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VISUAL AND RADIOGRAPHIC CONTRAST MEDIA AND METHOD OF USE

Nicholas G. Demy, 527 Foothill Road, Somerville, N.J.

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3 Claims. (Cl. 167—95)

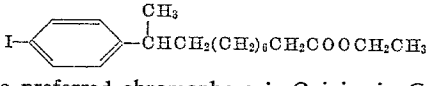
The present invention relates to a liquid radiographic contrast medium and more particularly to a distinctively colored iodinated oily substance, for example, an iodinated fatty acid, which exhibits marked radiographic opacity and yet is clearly distinguishable from aqueous body fluids when observed using ordinary light in the visible portion of the spectrum.

More specifically, the invention relates to a distinctively colored, radiopaque, oily liquid suitable for injection into various cavities of the human body for purposes of fluoroscopic and radiographic examination, the liquid being subsequently withdrawn after completion of the examination. During the withdrawal, which preferably takes place under ordinary light without X-rays, the distinctive color of the liquid and its oily consistency permit the examiner to determine with certainty when the liquid being withdrawn from the body cavity ceases to contain the iodinated substance and thus to ascertain when substantially all of the contrast medium has been removed.

Suitable colorless contrast mediums are, for example, fatty acids described in Strain et al., U.S. Patent No. 2,348,231, issued May 9, 1944.

The distinctively colored iodinated fatty acid solution of the invention is suitable for use in myelography; positive contrast ventriculography; lymphangiography; and radiography of the sinus tracts, fistulous communications, ducts and other body cavities.

In general, solutions embodying the invention are prepared by the addition of a fat soluble chromophore to the common esters of iodinated phenyl aliphatic acids. The chromophoric group may be D & C Green #6 (Quinizarin Green SS) having the chemical name of 1,4-bis (p-toluino) anthraquinone; or D & C Violet #2 (Alizurol Purple or D & C Blue #3) having the chemical formula of 1-hydroxy-4-p-toluionoanthraquinone; or a non-toxic metallic salt of alkannin, $C_{16}H_{16}O_5$. The preferred iodinated fatty acid which serves as the vehicle for the chromophore is a mixture of the esters of ethyl iodophenylundecylic acids having a specific gravity materially in excess of unity and more particularly having the formula of



and the preferred chromophore is Quinizarin Green SS having the chemical name of 1,4-bis (p-toluino) anthraquinone.

For example, one gram of Quinizarin Green SS is added to 100 grams of the ethyl ester of iodophenylundecylic acid. This results in a stable deep green-blue water immiscible, non-emulsifying, freely-flowing fluid which does not stain the body fluids or tissues. The solution contrasts sharply on a radiographic film and during fluoroscopic observation; at the same time, it is clearly visible under ordinary illumination to the unaided eye or the dark-adapted eye covered by red goggles as a deep green-blue oily layer which underlies and is readily distinquished from the colorless, aqueous spinal fluid.

The radiopaque oily solution consists essentially of a dye and a radiopaque vehicle, both of which have proven to be internally acceptable by the body and both of which are well known to be nontoxic. The Quinizarin Green SS is dissolved within the oily iodinated fatty acid without any accompanying chemical reaction forming a different compound. The resulting solution is injectionally acceptable to the human body and its cavities.

Although other nontoxic coloring agents may be used wherein the color is readily distinguishable from the colors of the fluids of the human body, a color in the blue end of the visible portion of the spectrum is essential when the medium is being withdrawn. While the radiographic photography may be performed in a fully lighted room, the fluoroscopy is performed in a darkened room and the examiner wears goggles with lenses formed of red-colored glass. The deep green-blue color of the radiopaque fatty acid makes it unnecessary for the examiner to remove the red goggles for observation and volumetric evaluation of the liquid being withdrawn from the body cavity which has been examined and thus destroy the dark adaptation of his eyes.

The method of myelography will be described as an example of the limitations which the current medium now imposes on the examination. Generally, from three to twelve cubic centimeters of the colorless radiopaque medium are injected through a long needle into the spinal canal. The location of the injected oily contrast medium is then observed fluoroscopically and the patient assumes a position such that the contrast medium flows by gravity into the region of the spinal canal where the abnormality is suspected. X-ray pictures are taken. The needle remains in place while the pictures are being taken and developed.

When the desired fluoroscopic and photographic information has been obtained, attempt is made to withdraw as much of the injected material as possible using a syringe connected to the needle. The conventional contrast medium is a colorless liquid immiscible with the spinal fluid and will hereinafter be designated as "oil." This oil may become slightly emulsified or dispersed into small globules when mixed with air and spinal fluid drawn into the syringe. This makes it difficult to distinguish between the spinal fluid and the oil during withdrawal into the syringe and also makes it difficult to estimate the amount of oil withdrawn. Time is lost in crude and cumbersome testing for oil, and in uncertain estimation of the amount recovered from the spinal canal. During this time, the examiner's eyes are covered with red goggles to preserve dark adaptation for the fluoroscopic identification, positioning and removal of the oil. Excessive spinal fluid is lost and manipulation of the needle in the spinal canal can be extremely uncomfortable to the patient. Patients refuse to have the examination repeated and physicians are reluctant to perform the examination even initially because of these technical difficulties. Often the attempt to remove the oil is abandoned in frustration and significant amounts remain behind.

