues between the shoulder-blades or into the arm. The patient should be kept in bed for a few days before the test is made, and his temperature taken four-hourly. I always commence with a dose of 0.001 of a cubic centimetre of Allen and Hanburys' old tuberculin. It is uncommon to get a reaction to this first injection. After three or four days I repeat the injection, giving 0.002 c.cm. If no reaction be noted I give a third injection of 0.004 c.cm. The test is not very delicate. It is uncommon for a reaction to follow the first injection, but this sensitizes the body, and the second or the third injection should cause a reaction in a tuberculous individual. It is not essential to increase the dose. In my last case my new house-surgeon misunderstood my directions and gave three successive doses of 0.001 c.cm. Reaction followed the third dose. It has been suggested that this sensitizing action may allow a normal non-tuberculous individual to react. This is not the case; several of my patients have failed to react, even to the third injection. Reactions are far more common after the third than after the previous injections. There are three kinds of reaction: the local, the general, and the focal. The focal reaction is by far the most important in eye work. I have not paid much attention to the local reaction; it seems to me too capricious in its action. It consists of swelling and redness at the site of injection, and may be the only reaction obtained. At present I disregard it as a sign of tuberculosis. In this I may be wrong. The general reaction consists of a rise of temperature occurring at from twelve to twenty-four hours after the injection, accompanied in some cases by general malaise and headache. I take it to signify that somewhere in the body there is a tuberculous focus. The focal reaction consists of increased injection of the eye, pain, lacrymation, and sometimes in the appearance of definite choroidal tubercles of a transient nature, or of nodules in a case of scleritis. I have also noted alterations in pigmentation in cases of tuberculous choroiditis. Up to the present I have never seen any harm done to the eye by a focal reaction to old tuberculin, and in many instances reaction has heralded a rapid recovery. I regard a focal reaction as an absolute indication of the actual presence of bacilli in the eye. Here again I may be in error. Perhaps it is given by an inflammation due to a tuberculous toxæmia.

The second great indication of ocular tuberculosis is the presence of definite tuberculous deposits elsewhere in the body. The most important are enlarged glands in the neck and abdomen, and tuberculous joints and bone disease. I have never so far detected pulmonary complications or pleural disease. In fact, as Straub points out, the chronic attenuated tuberculosis which causes secondary disease, either definitely bacillary or toxæmic, has immunized the organisms to the bacillus, and so serious tuberculosis is rarely seen.

I attach great importance to a family history of phthisis and other tuberculous affections. I obtain it in the majority of my cases. Finally, the actual appearance of the eye will often lead to a correct diagnosis of tuberculosis when the observer has become accustomed to this class of case.

In this paper I am dealing with struma of the eye, attenuated tuberculosis, but it is often impossible to draw a hard and fast line between this class of case and classical florid tuberculous processes, such as, for example, a tuberculous iritis with massive tubercles in the anterior chamber.

It is often difficult or impossible to differentiate between a definite infection where the eye actually contains bacilli and a tuberculo-toxæmia, and in most cases it is unnecessary to make this distinction.

Phlyctenular Ophthalmia.

I shall now after these general remarks consider in detail some of the common diseases of the eye in which

* A paper read before the Birmingham Branch of the British Medical Association.

struma is frequently, if not always, the exciting cause. The most common is phlyctenular conjunctivitis and keratitis. A careful study of this affection will elicit the fact that it is chiefly found in children of a decidedly strumous habit. At least 70 per cent. of my cases have enlarged glands or a very strong family history of tubercle, many of them have adenoids and enlarged tonsils, and with one exception every case that I have tested with a subcutaneous injection of tuberculin has given a positive reaction. Further, I have treated 5 or 6 cases by one injection of T.R., and in each instance the phlyctenule has disappeared within a couple of days. No local treatment was adopted. Dr. Wall, of Coleshill, speaking at the last meeting of the Birmingham Medical Society, said that in every case in which he had used this method of treatment it had been immediately successful. Phlyctenulae are not examples of tuberculous infection of the eye. They have been repeatedly excised and rigorously searched for bacilli, but they have never been found. We must regard the disease as the result of a tuberculo-toxaemia. This view receives confirmation from the fact that they often appear when old tuberculin is instilled into the conjunctival sac. It seems to me that the question with regard to phlyctenulae is not whether they indicate the existence of a tuberculous lesion elsewhere in the body, but in what proportion of cases this is the case. I have been able to regard a tuberculous etiology as exceedingly probable in 70 per cent. of my cases. Professor Straub, of Amsterdam, thinks that 100 per cent. is nearer the truth. I have had one case, as I mentioned above, in which I failed to get a reaction after three injections of old tuberculin in increasing doses, and I have frequently seen them in the East associated with other infections of the conjunctiva, more especially the Koch-Weeks bacillus. At present I can only say that a child with phlyctenulae, especially recurrent phlyctenulae, is probably strumous. Straub has pointed out that these strumous children have a lower specific gravity than ordinary healthy children. Phlyctenulae are very common in hospital practice, exceedingly rare in private practice—a fact that shows that they are associated with defective hygienic conditions. These views are by no means universally accepted. Bishop Harman, in his book, *The Conjunctiva in Health and Disease*, does not even discuss the question of a tuberculo-toxaemia as the usual cause, and says the word "strumous" should be dropped in this connexion. He scouted the whole idea at the Liverpool Meeting last year. The matter is of prime importance. Thousands of children annually have their sight terribly impaired by the ravages of this form of keratitis. I believe that when England gets a milk supply free from living tubercle bacilli the disease will become very uncommon.

