ureters intact, as described by Mr. Moynihan in the *Annals of Surgery* for last month, proves to be a further help in this direction.

There are other physiological points of much interest about these cases. It is well to realize the fact that a patient whose ureters have been implanted into the rectum is practically receiving a rectal enema of two to three pints of urine daily, and it apparently takes some time for the bowel to become acclimatized to the new conditions, and to learn to expel, without absorption, the fluid poured into it. Our knowledge of the physiological effect of the absorption of urinary constituents through the intestinal mucous membrane is very scanty, but the peculiar attacks of *malaise* which my patient suffered from at times suggested the absorption of urine of a higher toxic character on such occasions.

There is also another point of interest concerning this function of urinary reservoir action acquired by the rectum. For the most part the urine is passed at lengthy intervals, 10 oz. to a pint at a time, clear and free from admixture with faeces, and this act is followed in a morning by the further evacuation, a little later, of a normal firm motion without urine, while sometimes, in the early morning passage of urine, the first portion is more or less mixed with faeces. This phenomenon strongly confirms the suggestion that the rectum is habitually empty except shortly before the passage of a normal motion, and thus the urine collects in the rectal ampulla free from faeces, is voided when the rectum becomes sufficiently distended, and that this act is followed, when necessity arises, by the descent into the rectum and the later evacuation of solid faeces. This habitual emptiness of the rectum further suggests this portion of the intestinal tube as a more suitable site for implantation than the colon higher up, which habitually contains faeces.

Finally, one word about the peculiarities of the vesical mucous membrane so extroverted. No attempt was made in my case to remove or cover in the exposed vesical mucous membrane, and yet, owing to the change in environment, the exposed surface gradually changed its character and became a non-secreting skin surface, having all the appearance of cicatricial skin; this occurred all over, except at the angle formed by the abdominal wall and the epispadic penis, where a certain amount of moisture and mucus still collected, and here the epithelium preserved its mucoid type. In the language of heredity, the vesical, and probably the genito-urinary mucous membrane, possesses the inborn capacity of developing along two lines—the mucous membrane and the skin—while the environment determines the course development shall take in any case at any given time, the practical point being that it is not necessary to remove such portions of exposed membrane when the normal secretion bathing the surface has been arrested.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, 1905, vol. ii, p. 232.

TONSILLITIS IN CONVALESCENCE FROM DIPHTHERIA.

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THE occurrence of a non-specific inflammation of the tonsils in convalescence from diphtheria is not uncommon, and is of no little interest and importance. The concurrent symptoms suggest often in such cases the possibility of scarlet fever. On the other hand, a relapse of the disease may be suspected, and the advisability of serum treatment will at once have to be discussed. The following observations are based on observations made on 900 consecutive cases of diphtheria under my care during three years.

Apart from cases of inflammation of the tonsils which proved at the time or subsequently to be scarlatinal in origin, the tonsillitis occurred in 64 cases (7.1 per cent.) either within and usually towards the end of the first three weeks of the disease, or at a much later period. In the first class the tonsillitis found in 30 cases (3.3 per cent.) was invariably associated with late manifestations of serum, which consist in a rash generally of the type of a circinate erythema, and usually associated with pyrexia,

less frequently with pains in the joints or muscles, and adenitis of the submaxillary and cervical glands. This faucial affection, described by the French under the name of pseudo-relapse, or *angine de retour*,¹ may be conveniently designated angina redux. It occurs, as a rule, within a fortnight from the first injection of antitoxin, the average time in these 30 cases being 14.1 days after the first injection. Similar figures are given by Sevestre and Aubertin,² who mention the reappearance of angina and croup in the period of late serum phenomena on the tenth to the fifteenth day after injection.

The appearances presented by the throat in this condition vary from an injection of the fauces with a follicular deposit on the tonsils to large semi-confluent patches resembling the early stage of diphtheria. Unlike diphtheria, however, they are not adherent, and disappear often without any local treatment whatsoever as the other serum phenomena subside, leaving no ulceration. In only one of my cases was there any loss of tissue in the subjacent mucosa.

Bacteriological examination reveals rich growths of staphylococci and streptococci, which accords with the theory that the late manifestations of serum are due to the action of these micro-organisms.³ As a rule the patients do not complain of sore throat. Albuminuria may develop at this time, or pre-existing albumen in the urine may increase in amount. Pyrexia may persist for several days, and the constitutional disturbance, especially in older patients, be considerable. The average duration of the pyrexia was 5.2 days. In 2 cases the temperature reached 104°; in 5 it exceeded 103°.

