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THE EXAMINATION OF RENAL FUNCTION*

BY

F. S. FOWWEATHER, M.D., M.R.C.P., M.Sc., D.P.H., F.I.C.

READER IN CLINICAL CHEMICAL PATHOLOGY, UNIVERSITY OF LEEDS; CHEMICAL PATHOLOGIST, GENERAL INFIRMARY AT LEEDS

In his presidential address at the opening of this session Dr. G. W. Watson called attention to the large number of laboratory tests that patients are very frequently submitted to nowadays; he considered that many of them were superfluous, and, what was worse, there was a great tendency to allow these tests to take the place of sound, intelligent clinical examination of the patient. I agree with much that he said, but I should like to point out, in the strongest possible terms, that it is not the clinical pathologist who is responsible for this state of affairs, but rather that type of clinician who believes he sees in the clinical laboratory an instrument which can relieve him of much of the work of examination of his patient, and can be made to bear the labour and responsibility of making his diagnosis for him. In this connexion let me quote what I wrote in a little book published in 1928.¹ Other clinical pathologists have written in the same strain.

"The clinical laboratory should never be regarded as an institution which of itself is capable of supplying a diagnosis. It is a means of obtaining additional information about a patient, where it is felt that further information is needed, to add to that already obtained by careful and complete clinical examination. A diagnosis must then be made in the light of all the evidence available. But sound clinical observation is, and must remain, the principal means of arriving at a correct diagnosis. . . .

"The correct attitude of the clinician to laboratory work is that if in any case, after using all the available clinical means at his disposal, he is not thoroughly satisfied concerning the matter in hand, whether it be one of diagnosis, prognosis, or treatment, then he should consider in what way laboratory information may help him, whether to throw further light on a doubtful case, to confirm or negative a probable diagnosis, to decide between alternative views, or in any way to make more certain his knowledge of the matter in hand. This procedure involves the intelligent consideration of the relation of laboratory work to each individual case, and is the reverse of the method of routine application of numerous laboratory tests before a serious attempt is made to consider a case from the clinical standpoint."

The clinical pathologist never intended that his methods and his work should supplant the ordinary methods of clinical examination; but he does believe that, in suitable cases, they supplement these ordinary methods, and frequently add useful information that could not otherwise be obtained.

Acute and Chronic Nephritis

Renal disease is one of the subjects on which information beyond that obtainable by ordinary clinical examination is frequently desired. With regard to acute nephritis, examination of the patient and his urine gives, in the great

majority of cases, sufficient information to establish the diagnosis. (Here I should like to point out that I consider the simpler tests of urine—for example, for albumin, and examination of the centrifuged deposit—as part of the ordinary clinical examination of a patient, and not as special laboratory procedures.) But the matter of prognosis may call for laboratory assistance. There is always the possibility that a case may not recover completely, but that the acute nephritis may become subacute or chronic. Laboratory tests at intervals to show the state of renal function are here very useful, and give the best indication of the progress the patient is making.

So far as chronic nephritis is concerned, laboratory tests may frequently be required to establish the diagnosis: the symptoms may be far from diagnostic; there may only appear to be a general asthenia, or anaemia may be the most outstanding feature; in another case vomiting may be prominent, or headache may be the only symptom complained of. Oedema is, of course, usually absent. The urine, so far as the simpler tests go, may yield little information, for albuminuria is rarely more than slight, and often is absent altogether. Casts, too, are not a constant feature. But careful examination by approved renal function tests frequently makes the diagnosis clear. And in many cases where one feels certain that some renal impairment is present, such tests are useful in giving an indication of the degree of such impairment; for on this point symptoms and physical signs are not always very reliable. We are all familiar with the type of case in which signs and symptoms have appeared relatively slight or almost non-existent until a short time before death has occurred from renal failure.

Blood Urea Concentration

I do not propose to make anything like a complete survey of renal function tests. Many have been tried, but only a few are in anything like general use. Something must be said first about blood urea concentration as an index of renal function.