Photophobia in Children.

This is a symptom-complex caused by an increased irritability of the mucous membrane of the nose and of the conjunctiva. It is probably due more to the chronic rhinitis than to the catarrhal conjunctivitis. This condition is first cousin to phlyctenular disease. It is practically in its typical form only found in strumous children, who mostly have thick lips and enlarged cervical glands. Associated with the rhinitis and the catarrhal conjunctivitis we generally find eczema of the upper lip and of the skin over the malar bone. Adenoids and enlarged tonsils are frequently present. When a child is treated as an outpatient the photophobia may continue for months, even though atropine is used. If the child be removed from its unhygienic home conditions, and be taken into the hospital and given spinal douches with cold water every morning, it rapidly improves. Unfortunately it often relapses as soon as it returns home. I have tested a few of these children with tuberculin, and have obtained positive reactions. I regard this form of photophobia in which there are no lesions of the cornea as pathognomonic of struma.

Scleritis.

Scleritis is one of the diseases which probably is almost always caused by the *Bacillus tuberculosis*. A few cases of diffuse scleritis and some of episcleritis are syphilitic in nature, and some are due to a gonococcal metastasis, but tuberculosis is the prime factor. This has been rendered almost certain by the researches of Török, Verhoeff, and others. Stork succeeded in producing

experimental scleritis in rabbits by injecting living tubercle bacilli into the ear vein. My own results point most conclusively to the same opinion. In all cases in which I have used the tuberculin test I have obtained a general reaction; in four cases I got a focal reaction after an injection of $\frac{1}{5000}$ mg. of T.R. without any general reaction. Scleritis has been held to be due to a rheumatic diathesis, whatever this may mean, because patients with scleritis are apt to have articular rheumatism. I would suggest that the joint pains are due to a chronic arthritis caused either by actual infection with attenuated tubercle bacilli or to the toxic effect of blood chronically impregnated with the products of some distant tuberculous glands. This question of chronic articular rheumatism, not including osteo-arthritis, would seem to be a useful field of research with tuberculin. Scleritis is apt to be a serious disease. It is very chronic, and when cured recurs with aggravating persistency. Each attack leaves scars in the sclera, which may become ectatic, causing an intercalary staphyloma. The cornea is often implicated with a sclerotising keratitis which is, I believe, a tuberculous process, because I have seen it clear up considerably under the action of tuberculin. The origin of the disease is not generally in the sclera itself but in the ciliary body, where Verhoeff has demonstrated a caseating tuberculosis. Up to the present we have been impotent against the disease; there was no efficient treatment. But now tuberculin therapy gives us a potent weapon with which to combat it; but I would here sound a note of warning. Tuberculin in scleritis is a double-edged weapon, which, if not used with extreme caution, may precipitate the loss of the eye. I have on two occasions been faced with a condition of anaphylaxis. One case was a very severe one of scleritis of both eyes in an old woman. I treated her successfully with T.R. after a preliminary test with T.V., which gave a positive reaction. A severe relapse occurred a year later, and I gave her an injection of $\frac{1}{5000}$ mg. of T.R. The result was a little short of disastrous. Both eyes became intensely inflamed, and a severe and intractable iridocyclitis commenced. After seven weeks of careful treatment she is now a little better, but I fear that the tuberculin has hastened the total loss of both eyes, which was, perhaps, inevitable from the first. I strongly advise that when scleritis has been cured temporarily by tuberculin and a relapse occurs the second course of tuberculin should begin with very small doses, say $\frac{1}{10000}$ mg., and the patient should be kept in bed until it is certain that the second course will be well tolerated. I have had a second example, but the focal reaction which followed $\frac{1}{5000}$ mg. of T.R. fortunately did no permanent harm, although it made me very anxious for the eye for some time.

