quinine, and arsenic, didymin, thyroid, thymus, pituitary extract and x rays. Nothing seems to have had much effect upon him, and x rays seemed to aggravate the hallucinations. Thyroid gland only reduced his weight and so was soon discontinued. Pituitary extract seemed to quieten him for a time, and increased the quantity of urine, and apparently also the systolic blood pressure which sometimes went up to over 100 mm. Hg a day or two after injections of pituitary extract, but even these results were by no means consistent and might have been ascribed to normal variations. The one satisfactory feature of the case is that the vision and extent of the field in the left eye have not materially diminished during the last five years. The vision is decidedly variable and on some occasions it gets as low as counting fingers at 3 metres—this in fact was the record of the vision in the left eye in 1906 when that of the right eye was given as $\frac{3}{8}$. It is seldom less than $\frac{3}{8}$ at the present time.

CASE III.—*Ateliosis* (?) (Fig. 7).

Frank L., aged 15 years. Family history unexceptional. Patient was like other children until he was 6 years of age. From that time on he has been physically at a standstill and has retrogressed mentally. Latterly he has been under treatment for tabes mesenterica. At the present time he is 3 ft. 7 in. in height, and weighs 3 st. 2½ lb.

His general appearance suggests feeble mental and physical development. The skull is dolichocephalic, with marked frontal eminences; bridge of the nose undeveloped; mouth large, tongue pale and flabby; teeth good; heart and lungs normal. He has scoliosis, lumbar lordosis, and genu valgum. The abdomen is very prominent—23 inches in circumference at umbilicus. There is a fine growth of hair in the lumbar hollow, but there is no deformity of the neural arches.

There is complete testicular descent, and external genitals are normal. The skin over the abdomen and front of the thighs is markedly mottled (see photograph, Fig. 7), and the fingers and toes are of slight purplish tinge, but are quite warm to the touch. Intellectually he is very backward. He speaks, but will not answer questions. Eyes: Beyond having had phlyctenular keratitis, which has now healed up, there is nothing to note with regard to the eyes. There is no optic atrophy, and, as far as we can judge, no defect of the visual fields.

Radiographic examination shows that the sella turcica is smaller than usual, and is apparently encroached on by a bony spicule (Fig. 8).

There seems to be delayed ossification of epiphyses also, as

Fig. 8.—Case III. Radiograph showing small-sized sella turcica encroached upon by a bony process.

there is no union between the ischial and pubic rami. It will be easier to judge of the state of his bony development when he reaches the age when the epiphyses of the long bones are due to join the diaphyses.

The foregoing cases indicate the type of nutritional and other disturbances which result from pituitary insufficiency during the growing period.

The following cases kindly reported to me by Dr. Duncan Lawrie, of Oldham, show the results of hypopituitarism in the adult.

CASE IV.

Miss A. B., aged (?), complained of failure of sight, with frequent headaches and amenorrhoea of three years' duration.

In appearance she was a tall, broad-shouldered woman, and her hands and feet were large, but only in proportion to her size. She was bigger than her mother and sister.

Mentally she was normal or above the average of her class. The thyroid was markedly enlarged.

Pupils dilated, react sluggishly to light, active to accommodation and convergence. Left eye divergent. Nystagmus on fixation. Primary optic atrophy each eye.

R.V. = $\frac{3}{8}$, L.V. = $\frac{3}{8}$.
Reads J. 4.

Charts of visual fields show bitemporal hemianopia. Colour vision for red, green and blue good in parts of fields retained. Thyroid administration rapidly gave rise to tachycardia and tremors and did not improve other symptoms. She died with symptoms of cerebral growth. No autopsy.

CASE V.

Mrs. B., aged 35 years. Had noticed failure of sight for three years; menses, which were regular previously, became arrested four years ago.

Physically and mentally she shows nothing abnormal, and beyond the complaints mentioned feels perfectly well. The right pupil is larger than the left. Neither pupil reacts to light. The right eye is divergent. There is primary atrophy of the optic nerves, the right being more markedly atrophic.

R.V. = Fingers at 6 in.
L.V. = $\frac{3}{8}$.

Bitemporal hemianopia. The case has been lost sight of since.

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THE VACCINE TREATMENT OF GONOCOCCAL ARTHRITIS.

