Patented Jan. 13, 1942 2,269,489

UNITED STATES PATENT OFFICE

2,269,489

CONTRAST AGENT FOR X-RAY DIAGNOSES

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No Drawing. Application October 11, 1938, Serial No. 234,403. In Germany September 25, 1929

2 Claims. (Cl. 167—95)

This invention relates to contrast agents for X-ray diagnoses, and more particularly to contrast agents useful in the screen observation and photography of the genito-urinary system.

This application is a continuation in part of my copending application for U. S. Letters Patent Ser. No. 476,245, filed August 18, 1930.

It is an object of this invention to provide a method and means for the screen observation and photography of the genito-urinary system which are generally applicable.

It is a further object of the invention to provide a method and means of the afore-noted type which are readily available to the general practitioner.

It is a still further object of the invention to provide a method and means for the purpose stated which cause neither pain nor discomfort to the patient.

It is yet another object of the invention to provide for high contrast visualization and pictures of the tract under study.

Another object of the invention is the visualization of a wider area than hitherto rendered accessible.

Still a further object of the invention is to provide for visualization over an extended period to facilitate study of the function of the organs.

Other objects, and the manner in which the same are attained, will appear from the following description.

In many diseases, it is a very important task for the physician to acquire the most complete information about the condition as well as the function of the genito-urinary system. Heretofore, the only methods available for this purpose were retrograding pyelography or peroral administration of contrast agents, which methods, however, were found to be disadvantageous in various major respects.

Retrograding pyelography involves cystoscopy and catheterization, contrast substances such as lithium iodide or sodium iodide dissolved in water being introduced, through the catheter, into the bladder and the ureters. To the extent that the substances filled the organs, X-ray pictures showing in outline any irregularities were obtainable. However, this method failed in cases of physical obstructions or disorders in the channels employed and thus was far from being generally applicable. In view of the involved procedures required, it was not available to the general practitioner. These procedures, moreover, invariably result in pain and serious discomfort on the part of the patient during and after administration. To fill the calyces of the kidneys was rarely possible, and then only with difficulties. The area visualized did not extend far enough to permit of obtaining a complete picture. Finally, it proved impossible to keep the contrast substance in the inner parts of the organs long enough to permit observation over an extended period, as is required in the study of the function of the system.

Peroral administration was established to be similarly deficient. Substances given perorally display a tendency of appearing in the feces rather than in the urine, so as to defeat the purpose of visualizing the genito-urinary tract. Owing to the passage through the portal system and the liver before reaching the general circulation and hence the kidneys, these substances are so slowly resorbed that their contrast effect is anything but satisfactory. Moreover, the area visualized in this manner is very limited.

Although the various drawbacks of the afore-noted prior art methods were readily recognized, and in spite of the fact that numerous investigators in this field strove, over a great number of years, to develop a method and means for rendering the genito-urinary system more readily accessible to screen observation and photography by X-rays, no solution of this problem was forthcoming until the present invention was made.

The present invention is based on the concept that all the drawbacks of the prior methods can be eliminated, and a procedure can be obtained which is generally applicable, i. e. which is operative also under conditions of obstructions or disorders in the anatomical channels, which is available to the general practitioner, which eliminates pain or discomfort on the part of the patient, which results in high contrast visualization and pictures of the genito-urinary tract, and which increases both the area rendered visible and the period of time during which it is accessible to observation, if the methods of the prior art are critically departed from and a novel method is introduced which provides for the direct introduction of the contrast agent into the general circulation.

This concept was based on the recognition that the various drawbacks inherent in the prior methods was largely if not altogether caused by the more or less anatomical introduction of the contrast substance into the organism, whether this introduction took place through channels of the genito-urinary system or through the diges-

tive system. It was recognized that unless a purely physiological mode of introduction of the contrast substance could be provided for, the methods would be always lacking in high contrast visualization, general applicability, visibility in sufficiently large an area over an extended period, to name only a few of the drawbacks discussed above. After this had been established, it was concluded that the the physiological method called for should conform, as closely as possible, to the natural excretion processes in the organism, and it was this thought which led to the method now devised of introducing the contrast substance into the circulation, whence it is carried directly into the kidneys and excreted therefrom into the other parts of the genito-urinary system in a manner corresponding to the formation and transportation of urine.

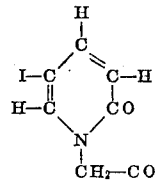
The most obvious and most effective mode of directly introducing the contrast agent into the circulation is to administer such substance by way of intravenous injection, and accordingly this is the method contemplated by the present invention.

