

## UROSELECTAN: EXCRETION UROGRAPHY.\*

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UROSELECTAN is the name given to a chemical compound which has been invented recently by Binz and Raeth, and employed in Von Lichtenberg's clinic, to delineate the urinary tract. It is neutral, is soluble in water to more than 50 per cent., and contains 42 per cent. of iodine. It is opaque to X-rays and is an extremely stable chemical compound. It can be introduced into the blood stream in relatively large amount. It is excreted by the kidneys, and thus during the course of its elimination it enables the entire urinary tract to be outlined by X-ray photography. "Excretion urography" has thus been accomplished—a discovery which has been anticipated since Graham introduced his method of delineating the gall bladder and biliary passages by the administration of sodium tetraiod phenolsulphone-phthalein, or "S.T.I.P.P." as it is called. Excretion cholecystography prepared the way for excretion urography.

There is this difference, however, when the two methods of diagnosis are compared and evaluated. Up to the present, duodenoscopy with catheterisation of the biliary passages has not been accomplished. It is thus not possible to instil an opaque solution into the bile ducts and gall bladder with a view to delineating them by X-ray examination. What I would call "infusion cholecystography" thus awaits discovery; whereas ordinary urography, or as we will call it now "infusion urography," where the renal pelvis, ureters and urinary bladder have their form and capacity rendered visible by X-ray examination after the introduction of a suitable opaque pyelographic solution, has long been practised, and is an essential part of the routine examination of the great majority of cases of suspected renal or vesical disease.

The information which infusion urography affords, is so accurate and so easily obtained that the question at once arises, "What advantage is to be gained by the employment of this new method of 'excretion urography' in place of a method of outstandingly proven value?"

We may say at the outset that in our opinion the introduction of excretion urography is an epoch in medicine. It

\* Read 2nd July 1930.

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has come to stay and within its limited field of usefulness will prove of great value as a diagnostic aid. In our opinion it will never replace the ordinary pyelographic examination in the great majority of cases. Already, however, during the few weeks we have used it, uroselectan has enabled us to accomplish what was never possible by ordinary pyelography, and to delineate the renal pelves, ureters and bladder in cases where ordinary pyelographic examination was impossible, difficult or contra-indicated. To enable you to estimate the value of this new means of diagnosis, we would remind you briefly how an ordinary pyelographic examination is carried out and some of the facts it reveals. Although possible under a general anaesthetic, it is advisable to conduct the examination on the conscious patient, whose co-operation is necessary to avoid over-distension of the renal pelvis. It is thus obviously eminently unpleasant, although usually painless. In children and in adults of unstable mind it is difficult to accomplish.

Sometimes the patient is sick and upset after the examination. At the same time it is devoid of danger. We have conducted the investigation of over four thousand patients and have not had one where any serious harm resulted from the examination. The bladder is first filled with a clear sterile solution. The channel of entrance—the urethra—must thus be pervious. A catheterising cystoscope is then introduced and the ureters catheterised. The bladder must thus have a capacity sufficient to permit of this, and the ureters must be visible and pervious. Through the ureteral catheters an opaque media, 12 per cent. sodium iodide solution, is then introduced into the renal pelves and photographs are taken. The picture thus obtained is known as a pyelogram, the procedure that of pyelography. By means essentially similar a ureterogram or cystogram may be made.

By means of a complete urological examination, of which urography forms a most important part, an exact diagnosis of all deformities or diseases of the urinary tract can be made. The modern urologist does not express an opinion at the conclusion of the examination; he states a fact. He is, however, human, and is thus sometimes wrong; but in our experience when he reviews such a case, he will note that the error in diagnosis is due to his having carried out an incomplete examination.

Every deformity of the kidney can be demonstrated by

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pyelography. The photographic appearances of the congenital cystic kidney, the horse-shoe kidney, the unilateral, fused kidney, the kidney with double pelvis, the pelvic kidney, are unique and diagnostic. Early tuberculous disease, when it has invaded the pelvis, has a characteristic appearance. More advanced tuberculous disease shows in the ureterogram a picture which also is diagnostic. The appearance of pelvic distension due to chronic pyelitis differs from that of an ordinary hydronephrosis.

By urography not only the presence of a stone in the urinary tract can be diagnosed accurately, but also the degree of damage it is producing estimated, and from its relative density its chemical composition judged.

By pyelography it is now possible to diagnose early malignant disease of the kidney. A shadow outline of innocent tumours growing from the wall of the pelvis can also be obtained.

If our means of diagnosis are thus so perfect and so safe, what scope remains for the application of excretion urography? Will it provide an equally safe and equally accurate method of delineating the urinary tract? It is a method wherein a running stream is photographed, and it will thus reveal when the springs have dried up or are absent and show clearly any obstruction to the flow. It is unlikely that it will outline a filling defect such as occurs in tuberculous disease or obliterative changes such as malignant disease produces. It also has not the advantage of accurately outlining the ureteral channel that the X-ray ureteral catheter affords in ordinary pyelography, which also permits of the urine from the two kidneys being segregated for examination chemically, cytologically and bacteriologically.

Under certain circumstances pyelographic examination is impossible, inadvisable or extremely difficult. A variety of circumstances may render a pyelographic examination impossible, such as :

- A. Impermeable stricture of the urethra.
- B. Pronounced prostatic hypertrophy, which so lengthens the urethral channel that the ordinary cystoscope will not enter the bladder cavity. When pronounced intravesical herniation of the bladder is present, the mound thus formed may obscure the ureteral orifices.

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- C.* The ureteral orifice may be inaccessible owing to its opening into a diverticulum or from the presence of a ureterovaginal fistula.
- D.* The ureteral orifice may be visible but cannot be catheterised owing to muscular spasm rendering it impermeable. External pressure may also render it impermeable. Catheterisation may be possible, but when the channel is inflamed owing to the pain experienced, the catheter may be expelled. Where a double pelvis with two ureters exists, the synchronous catheterisation of both is difficult and sometimes impossible.
- E.* The ureter may not be able to be observed owing to the bladder being in extreme systole or owing to extreme ulceration of the bladder wall.

