General tuberculosis is also not uncommon, while tubercle of the abdominal glands, and tuberculous ulcers of the intestine, are almost invariable, these last arising certainly from infection by swallowing the pus. Abscess in the brain, purulent pleurisy and tuberculous meningitis are also occasional causes of death. Hectic fever and emaciation always accompany fatal cases.

The part which the phosphorus plays in the process is not far to seek. The acid fumes (phosphorus and phosphoric acids) produced by its oxidation in the air have no effect on bone covered by gum or mucous membrane; but when they can penetrate to the bone directly through the aperture left by a decayed or extracted tooth or any injury, they erode the bone, weaken its nutrition and resisting power at this small spot, and make it susceptible to infection by tubercle bacilli. The bacilli having made good their foothold, spread slowly in some cases and with disastrous rapidity in others. I think I am correct in saying that the great majority of workers in match factories have carious teeth, and yet only a very small proportion of them become affected with cario-necrosis of the jaw—namely, those of them who, owing to their home surroundings or to individual predisposition, become readily infected by the tubercle bacillus. V. Bibra and Geist state that the disease may occur weeks or months after the patient has left the match factory, and in one of their reported cases the woman had actually been eighteen months away from the work before any symptoms began. This in itself is almost complete proof that the phosphorus fumes are only a predisposing cause, and that the disease depends on subsequent infection. It is well known that v. Bibra and Geist, and later Wegner, produced suppuration and cario-necrosis in the jaws of rabbits by injuring the periosteum and then exposing the animals to phosphorus fumes (on uninjured rabbits the fumes had no effect). The rabbits all died in from five to ten weeks' time and were found to have tubercle of the lungs. I experimented in a different way, as it is evident that these animals had become rapidly infected from the laboratory cages in which they were kept. I got new wooden hutches made, placed them in a room where animals had not been previously kept, and kept them scrupulously clean. In the hutches pieces of phosphorus were placed in a mortar on damp earth (to avoid risk of fire) in such quantity that the cages were constantly filled with the fumes in much greater amount than can possibly occur in any factory. Four rabbits were then placed in the hutches after the periosteum and gum had been removed over a considerable portion of the upper and lower jaws in each. In one a tooth was loosened in addition, the operations being all performed under chloroform. They seemed to suffer no inconvenience either from the operation or from living in the phosphorus-fume atmosphere. It has been very difficult to prevent the gum growing over the exposed bone, and after many weeks there is not the slightest trace of any jaw affection. The exposed surface of bone has become slightly eroded and rough, but whether from the action of the acid fumes or from that of the bacilli of the mouth it is impossible to decide.

TREATMENT.

The treatment hitherto pursued in cases of phosphorus jaw has been to wash out the mouth with deodorant and antiseptic lotions, and wait until the necrosed pieces of bone come away. This is always extremely tedious, and may last many years. In extreme cases the whole lower jaw, or half of it, or parts of the upper jaw have been excised. Sometimes by so doing the whole of the infected portion may be removed, but frequently the disease has again broken out in a neighbouring part of the bone. It is evident, however, that early operative interference is called for, and that the original tuberculous focus at the root of the tooth should be removed at once.

PROPHYLAXIS.

As regards prophylaxis, there is absolutely no risk so long as the bone remains protected by gum, and even when carious teeth are present the entrance of the bacilli can be prevented by careful stopping. Efficient ventilation of the workshops will dilute the acid fumes arising from the phosphorus, and make them less active in injuring exposed bone. The infection with the tubercle bacilli is a matter quite apart from

the factories, and cannot be controlled either by State regulations or workshop rules. It is acquired—as other tuberculous affections are acquired—by certain persons and not by others, and owing to the present all-pervading frequency of the organism persons with exposed bone eroded by acid fumes, and living under bad hygienic conditions, are very apt to become infected. Whether the fumes also weaken the mucous membrane of the lung alveoli and predispose to pulmonary phthisis among persons employed in match factories, I have no information which will enable me to decide. It is just possible that actinomyces or other organisms may also occasionally lodge in the weakened bone, and lead to caries and necrosis, but in those cases which I have hitherto examined I have only found the tubercle bacillus.