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THE occurrence of gonococcal arthritis signifies an infection through the blood stream, usually from the urethra or vagina, very exceptionally from the conjunctiva. The vitality of the gonococcus on these mucous membranes and the obstinacy of the local infection are well recognized, but from the comparative infrequency of visceral infections it is evident that the micro-organism has great difficulty in maintaining its existence in the blood serum. The tissues which it attacks from the blood, though very widely spread, are few in number, chiefly the fibrous structures of the joints, muscles, and fasciae, and the synovial membranes of joints and tendon sheaths, although the valves of the heart and the pleura are not exempt. All these structures, in fact, consist chiefly of white fibrous tissue.

Fibrous Tissue.

Once established in fibrous tissue the gonococcus may maintain itself very obstinately, but as a rule local reaction occurs, characterized by formation of new fibrous tissue, and after some weeks the organism dies out, leaving behind it a local fibrosis which is pathological in structure and gives rise to chronic muscular stiffness, pain or aching, contracture of joints, flat-foot, and other effects. Sometimes, but rarely, an abscess forms, and yields pure cultures of the gonococcus.¹

Joints.

In joints the fact that increased secretion takes place from the synovial membrane determines to a great extent the local symptoms. The gonococcal inflammation is often transient, although it can be very prolonged. Thus we find that many patients give a history of one or more attacks of polyarthritis which have cleared off in a few days, and frequently, when several joints have been affected, these cure spontaneously with the exception of one or two, which remain more or less obstinately inflamed. The exudation into the cavity of the joints contains many polymorphous leucocytes, and is rather

thick and turbid, but it very rarely becomes purulent. Immunity does not seem to be conferred, as joints which have once suffered are more liable to subsequent attacks, but some degree of resistance must be developed, as at first the pain and fever are at their worst, and later, even without treatment, the temperature tends to fall and the swelling of the joint to diminish. The incidence of the joint infection can often be traced to exposure to cold or wet, and to injury or strain.

Mucous Membranes.

On mucous membranes the formation of pus is a constant and marked feature. After a time a certain amount of local immunity is established, the organisms remaining virulent and infective to others, but ceasing to cause much appreciable local reaction or discomfort to their host. In the male urethra the discharge becomes "gleety" or is entirely in abeyance, but is liable to become purulent again under various forms of irritation. The infection of the mucous membranes may endure almost indefinitely or may finally die out. The amount of local immunity conferred by it must be very small, as reinfection can take place at once; nor is much, if any, general immunity induced, as the joints, conjunctiva, bladder, testicle, and other parts are often infected in persons who have suffered for months from urethritis.

The mechanism of the spontaneous cure of gonococcal infections is not yet clear. Possibly phagocytosis plays the chief part. In fibrous tissue no local leucocytosis has been observed, but in the case of joints the leucocytes in the exudation sometimes can be seen to contain gonococci, and it is generally assumed that the cocci lying in the leucocytes of a purulent discharge are in process of disintegration, even although they remain infective.

Toxin.

A urethritis seldom causes much fever or constitutional disturbance. On the other hand, a blood or joint infection causes both, and often to a very considerable extent. This is due to the action of a toxin, which is of the nature of an endotoxin, and is only set free when the cocci die and become disintegrated. De Christmas found that the injection of this toxin into the human urethra caused a purulent discharge, and that this recurred with succeeding injections, no local immunity being established. In the natural disease in man it is a matter of common knowledge that the body does not rapidly or efficiently immunize itself.

VACCINE TREATMENT.

During the last four years various papers have appeared describing the treatment of gonococcal infections by the subcutaneous administration of dead gonococci, the object being to stimulate the tissues generally to produce opsonins or antibodies. Allen,² Emery,³ Bosanquet and Eyre,⁴ and others speak very positively and enthusiastically of the curative results of vaccine treatment in all forms of gonococcal infection. Irons⁵ says, however, that it is of no use in acute gonorrhoea, and Pollock,⁶ Hartwell,⁷ and others that it is valueless in urethritis—results which accord with my own experience. In vulvo-vaginitis of children its use has been said to be satisfactory and the reverse, but a perusal of the published papers⁸ does not carry conviction as to its efficacy.

