SERUM AND VACCINE THERAPY IN CONNEXION WITH DISEASES OF THE EYE.

THE MIDDLEMORE PRIZE ESSAY, BRITISH MEDICAL ASSOCIATION, 1911.

By C. W. G. BRYAN, F.R.C.S. Eng.,

LATE ASSISTANT IN THE DEPARTMENT FOR THERAPEUTIC INOCULATION, ST. MARY'S HOSPITAL; AND HOUSE-SURGEON, OXFORD EYE HOSPITAL.

I.

THE subject of serum and vaccine therapy in relation to diseases of the eye is one which has received a large amount of attention, and on which a great deal of work has been done during recent years.

The treatment of eye diseases by serums and vaccines differs from similar treatment of disease in any other part of the body owing to the anatomical peculiarities of the blood and lymph supply of this organ.

The cornea and vitreous have in the healthy condition no blood vessels, and are feebly nourished by lymph; the lymph circulation of the intrinsic parts of the eyeball is, however, not free, and this is exemplified by the rarity with which malignant growths of the interior of the eyeball give rise to secondary deposits in glands until the growth by direct spread has extended outside the sclerotic coat.

Again, in those parts of the eye where there is a supply of blood vessels the distribution of the blood in these vessels is constantly varying owing to the unceasing movements of the eye as a whole, and of its various parts—the iris, ciliary body, etc. These movements are of importance when the eye is infected, as they cause the setting free of bacterial substances, toxins, etc., in the blood stream. This subject of autoinoculation will be discussed later in connexion with vaccine therapy.

Immunity against disease due to infection may be acquired actively or passively. Vaccine therapy is concerned in the production of active immunity, serum therapy deals with the production of passive immunity.

VACCINE THERAPY.

Active immunity can be acquired in two ways—either by auto-inoculation by bacterial substances set free in the blood stream from some focus of disease, or by the methods of hetero-inoculation—that is, by the absorption of vaccine, usually injected into the subcutaneous tissues. In disease of the eye auto-inoculation is an unsatisfactory method of producing immunity, owing to the limited blood and lymph flow in the eye, and to the fact that the size of the area of infection, as compared with the body as a whole, is small, and therefore great disturbance of this small area would be necessary to produce any marked auto-inoculation.

In using vaccines it is necessary as far as possible to prevent auto-inoculation by keeping the diseased part at rest, and this is a difficulty with which we have specially to contend in dealing with eye diseases. If auto-inoculation takes place at the time that treatment by hetero-inoculation is being carried out, substances of unknown amount may be set free in the blood stream at unfavour-

changes which vary with the amount of vaccine given. The opsonic index is a means of gauging the amount of opsonin in the blood serum, opsonin being some substance which so acts on bacteria that the phagocytes of the blood are able to ingest these bacteria. Injection of vaccine has as its aim the increase of the opsonins in the blood, but the effect of vaccine on the amount of opsonin, as shown by the opsonic index, varies with the amount of vaccine which is injected.

According to the amount of vaccine given, four effects may be obtained.

1. If a small dose be given to an infected person, no effect may be produced, as shown in Chart 1, of a patient suffering from undoubted tuberculosis. Here doses of tuberculin (bacillary emulsion) varying from $\frac{1}{1000}$ to $\frac{1}{100}$ mg. were given, and twenty-four opsonic indices taken with no variation greater than would be within limits of normal.

2. A dose which has only a slight effect causes changes in the amount of opsonin in the blood—first, a rapid slight rise of the opsonic index, then a gradual fall to the level at which the index stood before the inoculation.

3. The usual effect of an efficient dose of vaccine is to cause first a fall (this being called the “negative phase”) followed by a rise (“positive phase”) the index gradually again falling to the level at which it was before the vaccination. A slight variation of this curve is occasionally seen in a small rise, lasting a few hours, occurring before the negative phase sets in.

4. If an overdose be given, then the only effect is a negative phase lasting a long time, the index gradually rising to near its former level.

