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# Intravenous Urography by Means of the Sodium Salt of 5-Iodo-2-Pyridon-N-Acetic Acid\*

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IN 1923 ROWNTREE AND HIS CO-WORKERS (1) of the Mayo Clinic were the first to attempt to visualize the urinary tract by means of the intravenous injection of a 10 per cent solution of sodium iodide and also by the oral administration of that salt. The urinary bladder, and in some cases the pelvis and ureter, could be visualized.

The following year Rosenstein and von Lichtenberg (2) reported at the urologic congress in Berlin their results, repeating the work of Rowntree and his co-workers with sodium iodide but in conjunction with perirenal pneumoradiography.

In the same year Volkmann (3) reported his observations with the use of different halogen compounds; he found the intravenous injection of a 10 per cent solution of sodium iodide to be best.

In 1927 Lenarduzzi and Pecco (4) tying off the ureter and injecting sodium iodide intravenously in animals, obtained positive roentgenograms of the kidney, pelvis and ureter.

Hryntschak (5) at the urologic congress in Berlin in 1928 and in a publication in 1929 (6)

reported his results with the use of a large series of bromine and iodine compounds, aromatic in nature, carrying out about 200 animal experiments. Neither the names nor the chemical formulas of the substances used by him are stated. In his publication the only detail of the chemical composition of three of them applied and numbered 13, 27 and 48 is that the first two were iodine and the last a bromine compound. In some of his experiments he simultaneously used an adjuvant, such as caffeine, urea, pituitary extract and atropine, to influence excretion and the dynamics of the pelvis and ureter. He obtained some positive results in animals and in a female patient. In his conclusions he stated that although, two and a half years ago, he had been able to obtain useful intravenous pyelograms in a few cases, the method had by no means met the conditions set forth by him. He, however, expressed the hope of accomplishing his aims by continued investigations.

Ziegler and Köhler (7) reported at the urologic congress in Munich in 1929 and in a publication in 1930 (8) their results with the oral administration of 10 Gm. of sodium iodide and 10 Gm. of urea in milk in conjunction with pressure applied over the sacro-iliac articulation through the abdominal wall by means of a special apparatus.

All investigators who utilized the halogen compounds found that they could not be given in sufficiently large quantities to be of practical value in visualizing the urinary tract, though under favorable conditions in occasional cases, the kidney, pelvis, calices and ureters could be made out.

Roseno (9) was the first to achieve practical results by means of the intravenous use of a

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This work was carried out with the aid of a grant from the Emanuel Libman Fellowship Fund. It was initiated at the Staedtisches Krankenhaus, Altona, Germany (Prof. Dr. Leopold Lichtwitz, director), continued in the urologic service of the St. Hedwig Krankenhaus, Berlin (Prof. Dr. Alexander von Lichtenberg, director), and has since been pursued in the urologic service of Dr. Beer, the radiologic department of Dr. Jaches, and the Chemical Laboratories of The Mount Sinai Hospital, New York.

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combination of sodium iodide and urea, called "Pyelognost" [NaI, CO(NH<sub>2</sub>)<sub>2</sub>]. According to some reports it is stated that the substance employed by him is at times associated with reactions. The visualization of the urinary tract, however, is satisfactorily accomplished. Roseno also stressed the functional aspects of the problem. He gave an account of his investigations at the urologic congress in 1928. In 1929 he made a further presentation of his work before the urologic congress in Munich and published an extensive report of the method and the results. In the course of a discussion at the time of the first presentation, von Lichtenberg (10) expressed himself pessimistically concerning the possibility of intravenous urography.

This work (11) was begun with N-methyl-5-iodo-2-pyridon, synthesized by Professors Binz and R ath.