Circumstances—such as the presence of balanitis, urethritis, prostatitis or severe cystitis—arise where ureteral catheterisation and pyelography would be technically easy to carry out but are inadvisable owing to the risk of producing an ascending infection.

When acute pyelitis is already present, ureteral catheterisation and pyelography are contra-indicated owing to the risk of activating an already existing infection.

It will thus be seen that there are a number of cases where excretion urography, although it only provides a poor substitute for infusion urography, would prove a valuable diagnostic aid. We have tried it already in a number of cases. Several of these were selected to determine its value as an alternative to ordinary pyelography, but in others we consider catheterisation contra-indicated on various grounds. In others, ureteral catheterisation was attempted and failed; and in others, additional confirmatory evidence was desired after a previous pyelographic examination.

As illustrations, a man came under our care suffering from overflow incontinence of urine, of long standing. For this he had been wearing that filthy instrument known as a portable rubber urinal. As a consequence the penis was oedematous and a severe balanitis and anterior urethritis were present. Excretion urography demonstrated to us the degree of backward pressure on the kidneys, and the cystogram obtained showed graphically the amount of residual urine.

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Another patient came under our care. In 1927 he had been operated on for interstitial prostatitis and median bar formation ; no relief followed ; partial retention of urine and pyuria remained. A cystoscopic examination had been attempted without success owing to contraction of the vesical neck, and was followed by very serious ill-health and recurring rigors for seven days. When he came under our care he was very toxic, and the urine voided was very foul smelling and contained a mixed infection. His blood urea was 65 mgrms. per 100 c.c. Uroselectan again demonstrated the absence of bilateral, backward pressure and hydronephrosis, and the kidneys were apparently functioning satisfactorily. The cystogram showed a bladder containing about 10 ounces of residual urine.

In another case, on cystoscopic examination a healthy right ureter was catheterised. The orifice of the left was œdematous and could not be catheterised. The clinical symptoms indicated left-sided obstruction. We will demonstrate to you later that by uroselectan we were able to confirm that the right kidney was apparently healthy and that the left ureter was obstructed by narrowing of the lumen at its lower end. This was confirmed at operation as due to an inflammatory periureteritis.

In another case, that of a young woman who was referred to us by a gynæcological colleague who had cured her of a pelvic disease, persistent vesical discomfort remained. Her history indicated a previous acute pyelitis. The urine contained a few *B. coli* organisms. Under ordinary circumstances we would have certainly done bilateral pyelography and renal lavage. Uroselectan examination showed us clearly the absence of the atonic hydronephrosis of chronic pyelitis, and both kidneys appeared to be functioning well. A simple cystoscopic examination was therefore only done, which revealed slight trigonitis, the dregs of a healing urinary infection. A complete and satisfactory examination had been carried out free of any discomfort.

We claim therefore that in excretion urography we have at least a substitute of moderate value for infusion pyelography, where the latter is impossible or inadvisable. The more important claim, however, can be made that by means of it, as we already have said, there has been accomplished what was never previously achieved — the entire kidney has been clearly and accurately outlined. Not only when accumulated in the renal pelvis and ureter is the salt opaque,

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but also during its course of tubular excretion. Thus the renal parenchyma is also outlined and a photograph of the entire kidney obtained. Another result of very great value has been achieved. A graphic record of the amount of residual urine has been obtained, as in two cases referred to already, when a perfect demonstration of the amount of residual urine was obtained without catheterisation, with its attendant discomfort and danger.

We are enthusiastic as regards the value of this new method of examination for further reasons. Our predecessors reached pre-eminence in surgery through the dissecting room. They belonged to the great school of anatomical surgery. The generation that is passing sought success by the application of a knowledge of pathology to surgery. The surgeon of the future is going to be a surgical physiologist. Excretion urography is a graphic physiological demonstration.

The ordinary pyelogram obtained by infusion urography, upon which up to the present we have depended alone, delineates the morbid anatomy of the disease with equal accuracy in the living and the dead. Excretion urography by the injection of uroselectan demonstrates the course of a vital stream, the urine flow. We have already learnt much from observing this, and look forward confidently to learning much more.

The value of uroselectan as a test of renal functional activity by estimating the rate of its excretion in the urine will be described later; and when this is being judged in comparison with "chromocystoscopy," the phenolsulphone-phthalein test, phloridzin, urea concentration and other methods, we would ask you to consider the value of these from the standpoint of the surgeon who wishes to know not only the total functional activity of both kidneys, but also the functional activity of the individual organs, and up to the present this is most frequently impossible and often inaccurate.

The combination of excretion urography after the injection of uroselectan with the determination of the renal functional activity by estimating its rate of excretion gives promise of our being able to determine not only the presence of disease in one kidney, but also the health of the other.