The important point in this connexion is that a raised blood urea is simply evidence of urea retention; but urea retention is not always due to impaired renal function. Anything tending to produce an oliguria—reduced fluid intake, loss of fluid by vomiting, the formation of effusions, and thus the withdrawal of fluid from the blood—may cause a rise in the blood urea where the kidneys themselves are functionally normal. A similar rise may result from excessive protein intake, or excessive protein metabolism, as in fevers or starvation. If all extrarenal causes can be excluded, then a raised blood urea is evidence of deficient renal function. Any obstruction to urinary outflow also causes urea retention—for example, in enlarged prostate; often the removal of the obstruction

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results in a rapid return of the blood urea to normal, and where this occurs we have clear evidence that the urea retention was not due to primary failure on the part of the kidney itself, but to the interference with its normal action caused by back pressure. To the surgeon dealing with this kind of case determination of blood urea at intervals, and, in particular, noting the rate of disappearance of urea retention after removal of obstruction, is a very satisfactory renal function test.

But some impairment of renal function may coexist with absence of urea retention—that is, we may have a normal blood urea in cases in which renal function is deficient. One result of failing function on the part of the kidney is loss of concentrating power, and this occurs in nearly all cases sooner or later. But in earlier stages this failure to produce a concentrated urine may be masked by the ability to produce an abundance of dilute urine, so that actually the normal amount of urea and other waste products is still got rid of, and consequently there is no retention—failure of concentration is compensated for by polyuria.

On account of these limitations on blood urea figures as evidence of the true state of renal function, other tests have been devised in an attempt to obtain a more accurate picture of the real state of affairs, and my chief object now is to describe one of these tests in which I have been particularly interested, and which, so far as my experience goes up to the present, is the best test available.

A Simple Test of Renal Function

But before passing on to describe this I want, briefly, to draw attention to one very simple method of examining renal function which can be carried out with very little equipment or labour, which depends on principles well known to all, but which is generally overlooked.

The test is simply to instruct the patient, while continuing his normal routine, to preserve every specimen of urine passed during a complete twenty-four-hour period, to keep all the specimens separate, and to label each one with the time at which it was passed. At the end of the test he will present you with six or seven specimens. Determine the volume of each and also its urea content, or, failing the latter, the specific gravity is almost as good in nearly all cases; also add the approximate volume per hour for each specimen. Then tabulate the results; they will be somewhat as follows:

A: Normal				B: Nephritic			
Time	Volume	Urea per cent.	Approximate Volume per Hour	Time	Volume	Urea per cent.	Approximate Volume per Hour
11.15 p.m.	—	—	—	11.30 p.m.	—	—	—
7.30 a.m.	390 c.cm.	2.7	47 c.cm.	6.0 a.m.	550 c.cm.	1.4	50 c.cm.
11.10 a.m.	295 c.cm.	1.6	63 c.cm.	10.5 a.m.	350 c.cm.	1.3	84 c.cm.
1.50 p.m.	140 c.cm.	1.8	51 c.cm.	2.0 p.m.	340 c.cm.	1.4	85 c.cm.
4.10 p.m.	110 c.cm.	2.3	47 c.cm.	5.30 p.m.	315 c.cm.	1.5	90 c.cm.
6.0 p.m.	90 c.cm.	1.1	103 c.cm.	8.0 p.m.	210 c.cm.	1.3	84 c.cm.
11.15 p.m.	315 c.cm.	2.0	60 c.cm.	9.55 p.m.	165 c.c.m.	1.2	83 c.cm.
				11.30 p.m.	130 c.cm.	1.5	80 c.cm.
Total ..	1,140 c.cm.			Total ...	2,100 c.cm.		

Compare the volume and concentration of the urine secreted during the night with that secreted during the day. Note whether the volumes and concentrations show much or little variation. With normal function the night urine is less in volume, but greater in concentration than the day urine. As the kidneys become inefficient this difference becomes less marked, and as inefficiency advances, the reverse condition begins to appear—the kidneys have to make up during the hours of rest for what they were unable to do during the

period of bodily activity. Throughout the day period, with normal function, individual specimens vary much from one another, the kidneys being quick to respond to changed conditions of waste nitrogen production and fluid intake. With loss of efficiency there is loss of elasticity and ready response to varying conditions—the inefficient organs begin to work at a dead level.