### Formula 1

At the wish of Professor Binz, the efficacy of this substance in the therapeutics of streptococcus was under investigation in the clinic of Professor Lichtwitz in Altona, Germany. The study of its excretion through the kidney and into the bile and its iodine content (54 per cent) led to the thought that the substance might be applicable for roentgenologic purposes. Experiments on rabbits demonstrated the fact that the kidney parenchyma and urinary bladder could be visualized after the intravenous injection of the drug; the pelvis and the ureter, on the other and, were poorly seen. Ligation of the latter, however, did bring the upper tract well into view. The gallbladder was not visualized. Simultaneous studies of its excretion, limited to determinations of the iodine component, revealed about 75 to 80 per cent of the injected iodine in the urine in from twelve to sixteen hours.

Concerning the toxicity and tolerance, I found that 0.2 Gm. per kilogram of body weight could be administered intravenously to the rabbit without any demonstrable ill effects; 0.33 Gm. per kilogram, however, produced transient generalized disturbances. On the basis of these observations, one could theoretically give to a 60 kilogram individual 18 Gm. of the substance as a maximal dose. Because of marked individual differences in man, the quantity administered was far below the calculated one. The adult received 6 Gm. of substance. Headache, nausea, vomiting, generalized discomfort, and in two cases transient diplopia were disturbing factors. The oral and rectal administration of this drug also yielded similar roentgenologic

results and toxic manifestations. In all cases the urinary bladder was seen. The kidney parenchyma itself appeared to stand out more in relief. In man, the upper urinary tract was outlined only after producing a temporary artificial obstruction in the ureter by means of a bougie at the time of maximal excretion. The attained results, though not sufficiently good for practical purposes, were encouraging and pointed to the possibilities of further development.

The experience with this substance brought out the need for a modification, possessing better tolerance and greater solubility, so that a larger dose could be administered. In this way, a higher concentration of the excreted iodine component could be hoped for. The observation of double vision and the possibility that the methyl radical might be responsible were noted. At a conference between Professor Binz and his associates, Professor Lichtwitz and me, these results and observations were presented. Professor Binz, who followed these investigations with great interest, said that he felt that these needs could be fulfilled. He supplied us with several compounds which he states belonged to the selectan group, synthesized by him and Professor R ath at an earlier date, and which now were prepared in larger amounts for our purpose and studied with the aid of Dr. Hillgruber (12). One of them, insoluble in water, was soluble in very strong alkali. It could not be given intravenously and was therefore administered by mouth to a dog and in gelatinum duratum capsules to a male patient at Professor Lichtwitz's clinic with negative results. Professor Binz had furnished me with this drug one week before the conference mentioned.

Thereafter I continued the work in the urologic service of Professor von Lichtenberg in Berlin. To eight patients, 7.5 Gm. of the original substance, N-methyl-5-iodo-2-pyridon, were given by mouth with the already described reactions. The outline of the bladder was seen. Only in one case, that of a stone obstruction of the ureter about one inch below the ureteropelvic junction, was a useful roentgenogram of the pelvis and ureter above the stone obtained. The insoluble compound used at Professor Lichtwitz's clinic was now tried again at Professor von Lichtenberg's division with the same negative results. Another compound of this group, having a higher iodine content and a sodium acetate radical substituted for the methyl, was then tried. Though more soluble than the previous one, it was still unsuitable for intravenous application. The oral administra-



**Fig. 1.** Right-sided bifid pelvis in a man, aged 20; 40 Gm. of substance.

tion was likewise inadequate because of the poor absorption by the gastrointestinal tract. When a preparation having a lower iodine content and the sodium acetate group substituted for the methyl was furnished by Professor Binz, the clinically applicable and successful substance, 5-iodo-2-pyridon-N-acetate of sodium, was finally obtained. This compound differs from the original only in the substitution of sodium acetate in place of the methyl group. It was fortunate that this preparation, introduced abroad as "Uroselectan," proved to be free from all accompanying reactions, to have quite an extraordinary affinity for the kidney, and to be very soluble in water. These needs were therefore completely fulfilled and satisfactory roentgenograms could now be obtained, as reported by me at the urologic congress in Munich in 1929 (11). Professor von Lichtenberg, who took up the subject directly after me, stated that he considered that which had been communicated a significant advance (13). Some weeks later, my paper was published in the *Klinische Wochenschrift* and was followed by another contributed by Professor von Lichtenberg and me (14).