We have had already several cases of renal enlargement from disease where on ordinary pyelographic examination the urine channel was pervious, the pelvis only moderately enlarged, the renal parenchyma not destroyed and urine segregated by

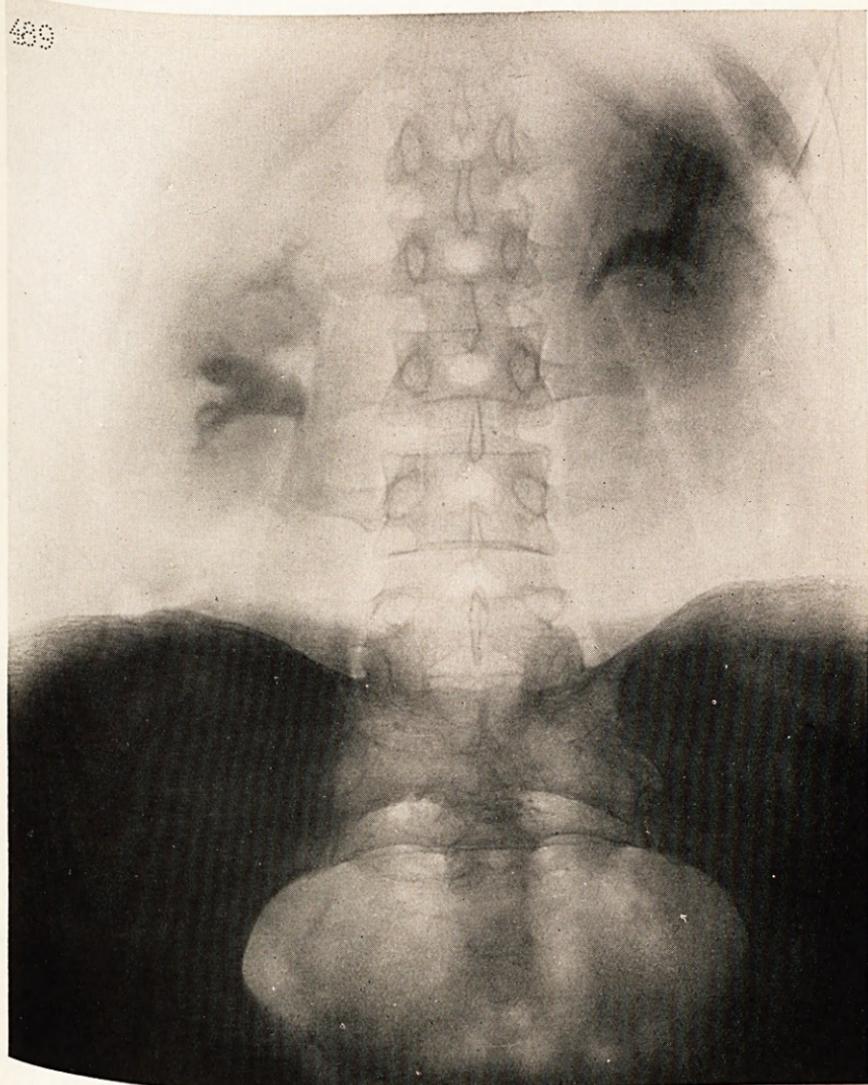


FIG. 1.—EXCRETION UROGRAPHY. BILATERAL DOUBLE PELVIS AND URETER.  
The outlines of the bilobed kidneys are faintly revealed. Each kidney possesses two pelves of normal contour with separate ureters passing from them.

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FIG. 2.—EXCRETION UROGRAPHY.

Double pelvis of left kidney with closed hydronephrosis of the upper sac. At the lower and inner margin of the large renal shadow on the left side a pyelogram of the lower renal pelvis is seen. The outlines of both ureters and the outline of a normal kidney and normal renal pelvis are well shown on the right side.

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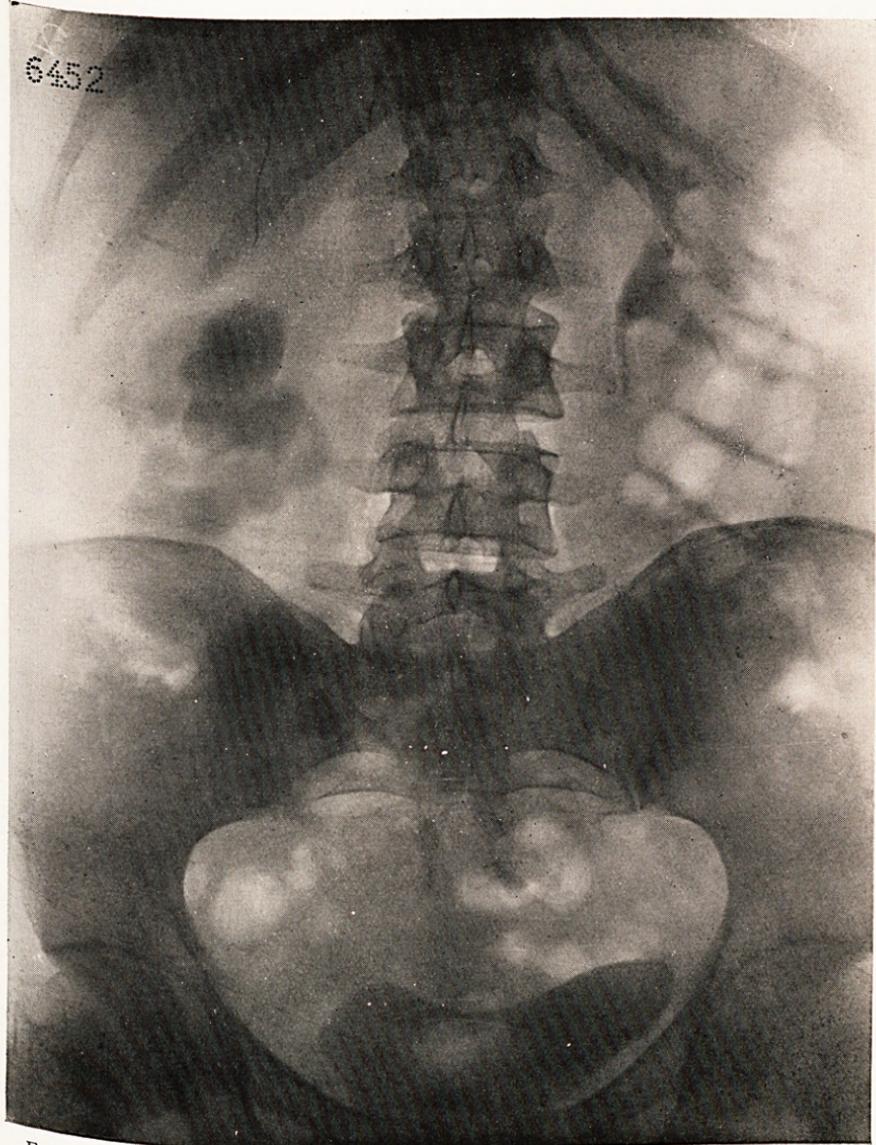


FIG. 3.—EXCRETION UROGRAPHY. TUBERCULOUS DISEASE OF THE RIGHT KIDNEY. The right kidney is observed to be enlarged. Its pelvis and calyces are dilated and irregular and the ureter dilated. The pycelographic outline of the left kidney is normal.

