article on Tumours, in Pitha and Billroth's well-known *Chirurgie*, mentions that dermoids sometimes follow injury (trauma) in early life, and as an illustration writes:

"A child, 6 years old, was seized in the right orbital region by a dog, but without actual wound of the skin; some weeks later a tumour appeared in this region, its presence had never been noticed before. It gave the characters of a dermoid."

Among my own cases I have an example of an implantation cyst in the forehead of a pretty girl, which formed in the scar of a wound, due to a blow from an angular stone, three years previously.

TETANUS ANTITOXIN; ITS PREPARATION AND PROPERTIES.

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A SHORT description of the mode of preparation of tetanus antitoxin may be of interest at the present time when antitoxins and the antitoxin treatment are occupying so much attention. The work, on which the following account is based, was carried out mainly on the lines followed by Roux and Vaillard,¹ and may be divided into the following stages:

PREPARATION OF THE TOXIN.

A simple method was adopted for the cultivation of the tetanus bacillus, and gave excellent results.² Glass flasks of a capacity of about 120 c.cm., and of the form known as "yeast flasks" were used; these have a narrow glass tube attached to the neck, for the first inch or so passing horizontally outwards and then bent downwards at right angles.

The neck of the flask is corked with a perforated rubber cork, through which a narrow glass tube passes to the bottom of the flask, projecting 2 inches above the cork. This projecting portion of the tube and also the end of the lateral tube are plugged with cotton wool, care being taken that the plugs are loose enough to allow gas to pass freely through them. The flasks are filled with a grape sugar bouillon, sterilised, and inoculated after momentarily withdrawing the rubber cork and tube. The air is expelled from the flask and replaced by hydrogen by connecting the projecting glass tube with a Kipp's hydrogen apparatus, the gas bubbles through the bouillon and escapes by the lateral tube.

After the hydrogen has been passing for half an hour, a small capsule containing mercury is applied to the free end of the lateral tube, so that its open extremity just dips beneath the surface of the mercury. The projecting end of the tube, which passes through the rubber cork, is then sealed off in the blowpipe flame. The flask is thus filled with hydrogen which cannot escape, nor can air enter on account of the mercurial valve, though if any gas be formed during the growth of the organism it can escape, while the glass flask can be used again and again. The flask, with the mercurial valve *in situ*, is placed in an incubator at 37° C. After a lapse of two days the bouillon becomes turbid, and gradually a small precipitate, consisting chiefly of bacilli and spores, falls to the bottom; a surface film never forms. The culture can be used after it has been growing for three weeks, but preferably for a month; after five weeks' growth the virulence seems to diminish. Such a culture is so toxic that after filtration $\frac{1}{100}$ c.cm. of the filtrate is sufficient to kill a guinea-pig weighing 300 to 400 g. The cultures are filtered before using, and an antiseptic is added to the filtrate to prevent subsequent putrefactive changes. At first thymol was used, but this was found to produce a slight precipitate after a time.

As I have elsewhere pointed out,³ thymol, though an efficient antiseptic for such a purpose, is a precipitant of proteid substances, and must be used with caution when these are present. Carbolic acid was afterwards employed, one part of a 5 per cent. aqueous solution of carbolic acid being added to every nine or ten parts of the fluid culture, corresponding to an addition of about .5 per cent. of carbolic acid.

This addition does not in any way modify the virulence of the filtered culture, which seems to keep indefinitely in a dark cool place; at any rate, there is no loss of activity after a lapse of four months. The mixture of carbolic acid and culture is then filtered through porous porcelain, preferably after previous filtration through paper, to remove the organisms. This can be conveniently carried out by means of a Chamberland filter, which is connected with an exhaust pump by a rubber tube, the filter "candle" being immersed in the fluid contained in a glass cylinder of suitable size. On exhausting, the fluid passes into the interior of the Chamberland filter, which, when full, is disconnected from the pump, and the clear filtrate shaken out into a stoppered bottle. The process is repeated as many times as necessary, and the fluid obtained forms the toxin which is used in the next stage—that of immunisation.

IMMUNISATION.

In order to obtain a quantity of antitoxin the animal chosen was a horse, which was injected with the prepared toxin after the method employed by Roux and Vaillard, except that it was found necessary to proceed more cautiously. To commence with: the toxin is weakened by the addition of an equal volume of Gram's iodine solution,⁴ of this mixture gradually-increasing doses are injected subcutaneously in the neck or shoulder, starting with .5 c.cm. and going up to 8 c.cm. or 10 c.cm. This took from May 2nd to June 22nd, three injections being given weekly. The next two doses were 4 c.cm. and 8 c.cm. of a mixture of 2 parts of toxin and 1 part of Gram's iodine solution. After this, commencing July 2nd, the pure toxin was injected, the dose being 1 c.cm., which was increased by degrees until 22 c.cm. were injected on July 23rd. On July 25th 4 c.cm. were injected into the jugular vein, followed by rather alarming symptoms half an hour after, the animal falling prostrate, with legs extended, laboured respiration, and rapid small pulse. These symptoms, however, lasted only about ten minutes, after which the animal seemed to recover completely. On three other occasions somewhat similar attacks occurred after intravascular injections.