The 5-iodo-2-pyridon-N-acetate of sodium (42.2 per cent iodine) is nontoxic, very soluble in water and neutral in its reaction.

### Formula 2

The iodine in the molecule exists in a stable organically bound state. Neither in the injected solution nor in its excreted form is iodine present in ionized state. These facts, despite the relatively large quantity of iodine in the amount of this substance that can be administered with impunity, would seem to explain, at least empirically, why iodism has never been observed. The tolerance for this compound is exceedingly great. A rabbit would receive 3 Gm. per kilogram of body weight without any harm. With the latter dose as a basis of calculation, it follows that 180 Gm. of the substance, or, in terms of iodine, 75.6 Gm., can be theoretically administered to a 60 kilogram person. The substance is excreted as such through the urinary tract, being recovered from the urine as the light yellow, insoluble acid on the addition of a dilute mineral acid. Because of the relative simplicity and accuracy and because I found it to be of assistance in the evaluation of the roentgenologic results, it has been considered feasible to apply a quantitative determination of this insoluble, precipitated acid-form as a basis for a test of renal function.

The recovery and identification of the excreted substance have been established in the following manner:

The addition of a dilute mineral acid — HCl or  $H_2SO_4$  — to urine containing the excreted soluble salt of the 5-iodo-2-pyridon-N-acetic acid results in the precipitation of the insoluble acid form. The precipitating agent should be added gradually until no more precipitation occurs. After one hour's settling the insoluble acid is filtered by means of suction on a Buchner funnel and is washed free from the precipitating agent with distilled water, as determined by the silver nitrate test for hydrochloric acid or the barium chloride test for sulphuric acid. The residue is dried to a constant weight at  $80^\circ C$ . For identification, a variety of samples of the urinary precipitate were analyzed for their iodine and nitrogen content; their acid equivalents and melting points were also determined. These were simultaneously controlled by comparison with similar determinations on substance precipitated from clean manufacturer's samples of the sodium salt. The results obtained are presented in Table 1.

Another series of melting point determinations (uncorrected) on twenty-four individual



**Fig. 2.** Intravenous urogram to exclude right urinary calculus, in a girl, aged 8 years. Slight dilatation of right kidney pelvis and blunting of calices (pyelitis). 25 Gm. of substance.

urinary precipitates yielded the following results: four times 236°C, five times 237°, four times 238°, four times 239°, four times 240°, two times 241°, one time 242°C. The control of precipitates from two manufacturers' samples simultaneously determined were 239° and 240°C. (The acid melts with decomposition. The determinations represent melting points of samples of different

urines and colors, varying from light yellow to brown, made with the same rate of heating.)

The brown color of the precipitate, recovered from some of the urines, is believed to be due to the admixture of urinary pigment; this is demonstrated as follows:

1. If animal charcoal is added to boiling water containing the brown colored acid-form in solution, the recrystallized substance no longer is brown; it now is light yellow, resembling pure precipitate.

2. Conversely, when a manufacturer's sample of the solution of a sodium salt is added to normal urine and then the acid-form precipitated from it (a procedure analogous to that of the recovery of the substance from the urine), the precipitate obtained is then brown. The same pure solution, however, with the addition of acid alone, yields a light yellow precipitate.

3. Qualitative analysis of the precipitate, following the scheme for the examination of urinary calculi, is negative for nonpigmentary urinary constituents.

The next consideration is whether the precipitation is quantitative. To determine this, two-hour urine specimens of patients injected with a known amount of the sodium salt were collected. On each specimen two simultaneous determinations were made, one for its iodine content by a sodium carbonate and sodium nitrate fusion method; the other by precipitating the acid and determining its constant weight. Since the acid by molecular weight contains 45.5 per cent of iodine, the quantity of iodine found by multiplying the weight of the precipitated acid by 45.5 should correspond to that of the total iodine de-

**TABLE 1**

*Analysis of Urine Containing Excreted Soluble Salt of 5-Iodo-2-Pyridon-N-Acetic Acid*