With regard to the doses necessary in diseases of the eye, the general statement may be made that larger doses of vaccine are necessary than in treating disease elsewhere, because the blood and lymph flow being limited, a less amount of opsonin will be brought in contact with the diseased area, and also the risk of toxic effect is less, as the area of infection is small.

It has been found that clinical symptoms vary directly with variations of the opsonic index. During the positive phase the patient's general condition improves, as shown by a drop in the temperature in febrile cases and alleviation of symptoms generally; locally also symptoms are relieved. In eye disease pain becomes less, discharge decreases, ciliary injection diminishes, vision improves, etc. Conversely, during the negative phase symptoms are aggravated.

The aim of Wright's system of inoculation is to produce by repeated injections negative phases as short as possible, followed by positive phases as long as possible, the vaccine being reinjected as the positive phase decreases. In this way the disease gradually becomes cured. The dose to produce this effect, at first small, has to be gradually increased in amount. The interval between inoculations varies according to the nature of the disease.

It is possible without the opsonic index to regulate the amount of vaccine by observation of clinical manifestations. In febrile diseases the temperature varies in inverse ratio to the opsonic index, as is shown by Latham and Inman,¹ and, after a suitable dose of vaccine, the temperature falls, rising again when the effect of the vaccine wears off. The vaccine is then repeated.

In eye disease, by direct inspection, we have a ready means of regulating the treatment by vaccines. In disease of the iris, cornea, and sclerotic vascular injection of the conjunctiva decreases after an efficient dose of vaccine, though if a negative phase is produced the injection may,

Chart 1.—A, Opsonic index. B, $\frac{1}{1000}$ mg. C, $\frac{1}{100}$ mg. D, $\frac{1}{10}$ mg. E, $\frac{1}{1}$ mg.

able times, interfering with the regulation of the dosage of vaccine.

Sir Almroth Wright and his disciples have shown by means of the opsonic index that the injection of vaccine into an infected subject causes changes in the blood,

while the negative phase lasts, be temporarily increased. This is well shown by a case of tuberculous keratitis which was treated by myself, the course of treatment being regulated by the amount of vascular injection. Whenever the eye became inflamed tuberculin was given, and each dose was followed by a period of absence of injection and of photophobia, until finally the condition became absolutely quiescent.

CASE.

R. M. suffered from keratitis for five years. From March to June, 1908, was treated with tuberculin B.E., regulated by observations of the opsonic index; after this treatment was regulated by the amount of conjunctival injection, which, when present, was associated with photophobia.

June 5th. Eyes quiet.
June 10th. Right eye inflamed.
June 11th. $\frac{1}{5000}$ mg. given.
June 14th. Both eyes quiet.
June 22nd. Slight conjunctival injection of left eye. $\frac{1}{5000}$ mg. given.
June 23rd. Both eyes quiet.
June 30th. Much injection of right eye. Photophobia. $\frac{1}{5000}$ mg. given.
July 1st. Slight injection of right eye.
July 2nd. Both eyes quiet.

After July 2nd the eyes showed no more sign of inflammation; corneae continued to clear and vision to improve. Tuberculin treatment was continued until August 26th.

Fromaget² mentions a case of tuberculous irido-choroiditis, treated by tuberculin, in which the first four doses were followed by ocular reaction, the fourth also by rise of temperature. Later doses led to marked improvement in local signs and in vision. Here, then, we have an example of negative phases shown by ocular reaction, and one by rise of temperature. The vision also improves during the positive phase as we should expect, and is diminished during the negative phase.

I now propose to deal seriatim with the various infective diseases of the eye which have been treated by vaccines.

TUBERCULOSIS.

Tuberculosis has been treated by vaccine since Koch first introduced his tuberculin in 1890. Disastrous results followed the use of this old tuberculin in the doses recommended by Koch. Treacher Collins³ mentions the case of a child, aged 9, suffering from tuberculous nodules in the right iris, who was treated by ten injections of old tuberculin, beginning with 1 mg., the dose rising in a month to 7 mg. The original four nodules invaded the whole iris, and the eye was excised.