My great difficulty all along has been to procure a sufficient amount of clinical material to enable me to make my observations more extensive and precise, and I shall be greatly indebted if any surgeon who has cases under his care, and more especially recent ones, will supply me with specimens of the discharge.

In conclusion, I have to express my great indebtedness to Mr. Garman and his son for a great deal of information and assistance, as without their active help and co-operation I could not have made these observations.

THE TREATMENT OF TETANUS BY THE INTRACEREBRAL INJECTION OF ANTITOXIN.

WITH PARTICULARS OF A CASE TREATED BY THIS METHOD, FOLLOWED BY RECOVERY.

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TETANUS TOXIN AND ANTITOXIN.

It is now a well-established fact that tetanus is a disease caused by the absorption of a toxin elaborated by the tetanus bacillus. The bacteria which produce this toxin are confined to the inner or outer surfaces of the body, site of inoculation, or devitalised tissues. Here they multiply and produce a very strong toxin, which after absorption is taken up by the cells of the central nervous system, is fixed there, and gives rise to the spasms which characterise the disease. All the symptoms of tetanus can be produced in susceptible animals by hypodermic injections of toxin free from bacilli.

In a case of tetanus the toxin reaches the central nervous system from the seat of its production by two paths, one part directly by the nerves, and on this account contractions may occur near the site of absorption before the general contractions set in. The other part reaches the central nervous system by the blood stream, and when it gets there it is, after a time, seized upon and fixed by the nerve cells in the same way that an aniline basic dye is fixed by a cell nucleus or a bacterium. This fixation of the toxin by the central nerve cells takes place in the spinal cord at an earlier period of the disease than it does in the higher nerve centres.

It appears that there exists a strong affinity between tetanus toxin and the cells of the brain and spinal cord. This affinity is easily manifested when they are mixed together *in vitro*.

Wassermann was the first to show that an emulsion of the brain or spinal cord of a susceptible animal, when mixed with tetanus toxin and injected under the skin of a guinea-pig (which is a very susceptible animal) produces no symptoms of tetanus, and the animal remains well. A control guinea-pig receiving the same amount of toxin *minus* the emulsion of brain or spinal cord dies with a typical tetanus. This experiment demonstrates that tetanus toxin is a neurotropic poison—that is, a poison which has a specific affinity for and joins itself on to nervous elements.

If a healthy animal, such as a rabbit, receives tetanus antitoxin hypodermically, it acquires passive immunity, and can resist large doses of tetanus toxin given subcutaneously or intravenously without any ill effects. In this case the tetanus toxin is neutralised as soon as it gets into the circulation by the antitoxin which is already there, and never reaches the central nerve cells at all. The animal is not, however, immune to a very small amount of tetanus toxin injected into

the brain substance, but, on the contrary, after this operation, it readily develops cerebral tetanus and dies. It is evident from this experiment that tetanus antitoxin, whether given hypodermically or intravenously, does not immunise the brain cells.

An animal suffering from tetanus cannot, as a rule, be cured by giving antitoxin in the usual way—that is, hypodermically. The toxin has already been fixed in the central nerve cells, and these cells evidently do not take up the antitoxin from the blood, and are not influenced by it. In this case the toxin may invade new areas by spreading itself from nerve cell to nerve cell under cover of the antidote. On the other hand, animals in the early stages of tetanus can be easily cured by the intracerebral injection of a small quantity of antitoxin.

With the help of these facts, which are the outcome of recent experiments by MM. Roux and Borrel,¹ on tetanus in animals (and which I have been able to verify at Netley and at the Pasteur Institute, Paris), we are in a position to treat tetanus in man on a more scientific basis than formerly.