In spite of the apparent risk, the injections into the jugular vein were continued in gradually increasing amounts, and on August 30th the animal received a dose of 70 c.cm. without ill-effect. There was then an interval of a month without injection, and blood drawn on September 29th was found to have an antitoxic power of about 50,000.⁵ This of course was not nearly sufficient, so the treatment was resumed on October 8th, when 6 c.cm. were injected into the jugular vein. The doses were rapidly pushed until November 19th, when 90 c.cm. were administered. At the beginning of December the antitoxic power of the blood serum tested on guinea-pigs was found to be about 1,000,000. The total number of injections, subcutaneous and intravascular, was 57, spread over a period of five months. It will thus be seen that the treatment was very tedious, and doubtless it might have been carried out more rapidly, but I desired to be on the safe side, as I had had the misfortune to lose my first horse. Roux and Vaillard obtained an immunity of 1,000,000 after a course of treatment lasting three months, and following their programme exactly my first horse developed tetanic symptoms after the fifth dose. I was also unable to increase the dose of toxin as rapidly as these authors seem to have done. The intravascular injection must be a risky procedure, and I question whether it is at all necessary, there being no need for it, for example, in the preparation of diphtheria antitoxin, and in another case I should certainly try to do without it. The smaller doses, up to 15 c.cm., were injected by means of a Loeffler syringe, the larger ones by an ordinary glass syringe attached to a large hypodermic needle by a short length of india-rubber tubing. The needles and syringes were disinfected with 1 in 20 carbolic solution before use, and in no instance did any trouble ensue from the puncture.

PREPARATION OF THE ANTITOXIN.

Allowing three or four days to elapse since the last injection

⁴ Iodine 1 part, potassium iodide 2 parts, water 300 parts.

⁵ By this is meant that 1 c.cm. of the serum will protect or immunise 50,000 grammes of guinea-pig against the minimum fatal dose of tetanus toxin. An immunising power of 1,000,000 means that 1 c.cm. of the antitoxic serum will protect 1,000,000 grammes of guinea-pig against the minimum fatal dose of tetanus toxin.

¹ *Annales de l'Institut Pasteur*, 1893, ii, p. 64.

² See also *Lancet*, 1894, ii, p. 64, and *Cent. f. Bakteriologie*, xvi, p. 1074.

³ *Proc. Physiol. Soc.*, 1894, No. ii, p. xi.

tion of the toxin, the horse is bled from the jugular vein by means of a sterilised cannula, the blood being collected in sterilised vessels and allowed to coagulate. After standing for twenty-four hours the clear serum is pipetted off into sterilised vessels. This serum contains the antitoxic substance and is the antitoxin, and may be used for injection. By working aseptically there is no difficulty in collecting and keeping the serum sterile; it should, however, be stored in a dark cool place, and a little camphor may be added to it. As cases of tetanus are not common it is customary to evaporate the serum to dryness, the dry substance being more conveniently kept without change. Heat destroys the antitoxin; therefore the evaporation must be performed *in vacuo* over sulphuric acid. A series of glass dishes are arranged one above the other on a metal stand in a large and strong glass receiver, which is connected with an exhaust pump. The glass dishes contain alternately sulphuric acid and the antitoxic serum, those used for the latter having been previously sterilised and covered with pieces of sterilised filter paper. The receiver is exhausted and the serum becomes dry in three or four days. The serum yields 9 to 11 per cent. of the dried substance, which is kept in stoppered bottles in a dark cool place. For use it should be powdered finely, and dissolved in sterilised distilled water without the aid of heat.

PROPERTIES OF THE ANTITOXIN.

Experimentally, the effects of the antitoxin are little short of marvellous. Minute doses injected into animals will completely neutralise fatal doses of the tetanus toxin injected eight to twelve hours afterwards. Thus 0.0005 c.cm. of the antitoxic serum was found to be sufficient to protect a guinea-pig weighing 400 to 500 grammes from the minimum fatal dose of the tetanus toxin, which in the present instance was about 0.01 c.cm. Mixtures of the toxin with the antitoxic serum, in the proportion of 40 or 50 parts of the former to 1 of the latter, are completely inert, and 2 c.cm. of such a mixture, containing nearly 2 c.cm. of the deadly toxin may be injected into a guinea-pig without producing any effect. The antitoxin also possesses considerable curative power, but much larger doses are necessary when the disease has declared itself than when used as an immunising agent.

TREATMENT OF TETANUS IN MAN.