However, by using smaller doses at longer intervals, good results have been obtained with old tuberculin in eye diseases. De Schweinitz⁴ describes two cases of scleritis and keratitis treated by old tuberculin—one case of eight years' standing cured by six weeks' treatment, the other case showing improvement, followed, however, by recurrence.

The general opinion is that the use of old tuberculin is attended by unjustifiable risk, and it has been superseded by less dangerous preparations. Many varieties of tuberculin have been placed on the market, each of which has had its supporters and opponents. It would be unprofitable here to mention more than a few of these products, many of which have been in use for but a short time.

Koch's new tuberculin (tuberculin T.R.) was very largely used, and it was with this preparation that Sir Almroth Wright placed the treatment of tuberculosis on a scientific footing, using small doses regulated by estimations of the opsonic index.

The next variety of tuberculin requiring special mention is the bacillary emulsion; this preparation has been, and is being, used extensively with good results. In a series of cases of ocular tuberculosis which I have treated I used this preparation of tuberculin, and I shall refer to some of my results later.

Mention must be made of the use by R. W. Allen⁵ of bovine tuberculin in the treatment of tuberculosis of the eye in human beings. He holds that tuberculosis secondary to phthisis is due to human tubercle bacilli, but that if secondary to cervical or mesenteric tuberculous glands, the disease may be due to bovine tubercle bacilli. He lays down the following rules:

1. If the disease is primary, commence treatment with

human tuberculin, and if no improvement takes place in two or three months, the bovine tuberculin, or a mixture of the two varieties, should be used.

2. If the disease is secondary use the appropriate tuberculin.

Allen claims good results in eye disease from the use of this method.

In recent years the two most important methods of dosage which have been employed in using tuberculin in eye disease are:

1. Wright's method, commencing with a small dose, $\frac{1}{50000}$ to $\frac{1}{100000}$ mg., gradually increasing the dose over a long period of treatment with about ten days' interval between each inoculation, the dosage being regulated by estimations of the opsonic index.

2. Von Hippel's⁶ method of treatment with tuberculin T.R., commencing with an initial dose of $\frac{1}{500}$ mg., repeating the inoculation on alternate days, increasing each time by $\frac{1}{500}$ mg. until $\frac{1}{50}$ mg. is reached; after this the dose is increased each time by $\frac{1}{50}$ mg. up to $\frac{1}{5}$ mg.; then, by $\frac{1}{5}$ mg. until a dose of 1 mg. is reached. During the treatment the temperature should not rise above 100° F.; if it does so, the previous dose, or a smaller one, is repeated until there is no rise of temperature after the inoculation.

In treating a series of cases at the Oxford Eye Hospital I have used Wright's method, regulating the treatment partly by estimation of the opsonic index, partly by observation of clinical signs and symptoms, temperature, amount of pain and photophobia, effect on vision, and conjunctival injection.

I wish to take this opportunity of expressing my gratitude to Mr. Robert Doyne and the other members of the staff of the Oxford Eye Hospital for their help and encouragement; it was at Mr. Doyne's suggestion that I undertook vaccine therapy while house-surgeon at Oxford, and he not only fitted up a laboratory for me, but gave me permission to make use of all clinical material which was suitable.

Extrinsic Tuberculosis of the Eye.

1. *Tuberculous Conjunctivitis*.—I have treated one case of tuberculous conjunctivitis over a long period with good result.

J. R., aged 61, was first seen in March, 1907, for a lump in the right lower lid of three months' duration; this was removed, but was followed by the appearance in the upper lid of a mass which was treated by caustics and scraping, but continued to increase in size. At the beginning of 1908 the whole of the inner aspects of both lids was covered with fungating granulations, the upper lid projecting over the lower and being thickened to about the size of a hazel nut. Owing to the thickening of the lids the eyeball was hidden, but on raising the upper lid the cornea could be seen, rough and opaque. In January, 1908, a scraping from between the coarse granulations was taken and stained, and tubercle bacilli were found. Treatment by Tuberculin B.E. was commenced in March. The effect of the first five doses on the opsonic index is shown in the following chart.