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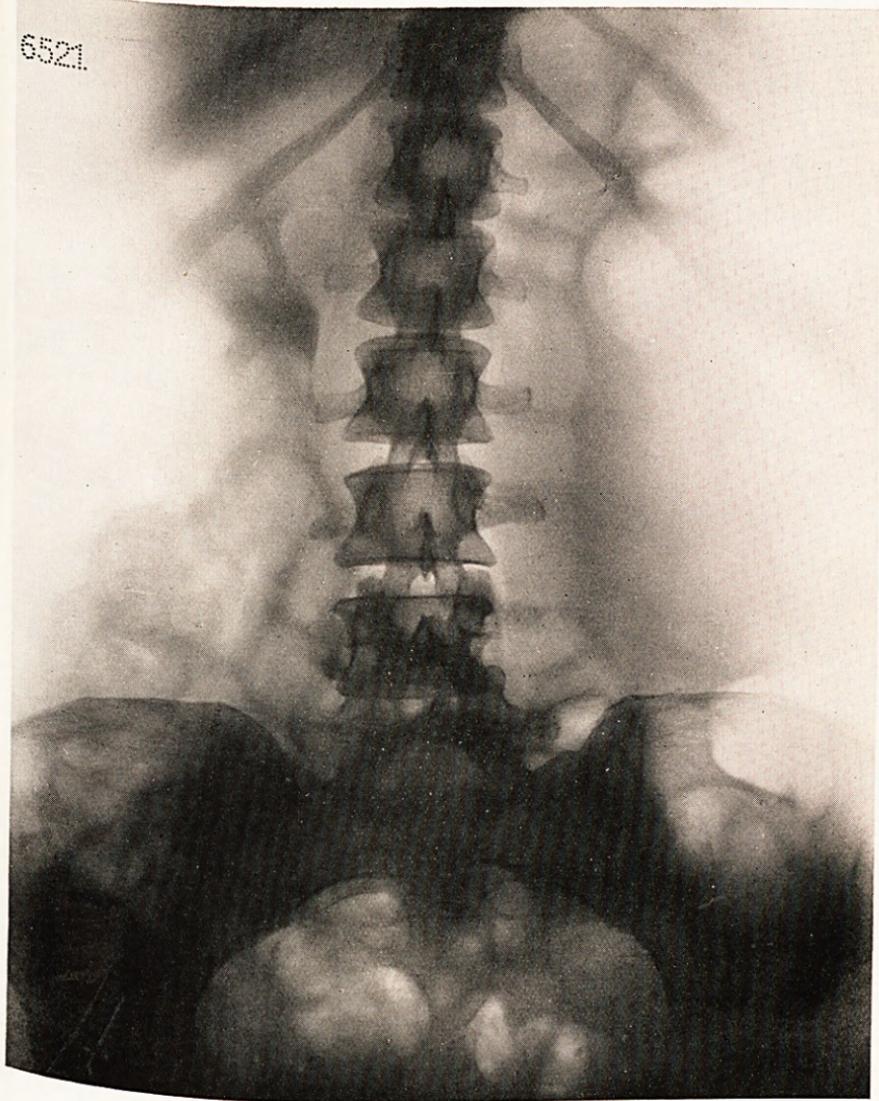


FIG. 4.—EXCRETION UROGRAPHY. TUMOUR OF LEFT KIDNEY.

The faint outline of the enlarged left kidney is shown, but no pyelogram was obtained.  
On the right side the pyelogram is normal.

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ureteral catheter from the diseased organ, and where by excretion urography after uroselectan no shadow was obtained from the diseased side the kidney was "silent." We wish to know the significance of this. What is its true clinical value? Is the threshold of uroselectan excretion the threshold of health? If so it is a great discovery.

**Technique of the Uroselectan Examination.**—Uroselectan, when prepared for injection, is a filtered sterile solution 100 c.cs. in bulk and of 40 per cent. strength. It is freshly made up on each occasion. Forty grams of the crystals are dissolved in 100 c.cs. of sterile, doubly distilled water. The solution is carefully filtered and the filtrate sterilised, the bulk being made up to the full 100 c.cs. during the process.

The method evolved for the investigation of the patient by uroselectan requires no material change in the ordinary routine of in-patient régime. A normal breakfast is allowed, and the patient is taken to the X-ray theatre at 9.30.

Firstly the patient empties his bladder naturally, and, with the patient in a recumbent posture, injection is proceeded with. The arm is constricted and a suitable vein selected. The skin is rendered aseptic in the usual manner with spirit and iodine, and an intravenous injection given by the tube and funnel method, the solution having been warmed to body temperature. It is advisable to administer the injection slowly, allowing seven to ten minutes for its completion. Thereafter the patient remains recumbent for the first period of half an hour, at the end of which interval he again empties his bladder. On this occasion the specimen is preserved.

The first X-ray photograph is now taken of both kidneys and the upper portions of the urinary tract, as well as the bladder and lower ends of the ureters. This may mean taking two pictures. X-ray photographs are taken again one and a half hours, three hours and six hours after the administration of uroselectan, the patient emptying his bladder before each group of photographs.