Submaxillary and cervical adenitis is relatively so common at this period⁴ without any striking corresponding inflammation of the throat, that an inspection of the fauces in such cases is often omitted. The absence of a more general recognition of angina redux is thus explained. This condition, though by no means common, is more frequent than relapses of diphtheria, the existence of which is not disputed. Relapses occurred twelve times—that is, 1.3 per cent.—in my 900 cases.

The statistics⁵ of the Metropolitan Asylums Board hospitals during the last six years give similar figures—1.16 to 2.11 per cent., or an average of 1.61. The occurrence of laryngeal symptoms at this period has been recorded by Sevestre and Aubertin,⁴ in some cases sufficiently severe to necessitate intubation. Such phenomena, which have been attributed to laryngeal oedema produced by the serum, I have never witnessed myself.

Secondary angina in convalescence from diphtheria, apart from serum manifestations, is not uncommon. It occurred in 34 of my cases (3.7 per cent.), the average time being the fortieth day. It is thus seen to be of more common occurrence than relapses, nor is the reason of this far to seek. Whereas the faucial tissues have gained a certain degree of immunity against the specific infection, their power of resistance against other forms of inflammation has been lowered.

A precisely similar event occurs in convalescence from scarlet fever where tonsillitis is a well-recognized sequela, occurring in 1.73 to 3.32 per cent., or an average of 2.44 per cent. for the last six years in the Asylums Board hospitals, as compared with the frequency of relapses,* which varied from 1.09 to 2.01 per cent. during the same period.⁵

Like tonsillitis in convalescence from scarlet fever,⁶ the late tonsillitis of diphtheria occurs more frequently in adults and older children, in females and in the damp months of the year. Thus, in 34 cases 11 were above 7 years of age, 16 were males, 18 were females. Seven of the cases occurred in January, 3 in each of the months of February, March, and April; 2 in each of the months of August, September, and October; and 12 in November alone. The accumulation of acute cases in the same ward was not found to have any influence in the causation of this late tonsillitis, as it is said to have in the case of late scarlatinal tonsillitis. It is possible, however, that the condition may be more common in hospital than in private practice.

The symptoms were slight, as a rule. In two cases vomiting first drew attention to the condition. The constitutional disturbance was not so great, nor the temperature so high, as in angina redux. The average duration

* It is more than probable that a large percentage of so-called relapses of scarlet fever are in reality primary attacks.

of the pyrexia was 4.0 days; 103.6° F. was the highest temperature recorded. In most of the cases the thermometer did not rise above 101°. The pulse was quick, but examination of the heart revealed nothing beyond hurried action, nor was there any other sign or symptom found to suggest a rheumatic origin for the condition of the throat. In a few cases patches of transient non-punctate erythema capriciously distributed over the trunk and limbs were observed. In one case a thick crop of herpes developed on the chin. Though albuminuria might have been present at an earlier stage of the disease it did not recur at this period. The faucial exudation was almost always discrete, disappearing in a few days with or without syringing of the throat. In only one case was antitoxin injected, as the patches showed a tendency to coalesce. Three successive negative cultures proved that the angina was not diphtherial.

Owing to the aggravated form which serum manifestations assume when antitoxin has been administered afresh, after an interval of a few weeks, faucial deposit occurring late in convalescence from diphtheria as distinct from that designated angina redux, which usually requires no treatment, should be dealt with first by local measures. As will be seen from the above figures, the chances in favour of the tonsillitis being non-specific in origin decidedly outweigh those of its being due to a fresh attack of diphtheria.

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¹ Deguyet Weill, *Traitement de la diphtérie*, 1902, p. 54. ² Sevestre et Aubertin, *La pédiatrie pratique*, 1903, No. 2; cf. Kault in Charcot, Bouchard, and Brissaud, *Traité de Médecine*, art. Diphtérie; and J. D. Rolleston, *Practitioner*, May, 1905. ³ Sevestre et Martin in Comby's *Traité des maladies de l'enfance*, art. Diphtérie, 1904. ⁴ Loc. cit.; cf. *Archiv für Kinderheilkunde*, Band xl, iv bis, Heft vi, ss. 460-462. ⁵ Metropolitan Asylums Board Reports, 1899-1904; cf. Gérard, *Les récurrences de la diphtérie*, 1904, and Narcisse Henry, *Rechutes dans la Scarlatine*, *Thèse de Paris*, 1904. ⁶ Caiger, in *Albutt's System of Medicine*, vol. ii, p. 158.

The Goulstonian Lectures

ON

AUTO-INTOXICATION: ITS RELATION TO CERTAIN CARDIO-VASCULAR DISORDERS.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON ON MARCH 13TH, 15TH, AND 20TH, 1906.

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LECTURE II.—[ABSTRACT.]

