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## Intravenous Urography (Swick Method)\*

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THE HISTORY OF THE DEVELOPMENT of this method and the chemical and pharmacologic properties of the substance employed are dealt with in greater detail in the paper by Dr. Swick presented before the Section of Urology.

Swick states that the present substance, prepared by Professors Binz and R  th, is nontoxic, very soluble in water, neutral in reaction and under normal conditions excreted as such through the urinary tract within eight to twelve hours to the extent of from 85 to 95 per cent. Iodism has never been observed. Its tolerance is exceedingly great. From about 45 to 65 per cent of the substance is normally excreted during the first two hours. For this reason, the urograms show their greatest intensity during this period.

The technic of administration is as follows: A 40 per cent solution is made up in doubly distilled water to a volume of 100 cc., filtered and then sterilized. Injection is done by means of several record hand syringes into the veins of the arm. The quantity administered is, for an adult, from 40 to 60 Gm. of the substance in a 40 per cent concentration. Younger persons receive proportionate doses. For children aged from 6 to 9 months the dose is 10 or 12 Gm. of



**Fig. 1.** — Normal urogram of an adult; 60 Gm. of substance injected.

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\*The original article is abbreviated in *The Journal* by the omission of six illustrations. This version has all 12 figures, as depicted in the author's reprints.

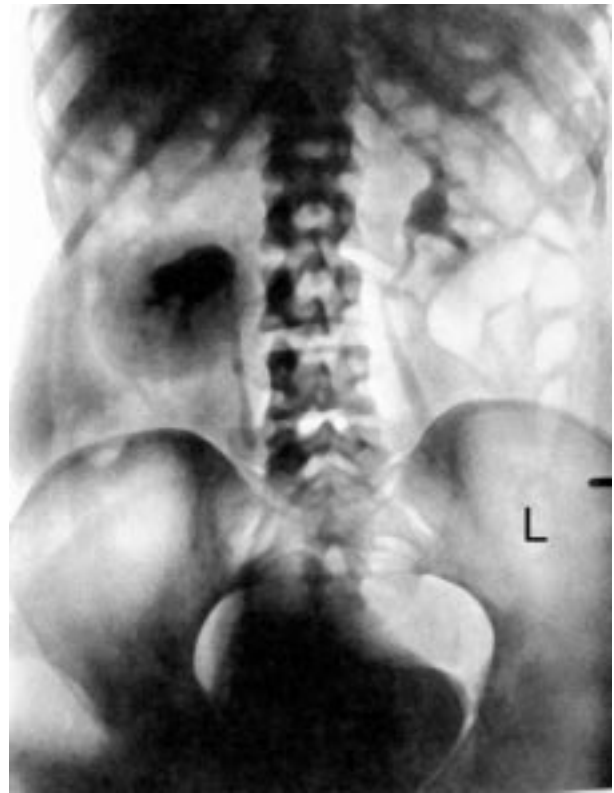
\*Read before the Section on Radiology at the Eighty-First Annual Session of the American Medical Association, Detroit, June 26, 1930.

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the substance; up to 2 years, 14 Gm.; 4 years and up, 16 Gm.; 7 years and up, 20 Gm.; from 10 to 13 years, 25 Gm., and 13 years old and up, 30 Gm. It was found roentgenologically that the injection in adults of from 50 to 60 Gm. of substance yields the better shadows. If 60 Gm. of substance is used, the full quantity of the solution may be injected continuously, or half is injected first and then the other half ten or fifteen



**Fig. 2.** Normal urogram of patient, aged 13 $\frac{1}{2}$  years; 30 Gm. of substance injected.



**Fig. 4.** Right nephropexy in woman, aged 31; 40 Gm. of substance injected; distortion due to operation; depression in left upper quadrant of bladder is due to the uterus.



**Fig. 3.** Right-sided pyelo-ureteritis in girl, aged 5 $\frac{1}{2}$  years; 16 Gm. of substance injected.

minutes later. The shadows obtained then are nearly, though not quite, as dense as those by the retrograde or cystoscopic method. During the injection the patient has an evanescent sensation of thirst and warmth; occasionally in the injected arm pain is experienced during the injection. I have observed no other reaction.

