kindness of Dr. William Harris, of the Pathological Department, Tulane University, histopathologic studies were made of the placentas, livers, and spleens of the fetuses. The placentas showed the presence of thorium, but none was found in the fetuses.

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Microscopic Changes Produced in Tissues of Animals Injected with Thorium Dioxide for Spleno-hepatography.

WILLIAM H. HARRIS AND A. V. FRIEDRICHS.

From the Department of Pathology, College of Medicine, Tulane University.

Many reports have recently appeared upon the results of the intravenous injection of colloidal thorium dioxide (Thorotrast-Heyden) in the experimental animal, most of them demonstrating tolerance and lack of toxicity even in large doses. Huguenin and Nemours[1] state that 18 cc. of thorotrast were tolerated by the rabbit without any after-effects. Later, however, with Albot,[2] they described the production of hepatitis and cirrhosis in rabbits with doses of 15 to 20 cc. Bauman and Schilling[3] found that 1 cc. administered intravenously in rabbits, was necessary for contrast shadows of the spleen and liver but that 3 cc. twice daily up to 12 cc. gave more distinctive shadows, with no ill effects. Fifteen minutes after injection, glossy colorless grains could be observed in the various stellate (Kupffer) cells and also in the reticulum cells of the spleen. Twenty-four hours later, such cells were swollen and filled with fine and coarse, glossy granules. After 14 days the same approximate condition existed. Popper and Klein[4] injected rabbits and dogs up to 8 times the quantity recommended for the human subject. They state it was harmless and that the blood was not affected. Lambin,[5] however, found that 5 cc. per kilo in rabbits necessary for liver visualization caused anemia whereas 1 cc. per kilo, sufficient for spleen visualization, caused an erythroblastic reaction, without producing anemia. When a pronounced anemia

[1] Huguenin, R., and Nemours, A., *Rev. de Path., comp. et d'Hyg. gen.*, 1931 **415**, 480.

[2] Huguenin, R., Nemours, A., and Albot, G., *Comp. rend. de Seances d. Biol.*, 1931, **35**, 879.

[3] Bauman, H., and Schilling, C., *Klin. Wschr.*, 1931, **27**, 1249.

[4] Popper, H., and Klein, E., *Muench. med. Wschr.*, 1931, **43**, 1829.

[5] Lambin, P., *Comp. rend. Soc. Biol.*, 1931, **28**.

was produced, the recovery was spontaneous. Kadrnka[6] reports haematuria in animals subsequent to intravenous injections of thorium dioxide. Thus conflicting observations have been recorded.

We injected 53 white rats in collaboration with radiological observations of Drs. Menville and Ané, with variable results as regards tolerance. The very moderate dosage was from 0.2 to 1 cc. introduced in the tail vein. In the human subject as much as 50 to 75 cc. has frequently been injected. About 4% died within 48 hours. Those surviving this period with the exception of the pregnant females continued to live after 3 months in apparently good health. The animals studied histologically included those dying early as well as those surviving and in good condition, sacrificed with ether anesthesia.

In the animals dying from the injection within 48 hours, the following microscopic changes were noted: The liver showed cast-like masses of small thorium granules in the sinusoids and marked parenchymatous degeneration with fatty changes were present in the hepatic cords. In the kidneys, larger glossy thorium granules were found in the glomerular capillary tufts. The renal tubuli showed in areas, occlusion of the lumen from swelling of the renal epithelium while others showed extensive parenchymatous degenerative changes. The spleen showed extensive collection of thorium granules which had replaced the splenic tissue in much of its structural extent. The deposits were present in the splenic corpuscles and the splenic pulp. The material was not phagocytized. In one animal in which the lungs were visualized the capillaries of the alveolar walls were laden with glossy thorium granules.

In the animals in apparent good health the changes noted in general were those described by most observers, *i. e.*, the selective reaction of the reticulo-endothelial cells, especially of the liver and the spleen, which structures apparently represent the accumulating foci of the thorium injections. It does not seem entirely accurate to state, however, that the selective affinity of the reticulo-endothelial system would account solely for the extensive and consistent splenohepatic accumulations. It is true that the bone marrow does show some collection of this material but the vascular supply of the lungs, kidneys, lymphatic glands and other structures forming a part of the Aschoff system is seldom visualized.

The cellular response produced is somewhat analogous to that seen in typhoid fever. The displacement of splenic structure, the apparent invasion and destruction of areas of hepatic cord epi-

[6] Kadrnka, S., *Radiology*, 1932, **18**, 371.

thelium and the deposition of the material in the portal tracts is, however, a more definite histo-pathologic change than simply a phagocytic reaction on the part of the reticulo-endothelial system.

It is possible that the white rat presents a somewhat different response than that of other animals. It is also possible that the thorium preparations vary slightly in the character of their constituents.

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Histo-pathological Effects of Thorium Dioxide on Lymphatic Glands of Animals Visualized by the Menville-Ané Method.

WILLIAM H. HARRIS.

*From the Department of Pathology, College of Medicine, Tulane University.**

The method of radiological visualization of the lymphatic glands by the injection of colloidal thorium dioxide (thorotrast) was described by Menville and Ané.[1] In this work the material was introduced subcutaneously in the area of the perivascular lymph spaces. The subsequent drainage to the lymphatic glands produced visualization not alone of the glandular structure but also, at times, the lymphatic vessels (Fig. 1). Through this means, the opportunity

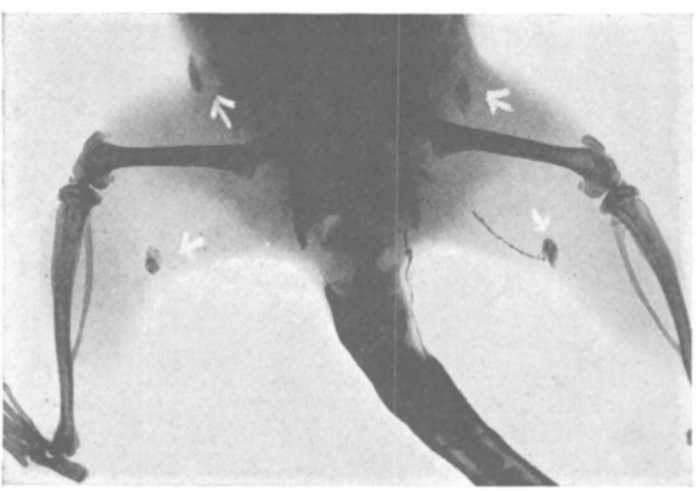

FIG. 1.

* Aided by a grant from the David Trautman Schwartz Research Fund.

[1] Menville, L. J., and Ané, J. N., *J. Am. Med. Assn.*, 1932, **98**, 1796.