Twenty-one cases of jaundice (Table I) and 7 other instances of liver and biliary tract disease without jaundice (Table II) were investigated. Since fever and anemia also influence the choline-esterase activity,[1] we have tabulated the temperature at the time of drawing of the blood and have recorded the hemoglobin. It is obvious from these figures that there is a tendency to depressed values in cases of hepatic and biliary tract disease. The mechanism of this depression has not as yet been elucidated. However, a series of experiments which were suggested by these data showed that bile acids,[3] added to the reaction mixture in the form of their sodium salts, caused inhibition ranging from moderate effects to almost complete inhibition of enzymatic hydrolysis.

It was stated in the original publication that the choline-esterase activity in the serum may be a factor which is inversely related to the vagotonicity of the individual. In view of this, it is of interest to speculate on the relation of the depressed choline-esterase activity to the sweating, bradycardia, and fall in respiration, vagotonic symptoms which not infrequently occur in cases of hepatic disease with and without jaundice.

Summary. The choline-esterase activity of the serum in patients with jaundice or biliary tract disease was found to be depressed.

9856

Passage of Sulfanilamide from Mother to Fetus.

HENRY M. LEE, ROBERT C. ANDERSON AND K. K. CHEN.

From the Lilly Research Laboratories, Indianapolis, Indiana.

Recent reports by Marshall and his associates[1, 2] indicate clearly that sulfanilamide when administered to animals and men is rapidly and uniformly distributed in different tissues. It is thus easy to conceive that the drug may also be detected in fetal circulation and amniotic fluid among pregnant animals. In order to substantiate this assumption, the following experiments were carried out.

Pregnant rabbits of not less than 3 weeks' duration were employed.

---

3 Sobotka, H., and Antopol, W., *Enzymologica*, 1937, **4**, 189.

1 Marshall, E. K., Jr., Emerson, K., Jr., and Cutting, W. C., *J. A. M. A.*, 1937, **108**, 953.

2 Marshall, E. K., Jr., Emerson, K., Jr., and Cutting, W. C., *J. Pharm. and Exp. Therap.*, 1937, **61**, 196.

TABLE I.

Rabbit No.	Body wt., kg.	Dose, mg. per kg.	Duration of pregnancy, days	Interval between administration and sacrifice of animal, hrs.	Sulfanilamide, mg. %					
					Maternal Blood		Fetal Blood		Amniotic Fluid	
					Free	Total	Free	Total	Free	Total
1	3.20	420	32	3¾	15.7	26.5	14.6	18.1	†	†
2	3.60	375	33	5¼	13.7	24.7	12.1	16.7	†	†
3	3.60	375	31	5⅓	2.6	21.0	2.7	12.5	10.5	13.1
4	4.92	375	23	4⅔	9.8	29.2	6.2	†	†	†
5	3.49	375	23	5	6.3	35.2	6.4*	10.3*	2.2	†
6	4.15	375	26	5½	4.4	11.5	3.1	7.3	2.8	5.2
7	4.78	375	26	4¾	20.3	22.0	16.9	20.0	15.7	19.4

*Amount per 100 g. of entire fetal tissue.
†Not determined.

Sulfanilamide dispensed in capsules was given by mouth. The dose was 375 mg. per kg. in 6 animals, and 420 in the remaining one. After a period varying from 3¾ to 5½ hours during which active absorption took place, maternal blood samples were taken either from the marginal vein of the ear or by cardiac puncture. The animals were immediately sacrificed by a blow on the head, the amniotic fluid if sufficient was obtained by aspiration with a syringe, and the fetuses were freed from their placentae. In order to eliminate any possible contamination by the maternal blood, the fetuses were washed in running water and dried with a towel. After decapitation, the fetal blood was pooled and analyzed for sulfanilamide content. In one case no fetal blood could be collected because obviously the pregnancy was not fully advanced. It was therefore necessary to grind the fetuses with sand, and extract the residue with alcohol. All determinations of sulfanilamide both as the free and as the acetylated product were made with the colorimetric method perfected by Marshall and his coworkers.[3, 4]

The results are summarized in Table I. There is indeed no question that sulfanilamide passes from the maternal to the fetal circulation. The total amount expressed in mg. % is uniformly greater in the mother than in the fetuses, although the amount of free sulfanilamide appears to bear a close relationship between the maternal and fetal blood. The relatively low content of conjugated sulfanilamide on the fetal side might be due to less efficient mechanism of acetylation in the unborn animals. As in mature rabbits, sulfanilamide is probably also well distributed in fetal tissues as shown by animal numbered 5 in Table I. The presence of the drug in amniotic fluid is not unexpected since the fluid is generally considered to be derived from the maternal serum.

Summary. Sulfanilamide when given by mouth in pregnant rabbits has been shown to pass from the maternal to the fetal circulation. The acetylated form is relatively lower in the fetal blood than in the maternal blood. Sulfanilamide can be also detected in the amniotic fluid.

[3] Marshall, E. K., Jr., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 422.

[4] Marshall, E. K., Jr., *J. Biol. Chem.*, 1937, **122**, 263.