The roentgen technic is that usually employed in urinary tract examinations: the Potter-Bucky diaphragm, a 14 by 17 film (occasionally a smaller size if only part of the tract is wanted), and compression by means of the rubber bag. The patient is kept on the table for at least one hour after the injection. The best roentgenologic results are obtained fifteen, thirty-five and sixty minutes after the last injection. After that period, good outlines are obtained only in cases of delayed renal function, combined with obstructive lesions. It is therefore important to have each film developed immediately in order to determine for how long a period the taking of roentgenograms should be continued. It may sometimes be necessary to take roentgenograms at one to three hour intervals until good shadows are obtained. Sometimes it is necessary to have the patient empty

the bladder in order better to demonstrate the lower ends of the ureters.



**Fig. 5.** Bifid right renal pelvis and forked ureter. A left retrograde pyelogram had been done three months before this intravenous urogram was performed. One week after the retrograde pyelogram was done, an intravenous urogram was performed which showed that the left kidney did not visualize at all, and the right kidney only slightly. This second intravenous urogram now shows that both kidneys are well visualized.

The intravenous method is indicated in all instances in which urography is desirable and is applicable in many more cases than the retrograde method, because the objections to instrumentation are eliminated. It has thus been possible to employ this method in children as young as 6 months and in adults with large prostates, cardiac disease or other contraindications.

Contraindications to the use of the intravenous method would be actual or latent uremia in which, as a result of the poor concentrating power of the kidney, meager or no anatomic information could be obtained. For functional data, much simpler and less expensive methods, such as the blood urea determination, the phenol-sulphonphthalein, indigo carmine, and the dilution and concentration tests can be applied. In addition, the procedure might prove dangerous. Therefore, it is strongly advocated by Swick that



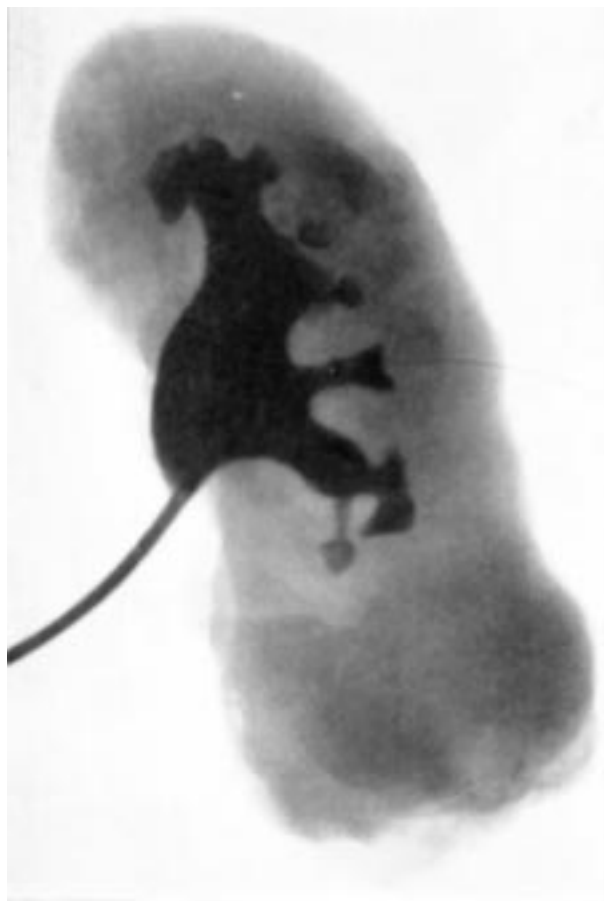
**Fig. 6.** Papillary carcinoma of urinary bladder extending from the left orifice to the internal sphincter, according to cystoscopic diagnosis, in woman, aged 62; 50 Gm. of substance injected. The left ureteral orifice cannot be seen. There was no indigo carmine excretion from left side; good blue from right. Intravenous pyelogram shows dilatation of left urinary tract, especially of juxtavesical and intravesical portions of the ureter. The denser shadow on the left than on the right normal side is due to partial obstruction at the left ureteral orifice.

patients about to be subjected to the intravenous procedure should have at least a blood urea, phenol-sulphonphthalein and concentration tests performed. The intravenous method, however, does not eliminate the retrograde or cystoscopic method; this is especially true in cases in which kidney function is impaired and therefore the iodine concentration is so poor that the tract is not sufficiently visualized. Here the retrograde method has to be resorted to in order to obtain an anatomic outline of the renal pelvis and ureter. The bladder will generally be shown well, unless both kidneys are below par. The faintest shadows are obtained with poorly functioning kidneys, the densest when obstruction is present. The roentgenographic contrast is heightened by means of the compression bag, which should be kept on for from five to ten minutes prior to and during the taking of the roentgenograms. One or more after each of these might also be taken without compression.