Sample	Color	Nitrogen Determination Micro Dumas Method	Iodine Determination Na <sub>2</sub> CO <sub>3</sub> + NaNO <sub>3</sub> Fusion Method	Iodine Determination Carius Method	Acid Equivalent	Melting Point Uncorrected
Manufacturer sample	Light yellow white	4.99%	46.77%	46.37%	277	235
Urine sample 1	Light yellow	5.23%	46.23%	46.4%	280	234 white
Urine sample 2	Slightly brown	5.04%	46.31%	47.98%	Not done	Not done
Urine sample 3	Brown	5.29%	46.65%	50.1%	279.5	235

Note: The determinations in columns 4, 5 and 6 represent averages. Theoretical iodine content, 45.5%; theoretical nitrogen content, 5.02%; theoretical acid equivalent, 279.

terminated directly from the urine. Tables 2 and 3 illustrate the results obtained.

Comparing columns five and six, that is, the calculated iodine values with the independent iodine determinations, one observes a constant, close agreement. The reason for the relatively small differences between the calculated (the lower values in column 5) and the quantitatively determined iodine (column 6) can be explained by the presence of the precipitated acid-form in the filtrate as a result of its slight solubility. It has been found that the iodine content of the filtrate plus the calculated iodine compare very favorably with that of the quantitatively determined iodine. There were isolated cases in which there were discrepancies, believed, however, to be due to an error in the technic of iodine determination. This phase is being investigated further.

Finally, in order to establish the percentage excretion of the iodine and of the precipitated acid, it is necessary to determine the actual amount of injected salt in terms of the iodine component, and also in terms of the precipitated acid. It is obvious that, in the preparation of the solution, losses will occur. The following are the factors and sources of error which should be considered:

1. Apothecary scale used — about 2 per cent.
2. Loss due to the moisture content of the salt — about 3 per cent.
3. Loss through double filtration of the solution — about 3 per cent.
4. An indeterminate loss due to the impossibility of a quantitative transfer of the 40 per cent solution from the glassware used in its preparation.

**TABLE 2**  
*Quantitative Determination of Urine Specimen\**

Urine Specimen	Volume Cc.	Specific Gravity	Weight of Precipitated Substance Gm.	Iodine Calculated from Substance Gm.	Iodine Determination of Urine Gm.
2 hours	850	1.014	19.79	0.004	9.6295
2 hours	200	1.034	9.395	4.275	4.76
2 hours	120	1.032	4.604	2.095	2.4578
2 hours	91	1.024	1.792	0.8154	1.0396
2 hours	93	1.014	No precipitate		
2 hours	150	1.008	No precipitate		
Total grams			35.581		17.889
Percentage of substance excretion					91.23
Percentage of iodine excretion					95

\*A woman, 25, with good renal function; 50 Gm. of Substance injected.

**TABLE 3**  
*Quantitative Analysis of Urine Specimen in a Case Presenting Poor Function.*

Urine Specimen	Volume Cc.	Specific Gravity	Weight of Precipitated Substance Gm.	Iodine Calculated from Substance Gm.	Iodine Determination of Urine Gm.
2 hours	335	1.019	6.70	3.05	3.12
2 hours	260	1.022	6.10	2.78	2.84
2 hours	145	1.025	3.86	1.76	1.82
2 hours	100	1.025	3.56	1.62	1.79
2 hours	138	1.022	2.71	1.23	1.26
Total grams			22.93		10.83
Percentage of substance excretion					53
Percentage of iodine excretion					52

A woman, aged 42; 55.5 Gm. of Substance injected.

5. The difference in molecular weight of the sodium salt (301) and the precipitated acid (279), 7 per cent.

6. Loss due to the solubility of the precipitated acid, a fraction of 1 per cent.

Thus, to establish the extent of inaccuracy in the quantity of iodine actually administered as against its theoretical content, a solution as for injection was prepared. Its actual iodine content, determined chemically, was found to be on the average 89 per cent of the theoretical. This figure can be designated as "the iodine factor."