If tetanus is suspected, but symptoms have not yet appeared, antitoxin given hypodermically, or into the circulation, confers passive immunity, and is a certain and efficacious preventive. If symptoms have already appeared, it almost always fails to cure or to prevent the spread of the disease when given hypodermically, for the central nervous elements have not the same affinity for the antitoxin that they have for the toxin. On this account the toxin already fixed in the lower nerve centres does not meet with the antitoxin which is circulating in the blood, and the higher nerve centres, which have not as yet taken up the toxin, are not immunised against a spread of the toxin from the lower centres, so the disease takes its course.

INTRACEREBRAL INJECTION.

The only way to convey immunity to the vital parts of the nerve centres and to prevent their nerve cells from fixing the toxin, is to inject the antitoxin into the substance of the brain. If this is done early in the disease, while only the lower nerve centres are as yet affected and before the higher nerve centres have become affected, the progress of the disease is arrested, the symptoms already present, which depend on fixation of the toxin in the lower centres, remain for some time and then gradually disappear, the toxin ceases to invade new territories, and recovery is likely to be the result.

The first case of tetanus in man treated by MM. Roux and Borrel's method of intracerebral injection of antitoxin was done by MM. Chaffard and Quenin in Paris on April 26th, 1898, and the patient recovered.² Since then some 20 cases have been treated in and near Paris by the same method and with very encouraging results. During a visit to Paris in October last I had the advantage of seeing this method of treatment carried out at the Civil Hospital, Versailles, by M. le Dr. Vilon and M. Borrel. To both these gentlemen I am greatly indebted for their kindness and courtesy in giving me every facility to see the operation and to visit the case afterwards.

The patient was a middle-aged man in the early stages of traumatic tetanus following a ragged wound of the hand. The muscles of the jaw (masseters) and neck only were involved. He could swallow without difficulty. After the intracerebral injection of antitoxin the symptoms remained as they were for a week, and then improvement slowly set in and went on to convalescence.

In the same hospital there was a convalescent tetanus patient who had also been treated by intracerebral injection of antitoxin. In this case tetanus followed amputation through the lower third of the thigh for gangrene of the leg, caused by a suppurating popliteal aneurysm.

On November 17th, 1898, a case of tetanus was diagnosed at the Cambridge Hospital, Aldershot. On receiving a telegram asking for tetanus antitoxin I proceeded to Aldershot to see whether it might be possible to carry out MM. Roux and Borrel's method of treatment in this case. The medical officer in charge of the hospital, Lieutenant-Colonel J. Martin, Royal Army Medical Corps, and the medical officer in charge of the case, Lieutenant G. B. Crisp, Royal Army Medical Corps, expressed their approval.

History.—The patient was Private A. G., Army Service Corps, aged 22, three months service. No previous admissions to hospital. He was a

strong, well-nourished man, of good physique, and a total abstainer. He was admitted on November 14th, for contusion of the testicles caused by a bump on the pommel of the saddle. For a fortnight before admission he had been going through a course of rough riding in the riding school, and stated that he had had several falls and bruises. There were no open wounds, and the contusion of the testicles was not severe.

Onset of Tetanus.—On November 16th, two days after admission, he developed symptoms of tetanus. The masseter muscles, and the muscles of the neck were contracted, and those of the abdomen slightly so. On November 17th, the spasm of the jaw muscles was marked, and there were also spasms of the muscles of the legs and arms, especially on examination. The abdominal muscles were also slightly contracted.

Injection of Antitoxin.—At 9 P.M. he was put under chloroform by Lieutenant Crisp, R.A.M.C., and with the assistance of Lieutenant-Colonel J. Martin, R.A.M.C., I injected 2½ c.cm. of doubly strong antitetanic serum into each frontal lobe of the brain. At the same time 20 c.cm. of antitoxin were given hypodermically in the flank.

After-History.—He had a good night, and on November 18th the tetanic spasms of jaws and stiffness of extremities continued as before, and his condition was unchanged; 20 c.cm. antitoxin were given hypodermically.