**Fig. 7.** Enlargement of the pelvis and calices of left kidney, but only slight distortion of one of the lower calices, in a man, aged 38; 60 Gm. injected. At operation a clear cell carcinoma was found.

The advantages of the intravenous method are manifold. It intensifies the kidney shadows, frequently bringing out irregularities in outline. Instrumentation is avoided which even under favorable circumstances is to say the least, very unpleasant and which, as will be seen from some of the illustrations, seems to cause a temporary inhibition of function of the kidney subjected to it. The entire urinary tract, including the bladder, is shown at one application of the method. With the cystoscopic method it has generally been found necessary to inject each side at separate sessions so as to avoid the severe reactions that frequently followed bilateral pyelography performed at one session. For the same reason the intravenous method is safer in case of solitary kidney. Anomalies in the urinary tract, such as double ureters, are revealed in some cases in which the cystoscopic method failed for technical reasons. It is not subject to failure in stricture of the ureter and is the only useful method in the study of the result of transplantation of ureters. It eliminates the artefacts which not infrequently complicate the other method and sometimes makes one hesitate to designate a transparency within the opaque ma-



**Fig. 8.** Specimen of left kidney of the patient shown in Fig. 7.

terial as a calculus rather than an air bubble or to say that a defective calix is due to a pathologic lesion and not to poor injection technic, especially when the urologist happened to be one of limited experience.

An added advantage of this method is that it demonstrates not only the anatomy of the urinary tract but also its function. The roentgenographic determination of function is, however, not sufficient in itself; according to Swick it should be supplemented by the quantitative determination of the excreted substance, which can be recovered from the urine. It will undoubtedly also give information regarding peristalsis of the ureters and the physiology of the pelvis and calices. In some cases of renal calculus, spasm of the calices was shown, probably as a reaction to the presence of the foreign body. In others in which the retrograde method preceded the intravenous, temporary nonvisualization on that side was present. It is important, therefore, to remember that the mere nonvisualization at a given examination does not necessarily denote permanent renal damage and



**Fig. 9.** Enlarged right renal pelvis, shown by intravenous urography, in a boy, aged 12; 30 Gm. of substance injected. The boy had pus in the urine when 1 year of age and urinary symptoms ever since. For seven years he had pain in the left upper quadrant and left loin. On the left side, the calices, which filled first, as they do in all hydronephrosis, were enormously enlarged.



**Fig. 10.** Later film of same case as Fig. 9, showing the pelvis to be of enormous size. The ureter was not seen at all. Left nephrectomy disclosed an infected hydronephrosis caused by narrowing of the ureteropelvic junction, probably congenital in origin.

therefore it is wiser to use the term functional inhibition.

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#### Abstract of Discussion

**PROF. LEOPOLD LICHTWITZ**, Altona-Elbe, Germany: Pyelography by way of excretion is an old desire. Dr. Rowntree was the first to attempt the visualization of the urinary tract by means of sodium iodide. Professor Binz of Berlin, who for a long time was greatly interested in chemotherapy, invented and prepared with his collaborators the group of selectans. Selectan and selectan neutral were sent by him to the clinic at Altona with the idea of attempting to influence coccus infections. In order to attempt treating infections of the kidney pelvis and gallbladder, we studied the output by the kidney and liver. We obtained evidence that the preparations did not cause iodism. The fact that these selectans are iodine-containing, exc-

retable by the kidneys and liver and cause no iodism, which had been the greatest obstacle in the earlier attempt, naturally led to the idea of testing them for the widely desired intravenous pyelography. Surely the invention of Professor Binz is the one leg of the new method. The second basis is the work of Dr. Swick. Important as is the existence of preparations, they become valuable only when the right person takes them for a special purpose. This is made clear by the fact that the preparations of Professor Binz were tested for the same purpose before Dr. Swick began his studies (without his knowledge) by a man of great experience in research work — without sufficient results. Between the important work of chemical preparation and final success, there came the hard work of a clever and energetic man, one with the deepest devotion to and greatest passion for research work. Therefore, we appreciate the work of both Professor Binz and Dr. Swick, and as this work is based on the invention of a famous German chemist and the investigations of a young American working in Germany, it may be considered as another hopeful symptom of scien-



**Fig. 11.** Deformity of left renal pelvis and calices, a cavity, absence of the middle calix, and a straight rigid ureter suggestive of tuberculosis, in a man aged 32; 60 Gm. of substance injected.