The method for establishing the "precipitated acid factor" was similar to the foregoing except that the prepared solution was then distributed among normal urines so that each two-hour specimen resembled approximately in its volume and substance content those excreted by patients injected with different amounts of the solution of the sodium salt. (In carrying out the renal function test by means of the quantitative estimation of the excreted substance, five or six two-hour urine specimens are collected.) Table 4 demonstrates the average established factor; namely, from 77 to 78 per cent.

In other words, to establish the basic acid value, 22 per cent is to be deducted from the theoretically administered weight of sodium salt when calculating the percentage of excretion in terms of acid substance. Similarly, 11 per cent is to be deducted from the theoretical iodine content of the injected sodium salt in order to estimate the percentage excretion in terms of the iodine component.

These aspects being clarified, it now becomes evident that quantitative determinations of the excreted substance in terms of the precipitated acid can form the basis of a test for renal function. (The quantitative estimation of the precipitated acid has been chosen in preference to that of the iodine because of its relative simplicity and reliability.) Normally about 85 to 95 per cent of the substance can be recovered from the urine within from eight to twelve hours after the injection. In two cases 98 per cent was recovered. From that period on, under normal conditions, as a result of the solubility of the precipitate, which during this stage occurs in such small amounts, its presence can be detected only by an iodine determination method. It is thus found that the excretion of very small amounts of the substance goes on from three to

**TABLE 4**  
*Corrected Acid Substance: Factor for Calculating Percentage of Excretion*

Druggist Scale			Chemical Scale	Per Cent of Loss
1. 40 Gm. of substance			39.523 Gm.	- 1.19%
2. Drying			38.2 Gm.	- 3.35%
3. Solution of 100 cc. filtration (Loss on filter paper = 1.125 Gm.)				- 2.95%
4. Aliquot for iodine determination, 4 cc. of total 96 cc.				
5. Distribution on basis of average urinary output by volume and by weight				
Specimen	Volume Cc.	Containing Approximately		Gm. Precipitated Acid Recovered
A. 2 hrs.	550	1/2 solution precipitated and filtered		16.96
B. 2 hrs.	175	1/4 solution precipitated and filtered		8.19
C. 2 hrs.	150	1/10 solution precipitated and filtered		3.515
D. 2 hrs.	90	1/20 solution precipitated and filtered		<u>1.555</u>
				29.850
				<u>1.24</u>
				31.090
				<u>31.09</u>
				40.0 = 77.7%
				<u>31.09</u>
				39.525 = 78.66%

This factor is variable within narrow limits depending on points enumerated

ten and perhaps more days after the injection. For example:

- First twenty-four hours, 850 cc., 0.3195 Gm. of iodine.
- Second twenty-four hours, 1,200 cc., 0.0218 Gm. of iodine.
- Third twenty-four hours, 1,400 cc., 0.0036 Gm. of iodine.
- Fourth twenty-four hours, 1,400 cc., none.

From the results already obtained, it is seen that the normally functioning kidney possesses the ability to excrete this substance in a relatively large quantity within a given short period. This may be characterized as the thrust excretion ability of the normally functioning kidney," present during the first two hours. To illustrate, from about 45 to 65 per cent of the total precipitable acid is recovered during the first two hours, about 20 to 33 per cent during the next two, and the remainder during the subsequent hours. Figure 3 illustrates the curves of excretion in a normally functioning and in a poorly functioning kidney.

Aside from the dose administered and the extrarenal factors influencing renal secretion, the thrust excretion ability of the normally functioning kidney plays a vital role in determining good roentgenologic visualization. During the later periods, in spite of the fact that the substance is still being excreted, poor or no visualization is obtained. Good visualization is dependent on a definite concentration of the shadow-producing element determined by the factors enumerated. When the additional mechanism of obstruction is present, visualization may be had although the normal height of excretion is absent, provided