It is more difficult to sum up and analyse the results of vaccine treatment in gonococcal arthritis as reported by different observers. For instance, Hale White⁹ records 4 cases, 2 of which were rapidly (three to five weeks) cured by three doses of 5 to 10 million gonococci, the third by four doses of 5 to 25 million, and the fourth by three doses of 100 to 200 million. W. R. Jack,¹⁰ in 4 cases, got somewhat similar results (cure in seventeen days to seven weeks with four to nine doses) with inoculations of 4 to 10 million gonococci; and Stewart and Eyre¹¹ state that 5 to 10 millions should only rarely be exceeded, and advise even 1 to 2 millions every three to five days as safe and satisfactory. On the other hand, Allen states that an initial dose of 500 millions is required, and that it should be raised to 1,000 millions. Irons speaks favourably but guardedly: "In certain cases at least of gonococcal arthritis recovery can be hastened by the injection of dead gonococci" (dosage 20 to 1,000 millions). He used other treatment freely along with it, as did Hartwell (dosage 10 to 600 millions). Cole and Meakins¹² gave

300 to 1,000 millions, and found the negative phase always ill-marked or absent. In most of their cases only three or four doses were administered, mostly at intervals of eight to twelve days. They say: "It is difficult not to feel that the treatment has been of value. We recognize, however, how difficult such conclusions are, and we prefer therefore to publish the cases as they are and allow others to decide whether they will carry out this treatment or not." Murrell¹³ gives short summaries of 3 cases which recovered, but not rapidly, under vaccine administration. There is also marked difference of opinion regarding the relative value of autogenous and heterogenous vaccines. Certain of the above writers hold that the former are much more efficient, while others maintain that the latter are equally powerful.

Personal Observations.

I wish to put on record here the results obtained by the vaccine treatment of 9 cases of gonococcal arthritis. The number is not large, but they were carefully selected as uncomplicated cases, all of which suffered only from urethritis or vaginitis, and arthritis, so that treatment was not made more difficult or prolonged by such complications as cystitis, conjunctivitis, prostatitis, etc. In all, the gonococcus was isolated from the urethra, vagina, or a joint, and cultures made. Autogenous vaccines were mostly used, but not exclusively. Three of them were treated at first with salicylates to make sure that they were not cases of true rheumatism; in the others vaccine treatment was begun at once. They were all cases of moderate ordinary severity, and otherwise in good health.

In all, the treatment was at first exclusively by the vaccine, but in most of the cases no distinct improvement followed, and after waiting a reasonable time ordinary local treatment was usually superadded or substituted. This was always followed by an immediate and distinct improvement in the local and general conditions, and was what finally led to cure. Only in one case (ix) did recovery take place under vaccine treatment alone, but improvement was so rapid and so marked after only one dose of 5 millions that, on comparing it with the results in the other cases, one cannot help feeling that the vaccine had nothing to do with it. The doses are marked on the charts, and a reference to these will show that varying quantities were used, this being done purposely owing to the different opinions prevailing as to the most suitable dose. I was unable to give the large amounts recommended by Allen, on account of the violent reaction which sometimes followed on much smaller quantities.

Before a correct judgement can be formed of the value of vaccine treatment in gonococcal arthritis considerable experience is necessary of the clinical progress of the disease under other forms of treatment. My experience has been that the great majority of uncomplicated cases of ordinary severity which require hospital treatment can usually be cured in from five to eight weeks.* For years past I have kept accurate records of such cases, and charts 10 and 11 indicate briefly the progress of two of average severity. They compare very favourably with the similar cases treated by vaccines. The ordinary plan of treatment which I now adopt is to administer full doses of copaiba, to apply to the affected joints or fibrous tissues a dressing of oil of copaiba (three parts to one part olive oil) after it has also been gently rubbed in, and to use bougies containing 2 or 3 per cent. silver nitrate for the urethra. In women the vagina is douched twice daily with solutions of mercuric chloride (1 in 1,000 and 1 in 2,000) or calx chlorinata (1 in 100) or potassium permanganate. These are frequently changed, and, after the douching, solution of hydrogen peroxide or silver nitrate is freely used and a certain amount left in. If the cervix is deeply infected it is a practical impossibility to free it from gonococci. If there is much fluid in a joint it should be tapped, and to avoid the formation of adhesions the joints should be gently moved several times daily. The pain of movement is often so severe, however, that patients will not allow this to be done. The results here detailed, along with those got in other cases, have forced me to the conclusion that the administration of dead gonococci exerts no curative

* By "cured" I mean that the gonococcus cannot be found in mucus expressed from the urethra or got by passing a platinum-wire loop along it, and that all active inflammatory symptoms have disappeared from the joints. Stiffness or contracture is, of course, a result of the infection, and can only gradually be removed by massage and movement.

Chart VI.—Case vi. Woman, 48. On admission both knees and both ankles painful and slightly swollen, left wrist and hand much swollen, right shoulder painful and swollen. Duration, eight days. Gonococci in vaginal discharge. 1, Salicylate treatment, no benefit. 2, Pain in joints very severe. 3, Pain less, wrist and shoulder stiff from adhesions. 4, Vaginal douching with 1 in 2,000 mercuric chloride. 5, Pain gone. 6, Shoulder-joint and wrist very stiff and muscles much atrophied.