Between the second and the last group of photographs the patient is allowed to return on a trolley to his ward or room so that the interval of three hours is spent comfortably in bed, and the patient may even have a light meal. No restriction as regards diet is made on the day of the investigation, but extra fluids are withheld. In all cases the samples of urine obtained during the period of the investigation are examined, and an

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estimation made of the volume and specific gravity of the urine and the weight and the percentage of the drug in each.

In certain cases the patient returns for an X-ray photograph twenty-four hours after the injection, and in such cases the urine passed in the interval between the six-hourly and the twenty-four-hourly X-ray examinations is also clinically investigated.

**The Effect on the Patient.**—Before using uroselectan on the human subject, the effect of its injection, both by subcutaneous and intravenous routes, was tried out in animals.\* In a healthy laboratory animal no toxic symptoms, either local or general, were noted. When the drug was allowed to perfuse the subcutaneous tissues, no local inflammatory process was set up, and in this respect uroselectan for use in intravenous urography differs from the local effect on the tissues produced by S.T.I.P.P. in intravenous cholecystography.

In the laboratory animal no change occurred in the secretion of the urine, either as regards quantity or proportion of normal constituents, by gross over-dosage, as compared with that used in the human subject, weight for weight. Similarly, when uroselectan is used clinically no local inflammation will be set up in the arm if by chance a leakage of uroselectan occurs into the tissues around the vein.

As regards general symptoms during the injection, in all cases a feeling of warmth, with slight flushing, is noted, and in the average surgical case coming for investigation a rise in the pulse-rate of a few beats may be found. In cases where there is some nervousness or tendency to hyperthyroidism, more marked flushing of the face, with a correspondingly greater increase in the pulse-rate, is found. In the small series of cases of severe chronic nephritis in which uroselectan was used, a more marked general reaction was present. With the sensation of warmth some apprehension or undue interest in the injection was expressed. The pulse-rate increased by ten beats a minute or more, and with a slight rise in pulse-pressure it became fuller in character. In every case these symptoms disappeared within a few moments of the termination of the injection. In one case a rise of temperature, with sickness and vomiting, occurred four hours after the injection, but a few hours later a complete return to normal took place. No other case showed any demonstrable after-effect from the use of uroselectan.

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It is suggested that the iodine factor in uroselectan brings about a temporary increased excitability following its injection. It is noteworthy that such symptoms only appear prominently when the renal function is exceptionally low and the rate of excretion of the drug at a minimum.

**The Interpretation of the Photographs.**—The urogram obtained following the use of uroselectan varies in its density with a number of factors. Firstly, if no excretion of uroselectan through the kidney occurs, there is no urogram. If the excretion of uroselectan is delayed, then only late in the course of the investigation is a satisfactory urogram made. If, from obstruction in the urinary tract, there is delayed emptying of the upper urinary passages, the renal pelvis and ureter, then from dilatation of the upper urinary tract, and consequent increased capacity for holding a larger quantity of excreted uroselectan, a broader and denser shadow, giving a better urogram, is obtained.

In cases where both kidneys are present, only one of which is diseased, while a study of the urogram of the affected side may or may not indicate the nature of the pathological process, certainly from comparison with its neighbour a valuable indication of the comparative functional activity of the two sides may be obtained. From the fact that tubular secretion or excretion in the renal parenchyma is going on, the shadow that is produced of the kidney gives a valuable indication of its shape and size. Accordingly, only when the kidney is absent, or relatively functionless, does one find complete absence of urographic shadow.

From the study of a series of urograms following excretion pyelography in cases of relative health and disease of the urinary system, one finds that, in the absence of pathology in the urinary tract, an excellent urogram is obtained half an hour following the injection. This includes a shadow corresponding to the size and shape of the renal parenchyma, and a definite pyelogram of fainter intensity than that produced by infusion pyelography. The definition of the margins of the renal pelvis and calyces is never so clean-cut and delicate as that found in infusion pyelography, and the finer irregularities or filling defects, which are of diagnostic importance in so many cases, are not brought out. The line of the ureter is imperfectly seen, except where some delay occurs in its emptying into the bladder.

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As the bladder has been emptied naturally prior to the taking of the photographs, only in those cases where there is residual bladder urine is a cystogram obtained. In these cases a valuable pictorial demonstration is provided of the amount of residual urine and any irregularities in the bladder outline.

Probably the best urogram is obtained one and a half hours after the injection, and a satisfactory photograph in that period means that renal function is well within normal limits. In health the later photographs gradually give poorer and poorer urograms, so that in six hours no pyelogram is visible. Where there is delay in the excretion of the drug, as when renal function is diminished, the urograms may increase in intensity and definition after three hours or more from the time of the injection; and in this group are found those cases of hydronephrosis where a slowly excreted but increased pelvic content gradually acquires a large bulk of uroselectan-containing urine, and accordingly gives an improved shadow late in the period of observation. In such cases also where there is delayed emptying, a better urogram is obtained later in the series.

In every case it is imperative to have a satisfactory preliminary routine X-ray photograph of the urinary tract, so that no pre-existing shadow of calculus, calcified gland or other foreign material may confuse the interpretation of those of the uroselectan-containing renal secretion.