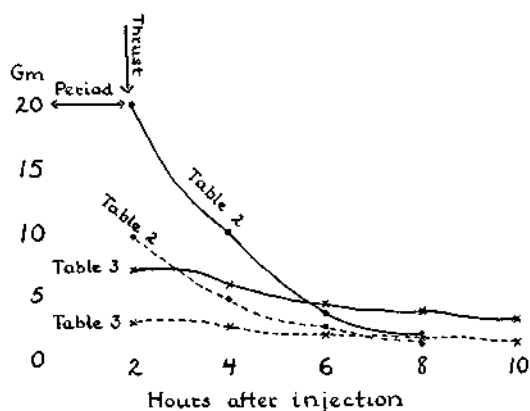


Fig. 3. Excretion of normal and of abnormal kidneys, 50 Gm. dose, tables 2 and 3: solid line, weight of precipitable acid excreted, in grams; broken line, weight of iodine excreted.

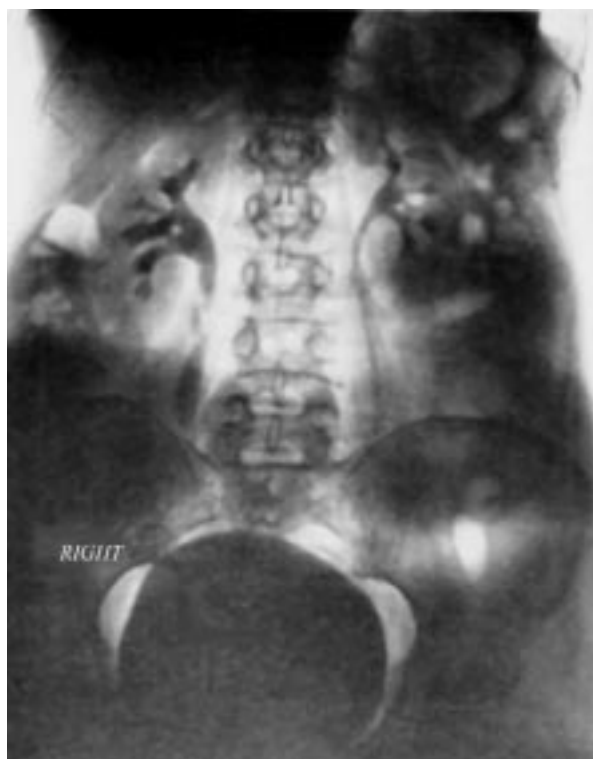
excretion takes place. On the other hand, under the same circumstances but with normal excretion, intensification of the shadow results. Thus, in a general way, it may be said that visualization, poor visualization, or no visualization is dependent on the functional activity of the kidney, in other words, its concentrating ability, as well as on extrarenal factors.

However, of the 122 cases studied at The Mount Sinai Hospital, one unexplainable exception has been noted. A woman, aged 54, with pain in the back and left kidney region, had an intravenous urogram done, June 2, 1930. Visualization was absent on the right side in all plates. The left urinary tract appeared normal. A large shadow of what looked like kidney was seen in the right upper quadrant. A faint curvilinear shadow in the bony pelvis on the right side was also observed (ureter?). June 4, cystoscopy and a right retrograde pyelogram revealed normal indigo carmine from both sides as well as the presence of a right sacral kidney. In order to gain an insight into this discrepancy, another intravenous urogram was repeated about two and one-half weeks later. The right kidney pelvis again was not visualized though the ureter could be definitely seen. This example serves to illustrate the need for caution in passing final judgment with absolute certainty on the functional state of the kidney by this method alone.

Moreover, it is also important to bear in mind that the functional activity of the kidney may be temporarily or permanently inhibited, and that the mere nonvisualization at a given examination does not necessarily signify permanent renal damage. The following case is illustrative:

Cystoscopic examination of a man, aged 41, was done, and a left retrograde pyelogram was made. At that examination normal indigo carmine excretion from both ureters was observed. The left pyelogram was normal. Following this examination, hematuria and marked pain in the left loin set in and persisted for about one week. When both symptoms had subsided, intravenous urography was done. Absent visualization of the pelvis and ureter with good kidney outline on the left side and a double pelvis and forked ureter on the right were noted. However, another intravenous urographic examination, about three months later, revealed a normally functioning and appearing left urinary tract in addition to the previous observations on the right; in other words, a case of temporary functional inhibition following retrograde pyelography.

