7. That associated with a high ratio of epileptics in urban relatively to rural districts is a similarly high infantile and early childhood mortality from tuberculosis, convulsions, and atrophy debility and marasmus, and also a correspondingly high proportion of occupied married women, which it would be well for employers of female labour to bear in mind.

8. That, except in terminal cases of active tuberculosis, loss of weight is not a valuable criterion of the presence of tuberculosis in epileptics.

9. It is contended that epilepsy may be an evidence of tuberculous infection in childhood, probably affecting the bronchial glands initially, and that the convulsions are due either to reflex irritation so set up or to the resulting toxæmia acting on an unstable nervous system, either inherited or acquired. Further, that the constantly recurring seizures not only establish a vicious habit as far as the nervous system is concerned, but also effect tuberculin autoinoculation, thus tending to keep the tuberculous process in check, so that, instead of a fatal termination, epilepsy results.

10. Consequently, the advisability of carefully searching for tuberculous foci in children the moment epileptic fits develop, and also the immediate use of tuberculin in their treatment, should receive consideration.

REFERENCE.

¹ Riviere, *Early Diagnosis of Tubercle*.

STRYCHNINE-TUBERCULIN TREATMENT OF HOSPITAL TUBERCULOUS CASES.

BY

J. H. WHELAN, M.D., R.N. (RET.).

ADMIRALTY SURGEON AND AGENT, PLYMOUTH; LATELY MEDICAL SUPERINTENDENT, SEAMEN'S HOSPITAL, CARDIFF.

RECENTLY I called attention to the good results obtainable in the different forms of tuberculosis by the combination of tuberculin and strychnine, the former given weekly, the latter practically daily by intramuscular injection in large single doses.¹ Since then I have given larger doses of strychnine with improved results. I give the strychnine injections to all kinds of tuberculous patients, including cases in which tuberculin injections are contraindicated, with the best results. I give strychnine in acute and chronic cases, in the pyrexial and the apyrexial, in the early stages and in the most advanced, and with invariably good results. It always improves the appetite and general condition. Patients who have a loathing for food soon regain their appetites under its influence. Strychnine will frequently do away with the painful necessity of adopting Debove's gastric lavage and over-alimentation. But the drug must be given by intramuscular or subcutaneous injection, preferably the former. Administered by the mouth it has not the same effects and in large doses will cause tormina and diarrhoea, with possibly disastrous results in advanced cases. These effects are never produced by the injections.

Haemorrhage from the lungs I have found to be no contraindication for the strychnine injections. I have given them in such cases with remarkably good effects when the circulation had been quieted by morphine.

Has strychnine any special action in cases of tuberculosis other than that of a tonic? A bacteriological friend of mine says it probably makes the patient more resistant to the attacks of the bacilli. Personally I incline to the belief that it stimulates the formation of antibodies, especially when combined periodically with tuberculin, and of course it acts as a general tonic and nerve stimulant.

It may be thought that giving these daily intramuscular strychnine injections would be found very trying both to the patient and to the practitioner, but such is not the case. No patient of mine ever objected to them. In fact, the bad cases seemed to look forward to them, as they felt better after "in themselves." There is no strain on the practitioner, and he can give over thirty in an hour if necessary. The site of the puncture—deltoid or gluteal—is dabbed with a swab wet with tincture of iodine by the nurse. The doctor pours 20 to 30 minims of 1 in 400 strychnine hydrochloride solution into the barrel of an all-glass syringe with a fine needle in position; the piston is then adjusted, the instrument turned with the needle

upwards, and the air expelled from the barrel along with the surplus solution, and the dose given. The needle is then quickly washed in hot carbolic solution, wiped thoroughly with a sterile swab wet with spirit, and is ready to give the next patient his dose. The following is the solution I invariably use:

R. Liq. strych. hydrochlorid. (B.P.) 100 minims.

Sterile normal saline solution made with camphor water, add to make 400 minims.