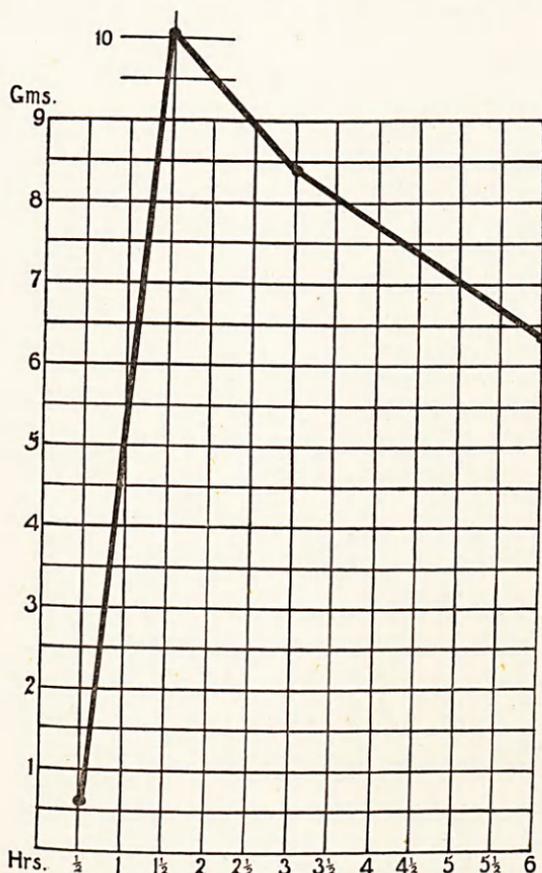
**The Estimation of the Rate of Excretion.**—In the ordinary process of investigation, four specimens of urine, representing the total bulk of urine passed in the period of observation, are obtained. These specimens are the urine passed half an hour, one and a half hours, three hours and six hours following the injection of uroselectan. The volumes of the individual specimens showed great variation, and accordingly the specific gravity reading lost considerably in value, although the specific gravity always gave a rough indication of the percentage of drug excreted in the specimen. Similarly the percentage of drug excreted made a variable reading.

The most useful estimation was the weight of the drug, and this was carried out through the co-operation of Dr C. P. Stewart in the Biochemical Laboratory. The specimen of urine was slightly acidulated with dilute mineral acid, which led to the precipitation of uroselectan. Excess of acid brought about a redissolving of the drug, so that a maximum

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precipitate was obtained by combined titration with acid and alkali. The precipitate was accurately filtered free from urine and measured in terms of dried weight.

It was found that in health a considerable weight of drug



### Double Pelvis

GRAPH I.—NORMAL UROSELECTAN EXCRETION CURVE.

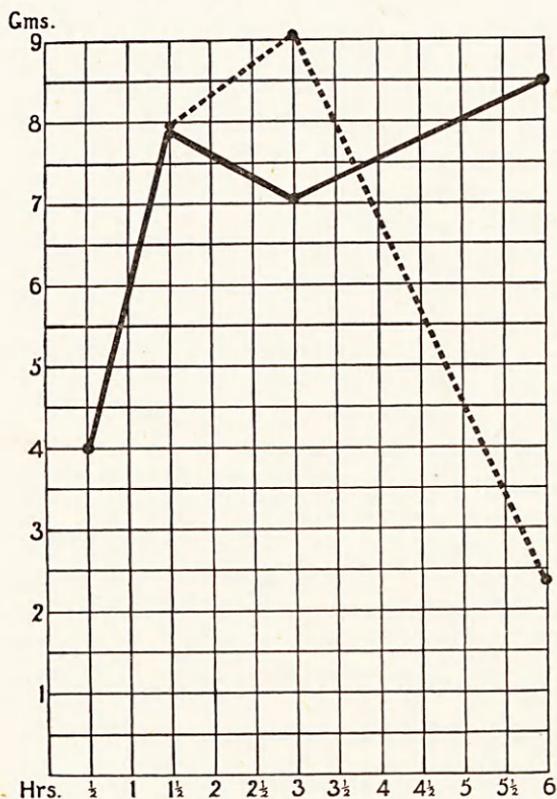
Total excretion in 6 hours = 25 grms. Rate of excretion = 70 per cent. in 3 hours.

was excreted shortly after the injection, and that the maximum weight excreted was obtained between the second and third photographs—that is, between one and a half and three hours from the time of the injection. Thereafter the weight excreted gradually fell, and either no drug, or only a trace, was present in the urine twenty-four hours afterwards.

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Where the disease present in the urinary system was slight, or unilateral and fully compensated for by the other kidney, a similar series of readings was obtained.

In cases where a clinical diagnosis of advanced disease in the urinary tract suggested the likelihood of diminished renal



### Renal Tumours

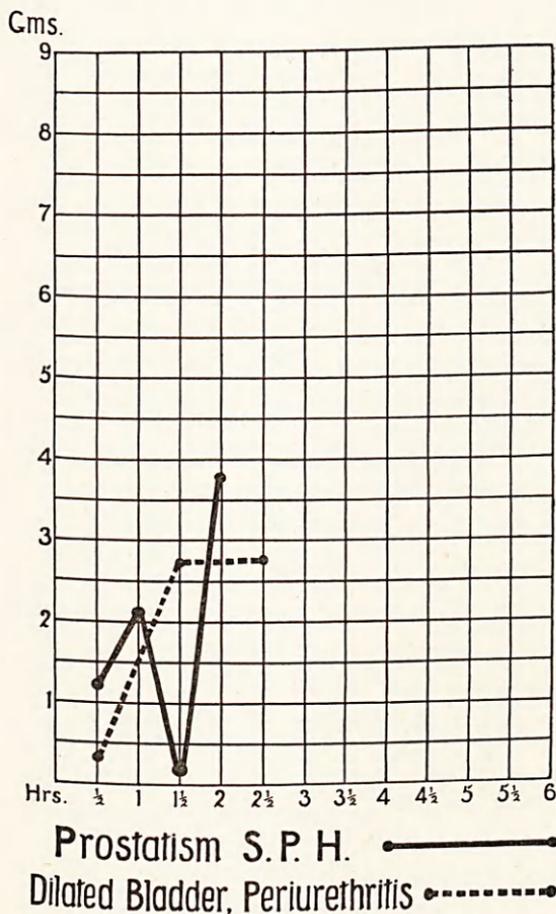
GRAPH 2.—NORMAL UROSELECTAN EXCRETION CURVE.