Until the end of 1908 the opsonic index was taken regularly and the injections were repeated every ten days, gradually increasing until at the end of the year $\frac{1}{3500}$ mg. was being given. Since that time till the end of 1910 Dr. Coventon, of Oxford, kindly carried on the treatment, and the patient had $\frac{1}{2000}$ mg. every fourteen days. In December, 1910, the conjunctivitis was cured; the conjunctiva was smooth, no injection being present except one small area the size of a pin's head in the upper lid. The thickening had disappeared, the lids being of normal consistency. The eye could be fully opened, and the cornea was smooth and showed only slight opacity at the upper part.

Saxl⁶ reports a case of tuberculous conjunctivitis in a woman of 23, treated for two months with tuberculin, and

showing improvement. Treatment then ceased, and the condition relapsed. On resuming treatment for a month the condition improved, but afterwards again relapsed and the lids were scraped. Here treatment does not seem to have been persisted in with sufficient patience.

Ormond and Eyre⁷ mention a case of tuberculous conjunctivitis in a child suffering from enlargement of cervical glands with sinus. The diagnosis was made certain by removing and microscoping a portion of the conjunctiva, where typical giant cell systems were found. Inoculation in a guinea-pig gave positive result. The patient was treated for eight months with tuberculin with good result, the vaccine being given ever three weeks. Von Hippel⁸ reports 3 cases of tuberculous conjunctivitis cured by tuberculin used according to his method. Torok⁹ gives the result of tuberculin treatment in 16 cases of eye disease (including 5 cases of tuberculous conjunctivitis) eight of which were cured, and four showed marked improvement.

The results, then, of the treatment of tuberculous conjunctivitis are good provided the treatment be persisted in over a long period.

2. *Interstitial Keratitis*.—I have treated one case of tuberculous interstitial keratitis with excellent result.

The patient, R. M., a boy of 11, had suffered from enlarged cervical glands and phlyctenular ophthalmia since 1901. In February, 1908, active interstitial keratitis was present in the left eye, the whole cornea was steamy, and there was intense ocular injection. The right cornea showed old nebulae and a recent ulcer. Treatment by tuberculin B.E. was commenced in March, regulated by the opsonic index. The effect of the first dose is shown.

The patient was treated until August, when $\frac{1}{100,000}$ mg. was being given. For the first two months treatment was regulated by estimations of the opsonic index; after this, however, clinical signs, onset of redness and photophobia, were sufficient to indicate when a fresh dose of vaccine was required, the administration of vaccine on each occasion being rapidly followed by alleviation of conjunctival injection and pain. Meanwhile the corneae were gradually clearing and vision improving, and treatment was discontinued in August, both eyes being quiet and corneae clear but for old nebulae.

Derby¹⁰ reports 9 cases of interstitial tuberculous keratitis treated with tuberculin with favourable results. Weeks¹¹ mentions 3 cases treated by von Hippel's method, all of whom recovered.

3. *Scleritis, Sclero-keratitis, Phlyctenular Ophthalmia*.—Nias and Paton¹² have shown the tuberculous nature of most cases of phlyctenular ophthalmia. They examined the opsonic index in a large number of cases, and believed that the condition was due to dead or attenuated tubercle bacilli escaped from a tuberculous focus elsewhere in the body. Allen⁵ however, has found that patients with phlyctenules and episcleritis do not always give Calmette's reaction, and are therefore presumably sometimes not tuberculous. In the majority of cases the patients are children suffering from tuberculous cervical glands, and subject to repeated attacks of scleritis and sclero-keratitis over a long period. In almost every case the condition is associated with some error of refraction, usually hyperopic astigmatism, but the photophobia is such a marked symptom that it is impossible to measure the patient for glasses. These cases react well to tuberculin, and if by this means the eye condition is alleviated, and then suitable glasses are fitted, the treatment by tuberculin, provided there is no obvious focus of tuberculosis elsewhere, can be given up, and the eye trouble does not recur. But, in my experience, if, when the eyes are quiet, the error of refraction is not corrected, there is a great tendency for the keratitis, etc., to recur. The following cases illustrate the effect of tuberculin treatment:

1. N. F., aged 4½. Eyes had been inflamed, with corneal ulcers and phlyctenules, and intense photophobia, for six months. $\frac{1}{100,000}$ mg. tuberculin B.E. was injected, and four days later both eyes were well except for faint nebulae. Glasses to correct hypermetropia were fitted. Treatment by tuberculin was continued for nine months, as the patient had had tuberculous cervical glands, which almost disappeared under the treatment; during this time there was no further eye trouble.

2. V. D. S., aged 4, came under treatment in May, 1908, for large phlyctenule in left eye. On May 6th $\frac{1}{100,000}$ mg. B.E. and May 15th $\frac{1}{100,000}$ mg. were given, followed by gradual

improvement. On May 22nd $\frac{1}{50,000}$ mg. was given, followed by a bad negative phase, as shown by the appearance of an ulcer of the right cornea, with hypopyon; the patient also suffered from fever and malaise. The ulcer was healing on May 30th, and after $\frac{1}{15,000}$ mg. tuberculin on June 6th the ulcer was quite healed, and both eyes remained quiet.

3. F. B., aged 11, suffered from recurrent attacks of phlyctenular ophthalmia in November, 1907, on February 13th, February 18th, and February 25th, 1908. Corneal ulcer March, 1908. Cultures from the conjunctiva were taken in February, and *Staphylococcus aureus* was grown. The patient had three injections of staphylococcus vaccine prepared from these cultures without any clinical effect. On July 2nd a fresh phlyctenule with conjunctivitis occurred, lasting thirteen days. The same condition set in on July 23rd, and on July 24th $\frac{1}{100,000}$ mg. of tuberculin was given, and next day the eye was quiet and the phlyctenule had disappeared. On September 19th conjunctivitis set in; $\frac{1}{100,000}$ mg. of tuberculin was given, and on September 21st the eye was perfectly quiet and well.

Here, then, we have a case in which tuberculin on the two occasions where it was used gave immediate relief to a condition which always before had proved very resistant to treatment. The patient showed no other signs of tuberculosis.

4. G. K., aged 1 year, came under treatment in November, 1906, and from then until April, 1908, suffered from phlyctenular ophthalmia and recurrent corneal ulcers; photophobia during all this time was intense. From April 17th to July 27th, 1908, tuberculin, in doses from $\frac{1}{50,000}$ to $\frac{1}{100,000}$ mg., was given, with gradual improvement. In August the eyes were quiet, and refractive error was measured; 3 D of hypermetropia was present. Glasses were worn, and the eyes remained well.

I have treated 17 other similar cases, all with good results, except one, a boy with enlarged cervical glands. In this case, in spite of tuberculin treatment in doses increasing from $\frac{1}{50,000}$ to $\frac{1}{100,000}$ mg., and very careful correction of hypermetropia, fresh attacks of phlyctenules continued to occur every few weeks. Derby¹⁰ reports 15 cases of sclero-keratitis treated with favourable results by tuberculin.

Weeks¹¹ using von Hippel's method, had 3 recoveries and 2 cases improved of 5 treated.

Hancock and Mayou¹³ have treated 4 cases with tuberculin, guiding the treatment by estimation of the opsonic index; the results were good.