Interstitial Keratitis.

In about 70 per cent. of the cases of interstitial keratitis is a manifestation of congenital syphilis, but the remainder of the cases are strumous in nature, and often yield to tuberculin treatment. The tuberculous affection is commonly confined to one sector of the cornea, and is not so liable to affect the whole cornea. It is, however, if untreated, more liable to leave behind a permanent nebula, and this is especially the case when the keratitis is contiguous to and part of a tuberculous scleritis.

Tuberculous Iritis.

I shall say nothing about florid tuberculosis of the conjunctiva, cornea, or iris, nor of miliary tuberculosis of the choroid. These conditions are caused by virulent bacilli, and are well understood. I shall at once pass on to a form of tuberculous iritis which is at present barely recognized. I am quite convinced that a certain proportion of iritides of the so-called "rheumatic" type are really due to tuberculosis. Whether there is a direct infection or a toxæmia I do not know. I may at once say that I am yearly becoming more and more sceptical of the existence of a "rheumatic" or "gouty" iritis. Most of these cases are gonorrhoeal in nature, many are caused by a distant septic focus, a septic mouth, otorrhoea, septic Fallopian tubes, boils, etc., others are caused by auto-intoxication from the alimentary tract, but a few are certainly tuberculous. My experiments with tuberculin have shown me that this is the case, and in two examples which I thought might be "rheumatic" I detected choroidal tubercles.

Cyclitis.

Cyclitis is frequently tuberculous, and I have obtained most encouraging results from tuberculin therapy.

Choroiditis.

I do not intend to say much about this subject because I recently read a paper upon tuberculous disease of the uvea to the Midland Ophthalmological Society, which was published in the *Birmingham Medical Review*, May, 1912. It is not an uncommon affection, and exists in three forms—the acute miliary form generally seen in association with tuberculous meningitis, the solitary form, and the disseminated form. The miliary form does not concern us because it is not a strumous disease—it is not attenuated tubercle, but a highly virulent form. It is, however, interesting to note that Stephenson and Marple have both stated that tubercles are present in a very large number of cases of tuberculous meningitis. Marple suggests that if only the examination be made with sufficient frequency they will be detected in every case. They may be very evanescent, appearing rapidly and disappearing within a few hours. The solitary form may advance steadily to the total loss of the eye, but I believe them to be generally benign. I have so far never seen a case which has not cleared up under tuberculin treatment, leaving a practically undamaged eye. I constantly find scars in the cornea, pigmented patches, which represent all that remains of a past tuberculous process. It is, however, a not infrequent occurrence that a fresh solitary tubercle develops close to an old quiescent one. In children obsolescent tubercle of the macula is not uncommon, and naturally their central vision is very defective. Disseminated choroiditis is more likely to be due to syphilis than to tubercle, but I believe that many cases ascribed to this disease are in reality caused by the tubercle bacillus in an attenuated form—to struma, in fact.

Lacrymal Sac.

The lacrymal sac is frequently affected with tuberculosis, especially in children, and should be extirpated at once.

TREATMENT.

We have in tuberculin a weapon which is of inestimable value in the treatment of struma or attenuated tuberculosis. The small chronic foci which originate the ocular manifestations, and the small deposits in the eye do not generally generate enough tuberculo-toxin to excite the formation of antibodies in the blood. In these cases the injection of tuberculin supplies the absent stimulus, and the circulation becomes flooded with the necessary antibodies, whatever they may be, and so the tendency to repair obtains the necessary advantage over the destructive influences at work in the small focus of disease. If, however, the local focus in the eye be but a part of a widely-spread tuberculosis, I believe that tuberculin is apt to be very harmful. The same is true when a state of anaphylaxis is present. Two cases will illustrate this point. Both were adolescents; both had florid tuberculosis of the iris, with large tuberculous masses in the anterior chamber. The first patient was a healthy lad with no other signs of tuberculous infection and a normal temperature. He failed to react to three increasing doses of old tuberculin, but reacted strongly to a small dose of bovine old tuberculin. After a year's treatment with T.R. he made a complete and absolute recovery. The second case had a similar condition in both eyes, but, in addition, had masses of palpable glands in her abdomen and a hectic temperature. After rest in bed, when the temperature curve had become normal in character, I gave her an injection of 100 mg. of T.R.; the result was disastrous, and hastened the inevitable total loss of both eyes. Probably—nay, almost certainly—the same thing happens when tuberculin is used in phthisis and other tuberculous affections where the actual tubercles are hidden from us, and it behoves us to be exceedingly cautious how we use such a potent agent for good or evil. If recent legislation leads to the indiscriminate use of tuberculin, the results can only be disastrous both to the patients and to tuberculin therapy.