On November 19th his condition was about the same; 20 c.cm. of antitoxin were given hypodermically.

On November 20th the spasms were less marked and not so easily excited by noise or other stimuli.

On November 21st the stiffness was less marked.

On November 22nd his condition was improving; he could open his mouth without causing spasms.

On November 23rd the muscles of the jaw and neck were free from spasms, but there was some stiffness of the limbs, and he started and had twitching of the muscles when he heard a noise, notably so when the camp gun went off on the hill a short distance from the hospital. The dressing was removed from the seat of operation and the stitches taken out. The wounds had healed by first intention.

On November 30th he was convalescent, but weak and anæmic. He was able to get out of bed, but had slight spasm of the arms on exertion. He presented no brain symptoms, ate and slept well. The temperature was practically normal throughout, pulse and respiration regular.

DESCRIPTION OF THE OPERATION.

The details of the operation are as follows: The patient is given an anæsthetic, and the hair shaved off over the fore part of the scalp, and the skin made aseptic. An imaginary line is taken over the head from one auditory meatus to the other. Another line is taken from the base of the nose to cross the first line at right angles on the top of the head, and a third line from the outer angle of the orbit to where the first two lines cross each other. The centre of the last line is the seat of operation, and is in front of the motor areas of the brain.

Having selected this site, an incision of about ½ or ¾ inch in length is made down to the bone. A small hole is now drilled through the bone with an Archimedean drill having a movable collar, so as to regulate the depth to which it penetrates. The hole in the bone need only be a little larger than the needle of the syringe which is to be inserted through it.

The syringe has a screw piston and the needle is attached by about 3 inches of rubber tubing. The needle is about 2 inches in length, and has a rounded point. It is inserted through the hole drilled in the bone, straight into the brain substance as deep as it will go, and an assistant holds it perfectly steady while the operator very slowly screws down the piston, so as to allow the antitoxin to soak into the substance of the brain drop by drop, to avoid breaking up any brain tissue. It should take at least ten minutes to inject 2½ c.cm.

When this amount has been injected the needle is withdrawn, and the edges of the scalp wound drawn together by two or three stitches, and the wound sealed up with collodion and cotton wool. The same operation is now repeated on the other side.

The object of using a round-pointed needle is to avoid puncturing a vessel. A sharp-pointed needle might possibly transfix an artery and produce hæmorrhage, whereas a round-pointed one would glide off a vessel and go past it.

The antitoxin used is double the strength of ordinary antitoxin, and although only 5 c.cm. are given (2½ c.cm. in each side), it represents the amount of antitoxin present in 10 c.cm. of the original serum.

The dried antitoxin from 10 c.cm. of the ordinary antitetanic serum is put up aseptically in glass tubes, and sent out from the Pasteur Institute, Paris, ready to be dissolved. The tube containing the dried antitoxin should be opened without contamination, then 5 c.cm. of sterile water added to dissolve it. When the antitoxin is in complete solution, it is filled into a sterile syringe of the pattern described (Roux's pattern 5 c.cm. syringe), and is now ready for use.

In addition to the antitoxin given intracerebrally, the patient receives 20 c.cm. daily for two, three, or four days, according to circumstances. The antitoxin given intra-

cerebrally immunises the higher nerve centres before the toxin has been fixed there. The antitoxin given hypodermically renders the blood antitoxic, and the toxin, as it becomes absorbed from the source of supply—wound, bruise, abrasion, or any other source, wherever it may be—is neutralised as soon as it enters the blood stream.

The advantage of giving the antitoxin hypodermically in addition to intracerebrally is evident when we reflect that the tetanus bacilli may still be cultivating themselves, and toxin still being absorbed.

In conclusion, it is my pleasant task to thank Lieutenant-Colonel Martin, R.A.M.C., and Lieutenant Crisp, R.A.M.C., for valuable assistance at the operation. I have also to thank the latter officer for the history of the case and notes.