[AFTER recapitulating his first lecture as follows:

(1) That in 12 out of 68 clinical cases hypertension was observed, and that there was with one exception proof that the kidneys were affected in these cases; (2) that the explanation of hypertension in renal disease was unsatisfactory—a toxic cause had been invoked, but not demonstrated; and (3) that experimentally he had shown that a rise of blood pressure occurred eighteen times out of nineteen, in which kidney extract was used, and that such frequency of a pressor effect was not noticed after the injection of extracts of other organs—moreover, the pressor effect produced by kidney extract was a prolonged one—

Dr. Shaw gave an account of work carried out by Tigerstedt and Bergman ten years ago.]

They had set themselves the task of elucidating the relationship between kidney and heart, being influenced by the teaching of Brown-Séquard on "internal secretion," and by the association existing between certain renal and cardiac diseases. Their first experiment was rewarded by a successful result.

Freshly-excised rabbit's kidney was rubbed up with glass powder and physiological salt solution. The fluid obtained was then filtered, and a few cubic centimetres were injected intravenously into rabbits. In a short time a well-marked and apparently protracted increase of arterial pressure was observed. In the first experiment, within 80 seconds of the injection of 5 c.cm. of the extract, the maximal pressure had risen from 70 to 68 millimetres before injection to 102 millimetres—that is, an increase of pressure of about 50 per cent. had ensued; in a second experiment the increase after the injection of 4 c.cm. was 25 per cent. within 100 seconds; in

the third experiment there was an increase of 18 per cent. in 60 seconds.

The investigation was further elaborated. They found that extracts which were prepared by boiling the fresh kidney with water or extracts prepared from the boiled kidney by means of cold water were inactive. Alcohol, either absolute or of 50 per cent. strength, was quite unable to extract from the preparation any active material. They were also able occasionally, but not always, to demonstrate that diluted glycerine extract had a definite pressor effect.

One of the objections to the use of the extract which has been injected into the series of cats already referred to is that the material injected was a coarse emulsion, and that until this emulsion could be made to yield a soluble substance capable of exerting a pressor effect the results obtained could not be quite convincing. Tigerstedt and Bergman have, however, succeeded in obtaining a solution of the active material which can be quite freed from any granular contents.

The kidney is rubbed up with absolute alcohol and filtered; the precipitate is dried in the air at room temperature and is then extracted with salt solution; 1 to 2 c.cm. of this extract exert as great a pressor effect as the fresh preparation; the active substance is not destroyed by alcohol. They speak of this extract as "Extract A." If it is boiled or heated in a water bath this extract loses its properties, but exposure to a temperature of from 54° to 58° C. does not apparently disturb the pressor effect.

The pressure substance to which these workers give the name of "renin" is not dialysable. From these various reactions it may be concluded that renin is a substance *sui generis*, and that the effects produced on the blood pressure are not due to any of the crystallizable substances which are excreted in the urine. Further, "renin" was present only in extracts made from the cortex of the kidney, and not at all, or only to a slight extent, in extracts of the medulla. Other experiments suggested that renin actually passes from the kidneys into the blood; that in the kidneys a substance is formed which under normal conditions may pass from the kidney into the blood by a process of internal secretion, and may exert a pressor effect. A preparation of fresh extract made by rubbing up fresh kidney substance with fresh defibrinated blood was also found to be active. The result of the analysis of the effects produced by injection of "Extract A" was to show that fresh renal extracts produce rises of pressure by acting on the peripheral nerve centres as well as possibly on the spinal cord.

Finally, Tigerstedt and Bergman considered the question of the fate of renin when it enters the circulation normally, and concluded that renin is partly got rid of from the body by the kidneys, but that it is also partially destroyed by the body or is possibly got rid of by the bowel.

[After criticizing these experiments Dr. Shaw proceeded:]

It seemed well to endeavour to secure results under the most exacting physiological conditions possible, and so a limited number of further experiments were carried out, using renal extract for injection purposes prior to the injection of any other preparation.

The analysis of these results shows that on three occasions when the experiment was carried out, as in my first series, under the influence of ether only with spontaneous respiration a fall succeeded the injection of renal extract.

When anaesthesia was procured by the administration of ether and morphine, respiration being carried out artificially, a rise of pressure followed the injection of renal extract on 4 occasions. No rise, and even a fall, occurred in 3 experiments. Another condition was to administer ether and morphine or curare, to carry out artificial respiration, and to cut the vagi. A rise of pressure followed the injection of renal extract in 3 cases, and a fall occurred in 2 cases.

These results are obviously unsatisfactory, for although the majority give some support to the view that there is a pressor substance extractable from the kidney, a good proportion of cases show the reverse.

Pressor substances have been demonstrated in the suprarenal medulla and in the posterior lobe of the pituitary body, and there has been abundant confirmation of the results.