Chart VII.—Case vii. Man, 24. Urethritis ten weeks. Left knee and both ankles swollen and painful. Left hip and back painful. Began six weeks ago. Gonococci in discharge. After each dose of vaccine there was a rise of temperature. Autogenous vaccine. Dismissed for breaking rules of hospital.

Chart VIII.—Case viii. Man, 33. Pain and swelling in right knee and ankle, pain in left hip and upper arms. Arthritis four months, urethritis five months. Gonococci in discharge. Nine years ago and five years ago had gonorrhoeal rheumatism. 1, Sodium salicylate 20 grains four-hourly. 2, Salicylate stopped, no improvement. The first two doses of vaccine caused no subjective symptoms; after the third, pain in heel and left shoulder. After dose of 300 million no subjective or objective symptoms. No improvement in joints. 3, Copaliba by mouth and oil of copaiba to joints. 4, Steady improvement since. 5, Discharged well except for stiffness. 6, Discharged well except for stiffness.

Chart IX.—Case ix. Man, 34. Urethritis for two months. Three weeks ago pain and swelling in knees, ankles, and great toes. Gonococci in discharge. 1, Pain and swelling almost gone from left knee. 2, Effusion almost gone from both knees, but still painful on movement. 3, Pain gone except on extreme flexion of joints. Autogenous vaccine.

Chart X.—Case x. Woman, 25. Pain in knees and ankles five days before admission. On admission left knee-joint swollen and painful. Sodium salicylate 20 grains four-hourly, methyl salicylate dressing on knee. 2, Knee-joint tapped and gonococci found. 3, Salicylates stopped, no improvement. 4, Vaginal douching 1 in 1,000 mercuric chloride, and oil of copaiba dressing to knee. 5, Pain gone, can walk. 6, Left hospital cured.

Chart XI.—Case xi. Man, 33. Pain, swelling and redness in right wrist, dorsum of hand and second and third metacarpo-phalangeal joints, pain in left knee. Urethritis. Gonococci in discharge. 1, Copaliba 30 minims thrice daily. Oil of copaiba dressing to joints. 2, Pain gone from knee. 3, Wrist nearly well. 4, No gonococci in urethra. 5, Recovered except for some stiffness in wrist and hand, due to adhesions.

toes. Urethritis for two months; gonococci present. There was marked improvement from the first, and after two injections of 5 million the pain and swelling in all the joints had greatly subsided. Each dose caused a slight rise of temperature, and 20 million was the largest given. No other treatment was employed.

CASE X.

Woman, aged 25. Five days before admission pain and swelling in knees and ankles, pain and stiffness in both shoulders. This cleared away except in the left knee-joint, which was tapped and gonococci found in the fluid. There was vaginitis with gonococci. There was fever, rising to 103° F. Salicylate treatment did no good. She then had vaginal douching (1 to 1,000 mercury chloride) and oil of copaiba dressing to the knee. The temperature fell at once, the pain and swelling disappeared more slowly, and after four and a half weeks she left hospital well.

CASE XI.

Man, aged 33. Urethritis with gonococci. Swelling with pain and redness had come on acutely in right wrist, tendon sheaths, and dorsum of hand, and in the second and third metacarpophalangeal joints. He was treated at once with copaiba internally and locally to the wrist and hand. Recovery took place in five weeks, but stiffness remained, due to adhesions.

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THE ALBUMEN REACTION IN TUBERCULOUS SPUTUM.

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THE difficulties in arriving at a correct diagnosis in early tuberculosis of the lungs are known to all of us, and in those cases which do not present physical signs it is almost impossible to form a correct opinion, much as we may suspect the presence of tubercle.

It is on this account that we welcome any new test which may assist us in a diagnosis, and to the patient it is of supreme importance that treatment should be commenced before the development of physical signs in the chest. The test which I propose to describe was introduced by MM. Lesieur and Prirey.¹ It is simple and can easily be applied at the bedside.

The technique is as follows: Five cubic centimetres of the sputum are mixed with 20 c.cm. of physiological salt solution in a test tube; 5 or 6 drops of acetic acid are added, and the whole well shaken up and then filtered. The filtrate is then tested for albumen by heat or nitric acid.