Up to the present I have only used T.R. I begin with 25 mg., unless I have special reasons for extreme caution. This dose I repeat once a week, and perhaps, after eight to ten weeks, increase it to 100 mg. It may, in some

cases, be advisable to again increase the dose to 250 mg., but generally I keep to the initial dose. A focal reaction obtained during a course of tuberculin treatment always does harm in eye cases, sometimes great harm. It is necessary to be very patient. Sometimes no improvement may be manifest for weeks or even months. My successful case of tuberculous iritis did not show the slightest sign of improvement for five or six months, and then he began to improve and got quite well.

In conclusion, gentlemen, the fact which I have brought to your notice, that attenuated tuberculous or strumous disease of the eyes is exceedingly common and generally amenable to treatment with tuberculin, should lead to the obvious conclusion that the eye is not likely to be the sole organ affected by attenuated tuberculosis. The presence of chronic rhinitis and of enlarged tonsils and adenoids in children should be regarded as indicating the probability of struma, and doubtless much of the chronic rheumatism so prevalent among us has a similar origin.

ON THE RIGIDITY OF CALCIFIED ARTERIES.

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(Communicated by PROFESSOR ADAMI.)

THE ordinary conception of calcification within the organism wherever it occurs is that it is of a stone-like rigid character, and this whether it occurs in a calcified fibroid of the uterus, a calcified obsolescent tubercle in the apex of a lung, or a calcareous plaque in an artery. A familiar expression is "the pipe-stem radial." Here it is true the calcareous deposit is not in the intima, but in the media, but in support of this view our museums show beautiful pipe-stem arteries, with dense white rings of calcification.

But is this view correct or constantly correct? Are there not data which are difficult to reconcile with such a view? Were the radial artery as rigid during life as we find it sometimes after death, why is it capable of expansion with each heart beat, as is indicated by the pulse tracing; why is it compressible by the finger; or why is it not shattered by the fingers of the numerous students during the clinic or ward round? And in the case of the aorta, if the saucer-like calcareous plates and scales which we find after death exist as such during life, why do we not have formed upon them, much more frequently, parietal thrombi, which, becoming free, cause emboli and gangrene? Why, again, do surgeons experience so little difficulty in ligaturing the arteries in a case of senile gangrene, although on examining the amputated limb later the proximal ends of the severed arteries are rigid and brittle?

As a matter of fact I would lay down as a general rule that arteries are not of a stony rigidity during life. (I shall later on give exceptions to this rule.) During life the calcareous matter in the arterial wall is not present in the form of rigid plates. It is there, but in the state that may be compared with unset mortar.

Let me place before you the following observations:

CASE 1.—C. D., aged 72, was a patient in Dr. Finley's service at the Montreal General Hospital. He had a blood pressure of from 180 to 205 mm. of mercury. The radial arteries were tortuous and could be rolled under the finger. He died somewhat suddenly, and permission for autopsy was obtained immediately. The radial arteries were dissected out within one hour of the patient's death. On removal they were no doubt more resistant than the normal, but they could be compressed and could be bent and curved like a moderately stiff rubber tube. About ten minutes after removal, however, the removed lengths of the vessel were found absolutely rigid, possessing "pipe-stem" characters. They crackled on compression and broke on being bent.

CASE 2.—Was one of senile gangrene of the foot in the service of Dr. Armstrong at the Royal Victoria Hospital, Montreal. Dr. Armstrong amputated at the upper portion of the popliteal space. The artery was much sclerosed, but on being severed bled freely, and was ligatured without difficulty.

The distal portion of the artery from Case 2 was immediately dissected out and disposed of as follows: A small length was allowed to stand in the open air; another was dropped into a one-half per cent. solution of sodium hydrate; another into a similar solution of hydrochloric acid; one into a normal saline, and another into a 20 per