Mackay¹⁴ describes a case of keratitis and scleritis of phlyctenular type, later becoming pustular. Treatment by a vaccine of *Staphylococcus aureus* was tried, with amelioration of symptoms, but later a relapse occurred. Tuberculosis was indicated, as the parents were phthisical. Tuberculin, therefore, was tried, and a positive phase, as shown by the opsonic index, was obtained. As I have mentioned, de Schweinitz¹ has obtained a cure in a case of scleritis and keratitis of long standing, using old tuberculin.

Internal Tuberculosis of the Eye.

In internal tuberculosis of the eye we have to deal sometimes with localized lesions of the iris or the choroid, but more often with a generalized tuberculosis of the inner parts of the eye, involving the iris, ciliary body, and the choroid. I have treated one such case over a long period.

M. B., aged 10, first came under treatment in November, 1907, with iritis in the right eye. The vitreous was cloudy, with numerous dustlike opacities, and a few more gross ones. Fundus view poor, but with the appearance of a mass down and out. V. $\frac{1}{2}$. Calmette's test gave a marked reaction in the diseased eye. This test seemed to have a very bad effect, and the eye, immediately after the test was carried out, became gradually worse. Patient was treated with tuberculin from March, 1908, beginning with $\frac{1}{25,000}$ mg., the dose being gradually increased, until in December, 1908, $\frac{1}{50,000}$ mg. was being given every ten days. The treatment was continued until October, 1909, and at that date the anterior chamber was occupied by a greyish exudate, there was exudation behind the lens, vision was only "hand reflex," and tension was soft. The dosage of tuberculin was regulated by the opsonic index, there being no clinical indications for guidance. The diagnosis was made certain by a positive von Pirquet's reaction, and a Wassermann test was also done and was negative.

In this case, then, the condition continued quietly to progress despite treatment. Better results than this have, however, been obtained in other hands.

Iritis.

Hancock and Mayou¹³ using Wright's method, report 5 cases of tuberculous iritis successfully treated. Weeks¹¹ reports a case of conglomerate tuberculosis of the iris cured by von Hippel's method. Shieck¹⁵ commences with

0.002 mg., repeating the dose on alternate days, each time increasing it by 0.001 mg. He has treated 5 cases of tuberculous iritis, which have improved either immediately or after a temporary increase in intensity at the beginning of treatment. Treacher Collins and Lawford¹⁶ mention good results obtained by tuberculin in the treatment of iritis. Clarke and Mayou obtained a cure in a case of tuberculous iritis in nine months, using $\frac{1}{100}$ mg. every two or three weeks. Von Hippel⁸ obtained cures in 23 cases of tuberculous iritis.

Many other cases of tuberculous iritis cured by tuberculin have been reported by Haab,²⁰ Wolfrum,²¹ and Ziegler.²⁴

Kerato-iritis.

Derby¹⁰ has treated 6 cases of kerato-iritis with favourable result.

Irido-choroiditis.

Fromaget¹⁷ reports a successful and interesting case. A female, aged 28, with no signs of visceral tuberculosis, for three weeks had had painful irido-cyclitis of the left eye; vision = $\frac{1}{2}$; fundus invisible. Two months of ordinary treatment did not improve the condition. In December, 1909, four injections of tuberculin were followed by ocular reaction, the last also by rise of temperature. In January and February, 1910, nine injections were given, and later more injections. The irido-cyclitis became much better, the vitreous cleared, the vision improved to $\frac{1}{2}$. When the fundus was visible there was seen an atrophic patch in the choroid, evidently a cured tuberculous lesion.

Choroiditis.

Using von Hippel's method, Weeks¹¹ has obtained improvement in four cases of tuberculosis of the choroid. Ernest Clarke and Wright,¹⁸ using the opsonic index as a control, cured a case of conglomerate tubercle of the choroid with tuberculin. The case was diagnosed by the varying tuberculo-opsonic index. Treatment by mercury and potassium iodide was carried on for the first nine months while tuberculin was being used. W. Kraus and A. Bruckner²⁵ report two cases of tubercle of the fundus treated successfully by tuberculin. Hay²⁶ mentions cases of tuberculous retinitis cured or treated with success by means of von Hippel's treatment.