Cases of renal tumour, in which the other kidney assumes sole function satisfactorily.

functional activity, and additional confirmatory evidence had been obtained from chemical examination of the blood and urine, it was found that the excretion of uroselectan half an hour to an hour after the injection was extremely low, and that a slightly improved reading was obtained in three and a half hours. Still later, the amount excreted again fell, small quantities still being present in the urine twenty-four hours

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afterwards. In one case a delayed excretion occurred, followed by a considerable rise in the weight of drug excreted three and a half to six hours after the injection.



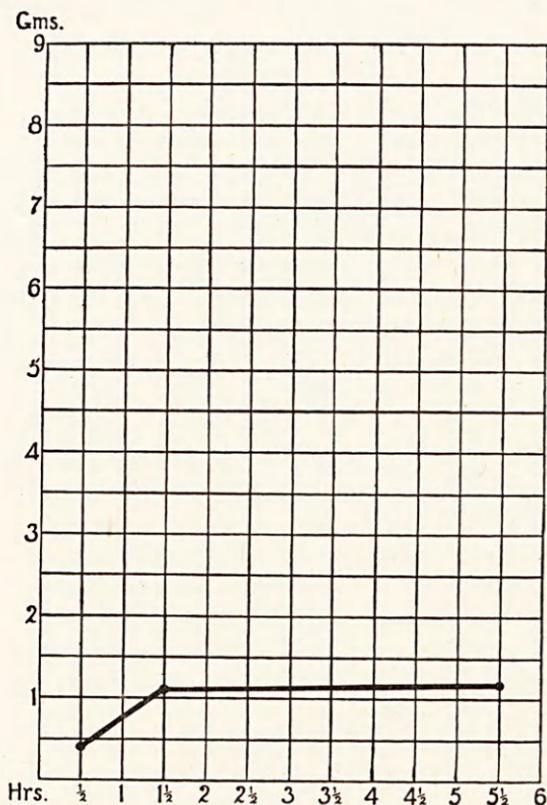
GRAPH 3.—LOW UROSELECTAN EXCRETION CURVE.

Cases of backward pressure in upper urinary tract, from over-distended bladder.  
Total excretion low. Rate of excretion uniformly low.

**Its Value as a Test of Renal Functional Activity.**—The series of cases investigated included those of both medical and surgical interest. From the medical side of the hospital, a limited number of cases of chronic nephritis and subacute parenchymatous nephritis were examined. These patients had been fully investigated, both from a clinical standpoint and

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by the standard clinical laboratory biochemical tests, including blood - urea and urea - output estimations. Their further investigation by uroselectan was carried out in order to determine what value the drug had as a test for renal functional



### Chronic Nephritis

GRAPH 4.—LOW UROSELECTAN EXCRETION CURVE.

Case of chronic nephritis, in which all routine renal function tests have given low results.  
Total excretion = 3.3 grams. Rate of excretion = uniformly low.

activity in well-established nephritic disease, when compared with such standard methods.

The average total excretion of uroselectan in normal functional activity during the period of observation of six hours is 25 grams. Seventy per cent. of this amount appears in the urine passed in the first three hours of the period of observation, of which 15 to 20 per cent. in the first half hour. The graphic

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representation of the figures thus obtained gives a normal uroselectan excretion curve. In the cases of chronic interstitial nephritis a uniform low excretion of uroselectan was found. In a severe case of chronic interstitial nephritis the total amount of drug excreted is extremely small—only about 3 grams ; that is, 12 per cent. of that excreted in health. Thus an important factor in the establishment of this method for use in the estimation of functional activity is brought out, viz., a high level is reached where that is normal and a low level where function is grossly impaired. There is thus room for wide variation in the figures obtainable during a uroselectan investigation carried out on those cases which occupy an indefinite category between genuine health and well-established disease.

The surgical cases included patients suffering from obstructive lesions of the lower urinary tract, in whom it was essential to obtain an indication of the effect of the condition on the functional activity of the kidneys above. Of necessity the effects of the lesion, from backward pressure or from ascending infection, were bilateral. In such cases a tentative opinion as to the state of the kidneys could be made following clinical examination and routine estimations of the blood-urea and urea-output in the urine. In advanced cases of prostatic hypertrophy with backward pressure, the tentative diagnosis of co-existing chronic nephritis, with dilation of pelvis and ureters, was borne out from the nature of the uroselectan excretion curve and urograms.

In certain cases, however, while it is known that an obstructive lesion is present in the lower urinary tract, which is liable to affect both kidneys above by its effect of backward pressure, the patient may be seen in a stage before any very apparent damage has been done. In those cases the uroselectan excretion curve commences at a low level, but shows a marked latent rise occurring three and a half hours or more from the time of the injection, and it is suggested, when such a uroselectan excretion curve is found, that, though function is impaired, the kidney is capable of returning to normal if the opportunity is given. Clinically this aspect has been substantiated from the extremely satisfactory progress of such patients following operation.

In many cases of surgical disease the nature of the pathological process brings up for consideration the question of nephrectomy. In such a case no satisfactory prognosis can be given unless it is known that the other kidney is able

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to assume entire functional activity. In certain of those cases the diseased kidney is already so destroyed that its neighbour has undergone compensatory hypertrophy. The use of uroselectan will indicate how far this compensation has met with success. Success implies a normal excretion curve.

### DISCUSSION.

*Dr Duncan M. Morison* said—The demonstration that Mr Wade and Mr Band have given is remarkably clear and convincing despite the fact that probably many of the photographs have lost definition through the process of reproduction. Mr Wade has clearly outlined the advantages of employing uroselectan in certain types of cases which previously could not be fully determined. It is of particular interest that Mr Wade and Mr Band have evolved the idea of utilising the excretion of uroselectan as a means of estimating renal function. The value of such a method can be fully appreciated, though at present the test involves somewhat precise laboratory technique.