Rate of Urea Clearance

In many cases such a simple test is capable of giving quite useful information. But where its indications are doubtful, or where it is felt that the best available information not only as to the presence but also the degree of functional deficiency is required, other tests are called for, and I want to deal now with the determination of the rate of urea clearance, as a measure of the efficiency of renal function. This conception of rate of urea clearance was introduced by van Slyke and his collaborators, and is dealt with in a series of papers from the end of 1923 onwards.

They had shown that when the urine volume output exceeds about 2 c.cm. per minute (called the augmentation limit) urea excretion proceeds at maximum speed, and the output per minute represents the urea content of a maximum blood volume, which in normal men averages about 75 c.cm. This they termed the maximum blood urea clearance (C_m), or simply the maximum clearance. This is given by the formula

$$C_m = \frac{UV}{B}$$

Where U = urea concentration of urine, B = urea concentration of blood, V = urine volume per minute.

Below the augmentation limit urea excretion is not constant, but varies with the square root of the urine volume. Hence, if we wish to compare urea excretion below the augmentation limit, either we must have a definite standard worked out for every volume below 2 c.cm. that we are likely to encounter, or we must arrange that the subject excretes a fixed volume per minute for which standards are known, or we must be able to calculate from observations for any volume occurring during a given test what would be the clearance if the urine output were a certain definite standard volume. The last is the only practicable procedure, and from observed volumes of U, B, and V it can be shown that the clearance which would occur if the urine volume were 1 c.cm. per minute (called the standard clearance, C_s) is given by the formula

$$C_s = \frac{U}{B} \sqrt{V}$$

The average value of C_s in the normal adult was found to be 54 c.cm.

The results as worked out from these formulae are in cubic centimetres. For clinical work it is much more convenient to have the results expressed as a percentage of average normal function. This can be done if we write the formulae

$$C_m = \frac{100 UV}{75 B}$$

and

$$C_s = \frac{100 U}{54 B} \sqrt{V}$$

Möller, McIntosh, and van Slyke² give line charts which simplify the calculation.

For children, or others whose size differs considerably from that of average adults, a correction is introduced by multiplying the observed V by the factor

$$\frac{1.73}{\text{square metres surface area}}$$

Now when renal function becomes inefficient the rate of urea clearance falls below the normal. Hence the determination of the urea clearance will tell us whether renal

function is normal or impaired, and also, where impairment is present, will indicate, at any rate approximately, the degree of impairment that is present.

The test is not difficult to perform. It requires only the determination of the blood urea, the urine urea, and the volume of urine excreted over a known period. It is not necessary to resort to any special preparation of the patient, nor is it necessary to withhold food for some time before the test; vigorous exercise, however, is avoided, and the previous meal should be a moderate one, preferably without coffee. The most desirable time of day is found to be the hours between breakfast and lunch. Moreover, it is not necessary to keep the patient in bed during the test.

In the original van Slyke method urine was collected over two successive hour periods, blood being taken a few minutes before the end of the first hour. The clearance was calculated for each hour period, and, presumably, the average of the two results is taken, though the original paper is not definite on this point. If the urine excreted in the hour period exceeds 2 c.cm. per minute (or if the corrected volume $V \times \frac{1.73}{A}$ exceeds 2 c.cm. per minute in a child) the maximum clearance is calculated; if the urine is less than 2 c.cm. per minute, then the standard clearance is calculated.