In internal tuberculosis of the eye, then, we find that the results of treatment by vaccine are good, especially where the iris is the diseased tissue. The iris is favourable for treatment because it has a good blood supply. In tuberculosis of the fundus, where the blood and lymph supply are poor, treatment has to be prolonged, and is less certainly successful. It may be mentioned here that in disease of the iris it is necessary to use mydriatics to prevent the formation of synechiae, and, the blood supply in this way being diminished, treatment rather tends to be prolonged, owing to the difficulty of getting sufficient opsonins into the diseased tissues.

REFERENCES.

- ¹ Latham and Inman: *Lancet*, 1908.
- ² Fromaget: *L'Ophthal. Provinciale*, Juin, 1910.
- ³ Treacher Collins: *Ophthalmoscope*, 1907.
- ⁴ De Schweinitz: *Therapeutic Gazette*, October 15th, 1910.
- ⁵ Allen: *Practitioner*, 1908, p. 737.
- ⁶ Saxl: *Archiv. f. Augenheilk.*, June, 1907, p. 328.
- ⁷ Ormond and Eyre: *Trans. Ophthal. Soc. U. K.*, vol. xxviii.
- ⁸ Von Hippel: *Arch. f. Ophthal.*, B. 6, 59, p. 1.
- ⁹ Torok: *Arch. f. Ophthal.*, September, 1907.
- ¹⁰ Derby: *Trans. Amer. Ophthal. Soc.*, vol. xii, Part II, 1910, p. 614.
- ¹¹ Weeks: *Trans. Amer. Ophthal. Soc.*, vol. xii, Part II, 1910, p. 598.
- ¹² Nias and Paton: *Lancet*, December 1st, 1906.
- ¹³ Hancock and Mayou: *Ophthalmoscope*, July, 1907.
- ¹⁴ Mackay: *Trans. Ophthal. Soc. U. K.*, vol. xxviii.
- ¹⁵ Schieck: *Arch. f. Ophthal.*, 1900, II, p. 247.
- ¹⁶ Treacher Collins and Lawford: *Trans. Ophthal. Soc. U. K.*, vol. xxx.
- ¹⁷ Fromaget: *L'Ophthal. Provinciale*, Juin, 1910.
- ¹⁸ Ernest Clarke and Wright: *Trans. Ophthal. Soc. U. K.*, vol. xxviii, p. 192.
- ¹⁹ Clarke and Mayou: *Trans. Ophthal. Soc. U. K.*, vol. xxviii.
- ²⁰ At Ophthalmological Congress in Heidelberg, 1905.
- ²¹ Rennert: *Deut. med. Woch.*, 1905.
- ²² Dorschleg, Inaug. Dissert., Griefswald, 1905.
- ²³ Wolfrum: *Arch. f. Augenheilk.*, B. 1, p. 1.
- ²⁴ Ziegler: *Trans. Amer. Ophthal. Soc.*, 1906.
- ²⁵ Hay: *Ophthalmoscope*, 1908.
- ²⁶ Kraus and Bruckner: *Arch. f. Augenheilk.*, May, 1907.

(To be continued.)

THE annual report relating to the Nurses' Co-operation, 8, New Cavendish Street, shows that last year's work was satisfactory, the fees received by members of the nursing staff aggregating a higher sum than in any previous year. The sickness and accident insurance policies, for which arrangements were made for the benefit of the staff some three years ago, continue to prove highly advantageous.

An Address

ON

CASES ILLUSTRATING SOME INTRACRANIAL CONDITIONS OF GENERAL INTEREST.

DELIVERED BEFORE THE BRADFORD MEDICO-CHIRURGICAL SOCIETY, OCTOBER, 1911.

By SAMUEL LODGE, M.D.,

SURGEON TO THE EYE, EAR, AND THROAT DEPARTMENT OF THE ROYAL HALIFAX INFIRMARY; PRESIDENT OF THE SOCIETY.

