a perfect anaesthesia with good muscular relaxation sufficient for any abdominal operation. With the adoption of this position for the injection it is important to keep the head and upper cervical area lowered; this can be done with safety by placing the shoulders on a level with the cephalic joint of the table, and by lowering the headpiece. This simply means that during the injection the thorax is raised 7 to 10 degrees, but the head and neck are dropped; and this position, with the head dropped after the patient is turned on his back, is maintained throughout the operation. In the event of a fall of blood pressure taking place, or should the operation require it, the table can be placed level, or even in the Trendelenburg position after ten to fifteen minutes; this does not appear to affect the anaesthesia, the solution being apparently fixed after this period of time. We have not found the controllability to be as accurate as Dr. Pitkin would lead one to believe: in the case of an extremity, however, the anaesthesia can certainly be confined to the lower reaches of the cord by using a sufficient tilt, say 12 to 15 degrees.

Duration of Anaesthesia.

Dr. Hill states that "duration is a variable quantity." Possibly it is, if only 2 c.cm. be used, but if 3 c.cm. be given there is no fear of the anaesthesia passing off under $1\frac{3}{4}$ hours. Since adopting the reversed Trendelenburg position we have frequently had anaesthesia lasting $2\frac{1}{4}$ hours, and no case has required general anaesthesia to finish off with.

Comparison with Other Spinal Anaesthetics.

We have had no experience in using percaine or a 10 per cent. novocain normal saline solution. Prior to the introduction of spinocain we have employed Barker's solution of stovaine as a routine. Dr. Howard Jones (*Lancet*, January 25th, 1930, p. 211) seems to be unnecessarily severe in his criticism of the Pitkin method. We have found spinocain to be superior in many ways to stovaine; true, the muscular relaxation may not be so good, but this is more than counterbalanced by the absence of toxic symptoms, so often seen with stovaine, by an increased measure of safety, and lastly by an increased duration of anaesthesia.

Summary.

We regard spinocain as a distinct advance in spinal anaesthesia. Whether the addition of amylo-prolamine is of importance in preventing too rapid absorption of the novocain or not we cannot say; we have certainly found it an ideal spinal anaesthetic which can be given to patients in a critical condition, with little or no fear of a catastrophe. Age does not appear to be any bar, and some of our best results have been in old and enfeebled patients in whom only a local or regional anaesthesia would have been permissible. We regard the most important points in connexion with it to be:

1. A preliminary injection of omnopon and hyoscine half to three-quarters of an hour before the operation.
2. An accurate technique during the spinal injection, which should be painless.
3. Comparatively little mixing of the solution with the cerebro-spinal fluid.
4. For upper abdominal work a 7 to 10 degree reversed Trendelenburg position of the table during the injection.
5. Close attention to the blood pressure readings throughout the operation.
6. Adoption of the Trendelenburg position in the ward for some two hours following upon the operation.

Provided the above details are attended to we are confident that a safe and lasting anaesthesia can be obtained, sufficient for any present-day abdominal operation.

I am greatly indebted to Sir H. A. Ballance for permission to publish these cases, and for his kindly help and criticism of this article.

REFERENCES.

- ¹ Pitkin and Kelly: Spinocain, the Controllable Spinal Anaesthetic, *British Medical Journal*, August 3rd, 1929, p. 183.
- ² E. Falkner Hill: Spinal Anaesthesia, *Lancet*, January 18th, 1930, p. 124.

REMARKS BY SIR HAMILTON BALLANCE.

Additional cases of operation under spinocain and planocain anaesthesia have been performed since the above was written, bringing the total to 50 with uniformly satisfactory results, including a difficult case of renal calculus in an old man. Although novocain has been used for spinal anaesthesia for many years, Dr. Pitkin deserves credit for again directing attention to its advantages and for describing a method of painless administration. In the past I have had many anxious times with such drugs as stovaine, tropacocaine, etc., but there has been no anxiety after administration of the novocain solutions. The hypodermic injection of omnopon and scopolamine about three-quarters of an hour before the spinal injection is a distinct advantage; some patients state afterwards that they do not remember coming into the theatre for the operation. The temporary upward tilt of the thorax ten degrees during the injection, but with the head low by means of lateral flexion of the neck, is recommended if anaesthesia to the nipple line is essential for the operation, and I believe this position to be perfectly safe.

The precise action of novocain on the spinal nerves, motor and sensory, may be a matter for discussion, but I have been impressed with the reliability and controllability of the method, the completeness and duration of the anaesthesia, and the absence of bad after-effects on the patients.