The antitoxin treatment of tetanus would seem to be the one which gives the best hope of cure, though it can hardly be so successful as the corresponding treatment for diphtheria is reported to be. The explanation of this is that tetanus is only recognised as being tetanus at a late stage when the toxins are circulating in the blood; the disease is far advanced before it can be diagnosed. Gowers⁶ estimates the mortality in traumatic tetanus at nearly 90 per cent., and in idiopathic at 50 per cent. I have been able to collect records of 42 cases of tetanus treated with antitoxin, nearly all traumatic, and of these 15 died and 27 recovered, giving a mortality of about 36 per cent. If these figures can be relied on, the result is encouraging, but the tendency is always to report successful cases only. The antitoxin must be administered by subcutaneous injection. It is difficult to state what the dose should be, for this has varied enormously in the recorded cases, from 10 c.cm. to 165 c.cm. Probably 20 c.cm. to 40 c.cm. for a first dose, followed by 10 c.cm. every six or twelve hours would be found most suitable.

Of the dry antitoxin, 1 gramme corresponds to about 10 c.cm. of serum, so that the dose of this would be 1 to 4 grammes. If reduced to an impalpable powder, it dissolves fairly readily, 1 gramme to every 5 c.cm. or 10 c.cm. of sterilised distilled water.

In conclusion, my thanks are due to Professor Crookshank, in whose laboratory part of the above work was carried out, and especially to Professor MacFadyean, Principal of the Royal Veterinary College, where the horse was kept, for kind advice and assistance during the progress of the work.

[NOTE.—The above work was carried out by means of a Government grant. By permission of the Grant Committee of the Royal Society, the immunised horse has been transferred to the British Institute of Preventive Medicine, and the tetanus antitoxin can be supplied on application to the Director, 101, Great Russell Street, W.C.]

⁶ *Manual of Diseases of the Nervous System*, 2nd edition, 1893, p. 685.

REMARKS ON CHRONIC RENAL DISEASE: ITS FREQUENCY IN ASYLUM NECROPSIES, AND ITS POSSIBLE CONNECTION WITH ALCOHOL AS A CAUSE OF INSANITY.

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THE object of this paper is: first, to endeavour to bring into greater prominence the great frequency with which renal disease is seen in asylum *post-mortem* examinations, and at the same time to attempt a comparison with the amount found in a *post-mortem* room of a general hospital; and in the second place, to inquire how far these renal changes may be regarded, as a factor in helping us more accurately to gauge the part alcoholic abuse plays in the etiology of insanity.

The report of the Commissioners in Lunacy for the year 1894 shows that during the five years 1888 to 1892 inclusive the yearly average number of admissions into the various asylums in England and Wales was 7,793 of the male sex, and 8,246 of the female sex, and that the percentage of these set down as caused by intemperance in drink was 20.5 for the former and 8.1 for the latter, or rather more than 14 per cent. of the total admissions of both sexes. The annual reports of individual asylums show a wide variation on each side of this figure. Thus, from the reports before me, the lowest percentage recorded is 5, and the highest is 30, including both sexes, while in the male sex the number sometimes goes up to over 40 per cent. It is very questionable, however, if the whole truth, or anything like it, is represented in these statistics. It so often happens that no trustworthy history of many asylum cases can at all be obtained, and these are then recorded in the table of causes as "Unknown." The number of these unknown causes is usually highest in those reports which show the lowest proportion of cases due to alcoholic excess. How many of these cases should fall under the heading of intemperance?

One of the first things that impressed me in the *post-mortem* room here was the large number of cases in which I found renal disease, chiefly in the form of interstitial changes; and it occurred to me that if they were collected and tabulated, they might perhaps be of service in the above direction.

From the literature regarding diseases of the kidney as seen in asylum necropsies, it would seem that at any rate in former years any special frequency was not noted. Thus, for instance, Bucknill and Tuke distinctly stated that the kidneys are remarkably free from disease in all forms of insanity.¹ Maudsley² observed that there was nothing special to be said concerning diseases of the abdominal viscera. But Dr. Howden many years ago pointed out that in the necropsies at the Montrose Asylum renal disease was frequently to be observed. More recently, especially from America, further facts have been brought forward indicating that, among asylum cases, the kidneys are much more frequently found diseased than was formerly thought; but, as far as I am aware, no attempt has been made to compare numerically the proportion found diseased in asylum *post-mortem* rooms with that in a general hospital.

The following are the results obtained from an examination into the records of the necropsies made at Banstead Asylum from April, 1893, to December, 1894. They numbered 154 (85 males and 69 females), and in 74, or 48 per cent., I found marked renal changes. These changes were visible in the males in 40 per cent., and in the females in 58 per cent. These figures are not intended to represent the entire number of instances in which the kidneys were found diseased, for in arriving at them I have excluded those cases in which there was solely a fatty, tuberculous, or waxy change, and have limited myself to the morbid conditions which might have been brought about by over-indulgence in alcohol. And thus, speaking broadly, the conditions included in my table are two—typical red granular contracted kidneys (with or

¹ In an earlier part of their *Manual* attention is drawn to the fact that alcoholic insanity was then certainly on the increase.

² *The Pathology of Mind*.