Urea Clearance After Dose of Urea

When this work came to my notice I found that I had data from a previous investigation which enabled me to calculate urea clearances not only under conditions similar to those laid down by van Slyke, but also for periods after the patient had taken a 15-gram dose of urea. An important fact which assisted me was that I found the blood urea at the beginning and end of the second hour after this dose of urea to be approximately the same, at an average of about 15 mg. urea nitrogen per 100 c.cm. in excess of the value before urea. The blood

FIG. 1.—Before urea. FIG. 2.—After urea.

urea, therefore, during this second hour period is approximately constant (though raised above normal) and a value obtained at any time during this period serves for clearance calculations for the period. On working out clearances before urea and during the second hour period after urea, I found, in persons with presumably normal function, that the values after urea lay within a narrower range than those before urea. It is an obvious advantage to have the normal range as narrow as possible; hence this point seemed worthy of closer investigation under properly controlled conditions, and I therefore made a careful re-examination of the point, using fifty presumably healthy male students as subjects. The results are shown in Figs. 1 and 2.

In these tests the students were allowed their ordinary breakfast, except that they were instructed not to take coffee; they were also allowed to carry on their usual activities in the hospital, only interrupting these when it was necessary to come to the laboratory for specimens of blood and urine to be taken. A further series of tests was also carried out on hospital in-patients. Besides being in bed during the test, food had been withheld from the previous evening. Two classes of patients were dealt with—namely, those in whom renal disease was believed to be absent, and those in whom it was believed to be present. The results on the non-nephritic group are in Table I.

TABLE I

Sex	Age	Blood Urea Clearance		Diagnosis
		Before Urea	After Urea	
1 F	32	39	82	Osteitis fibrosa
2 F	47	54	82	Hyperthyroidism
3 M	32	74	83	Nervous vomiting
4 M	45	82	73	Vitreous haemorrhage
5 F	24	71	95	Cerebral tumour. (Death 16 days later. At necropsy small glioma of sup. corp. quadrigemina found)
6 F	38	55	78	Dyspepsia
7 M	62	90	85	Diabetes.
8 F	54	76	76	Hyperchlorhydria
9 M	35	66	74	Dyspepsia
10 M	47	61	86	Polyarthritides
11 F	—	86	120	Morning vomiting with pregnancy; subsequently cleared up
12 F	—	49	81	Morning vomiting with pregnancy; subsequently cleared up
13 M	63	65	69	Nervous dyspepsia
14 F	28	65	96	Refinitis proliferans
15 F	12	76	76	Delinquency and backwardness; no unhealthy signs apparent
16 F	19	82	85	Fibrositis
17 F	59	28	65	Otosclerosis
18 F	46	48	70	Atrophic gastritis
19 F	50	66	72	Vertigo—(considerable improvement in a few days and patient discharged apparently well)
20 M	26	87	88	Functional albuminuria

Facts Revealed by Test

At this stage it will be convenient to consider some of the facts brought to light by the results so far obtained.

Van Slyke's normal range for Cs, calculated from data obtained from nineteen subjects, some of whom had been examined a number of times, is from 76 to 120. His range for Cm is very similar, and for practical purposes may be considered the same. In my own cases I have made no distinction in the table between Cs and Cm. Actually only a few of the latter occurred.

In the results on students the range before urea is from 29 to 107, while after urea it is 73 to 120.

Of the twenty cases in Table I, seventeen give results, after urea, between 73 and 120 as in the case of students; of the remaining three, two, giving values of 69 and 65, were elderly patients (63 and 59 years respectively), and the third, a patient of 46, gave a value of 70. Before urea the results in these twenty cases lie between 28 and 90.

The great similarity of these results to those on healthy students shows that the difference in conditions observed during the tests has no appreciable effect on the actual results—that is, whether you allow breakfast and mild exercise during the test, or withhold breakfast and keep the patient in bed, does not matter.