TREATMENT OF EYE DISEASE BY TUBERCULIN.

BY

W. CAMAC WILKINSON, M.D.LOND., F.R.C.P.

THE ophthalmic surgeon is not infrequently faced by cases of inflammatory trouble in the eye which do not yield to ordinary methods of treatment, and in some instances progressively get worse until partial or complete blindness results. I am convinced that in some of these cases the trouble is due to tuberculous disease of the eye, and for the last seven years I have been observing the effect of tuberculin in the diagnosis and treatment of certain refractory cases of chronic conjunctivitis, irido-cyclitis, scleritis, episcleritis, and even some obscure forms of retinitis. Apart from tubercle in the choroid in acute tuberculosis, it would seem that tubercle bacilli may reach the choroid and cause a simple choroiditis.

These tuberculous lesions of the eye have some special characters that have helped to obscure their diagnosis. Like the secondaries of syphilis they occur in the secondary stage, when tubercle bacilli are circulating in the blood; therefore one must not expect any phthisical lesion of the lungs. Examination of the lungs may not help in the diagnosis of tuberculosis of the eye, for these eye diseases are earlier in time than the chronic or phthisical lesions of the lungs. They develop slowly—in the course of years rather than months. They tend especially to recur, and they remain localized; yet in course of time one attack after another causes severe symptoms, and though the lesion is limited, it may give rise to pain, headache, and photophobia, and may greatly impair or destroy sight.

Within the last two or three years I have been given the opportunity of making more extended use of tuberculin, through the interest and co-operation of several ophthalmologists, notably Mr. C. L. Gimblett of the Royal Westminster Ophthalmic Hospital and Dr. Douglas McAlpine of the Middlesex Hospital. The necessary ophthalmoscopic examinations during the progress of treatment were made by surgeons interested in their respective cases. The following notes are of cases that have been referred to me for diagnosis, and for treatment when suitable.

CASE I.

An unmarried woman, aged 31, was described by Mr. Gimblett in June, 1928, as being a case of obscure irido-cyclitis of four years' duration, ending in secondary glaucoma. On incising with the keratome the lens was found to be disintegrated and destroyed. A similar condition has appeared in the left eye, which threatens to go the same way as the right. Tested with

tuberculin by the intracutaneous method the result was positive (++). She was treated with subcutaneous doses, beginning with 0.00001 c.cm. TR. When 0.00006 c.cm. was reached, the temperature was raised to 99.6°, and there was a track reaction (++). In one month there was some improvement, and in January, 1929, Mr. Gimblett wrote: "Patient is very strikingly better, and nothing until she started under your treatment did her the least good. In a few more months she would have been blind. Keratitis punctata has almost disappeared even from the right eye. As to the two anterior chambers, the vitreous chamber is still crowded with exudate." Treatment was continued until 1 c.cm. TR was given in one dose; there was then severe track reaction (+++), but the temperature was only 99.4°. As progress seemed to have come to a standstill, though the patient was very much better from treatment, I proceeded to graduated doses of BE, until 1 c.cm. was given at one dose. The temperature hardly rose above normal. In November, 1929, Mr. Gimblett wrote: "Both eyes quiet and the left vision with a +0.75 D. cylinder 80° is 6/18 all. There are deposits on the lens, but no keratitis punctata now. Is there any possibility of her working?" By December, 1929, the patient had gained half a stone in weight and looked a new woman; her eyes were so improved that she hoped to do some work after years of incapacity, and her general health was very much improved.

CASE II.

A girl, aged 16, was treated at Great Ormond Street Hospital for rheumatism at the age of 12, and the heart was thought to be affected; in 1928 it was quite normal. In March, 1923, the eyes became red and painful, and the patient attended the Western Ophthalmic Hospital, where she was treated by Mr. Robinson for seven months, during which time the legs also became inflamed and discharged as the result of erythema induratum. In 1927 the eyes were again affected, and the patient was again treated by Mr. Robinson, being sent to Bournemouth for two months. The eyes became worse and were very painful; there was sharp pain in the head, and the patient was unable to sleep, leeches being applied without benefit. She attended the Ophthalmic Hospital twice a week and had drops instilled. Dr. Douglas McAlpine could find no trace of tuberculosis in the lungs (December, 1927), but sent the patient to the tuberculin dispensary for specific diagnosis. The result was positive, and after prolonged treatment with tuberculin, until very large doses were being taken without any serious reaction, the patient was restored to apparent health. The eyes are now quite normal in appearance and function, and the legs are completely healed. The patient has been back at her usual work (carpet sewing) for more than twelve months.