**Fig. 12.** Same case (as Fig. 11). Left retrograde pyelogram two days later presented same appearance but did not visualize the cavity as clearly. Subsequent nephrectomy disclosed an isolated tuberculous cavity in the kidney as shown in Fig. 11.

tific cooperation and friendship between our two countries.

**PROF. ARTHUR BINZ**, Berlin, Germany: It was my idea in 1921 to attach arsenic, or other elements such as iodine, to heterocyclic nuclei, such as those of the alkaloid group, and possibly thereby intensify therapeutic efficiency in the treatment of syphilis. My assistant, Dr. R ath, and I chose the simplest heterocyclic nucleus, the pyridine, and transformed it into about 700 new arsenic and iodine compounds. Expecting them to be very toxic, we were much surprised to find several of an unheard of tolerability when compared with the known arsenic and iodine compounds. This new biochemical principle, which we ascertained in animal experiments, caused me finally to select sodium-2-oxo-5-iodo-pyridine-N-acetate ("Uroselectan") for intravenous urography. This new relationship between chemical structure and biologic action we published in the *Zeitschrift f ur angewandte Chemie*. Sodium-2-oxo-5-iodo-pyridine-N-acetate, in its present form, was made in 1927, long before Dr. Swick came to Germany. Its selection by me for the purpose of intravenous urography was not due to suggestions of Dr. Swick but was in answer to clinical principles which had been agreed on by Professor von Lichtenberg and me, before Professor von Lichtenberg's trip to America last year. Concerning priority, Hryntschak of Vienna in 1927 was the first to investigate selectan compounds for intravenous urography, including what is now known as sodium-2-oxo-5-iodo-pyridine-N-acetate. Hryntschak obtained but partial success. Professor Lichtwitz of Altona in 1929 in his investigation of the treatment of human infections by selectan neutral, which I had sent him, observed that this compound had another effect which concerned intravenous pyelography. But all these results were clinically negligible. After working with selectan neutral and other selectan compounds, in Professor von Lichtenberg's clinic, and obtaining disappointing results, final success was achieved when I selected sodium-2-oxo-5-iodo-pyridine-N-acetate for use. It was given by me to Dr. Swick, who had been appointed by Professor von Lichtenberg to try out the compounds that I would give him.

**DR. MOSES SWICK**, New York: When I began my studies, as Professor Lichtwitz has pointed out, a substance synthesized by Professors Binz and R ath, having the formula m-

methyl-5-iodo-pyridon ("Selectan Neutral") was being tested for coccus infections at his clinic in Altona, Germany. Studies on its excretion, and its iodine content, led to the idea of applying it for roentgenologic purposes. The encouraging results pointed to the possibilities of further development. Following a dose of 6 Gm. (one third of the calculated maximal dose), certain disturbing symptoms resulted. Some were headache, nausea, vomiting and general discomfort. Of particular interest was the occurrence of transient diplopia in two cases. This suggested the possibility of the methyl radical being the toxic factor. My experience with this substance brought out the need for a modification, possessing better tolerance, greater solubility, and a higher iodine content, so that a larger dose could be administered and a higher concentration of the excreted iodine component be obtained. This work had been carried out at the clinic of Professor Lichtwitz for seven months before conferences were held with Professor Binz. The full data concerning these conferences and other matters here discussed will be presented by me tomorrow before the Section on Urology. As a result of my first presentation of the needs to Professor Binz, he furnished me with a compound, which, because of its insolubility, had to be administered by mouth and gave no results. At the second conference, in which Professor Lichtwitz participated, the whole ground was gone over again. Professor Binz felt confident that our needs could be fulfilled. Thereafter I continued the investigations in the clinic of Professor von Lichtenberg. There again I tested "Selectan Neutral," the second substance, and a third furnished by Professor Binz, which also had to be given by mouth and was unsuccessful. Finally, Professor Binz gave me a substance of the selectan group, which had a sodium acetate radical substituted for the methyl (sodium-2-oxo-5-iodo-pyridine-N-acetate). This compound fulfilled the needs, and satisfactory urograms could now be obtained. Professor von Lichtenberg, who was in the United States at the time, was promptly informed of the results. These were reported by me in detail at the Urologic Congress in Munich in September, 1929. I am not a chemist but have interested myself along the chemical lines required by the theoretical side of my problem and the chemical examinations needed in the course of the clinical investigations.