The results also make it quite clear that figures, on non-nephritic subjects, obtained without giving urea cover such a wide range as to be really useless as a practical

test; the figures after giving urea, however, do lie within a well-defined range, which can be conveniently used as a standard of comparison. Considering all the results after urea, it seems justifiable to regard the normal value as anything exceeding 70. (The maximum doesn't really matter in this case: it is the minimum that counts.) Some allowance, however, should be made for advancing age, for which a figure of 65 might be taken, from about the end of the sixth decade. Now let us see what results are obtained in patients suffering from renal disease. These are shown in Table II. There

TABLE II

Sex	Age	Blood Urea Clearance		Diagnosis
		Before Urea	After Urea	
1 M	31	42	52	Chronic bone tuberculosis; parenchymatous nephritis. (Subsequently died; at necropsy subacute nephritis; sinus from tuberculous disease of 5th lumbar vertebra and sacro-iliac region)
2 F	23	46	57	Acute nephritis
3 M	36	60 35	48 (21/2/33) 50 (16/3/33)	Albuminuria; oedema— ? subacute nephritis
4 F	17	5.4	6.5	Renal rickets
5 M	17	39	12	Renal rickets
6 F	53	8.7	9.5	Polycystic disease of kidneys
7 M	29	8.4	11.5	Chronic nephritis. (Subsequently died; no necropsy)
8 F	—	22	42	Pregnancy; persistent albuminuria; pyelitis
9 F	47	36	45	? Polycystic disease of kidneys
10 M	34	21	11.2	Chronic interstitial nephritis
11 F	20	35 31	49 (2/1/33) 45 (2/7/33)	Acute nephritis becoming chronic
12 M	25	33	37	Acute exacerbation of chronic nephritis
13 M	35	50	52	Acute nephritis, becoming chronic
14 M	37	41	47	Interstitial nephritis
15 F	29	34	42.5	Pyelitis
16 F	58	53	56	Chronic nephritis
17 F	62	30	9.5	Hypertension; epistaxis. ? Chronic nephritis
18 M	22	58	57	Chronic nephritis
19 F	60	48	52	Granular kidneys; chronic uraemia
20 F	23	31	33	Acute nephritis

is again a difference between the results before and after urea. If we considered the range, on normal patients before urea, of the figures before urea in this table, seventeen would fall within that range. Of the figures after urea, however, the highest is 57—that is, not one falls within the normal range found after urea. This clearly shows that the urea clearance obtained after urea is a better indication of the state of renal function than figures obtained without giving urea; and since it is shown that where renal disease is present figures are obtained which are definitely below what are considered normal, the use of the test for investigating possible departures from the normal is clearly demonstrated.

Technique of Test

The method of carrying out a urea clearance test after urea is as follows:

At 7 a.m. the patient may be allowed a light breakfast; coffee must be avoided, but tea, if weak and in small quantity, may be permitted. At 9 a.m. the bladder is emptied, and immediately afterwards the urea is given. At 10 a.m. the bladder is again emptied. At about 10.45 a.m. a specimen of blood is taken for urea determination, and at 11 a.m. the bladder is once more emptied. The clearance value is of course calculated from data obtained from the

third urine specimen (exact volume, exact time of secretion and urea concentration) and the blood specimen.

These times I have selected as being most suitable for hospital practice; but they can be modified somewhat, so long as the intervals are the same, to suit the convenience of the persons concerned.

Two points are of especial importance—namely, that the bladder must be completely emptied on each occasion urine is passed, and the exact time of secretion represented by each specimen must be known. For the latter purpose it is best to instruct the nurse, or whoever is in charge of the patient during the test, to label each specimen passed with the time to the nearest minute at which it was passed, rather than to insist that specimens shall be taken at exact 60-minute intervals. In the latter case, if, as often happens, the attendant is engaged in some other task when she should be instructing the patient to pass urine, the interval becomes extended to sixty-five or seventy minutes, but she rarely owns up to this, whereas if she is told that a few minutes' variation on either side of the sixty is permissible, so long as the exact time the specimen is passed is recorded, one generally gets more exact data. With an intelligent patient, the requirements of the test can be explained to him, and he will do the time-keeping himself.