CASE III.

In October, 1927, a patient was sent by Dr. Carter of Wolverhampton, the symptoms being violent pains in the eyes with photophobia; the eyes were very bloodshot, there was sickness and giddiness, and the temperature was often 99.2° to 99.4° in the evening. The patient was absolutely incapacitated, and was confined to a dark room for many months. The weight was 8 st. 4 lb. Tested with tuberculin (Pirquet method) the reaction was positive. Subcutaneous injections of TAF were given, beginning with 0.0000125 c.cm. The temperature rose to 99.6°. In November the patient wrote: "The sight of both eyes is almost normal now, which is surprising, as the right eye has been short-sighted for several years, and there has been no return of the pain or fear of light that I have had for so many months, and in addition to this I have gained weight—six pounds since I was last weighed in August—so the treatment seems to be eminently satisfactory." In December he wrote again, "The eye is still clear, and it is having quite a normal amount of use." The patient was treated with TAF up to a dose of 0.6 c.cm. (September, 1928); by February, 1929, a dose of 0.95 c.cm. TR had been reached. The weight was 8 st. 9½ lb., and in March, 1929, the patient wrote: "My general health is most satisfactory."

CASE IV.

A married woman, while at the seaside in 1923, had a severe attack of conjunctivitis, the eyes being intensely inflamed, painful, and discharging. They recovered in six weeks; but each summer the sunlight caused recurrence of the inflammation, and dark glasses have been required. In 1928 the eyes were again inflamed and painful, and the vision was blurred; she went to the Central Hospital twice a week for two months, and atropine ointment was applied night and morning. The patient was then almost blind, her vision being gravely distorted. She was seen by Dr. Leech of Watford, who advised that a specific test should be made at the tuberculin dispensary. Her weight was 8 st. 11 lb. At the commencement of specific treatment one eye was completely blind and the other partially so. After treatment with increasingly large doses of tuberculin for eight months the sight became quite keen, and the weight increased from 8 st. 11 lb. to 9 st. 9 lb. In August, 1929, the vision being again impaired, a further course of tuberculin was given. In October, 1929, Dr. Leech wrote: "Her sight is now quite clear and she can read

small print, whereas when she started treatment she was unable to see even the largest test-type clearly." Mr. Gimblett wrote: "Evidence of old iritis in right; no keratitis punctata now. Venous engorgement of both discs. Everything appears quiet. No doubt she has had an inflammation of all the ocular structures, even the optic nerves, which is gradually subsiding."

CASE V.

A woman, aged 56, who was sent in July, 1928, by Mr. James of St. George's Hospital, had attended there since 1914 for iridocyclitis. The left eye was blind and the right was gravely affected. She had to be led to the dispensary by her sister, being able to see nothing, not even light. She reacted severely to the intracutaneous test with tuberculin. She was treated at the tuberculin dispensary, the final dose being 1.1 c.cm. TAF. In February, 1929, the sight was so much improved that she could walk through London streets to the dispensary by herself; the general health had also improved. In August, 1929, she could still go about by herself.

CASE VI.

In July, 1928, a female patient with a very bloodshot eye, attributed to ulcers, was given drops and tonics for one month with no improvement; the eye was greatly swollen and red, and she had severe pain. At the Western Ophthalmic Hospital iridocyclitis of eight months' duration was diagnosed. Mr. Taggart suspected tuberculosis, and Dr. Douglas McAlpine sent her to the tuberculin dispensary for specific tests, which were positive. Tuberculin treatment was begun in February, 1929, and the sight is now completely restored; the general health vastly improved, and she "feels a different person."

CASE VII.

A married woman, aged 32, saw Mr. Gimblett in 1925 and was ordered glasses. In October, 1928, she had headaches, and he found retinitis. A blood test was negative. She was sent to the tuberculin dispensary and tested with tuberculin. After a subcutaneous dose of 0.0015 c.cm. T.A.F. the temperature rose to 102°, and the track reaction was ++. She was treated with tuberculin until July 20th, 1929, when with 1.5 c.cm. TAF there was a reaction temperature of 100°. Her improvement was marked, and all pain has been lost since treatment. In April, 1929, Mr. Gimblett wrote: "She has now very much less floating opacities in her right eye and no further fresh patches of retinitis in the left; so far so good."

CASE VIII.