Signa: 1 in 400 strychnine solution. Dose, 18 to 25 minims.

In febrile, haemorrhagic, and third-stage cases tuberculin injections are generally considered inadmissible. With this my experience coincides. But tuberculin may yet be used in these cases with good results in the form of Sahli's inoculation method. This is simply a multiple von Pirquet's test done weekly. Personally I make the inoculation over the affected parts. When reaction occurs there is, I take it, a local anaphylaxis with the formation of antibodies which find their way into the circulation, whereas the tuberculin does not. Patients who are having tuberculin injections react powerfully to the inoculations. In a few cases of severe pleuritic pain in chronic phthisical patients, the inoculations quickly relieved the trouble.

In suitable cases, as I have already said, I inject tuberculin once a week or less often. I generally use T.R., human and bovine mixed, but sometimes B.E. or T.O.A. I am a follower of Wright. Rapidly saturating a patient with tuberculin seems to me to be entirely wrong. We are not dealing with an autotoxin in tuberculin, but with a toxin whose only power for good resides in causing mild reaction and the stimulation of the production of antibodies—a process which takes at least a week in developing. To give it oftener than that does no good, in my experience. This is strikingly shown to be the case in the paper by Dr. E. H. T. Rigg, reporting the results of tuberculin treatment at the Brompton Hospital, printed in the JOURNAL. He says:

The dose was increased every second day at first and afterwards at intervals of four days.

The results as compared with patients not treated with tuberculin were strikingly bad.

Throughout my patients were fairly well fed. Cod-liver oil and creosote were given to all who could take those medicines. Antiseptic inhalations were freely used. I do not say as good results, if not better, are not obtainable by other forms of hospital treatment, but I have not seen such.

The function of the hospital in cases of tuberculosis on the medical side is to treat the febrile stages of the disease and arrest its progress in the shortest possible time. Another function is the segregation and modified isolation of patients whose sputa swarm with tubercle bacilli, and are therefore a real public danger outside.

I give in brief the last twelve cases I treated in hospital.

1. Lascar, aged 25, admitted with small cavity in left apex. Haemoptysis twice. Sick several months on board ship. Night sweats, cough, and anorexia. Had two tuberculin and eight strychnine injections, and left "cured" in three weeks.

2. Finnish seaman, aged 26, admitted with both lungs riddled with cavities and both petrous bones diseased. Cyanosed and apparently moribund. Hyperpyrexia. Case hopeless, but condition ameliorated by injections. Intolerable earache and cough disappeared, and he became contented and cheerful. Sent to workhouse infirmary after a month's treatment.

3. English apprentice, aged 19. Suppurating glands in neck. Reacted violently to second injection of Banderier and Roepke's tuberculin test. Well in three weeks, but relapsed six months later, when a month's treatment effected another cure.

4. Lascar, aged 26. "Skin and bones only." Crepitus over both apices. Chronic diarrhoea, anorexia, fever. Sputum very scant. Von Pirquet reaction positive. Sick two months. In six weeks had three tuberculin and sixteen strychnine injections. Left feeling quite well, only physical sign remaining feeble respiratory sounds over left apex. Gained 6 lb. last week of stay.

5. Irish stoker, aged 37. On admission, right side wet pleurisy, blood spitting, and night sweats. Von Pirquet's reaction strongly positive; 22 oz. of serum drawn off, and ten days later 40 oz. of sero-pus. Pyrexia quickly subsided. In six weeks had two tuberculin and twenty-eight strychnine injections. Gained 6½ lb., and left feeling quite well.

6. French stoker, aged 30. Admitted for "bronchopneumonia." Ill seventeen days. Profuse sputum; tubercle bacilli 10 to 50. Fever, but in a week temperature fell to normal.

In a month's treatment had two tuberculin and twenty-

six strychnine injections. Gained 1 lb., and sputum and cough nearly disappeared.