Complete emptying of the bladder at the beginning and end of the second hour is, of course, of paramount importance, and this must be carefully explained to the patient. Incomplete emptying of the bladder is, I think, the chief cause of the wide variation of results before urea, for in most cases the volume of urine secreted over the first and second hours after urea is greater than that before urea. At the beginning and end of the second hour, then, there is a more satisfactory stimulus for the bladder to empty itself than when no urea is given. Frequently, in tests of this nature, what occurs immediately before the test is not sufficiently controlled. Thus, a short time before a test begins, a patient may require to empty his bladder. If he does so, when the time for a test specimen arrives the amount of urine secreted during this interval is so small that the impulse to empty is insufficient, and complete emptying does not occur. Or it may be that he is told not to empty his bladder when the impulse arises, but to wait until the test specimen is required. When this time does arrive, over-distension may have occurred, and again we get incomplete emptying. It is for this reason that in the directions for the test I have advised emptying of the bladder at 9 a.m., although it is only the specimen secreted between 10 and 11 a.m. that is really required for the test.

Occasionally one meets with persons who exhibit a psychical inhibition to micturition to order. This occurred twice during my investigation of students—in one case the patient thought he was being overlooked during the act. If the patient is not fussed, rushed, or observed during the act, this difficulty will not often arise. Where retention is believed to be present, or if for any reason it is thought that emptying of the bladder may be incomplete, a catheter should be used.

Advantages of Urea Clearance Test

Having so far described the urea clearance test and its technique, what are its advantages? The greatest appears to be that it takes mathematical account not only of the urea concentration of the blood and urine, but also of the urine volume output. Not only is the ability to excrete urea examined, but the ability to excrete water is also included.

The renal function test hitherto most frequently employed here has been the urea concentration test, together with a blood urea determination. In this test, however, difficulties in interpretation frequently arise when the urine volumes differ greatly from the average, for, although attention is chiefly directed to the urea concentration, the implication of large volumes of urine cannot be entirely ignored; urea is itself a diuretic, and where large volumes of low concentration are obtained, it is frequently impossible to say whether we are to accept this as evidence of a nephritic polyuria, due to loss of concentrating power, or whether we have the

results of a simple diuresis induced by the urea. This difficulty is avoided to some extent by limiting the patient's fluid intake for some hours before the test, but it is not entirely eliminated. No such difficulties arise in the urea clearance test, since volumes as well as urea concentration are taken into account mathematically by the van Slyke formulae.

In all the cases shown in Table II the routine renal function test, consisting of blood urea determination before urea, followed by a urea concentration test, was carried out, in addition to the clearance test already described.

In eight of them this routine test failed to show any impairment of renal function, yet all gave a urea clearance very definitely below the normal range. A careful consideration of all the facts obtainable clearly showed that renal function in these cases was definitely impaired, and left no doubt that the blood urea clearance value is the more correct index of the true state of the kidneys.

I have been making urea clearance determinations for some time now, in all cases where a renal function test has been required, and provided sufficient care and attention are paid to the two points I previously stressed—namely, complete emptying of the bladder and accurate timing of the specimens—I am convinced that the urea clearance is a much better index of the true state of renal function than the test formerly in routine use; I believe it to be, in fact, the best renal function test we possess.

REFERENCES

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² Möller, McIntosh, and van Slyke: *Journ. Clin. Invest.*, 1928-9, vi, 427.

REVIEW OF BLADDER-NECK OBSTRUCTIONS

WITH SPECIAL REFERENCE TO TRANSURETHRAL PROSTATIC RESECTION*

BY

DUNCAN M. MORISON, M.D., F.R.C.S.ED.

HONORARY UROLOGIST, ROYAL HOSPITAL FOR SICK CHILDREN,
EDINBURGH, AND DEACONESS HOSPITAL, EDINBURGH

It is perhaps not yet fully appreciated that the symptoms which are regarded as characteristic of an enlarged prostate are common to a number of other causes, not only in elderly men, but in other decades, as well as in the opposite sex. The same symptom group is referred to as diurnal or nocturnal enuresis in the young, frequency in adult life, and prostatism as senility is approached in the male.

The French were probably the first to point out that the urinary difficulties observed in elderly women were similar to those of prostatitis, but obviously due to other causes. From the same source we have the term "prostatisme sans prostate," when the symptom group is present without any obvious prostatic enlargement being felt per rectum. Accordingly, since this symptom group is common to various ages and both sexes, it is evident that full data should be obtained in each instance before an accurate diagnosis can be given and appropriate treatment instituted. In this paper, however, it has been considered advisable to review only the commoner conditions found in the male, and to exclude malignant disease.