In August, 1928, an unmarried woman, aged 24, complained that her eyes were misty; she could hardly see, and went to the Middlesex Hospital; she attended for three months with no improvement. In November, 1928, she went to the Royal Ophthalmic Hospital and saw Mr. Gimblett, who sent her to the tuberculin dispensary for "double irido-cyclitis of three months' standing." Her weight was 6 st. 7 lb. She was tested with tuberculin, the reaction being +++, and was treated with small doses. In December Mr. Gimblett wrote: "The keratitis punctata has practically disappeared, although both vitreous chambers contain much floating opacities." In March, 1929, he added: "The patient is very greatly improved, and all the keratitis has disappeared. The left pupil is almost fully dilated, and the vitreous is very much clearer." In August, 1929, he wrote: "The eyes are quiet"; and in November, 1929, "The right eye is well; I think the left eye has no keratitis punctata, and apparently no active lesion." In January, 1929, after an absence of fifteen months, the patient returned to work (fine needlework). Her weight was 6 st. 12 lb., a gain of 6 lb. and the general health had greatly improved. She is extremely sensitive to tuberculin, and still needs treatment for a long time.

CASE IX.

In a married woman, aged 44, the right eye was affected at the ages of 25 and 28. In February, 1929, she visited the Western Ophthalmic Hospital, where the eyes were reported weak, and reading glasses were ordered. Six weeks later she had an operation on the left eye, followed by complete loss of vision. She was advised by Mr. Taggart to attend the Hospital for Epilepsy at Maida Vale, where she saw Dr. McAlpine, who sent her to the tuberculin dispensary. The eye was still blind and very painful. A tuberculin test resulted in a reaction of +++, and a course of treatment was begun in May, 1929. In July there was less pain, and the sight was clearer. In August the eye was weak again, and there was pain and inflammation; a fortnight later the eye was much better; the discharge had ceased, and the eye was clearer than before. The sight is now so much better that she can read, and her general health is excellent. The treatment has been uninterrupted in spite of relapse. In December, 1929, she reached the highest dose so far, 0.5 c.cm. TAF; the treatment is still continuing.

Four other patients who were sent to the tuberculin dispensary for diagnosis gave negative reactions both to intracutaneous and to subcutaneous tests, showing that it

is far from true that all persons react to tuberculin. In these cases tuberculin treatment was not undertaken.

The cases I have recorded above seem to offer prima facie evidence that there are patients with inflammatory trouble in the eyes who do not benefit by ordinary methods of treatment; that many of these patients react to diagnostic doses of tuberculin; and that treatment with tuberculin produces marked improvement, or even arrest of the trouble, in a considerable number of these reacting patients. Since the use of tuberculin, for both diagnosis and treatment, by the methods I advocate is completely innocuous to the patient, I submit that its employment in such cases is amply justified. The satisfaction of the patients who have been treated at the tuberculin dispensary, coupled with the recorded opinions of the ophthalmic surgeons under whose care they were, encourage me to suggest that wider trial of these methods should be made in the treatment of eye diseases.

ON SPECIFIC ANTITOXINS IN STREPTOCOCCAL INFECTIONS.

BY

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WHILE it has long been common knowledge that streptococcal infection was responsible for a number of clinical varieties of disease—for example, cellulitis, erysipelas, tonsillitis, puerperal fever, scarlet fever, ulcerative endocarditis, etc.—it is only in recent years that it has been possible to differentiate and classify special groups of streptococci.

It was found that streptococci could be differentiated by their fermentative action on different sugars, and also by their haemolytic action on blood corpuscles, certain streptococci when grown on blood agar plates producing a clear red halo of haemolysis around each colony. These haemolytic streptococci are of special importance, as they are responsible for some of the most serious infections—for example, puerperal septicaemia, erysipelas, and scarlet fever. In 1924 the Dicks described a soluble toxin, derived from culture of haemolytic streptococci obtained from the throats of scarlatinal patients, and with which experimental scarlet fever had been produced. This toxin when injected intradermally produces a pronounced erythematous blush in the surrounding skin of patients whose blood does not contain enough of the specific antitoxin to neutralize it, and is widely used to test susceptibility to scarlatinal infection (the Dick test), exactly in the same way that the diphtheria toxin is used to test susceptibility to diphtheria (the Schick test).