7. Scottish apprentice, aged 19. After admission for trivial injury of wrist developed symptoms of acute general tuberculosis. Pyrexia, rales at left apex, obstinate constipation, abdominal pain and retraction and vomiting; dry cough and night sweats. Von Pirquet's reaction strongly positive, but very slow in developing. Had one tuberculin and ten strychnine injections. When he left felt well, but there was dullness over left apex.

8. English A.B., aged 31. Cavity left apex. Tubercle bacilli in sputum $\frac{0}{1}$ to $\frac{5}{1}$. Von Pirquet's reaction feebly positive. Ill some months. In thirty-two days had three tuberculin and twenty-four strychnine injections. Sahli's inoculations over site of trouble seemed to ease cough and sputum. Patient left practically free from cough with scant sputum. No night sweats, and with a good appetite.

9. Greek stoker, aged 34. Ill six months. Both apices affected. Excavation. Anorexia and night sweats. Severe pain over right apex relieved by Sahli's inoculations. Three tuberculin and twenty-five strychnine injections in thirty-one days. Gained 2 lb., lost cough and night sweats. Regained appetite.

10. Swedish carpenter, aged 37. Ill fifteen months (?). Evident fibrosis. Three attacks of pleurisy with effusion. Rapidly losing flesh lately. Intense loathing for food. Severe pleuritic pains (which were relieved by inoculations). Von Pirquet's reaction positive. Fingers and nose congested and clubbed. In thirty-one days had three tuberculin and fifteen strychnine injections, and left with a good appetite, feeling fit, but still occasionally sweated at night. Physical signs *statu quo*.

11. Irish A.B., aged 36. Acute dry tuberculous pleurisy and lung fibrosis. Great anorexia; made what seemed to be a good recovery in forty-six days. Had five tuberculin and thirty-four strychnine injections. Sahli's inoculations relieved chest and shoulder pains. Each scarification developed an erythema bump larger than a five-shilling piece. There was a history of plumbism.

12. Australian seaman, aged 32. Ill over eighteen months. Expelled from workman's home on account of cough keeping the inmates awake at night. Both apices excavated. Five tuberculin, thirty-four strychnine injections, and three inoculations in thirty-eight days. Gained 4 lb., and practically lost cough. Tubercle bacilli fewer in sputum.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, September 28th, 1912.

THE CUTANEOUS TUBERCULIN REACTION OF VON PIRQUET.

By A. J. BRUCE LECKIE, M.D. EDIN.,

LATE RESIDENT MEDICAL OFFICER, ROYAL MINERAL WATER HOSPITAL,
BATH.

The cutaneous reaction was introduced by von Pirquet, who described the test in the *Berliner medizinische Gesellschaft* in 1907. It consists of vaccination with Koch's old tuberculin, said to be followed in tuberculous subjects by inflammatory phenomena.

The Tuberculin Employed.

I employed two solutions of tuberculin of different dilutions, making a series of observations with each. The weaker solution consisted of 25 per cent. solution of Koch's old tuberculin, the diluting medium consisting of 0.3 to 0.5 per cent. of carbolic acid in normal saline solution drawn up in fine sealed glass capillary tubes supplied by the Clinical Research Association. The stronger solution consisted of undiluted Koch's old tuberculin, issued in similar form to the previous by Parke, Davis and Co. Small rubber bulbs are supplied to facilitate expression of the fluid.

Application of the Test.

The method which I employed in applying the test may be shortly stated as follows:

The flexor surface of the forearm was cleaned with ether a sterilized large surgical needle was taken and the skin gently scarified in two places about 2 in. apart, sufficiently to remove the surface epithelium, leaving a reddish area, care being taken to avoid too much effusion of blood. Slight presence of blood is an advantage, as it denotes a small lesion which will render absorption more certain. To one area tuberculin was applied, to the other glycerine as a control. No dressings were applied, but instructions were given for the arm to be kept uncovered until the areas had dried. In children the attentions of the nurse are necessary. Sometimes scarification was performed through the tuberculin, at other times the application was made after scarification.