If the reaction is obtained it is claimed by the writers to be strong evidence in favour of pulmonary tuberculosis, although they admit that the reaction occurs in other diseases, to which I will refer. Lesieur and Prirey claim that the reaction is present invariably in cases of pulmonary tuberculosis, even in its early stages, when it may be difficult or impossible to discover tubercle bacilli in the sputum. They find this reaction present before the appearance of any physical signs in the lungs in 75 per cent. of cases, and declare it to be a more useful test than the microscopic examination of the sputum. In miliary tuberculosis or in pleurisy it is not constantly given.

They also find the reaction present during an attack of acute lobar pneumonia due to pneumococci, and its persistence in this disease during convalescence points to the probability of a new focus of infection or a complication. The reaction is found also in acute pulmonary oedema, acute congestion, and acute bronchopneumonia. As a rule it is negative in acute bronchitis, and it is always negative in chronic bronchitis and emphysema. In cardio-renal cases it is often positive.

They give a total of 840 observations from various authors in which the reaction was positive in 100 per cent. of cases, confirmed by microscopic examination of the

sputum for tubercle bacilli in 83 per cent. of cases of probable pulmonary tuberculosis, and in 37 per cent. of cases of non-tuberculous sputum. They find that the intensity of the reaction is in direct proportion to the importance and gravity of the lesions and the abundance of tubercle bacilli, and so consider the reaction to be valuable in prognosis as well as diagnosis. A negative reaction would, according to their opinion, appear to exclude pulmonary tuberculosis.

My junior colleagues at the hospital have very kindly undertaken to make a thorough test of this reaction, and the results of their work in the wards, and my own in private, are here given.

In cases of suspected tuberculosis we can obtain very valuable information by using tuberculin; and although this is not the time to mention the various tests that are employed by that method, it is my practice to perform the cuti-reaction (von Pirquet's test), which consists of scratching a few drops of concentrated human or bovine tuberculin into the skin and watching the effect. If the patient is tuberculous a pinkish areola surrounds the scratch, occurring in about twelve to twenty-four hours and persisting, as a rule, for five or six days.

A positive von Pirquet test, however, is no evidence of pulmonary tuberculosis, but is simply an evidence that there is or has been a focus of tubercle somewhere in the body; of course, if there are physical signs in the lungs, then the presumption is strong that the case is one of pulmonary tuberculosis. I attach great weight to a negative von Pirquet reaction, as we can almost certainly exclude tuberculosis excepting in those cases in which the disease is too acute or too advanced to give a reaction. In the 110 cases in which the reaction was sought for in the wards of Mill Road Infirmary the diseases were as follows:

Pulmonary tuberculosis	...	...	...	90
Pneumonia	...	...	...	9
Bronchopneumonia	...	...	...	4
Bronchitis	...	...	...	2
Asthma	...	...	...	2
Tuberculous joints	...	...	...	2
Neurasthenia	...	...	...	1

As far as was possible the von Pirquet reaction was obtained, and in addition the sputum was stained for tubercle bacilli.

There can be no doubt that in the large majority of cases of pulmonary tuberculosis the reaction is easily obtained, and out of the 90 cases which were diagnosed as pulmonary tuberculosis, 75 gave a positive reaction and 15 gave a negative reaction. The latter 15 cases presented the physical signs of tuberculosis with a positive von Pirquet reaction, but in 9 of the cases no tubercle bacilli could be obtained, so that it is possible that our diagnosis was at fault. In 6 cases, however, tubercle bacilli were found, and this test was found to be negative in these 6 undoubted cases of pulmonary tuberculosis.

In the cases of pneumonia in the acute stage the reaction is generally positive, although in one case the reaction was not present until the sputum became rusty.

In chronic bronchitis and emphysema the reaction is usually negative. In the two cases of tuberculous joints the reaction was negative, and in one case of neurasthenia without lung symptoms the reaction was positive.

CONCLUSIONS.

From this list of 110 cases I would not like to dogmatize on the certain value of the test to make a diagnosis of tubercle of the lungs before the onset of physical signs, and before tubercle bacilli appear in the sputum, and I propose to continue the investigation in a few hundred more cases before coming to a conclusion. In the meantime, however, I am of opinion that the test is valuable in certain doubtful cases, and, taken in conjunction with a positive von Pirquet reaction, we would be justified in making a diagnosis of pulmonary tuberculosis; moreover, the test has the advantage of being very simple and easily applied, whereas it is often difficult in private practice to apply the von Pirquet test.

I would like to express my indebtedness to Dr. Williamson and Dr. Joseph for the work they have done in the wards.

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