**DR. THEODORE SOKOW**, Kenosha, Wis.: The use of this new method necessitates changing one's conception in explaining and diagnos-

ing roentgenograms. With the cystoscopic method, a forcibly dilated kidney pelvis is obtained, not corresponding to the anatomic conditions. With the intravenous method, the physiologic dynamic conditions of the kidney and ureters are observed. That explains why pictures taken at the moment of the kidney contraction may show the pelvis very small and the calices not at all. Only in the diastole is a perfect picture obtained. Certain technical procedures may improve the results, as elevation of the pelvis of the patient and compression of the region of the lower ureters. In one of the latest articles, Dr. Hryntschak of Vienna is recommending the use of solution of pituitary to increase the concentration of the dye in the kidney and atropine to delay the excretion of the dye. It seems worthwhile to try these and other drugs for the same purpose. In my experience, sodium-2-oxo-5-iodo-pyridine-N-acetate has given very good results and few after-effects. About two months ago, at the annual convention of the German Roentgen Society in Berlin, different authors mentioned a new product, produced by another chemical concern in Germany. I was able to secure lately a small amount of this chemical, and used it in different cases with very satisfying results.

**DR. L.T. LE WALD**, New York: Dr. Jaches has brought out two or three uses that seem to me very important. As I have had one case of implantation of both ureters into the sigmoid, similar to his case, and as I know of several cases at the Mayo Clinic, I would be interested to learn whether the rest of these cases could be examined and see whether dilatation of the ureters has occurred in the other cases in which there was exstrophy of the bladder. The second point relates to the possibility of misinterpretation, because one kidney didn't show function temporarily which might lead one into error. Dr. Jaches, however, has emphasized the fact that either repeating the test or roentgenographing the patient at a little later time shows that the kidney did function, thus avoiding erroneously diagnosing a single kidney because of this possibility of spasm interrupting the secretion. And then in case of horseshoe kidney, I think it is exceedingly valuable. Occasionally in a thin subject, at least in one case, I was able to see the shadow of the kidney going across the median line, but as a rule one would be in doubt in a case of that sort. In Dr. Jaches' case, the shadow was certainly very conclusive after the use of sodium-2-oxo-5-iodo-pyridine-N-ac-

etate. I would like to ask Dr. Jaches if any alarming reactions have occurred. A urologist in New York told me that in his first case in which the injection was given through rubber tubing he had had some reaction and he did not give more than half the dose and then desisted from finishing the examination, saying that the patient had some dizziness and collapse, and he didn't feel safe in going on. I wish Dr. Jaches would say a word or two more about technic.

**DR. B. R. KIRKLIN**, Rochester, Minn.: You might be interested to know of a little Scotch trick that we have employed at the Mayo Clinic. Dr. Braasch and his associates have been collecting the urine of the patients after they have received sodium-2-oxo-5-iodo-pyridine-N-acetate and sending it to the chemist, who has been able to recover approximately 65 per cent of the amount originally injected. I am informed by the chemist that the substance recovered in this way is a purer product than the original drug.

**DR. LEOPOLD JACHES**, New York: In 122 cases there have been no unpleasant reactions. What was the cause of the reaction in the case quoted by Dr. Le Wald, I do not know. It may be that this patient was an unsuitable subject. I suggest that this case be reported with all clinical data, so that more can be learned about all possible contraindications than is known today. I am glad to hear from Dr. Kirklin that at the Mayo Clinic the material was used over again. Dr. Swick has proposed the same thing to me but as yet I have not followed his suggestion. I made up my mind to keep out of the controversy regarding the origin of this matter. I would like, however, to say in connection with what has been stated concerning Dr. Hryntschak, that a real practical success did not result from his studies. As Dr. Swick is much more familiar with this phase of the subject, he should be permitted to discuss it for me.

**DR. MOSES SWICK**, New York: At the Urologic Congress, in Munich in 1929, where I presented my paper, Dr. Hryntschak was present. He did not discuss the subject but in his article which appeared at that time in the *Zeitschrift für Urologie* in 1929, he said on page 904 that although he had succeeded two and one-half years before in obtaining useful 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. I might add that he gave neither the name nor the chemical formula of any of the substances employed, but he mentioned three of them by number as 12, 27 and 48.



**DR. LEOPOLD JACHES**