Most methods are the same in essentials but differ in minor details. Von Pirquet makes three scarifications; to

two of them he applies tuberculin, and the third is left free, forming the control. He also applies a few fibres of cotton for five minutes to prevent flowing. This, however, can be avoided by a little care on the part of the patient. McNeil rubs in tuberculin by boring into the skin with a blunt-pointed instrument, others employ a special chisel-shaped scarifier.

The Reaction.

Scarification rapidly produces fleshy-looking wheals surrounded by slight hyperaemia; these phenomena are traumatic, and disappear in twenty to thirty minutes. In an hour or so a faint erythematous ring gradually appears round the inoculated area, which slowly increases in intensity and breadth. It occurs in most cases whether they are going to react or not, but is not seen round the control. It, and it only, may be the only sign of activity at the end of fourteen to fifteen hours, when it will either disappear or increase, forming a red zone $\frac{1}{4}$ in. to $\frac{1}{2}$ in. in breadth, varying in different individuals. This zone is the first phenomenon of a positive reaction showing definitely in fifteen to sixteen hours. From fifteen to twenty-four hours we find slight swelling of the area and its surroundings, reaching its maximum in forty-eight or fifty hours, when a reddish or brownish papule presents itself, the brown hue being produced by coagulated serum and pigment in the tuberculin. This may not be the final stage. In some cases the papule edge separates into small discrete papules sometimes surmounted by vesicles; meanwhile the summit of the original papule subsides, so that a ring of elevations surrounds a depression, the whole encircled by an erythematous zone. The edge of the papule may be raised without subdivision. The subsidiary papules appear on the second or third day. In some cases a papule is not produced, but simply a persistent injected area which may subside at the end of the second day. A well-formed papule begins to subside at the end of the third day, and in a week or ten days a scaly, brown, quiescent area remains, which daily decreases until at the end of three to four weeks a small brown pigmented area alone remains. The pigmentation persists for weeks or months, and is due to pigment in the tuberculin, not to pigment derived from the blood, as it is never observed in the control. No reaction was observed in the controls, except an occasional evanescent hyperaemic ring. Von Pirquet observed several reactions in controls, probably due to contamination. The test is painless, unaccompanied by constitutional symptoms or inconvenience. I regard cases as positive which, after twenty-four hours, show even slight elevation or a persistent hyperaemic zone.

Abnormal Reactions.

Sometimes the inoculated area may have an irregular outline sharply delineated; in one case it resembled a "port wine stain," and appeared on the sixth day in a non-tuberculous subject; scattered over it were petechial haemorrhages. In several other cases haemorrhages appeared on the edges of the papules in four to five days. Never have I observed these on the controls; hence they are not due to trauma. One case showed a papule surmounted by a crop of vesicles, which subsided in twelve hours. The only excessive reaction which I have seen occurred in a case clinically free from tuberculosis. In forty-eight hours the test area was converted into a red oedematous swelling, 5 by 8½ cm. in breadth, the centre occupied by the papule; from this area a red lymphatic could be traced to the axilla. Pain was present, but there was no pyrexia or other constitutional symptoms. No enlarged glands were detected. Under treatment by fomentations, all except the papule had disappeared in twelve hours. Pyogenic infection, of course, cannot be absolutely excluded, but susceptibility to tuberculin must also be considered. These abnormal results occurred where a positive reaction was obtained. Four out of six cases showed no evidence of tuberculosis; two of them occurred with the 25 per cent. solution, including the excessive reaction. Atypical reactions may be exhibited by the reaction time, a pronounced latent period, or rapidity of onset. An early reaction may appear as a well-formed papule in a few hours, maintained for two or three days; papulation within twelve to fourteen hours may be regarded as early. Three of my cases exemplified this, one showing a papule in three hours,