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THYMUS EXTRACT IN EXOPHTHALMIC GOITRE.

By W. RUSHTON PARKER, M.A., M.D. CANTAB.

THERE being still some difference of opinion about the efficacy of thymus extract in exophthalmic goitre, notes of four cases, in which its effects were closely watched, may be of interest.

CASE I.—Mrs. A. aged 28, had been troubled with palpitation for three years, especially during the past twelve months. Her eyeballs protruded conspicuously; the upper lids were retracted so that the sclerotics were visible all around the cornea, and blinking was infrequent, giving her a very staring look, and the upper lids had a lagging, jerky movement when lowered, but she was not aware of any unusual appearance about her eyes. A systolic murmur was audible all over her moderate-sized throbbing goitre, but she had only noticed the enlargement a month previously. Her pulse was 140. She had noticed tremblings for some months. The bowels were inclined to costiveness, and the skin was not unduly apt to perspire. She could walk two or three miles, and do her household work. She was rather anæmic, without any menstrual abnormality either during her twelve months of married life or before.

Fig. 1.

During six months she swallowed 2,000 5-grain thymus tabloids, mostly ten or twelve daily, and ate a large number of lightly-cooked lambs' thymus glands without the slightest perceptible effect upon any symptom, especially upon the rapidity of pulse, a note of which was made thrice daily for eight months, or upon the goitre, which remained as large

and apparently as active at the end as at the beginning. Nor was she apparently in any way benefited by iron, digitalis, bromide, belladonna, arsenic, or blistering, each of which was persisted in for many consecutive weeks; indeed, the best pulse-record was undoubtedly during a three weeks' holiday, when she was freed alike from all medicinal treatment and from household cares. Nevertheless, she somehow professed to feel better at the end of the treatment than at the beginning. The photograph, taken towards the end of the treatment, represents her appearance throughout the course.

CASE II.—Miss B., aged 35, born of a goitrous stock in a goitrous valley, noticed her goitre in her thirteenth year, and palpitation, tremblings, cramps, and weakness in her nineteenth year. There was slight drooping of the upper lids, but no protrusion of eyeballs or other ocular abnormality; her neck measured 16½ inches, and a systolic murmur was audible all over the large throbbing goitre; she complained of frequent faint feelings, had a pulse-rate of 120, and a systolic murmur at the base; she complained of always feeling hot, with a burning sensation in head and eyes, but no great tendency to perspire; her bowels were loosely moved twice daily; there was no menstrual abnormality; she was too weak to be of much use in household work.

During 18 months she swallowed 5,000 5-grain thymus tabloids, usually twelve daily, and ate many scores of lightly-cooked lambs' thymus glands; the neck continued to measure exactly as before, though she thought it was less tense and more flexible; the looseness of the bowels ceased; palpitation lessened; the sensation of heat, and burning in head and eyes ceased, and also the tremblings and cramps; the pulse slowed to 90; she could bear exertion better, bicycling with ease; she perspired less easily, and had faint feelings less often. Her own impression was that the treatment had a very beneficial effect upon all her most troublesome symptoms; but it is important to note that some improvement had already spontaneously set in five years prior to the treatment, leading to a marked diminution of many annoying symptoms, during the two preceding years more especially. Digitalis, strophanthus, and blistering were persisted in for some weeks without any noticeable benefit; no other drugs were used. The photograph, taken on the first day of treatment, equally well represents her appearance at the end.

Fig. 2.

CASE III.—Mrs. C., aged 45, had suffered about a year from goitre, palpitation, tremblings, nervousness, weakness, looseness of bowels, and easily perspiring skin; she had only lately noticed a peculiarity about the eyes; there was some retraction of the upper lids, so that the entire cornea were ordinarily just in view, and blinking was infrequent, giving her rather a staring look, and the upper lids were lowered in a lagging and jerky fashion, but there was no obvious protrusion of the eyeballs. Her neck