Therefore, to evaluate intravenous urography and to interpret correctly the results ob-



**Fig. 4.** Intravenous urogram to exclude a right renal neoplasm in a woman, aged 48. Demonstrates ptosed kidney, ureteral kink with dilatation. 50 Gm. of Substance.

tained from it, it is of paramount importance to consider this method as an excretory one and to bear constantly in mind the processes occurring in the renal and extrarenal systems.

As an adjuvant in assisting one to interpret and to evaluate the radiologic results, it is felt that simultaneous determinations of the substance recovered in the urine as described are sometimes helpful. It is not assumed that this test is superior to other tests of renal function; but, in view of its relative simplicity and the fact that it forms part of the intravenous examination, its use is advocated solely as a confirmatory aid in the interpretation of the intravenous urogram.

The blood urea, phenolsulphonphthalein, the indigo carmine, and the dilution and concentration tests are of great assistance in establishing the contraindication to the application of this method in a given case of bilateral advanced kidney disease. Where the blood urea is high and the concentrating power of the kidney poor, the method yields few anatomic data and becomes not only superfluous but perhaps attended by danger. For information of renal function under such circumstances, more simple and less expensive means, such as the blood urea and phenol-



**Fig. 5.** Marked dilatation of ureter, kidney pelvis and calices in a boy, aged 10 years. 25 Gm. of substance. (Case of Drs. Leopold and Stewart of the Lenox Hill Hospital, New York.)

sulphonphthalein determinations, serve the purpose.

In addition to anatomic data derived by this physiologic procedure, another vitally important phase of the urinary tract that can be studied without the introduction of instruments is the functional dynamic activity of the pelvis, ureter and bladder.

#### Method of Administration

For an adult, the usual dose, 40 Gm. of substance, is added in small quantities to doubly distilled water, which has been previously warmed to a moderate degree so that the resultant volume is about 100 cc. Stirring aids the process of dissolving. The solution is filtered twice through ordinary filter paper into a 250 cc. clean Erlenmeyer flask, which is preferably stoppered with fresh wax paper. It is then sterilized in a water bath for half an hour or autoclaved at 15 pounds pressure for twenty-five minutes. The syringe method, in preference to that of the gravity, is chosen, in the feeling that it is more apt to avoid the possibility of a foreign



**Fig. 6.** Same patient as in figure 5, with bladder partially empty, now demonstrating stricture (congenital) ureterovesical junction with marked dilatation of lower part of ureter, which was hidden on previous film by distended bladder. (Case of Drs. Leopold and Stewart of the Lenox Hill Hospital, New York.)

body reaction. A sufficient number of record syringes plus injection needles is sterilized in distilled water. The injection is done in two or three stages at intervals of from three to five minutes. The first roentgenogram is usually taken about fifteen or twenty minutes after the last injection. The subsequent three plates are made about twenty-five minutes apart. When functional disturbances are present, it is advisable to have additional later plates, at approximately one to three hour intervals, taken to determine definitely the absence of visualization, or the presence of late visualization. Particularly in those cases in which there is the added factor of obstruction — ureteral stone, prostatic enlargement, or ureteral strictures — there may be a late, but good or poor type of visualization. Experience alone will guide one in the interpretation of the plates, as well as the number of plates that may be necessary.

An added factor of great importance which has improved the results as far as density, clarity and consistency of shadow are concerned has been the



**Fig. 7.** Impassable stone obstruction, lower third of the left ureter, in a boy, aged 19. Intravenous urogram — good function — showing dilated ureter, pelvis and calices above stone. Right side normal. 50 Gm. of substance. Arrow points to stone.

application of a moderate degree of compression by means of an air-inflated rubber balloon (basket ball bladder), maintained over the urinary bladder region for from five to ten minutes prior to and during the taking of each roentgenogram. It is also advisable to take one or two plates without compression several minutes after any of the preceding ones and to have the patient empty his bladder after the second or third plate.