I PROPOSE in this address to describe some conditions illustrating most widely the diagnosis and treatment of some intracranial diseases which arise independently of local suppuration in the ear, the accessory cavities of the nose, and in the orbit. The cases include examples of intracranial tumour, hydrocephalus, disease of the pituitary body, and others of equally general interest.

Herrick has very truly said that "typhoid fever is not only an imitator of disease, but many diseases imitate typhoid fever." This is illustrated by the following case:

CASE I.—*Extradural Abscess over Both Frontal Lobes, of Traumatic Origin: Pseudo-Typhoid Symptoms: Pott's Puffy Tumour over Right Frontal Region: Operation—Cerebral Symptoms Relieved: Death from Chest Complications.*

A quarryman, aged 21 years, was admitted to the Halifax Fever Hospital on August 15th, 1911, under Dr. Neech. The duration of illness prior to admission was ten days. On admission the temperature was 105.4°, the pulse 92, and respirations 24. Next day the highest temperature was 107.4°, and highest pulse-rate 96. On the third day the highest temperature was 106°, and the highest pulse-rate 84. On the fourth day, on which he was transferred to the Royal Halifax Infirmary, the highest temperature was 99.2°, and the highest pulse-rate 68. Up to the time of his death the evening temperature rarely exceeded 103°, when the morning remissions usually exceeded 2°. During the day the patient lay in a typhoid state, but at night frequently rose from his bed and attempted to leave the ward. He constantly threw off the bedclothes, and complained of there being a bird's nest on the next bed; hypodermics of hyoscin and morphine were required every evening. Splenic enlargement and rose spots were never present. Diarrhoea of "pea-soup stools" was a prominent feature. Incontinence of urine and faeces. On two occasions Widal's reaction proved negative. Until the last week there were no chest symptoms. About the second week after admission to the Royal Halifax Infirmary a fluctuating swelling over the right frontal eminence was incised and pus was evacuated.

Towards the end of the third week the swelling reappeared. Rigidity of the neck muscles, retraction of the head, and Kernig's sign were more pronounced. There was conjugate deviation of the head and eyes to the left and optic neuritis was well marked in both eyes. Some inco-ordination of the arms (dysidiadocokinesia) was present. The right knee-jerk was brisker than the left. Plantar reflexes were flexor in type, and the abdominal reflexes present. Incontinence of urine and faeces. No sensory or motor changes. A history of falling against a fender and bruising the right frontal region, and of suffering from headaches all the summer was now elicited for the first time.

Operation.

On September 5th a scalp-flap, including the pericranium, was reflected with its convexity upward, its centre coinciding with the old incision for the evacuation of the subpericranial abscess. A portion of the frontal bone, oval in shape and about $\frac{3}{4}$ in. long in its largest diameter, was slightly greenish in colour, and presented a narrow but definite fissured fracture of about $\frac{1}{2}$ in. in length. On chiselling away the outer table of the bone in this situation pus escaped from the diploë. The bony opening was enlarged to the extent of 2 square inches. As the pus welled out the pulse and respiration improved. The dura mater was found to be separated from the frontal bone and covered by granulation tissue over a wide area. The pus appeared to be confined in the extradural space. Some of the pus was preserved for bacteriological examination, and was reported on as follows: In films a few diplococci (possibly pneumococci) are found. Culture on agar at 37° C. for forty-eight hours has yielded no growth.

After evacuation of the extradural abscess the typhoid state passed off, the patient no longer required hyoscin and morphine, and now answered questions readily. He became constipated. Towards the end of the fourth week my colleague, Dr. Whitaker, detected serious chest complications, from which the patient died.

Post-mortem Examination.

The bony margins of the skull and the subjacent dura mater disclosed healthy granulating surfaces. On opening the dura the frontal lobes were seen to present saucer-like depressions on their superior surfaces. About the Pacchionian bodies there was inflammatory thickening of the pia mater. Both lungs