Similar toxins were discovered in 1926 by Birkhaug in the case of erysipelas, and by Lash and Kaplan in the case of puerperal sepsis, the toxin of which differs from the Dick scarlatinal toxin in being heat labile, whereas the Dick toxin is not destroyed by boiling. These toxins also produce skin reactions similar to those of the Dick reaction in persons susceptible to erysipelas and puerperal fever respectively. The toxin prepared by Lash and Kaplan was made use of for testing the susceptibility of pregnant and non-pregnant women to puerperal sepsis. Antitoxic serums were produced by Birkhaug by immunizing animals with erysipelas toxin. This serum agglutinated haemolytic streptococci from erysipelas, and also had a striking therapeutic effect in erysipelas infection. Similar antitoxins have been prepared from toxin from puerperal septicaemia. Some doubt, however, has been thrown on the specific nature of these toxins and antitoxins during the last few years, especially by some investigators in this country. It would appear probable that there is a factor common to all three groups, that there is also a factor special to each of the toxins and antitoxins, and that to produce the most satisfactory therapeutic effect the specific antitoxin should be injected.

With regard to the specificity of the scarlet fever and erysipelas toxins, the Dicks have lately conducted a series of experiments which should be conclusive.¹ They demon-

strated that there was no direct relation between spontaneous immunity to scarlet fever and erysipelas toxin. It was shown that an attack of scarlet fever does not confer immunity to erysipelas, and that artificial immunization by scarlet fever toxin confers no immunity to erysipelas toxin; also that scarlet fever antitoxin prepared by immunizing a horse with toxin from scarlet fever streptococcus neutralizes scarlatinal toxins, but does not neutralize erysipelas toxin, and erysipelas antitoxin neutralizes toxins derived from strains of erysipelas streptococci, but not scarlet fever toxin. The Dicks conclude, therefore, that the soluble toxins produced by scarlet fever and by erysipelas haemolytic streptococci are immunologically specific and distinct.

Working with scarlet fever, erysipelas, and puerperal fever toxins, and with convalescent serums and antitoxins, Ferry and Fisher found that in low dilutions of the serum there was more or less cross-neutralization of the toxin by the serum, but in high dilutions the serums neutralized only their homologous toxins. If these results are accepted it is evident that to get the fullest advantage from antitoxic treatment the special antitoxin should be employed. In the case of puerperal fever, although the great majority of severe infections are due to the haemolytic *Streptococcus pyogenes*, other organisms are occasionally responsible, and a culture from the cervical canal and from the blood should be taken.

A case which has recently been under my care is a very striking illustration of this specific action.

The patient was attacked by a throat infection with a haemolytic streptococcus, which in the course of two or three days from the beginning of the illness invaded the middle ear and the mastoid cells on the right side. I saw her on the third day; her evening temperature was 101° F., and there was tenderness and slight oedema over the mastoid. A swab from the throat was taken, and 10 c.cm. of polyvalent antistreptococcal serum administered. On the following day an operation was performed upon the mastoid by Mr. K. D. Mackenzie. All the mastoid cells were infected, and a pure culture of a haemolytic streptococcus was obtained. The throat culture showed haemolytic streptococci and *Micrococcus catarrhalis*. The culture was incubated with the patient's blood by Dr. Biddle, pathologist to the East Suffolk Hospital, and the blood was found to have no bactericidal effect upon the streptococcus.

Following the operation there was free suppuration, and the temperature showed no diminution, reaching 101° F. each evening. On the fourth day after the operation 10 c.cm. of concentrated scarlet fever antitoxin was given intramuscularly in the morning, and the injection was repeated in the evening. On the following

A, Operation. B, 10 c.cm. scarlatinal antitoxin. C, 10 c.cm. polyvalent serum. D, 15 c.cm. colloidal silver (intravenous). E, 10 c.cm. erysipelas antitoxin.

day, the fifth after operation, the temperature reached 103° at 2 p.m., and definite erysipelas infection of the pinna of the ear and the skin in the temporal fossa was evident. The pulse rate went up to 110; it had previously ranged between 80 and 100. The leucocyte count was 13,000.

During the next few days the erysipelas continued to spread in the skin of the forehead to the nose. On the eighth day after the operation the temperature was 104° in the morning and 104.4° in the evening; the pulse rate was 116. The patient was given 10 c.cm. of scarlatinal antitoxin intramuscularly in the morning, and a similar amount in the evening. On the next day the temperature was 101° in the morning and 104° in the evening. On the tenth day the temperature was 101°, and 10 c.cm. of polyvalent streptococcal serum were administered. The leucocyte count was 10,000. On the eleventh day erysipelas infection had reached the left side of the face. The temperature was 102.6°, and 15 c.cm. of colloidal silver was given intravenously. No improvement followed, and on the thirteenth day the temperature again reached 103° F. An intramuscular injection of 10 c.cm. of concentrated erysipelas antitoxin was given on that afternoon.