*Dr C. P. Stewart* said—As a biochemist I am very much interested in this work of Mr Wade and Mr Band from the point of view of functional tests, because it has always struck me in working in the laboratory that no renal function test at present employed is of any use in the diagnosis of relatively mild kidney damage. I think it is probably fair to say that even with the most accurate tests we have (amongst which are the phenolsulphophthalein and the urea concentration tests), it is impossible to demonstrate damage definitely unless at least 50 per cent. of the kidney tissue is out of action. The uroselectan method seems to me a possible (not probable as yet) one by which we may be able to detect kidney lesions of a milder character, which will mean a very important advance in diagnosis. I think, therefore, that research should be directed not towards the investigation of very severe cases of nephritis, but towards the investigation of milder cases, in order to see whether those relatively mild cases show, in the excretion of uroselectan, either deficiency in amount or abnormality in regard to time, as compared with normal excretion. That seems, to my mind, the line of advance.

It is unfortunate that uroselectan is an expensive drug—and any investigation along these lines would involve the examination of large numbers of cases. I think, however, that as the demand for the drug becomes greater, the price will become less. There is also the possibility of recovering the drug from the urine in a form in which it may be used again.

The method of uroselectan estimation is very simple—it might be classed under “sideroom work.” The method which we have used for the estimation consists in slightly acidifying the urine—which

## Uroselectan : Excretion Urography

converts the sodium salt uroselectan to the corresponding, almost insoluble acid—filtering off the precipitate, drying it, and weighing. The quantities dealt with are so considerable that a very fine balance is not needed, and sufficiently accurate results are obtained with great ease.

The only difficulty is in interpreting the results. It does not follow that when the test has been fully worked out the analytical results will be treated as Mr Band has done to-night. He has plotted his curves from the total amount of drug in the sample of urine passed, and one may have to consider instead, or as well, the concentration of drug in the urine, because one finds a considerable variation in what may be regarded probably not so much the power of the kidney to secrete uroselectan as its power to secrete water. We would have to take that into consideration in the future, and it might be found desirable to alter the present technique of the test, giving water to promote secretion of urine. One is reminded of the development of the phenoltetrachlorphthalein test of hepatic function. In its original form the output of dye was estimated in the fæces; then the time required for the dye to appear in the duodenum became the criterion, but both these methods were able to detect only gross damage to the liver. More recently Rosenthal in America has measured the rate of its disappearance from the blood, and his results are more reliable. In animals, at any rate, he has been able to detect definitely the removal of 12 per cent. of liver tissue, and from the blood concentration curves he has been able to calculate the amount of liver tissue removed with a fair approximation to truth. It seems possible that the uroselectan test may develop along these lines.

*Dr Eason, Mr J. J. M. Shaw and Mr Struthers* also spoke.

*Mr Wade* (in reply) said—I do not propose to make any detailed reply as Mr Band is following me. I would like, however, to thank the Society for the way in which they have received our paper. We are enthusiastic on the subject and I have formed the impression that the Society is in agreement with us in considering uroselectan as a method of clinical diagnosis which in the future will prove most helpful.

The surgeon is always very keenly interested in the functional power of the kidneys, especially when any operative procedure has to be carried out on the urinary tract. This can be illustrated in two ways. Before any surgeon will carry out an operation on a kidney, he must first know that two kidneys exist and that the functional activity of the other organ is good. Even although painless, a cystoscopic examination must of necessity be usually an eminently unpleasant procedure, but up to the present I know of no method whereby you can demonstrate the presence of two kidneys and estimate their relative functional activity without carrying out a cysto-

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scopic examination and passing ureteral catheters. By excretion urography, as we have demonstrated, it will be possible in many of these cases to gain the desired information without a cystoscopic examination.

Again the surgeon is frequently very keenly interested in chronic renal disease, especially when he has to treat a case of prostatism with backward pressure. In these circumstances the problem is essentially a renal one, and on the state of the kidneys the success, or otherwise, of the operative treatment carried out will largely depend. To determine their functional activity has been difficult, for in the majority of them cystoscopic examination with ureteral catheterisation is impossible, and where possible is usually contra-indicated. We hope in these cases to gain much information of value from excretion urography, which will give us an idea of the degree of damage the backward pressure has produced and help us to estimate not only the renal function, but also to a certain extent the renal reserve.

*Mr David Band* (in reply) said—Undoubtedly uroselectan was primarily investigated for its use in cases of surgical conditions of the urinary tract in which one kidney had to be dealt with and treated by operation, provided always the other could be proved healthy and efficient to carry on renal function. Thus we were led to its use from a renal function standpoint. For purposes of control, cases of established nephritis were examined and the use of uroselectan compared with the routine renal function tests, and it was in this part of the investigation that the problem of nephritis, parenchymatous and interstitial, made itself obvious. We were struck with the fact that possibly uroselectan may aid in the definition of the various types of nephritis which may be rendered more apparent by this method. This aspect of the use of uroselectan has just been touched on and no more. Otherwise gross impairment of function or loss of function is estimated both photographically and chemically by the use of uroselectan. The estimation of the total excretion of uroselectan in the urine indicates how both kidneys are performing functionally—and if there is only one functional kidney, its degree of efficiency.

This brings me to the very great debt we owe to Dr C. P. Stewart for his sympathetic and practical help in dealing with the biochemical aspect of this work. We are particularly grateful for the simple method he has evolved for estimating the weight of the drug excreted in the urine.

Mr Shaw has mentioned in his remarks a very important thing. The use of uroselectan as an aid to diagnosis has only become possible because of the accurate knowledge of pathology to which we are heirs. Without that fundamental knowledge no diagnostic method depending on functional activity can have any value.