From studies controlled on the same patient with different doses several days apart, the impression gathered is that the administration of a 50 to 60 Gm. dose of substance in 40 per cent concentration, given in divided portions at about a ten-minute interval, yields denser and clearer roentgenograms. However, in view of the fact that this increased dosage means additional expense and that with a 40 Gm. dose sufficiently good practical results are usually obtained, particularly with compression, this change is at present advocated with some reserve. A 20 Gm. dose in adults has also given positive results.

The doses (40 per cent concentration) for children are as follows: 13 years of age, from 25 to 30 Gm.; 9 years and up, 25 Gm.; 6 years and up, 20 Gm.; 4 years and up, 16 Gm.; 2 years, 14 Gm.; 6 months, from 10 to 12 Gm.

### Reactions

During the injection the patients experience transient thirst and generalized warmth, particularly involving the face and bladder regions. Nausea and vomiting of transient duration have occurred twice. Occasionally there is pain up the arm of injection, which, however, disappears shortly afterward. Paravenous infiltration produces pain but no necrosis. Thrombosis at the site of the injection has not been observed. The urine does not reveal any evidence of renal damage by the substance.

### Application

The field of application of intravenous urography is evident whenever cystoscopy, ureteral catheterization or retrograde pyelography is dangerous or impossible for infectious or mechanical reasons, and whenever these procedures in general are indicated. The method, aside from offering a bilateral urogram, is also helpful in the presence of hematuria, in cases of implanted ureters, in children, and in individuals in whom instrumentation is taxing and harmful.

### Contraindications

Patients with uremia or latent uremia, as determined by the usual clinical methods, do not lend themselves to the application of this method. It is therefore wise to precede the examination by a determination of the blood urea. Experience with hyperthyroid patients is still wanting. The drug in cases of pulmonary tuberculosis does not seem to have any deleterious effect.

For pyeloscopic purposes this method will be feasible only when the density of the excreted substance is sufficiently great. When the function is poor, pyeloscopic results will be correspondingly deficient.

In my original paper published in the *Klinische Wochenschrift* in November, 1929, I (11) stated that the iodine component could not be demonstrated in the circulating blood. In the report by Heckenbach (15) from von Lichtenberg's clinic, Tourné and Damm have shown this to be incorrect. Studies which I was making at the time confirmed their observations. I could detect its presence in the blood as late as ten hours after a 50 Gm. dose. The stools and sputum of the patients injected show the presence of the iodine component in relatively small amounts. In the stool this element could be detected in a bowel movement as late as three to four days. It is also



**Fig. 8.** Ptosis of right kidney, dilatation of pelvis and twist of ureter behind pelvis, in a woman, aged 28. 50 Gm. of substance.



**Fig. 9.** Intravenous urogram of a woman, aged 45, showing nonfunctioning sacculated right kidney, proved at operation to be a tuberculous pyonephrosis. Retrograde pyelogram impossible. Ureter could not be entered. Left side normal. 40 Gm. of substance.

of interest to note that the skin of rabbits injected intravenously with a solution of the substance contained the iodine component.

In closing, I wish to express my deep sense of obligation to Dr. Emanuel Libman and to the directors of the Emanuel Libman Fellowship Fund with whose aid this work was made possible. I am extremely grateful to Professor Binz for his untiring help and cooperation. I am deeply indebted to Professor Lichtwitz for the invaluable aid and facilities which he placed at my disposal. I thank Professor von Lichtenberg for the opportunity and facilities, and also Dr. Rave, the roentgenologist of the St. Hedwig Krankenhaus in Berlin, for his aid. I am also thankful to Drs. Beer, Jaches, Gross and Sobotka, in whose departments at Mount Sinai Hospital this work was further developed, and to the Schering-Kahlbaum Corporation of Berlin, Germany, for its aid and supply of material. I am appreciative of the courtesies extended me by Drs. Bumpus and Alcock, and the

members of the Section on Urology of the American Medical Association.

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