Proceeding from the recognition that intravenous injection would afford the most appropriate method for administering contrast agents for the purpose stated, it was possible, after a thorough investigation into the prevailing conditions and requirements, to determine the class of substances which would lend themselves to administration by the novel method so as to avoid the drawbacks of the prior art and yield the improved results aimed at by the invention. The class of substances thus established is distinguished by a combination of properties common to all its members, as follows: the substances are organic compounds containing iodine or bromine, have the halogen linked to carbon in a stable non-ionizing form, are highly soluble, and are substantially inert with respect to the human body.

More particularly, the contrast substances employed according to the invention may be characterized as being salts of compounds having the general formula A—B—C, where A constitutes the shadow-forming part of the molecule and comprises an aliphatic or aromatic or pyridine ring substituted by halogen; B constitutes a link connecting the groups A and C and comprising one or more carbon atoms in a chain, or an oxygen or an amino group, or a combination of several of these; and C constitutes the group responsible for the high solubility of the compound, particularly in water, and comprises a carboxyl or sulfoxyl group. It is noted that while A and C must always be present, the intermediate link B may be non-existent, its part being taken by part of the group A.

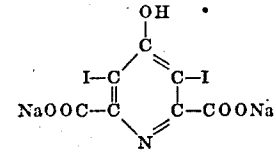
As examples of substances the following compounds may be mentioned as members of the class contemplated by the present invention:

1. The sodium salt of 2-oxo-5-iodopyridine-N-acetic acid, of the form



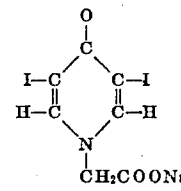
This compound has become generally known as "Uroselektan."

2. The disodium salt of diiodochelidamic acid, of the form



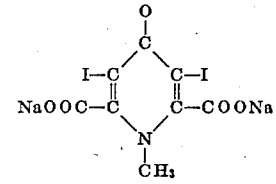
This compound has been designated as "D 34."

3. The sodium salt of the 3.5-diiodo-4-oxo-pyridine-N-acetic acid, of the form



This compound has been designated as "Perabrodil."

4. The disodium salt of N-methyl-3.5-diiodo-chelidamic acid, of the form



This compound is known as "Uroselektan B."

In the execution of the invention, a solution of one of the novel contrast agents in water is prepared under sterile conditions, the concentration of the solution being preferably provided as between approximately 40 to 80%. The sterile solution is then preferably warmed to body temperature and intravenously injected into the cubital vein. The injection should proceed slowly so as to avoid any discomfort on the part of the patient. After the injection is completed one has to wait for about from 5 to 10 minutes before the first screen observation may be made, or the first picture may be taken in the usual manner. Subsequently, a great number of pictures may be taken at intervals, the next following ones, e. g. after about 30 and 50 minutes.

Numerous advantages result from the novel method and means according to the invention. The method is generally applicable, even in cases of obstruction of the channels formerly utilized in retrograding pyelography. The method is available to the general practitioner. In years of experience, the method has been established to eliminate pain or discomfort on the part of the patient. High contrast visualization and pictures are readily obtainable. The area rendered visible is considerably increased when compared with that previously rendered accessible, owing to the utilisation of the entire tract as channel for the agents. The period of time over which visualization may be readily had is likewise considerably increased, the agent being kept in the tract for the length of time taken up by the physiological excretion processes.

Various changes may be made in the details disclosed in the foregoing specification without departing from the invention or sacrificing any of the advantages thereof.

I claim:

1. A contrast agent especially useful for rendering the urogenital system less pervious to X-rays, comprising essentially a water-soluble pyridine

carboxylic acid salt containing as a further substituent in the nucleus a member of the group consisting of bromine and iodine joined directly to nuclear carbon in non-ionizing form, said agent being adapted for direct injection into the human blood stream and readily conveyable by the blood stream to the urogenital system, and being non-toxic and stable in its passage through the human system.

2. In the diagnosis of disorders of the urogenital system by means of the X-ray, the step which comprises rendering the urogenital system less pervious to X-rays, and thereby visible on the screen, by injecting into the blood stream of the patient, and thus conveying through the latter and to the urogenital system, a solution of a soluble, stable, non-toxic pyridine carboxylic acid salt containing as a further substituent in the nucleus a member of the group consisting of bromine and iodine joined directly to nuclear carbon in non-ionizing form.

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