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Roentgen-ray Study on Non-permeability to Thorium Dioxide of Placenta of Albino Rat.*

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Experimental work on the permeability of the placenta to certain dyestuffs has been reported by a number of investigators. Wislocki[1] reports that when phenolsulphonephthalein is injected into the peritoneal cavity of a guinea pig fetus it is absorbed and passes slowly from the fetal blood stream through the placenta into the maternal blood stream and is excreted by the maternal kidney. A similar injection of trypan blue is also absorbed from the peritoneal cavity of the fetus, but is not transmitted by the placenta to the maternal organism. According to Wislocki's observations the placenta is incapable of transmitting an inert foreign colloid from the fetus to the mother. Shimidzu[2] injected pregnant rats subcutaneously between the scapulae, using 23 different dyes, 8 basic and 15 acidic. He found that the placenta was permeable to all of the basic dyes, and only 8 out of the 15 acid dyes penetrated the placenta; also that the permeable dye solutions were slightly colloidal or non-colloidal in character, with the exception of Biebrich's scarlet, a highly colloidal dye. Dyes largely in the colloidal state do not,

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1 Wislocki, G. B., *Bull. Johns Hopkins Hosp.*, 1921, **32**, 93.

2 Shimidzu, Y., *Am. J. Physiol.*, 1922, **62**, 202.

with rare exceptions, penetrate the placenta. These experiments were made on animals either at operation or after death.

We were unable to find in the literature reports of experiments on the permeability of the placenta to colloidal substances opaque to the roentgen ray. We appreciated that but few colloidal substances have been found which penetrate the placenta because of the size of the particles in these substances. We used thorotrast, a colloidal thorium dioxide, miscible in all proportions with body fluids. We hoped that its particles of thorium would be small enough to penetrate the placenta, as in the instance of Biebrich's scarlet, and thereby visualize the reticulo-endothelial system of the fetus.

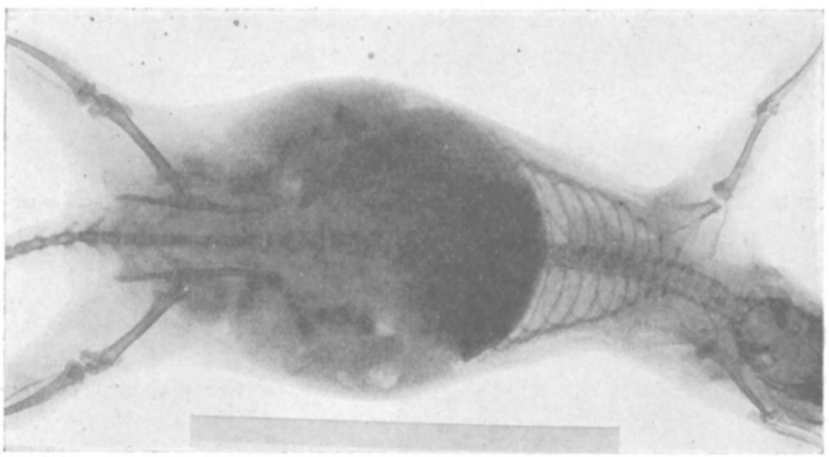

FIG. 1.
Pregnant rat, showing the visualized placentas. The liver and spleen of fetuses not visualized.

We used four pregnant albino rats, at or near full term. Three were injected with 1 cc. of thorotrast, and shortly after were roentgenographed, the liver and spleen being clearly visualized. The livers and spleens of the fetuses did not show the presence of thorium at that time. These rats were roentgenographed several times before delivery, with the same results. Roentgenograms were also made of the newborn shortly after birth, and we were unable to detect thorium in their livers or spleens. From the roentgenograms of these 3 rats there was no roentgen evidence that the thorium had reached the placenta. We then injected 1.5 cc. of thorotrast in the tail vein of the 4th pregnant rat, and a roentgenogram, made shortly after, clearly showed the liver, spleen, and 9 placentas, but the thorium, as far as we could observe, had not penetrated the placentas. This rat died 24 hours after injection, and through the

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.

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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**.