The symptoms referred to are generally a gradually increasing urinary frequency by day and night, the quantities of urine voided at each act becoming smaller. The act may be precipitate, or there may be initial delay; the stream lacking in force and being smaller than normal, it thus takes longer to perform the act, which concludes with dribbling. Variations and additions to the above

will be noted as the individual causal lesions are discussed. This group of symptoms usually indicates some change at the bladder neck which is interfering with the proper emptying of the bladder. To appreciate the various types of obstruction that occur, and the changes they induce, let us briefly refresh our memories with the anatomy and physiology of the parts involved.

Anatomy

The Bladder.—The musculature of the bladder is described as divided into three parts: (a) The walls. (b) The trigone. (c) The vesical neck.

(a) The bladder is lined by a transitional epithelium which is continuous with that of the ureter and the urethra. The wall, aside from this epithelial lining, is made up chiefly of muscle fibres, arranged in an outer longitudinal and an inner circular manner. Because of these acting together on the bladder contents it is better to consider them as one muscle, the "detrusor" of the bladder. Between the musculature and the epithelial lining, or mucosa, is a loose cellular tissue, which is only absent over the trigone. Over the trigone the epithelial lining is firmly attached to the underlying muscle, while in all other portions of the cavity the epithelial lining is so loosely attached to the detrusor that when the organ is empty the epithelial lining falls into folds.

(b) The trigonal muscle develops in the embryo from the muscle layers surrounding the lower ends of the Wolffian ducts and ureters. Later in foetal life these muscles come to lie in the bladder, and their main bundles run from the ureteral orifices to the vesical orifice, where the bundles from the two sides join and run down, just beneath the urethral mucosa on the aspect posterior to and beyond the verumontanum. The upper margin of these bundles passes across from one ureteral orifice to the other, forming a slight elevation—the interureteric ridge—at either end of which the ureteral openings are situated.

(c) The term "neck" of the bladder is employed to designate the region around the vesical orifice. Here the division of the detrusor muscle into two layers is more marked. From each of the two layers, just posterior and lateral to the vesical orifice, is sent a strong band of muscle fibres, which runs down and forward to the prostate to form a loop around the front of the urethra. The bundle from the external longitudinal layer is thicker than that of the internal circular. These together form the "internal sphincter," which is not a circular muscle like the sphincter ani, but only forms an arch around two-thirds of the vesical orifice. The external sphincter is a voluntary muscle, while the "internal sphincter," being supplied by sympathetic and parasympathetic fibres, is an involuntary muscle.

The Prostate.—In the development of the prostate it will be recalled that, in about the twelfth week of foetal life, five groups of tubules grow out from the posterior urethra towards the bladder. At first the five lobes are distinct, but later the two lateral and the middle lobes tend to coalesce. The posterior lobe lying behind the ejaculatory ducts remains distinct. The anterior lobe, which commences by being the same size as the others, retrogresses after four weeks and is completely atrophied before adult life. In a few instances the tubules of the anterior lobe may persist and even be the seat, ultimately, of an enlargement. The lateral lobes, however, are the most active as to growth, and comprise the major portion of the adult prostate.

The Submucous Glands.—Lying under the mucous membrane of the posterior urethra and trigone, and independent of the prostate, are certain accessory glandular structures. They are localized in three situations: (a) the prostatic urethra; (b) the vicinity of the bladder neck; and (c) the trigone. These submucous glands are of importance, since, like the prostatic tubules, they are liable to undergo enlargement in middle and old age, and on account of their situation are likely to give rise to obstruction.

The subcervical group, known also as the glands of Albarran, consist of some thirty branched tubules, whose ducts open into the floor of the urethra proximal to the verumontanum.

The subtrigonal glands lie anywhere between the mid-point of the trigone and the bladder outlet, and are similarly composed of branched tubules. Enlargement of either of these groups may be sufficient to cause typical symptoms of

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