The remaining oil which has not been removed is very slowly absorbed and residues are often seen on X-rays of the spinal column ten or more years after the examination. This residual oil can be a source of grave diagnostic error during the lifetime of the patient if radioactive iodine uptake studies of the thyroid gland are attempted later.

For a more detailed description of myelography using uncolored contrast media and the problems involved, reference may be had to a book entitled, "Myelography," by Robert Shapiro, M.D., Yearbook Medical Publishers, Inc., Chicago, 1962, Library of Congress Catalog Card No. 62–11257. Chapter 4 is particularly relevant.

The green-blue color of the injectionally acceptable oily contrast medium described above avoids many disadvantages of an uncolored contrast medium. Because of the distinctive color, the amount of contrast medium may easily be measured with accuracy and the amount which remains within the patient's body is readily and accurately ascertainable. This enables the neurosurgeon, ortho-

pedist or radiologist to tell whether he is withdrawing spinal fluid or contrast medium into the syringe; it technically facilitates the operative procedure and spares the patient discomfort and pain; it prevents excessive loss of spinal fluid; it makes possible the use of 10 to 30 cubic centimeters of contrast medium instead of 3 to 12, thus improving diagnostic accuracy by outlining a greater length of spinal canal; and it decreases the time of the fluoroscopic examination. Most important of all, it facilitates removal of most, if not all, of the oily contrast medium and thus prevents later confusion if radioactive iodine is to be used in the diagnosis of thyroid gland disease. Any of the residual distinctively colored oil can be identified and removed by the orthopedist or the neurosurgeon if an operation on the spinal canal should be performed at a later date.

Heretofore, the entire ventricular system of the brain has been examined by injection of air because the large volume of the ventricles precluded the use of a liquid medium which would be difficult to remove. With the use of an easily identifiable colored medium, positive contrast of ventriculography becomes a feasible examination.

In lymphangiography, regional lymph nodes which are the seat of primary or metastatic tumors, after X-ray examination using the colored oil, become visibly pigmented, thus enabling the surgeon to find and remove these tumors after preliminary identification on the X-ray film.

In the examination of fistulae, sinuses, ducts and cavities, the diseased or abnormal tracts may first be studied using X-rays in conjunction with the colored radiopaque oil described above. By permitting a certain amount of the colored oil to remain, the affected tracts which appear in the X-ray film may be visually identified with precision during the course of a correctional operation.

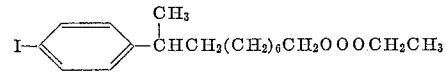
Reference is made to Tainter and Grayson: Radiopaque Diagnostic Agents, Annals of the New York Academy of Science, volume 78, art. 3, page 965 (Summary). July 2, 1959, stating on authority:

The medicolegal implications of residual dye are frightening. From the medical viewpoint residues of this dye (Pantopaque) preclude the use of radioactive tracer studies for the lifetime of the patient. A new radiographic agent for myelography is urgently needed.

While there are described what are believed to be the best embodiments of the invention, it will be understood that various changes and modifications may be made therein without departing from the spirit and scope of the invention as defined in the appended claims.

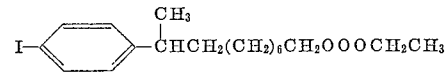
What is claimed is:

1. A radiographic contrast medium consisting essentially of



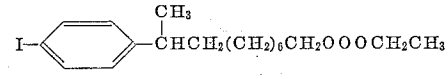
having about 1% by weight of a coloring agent dissolved therein, said coloring agent being selected from the group consisting of: 1,4-bis (p-toluino) anthraquinone; 1-hydroxy-4-p-toluino anthraquinone; and a metallic salt of alkannin, $C_{16}H_{16}O_5$.

2. A radiographic contrast medium consisting essentially of



having about 1% by weight of 1,4-bis (p-toluino) anthraquinone dissolved therein.

3. A radiographic contrast medium consisting essentially of



having about 1% by weight of 1-hydroxy-4-p-toluino anthraquinone dissolved therein.

References Cited by the Examiner

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2,307,187 1/43 Bell et al. ---------- 167—95

OTHER REFERENCES

Tainter et al., Annals of the New York Academy of Sciences, vol. 78, article 3, pp. 956 and 958, July 2, 1959.

LEWIS GOTTS, *Primary Examiner.*

FRANK CACCIAPAGLIA, JR., *Examiner.*