

as in unoperated cases and the baby nursed and developed according to expectation up to the time of this report (July, 1941).

Strangely enough, nursing, like pregnancy, proved an efficient stimulus for the maintenance of bright red color of the sex skin even in the absence of ovarian tissue. For about 2 weeks postpartum the color was distinctly less intense (6 on a scale of 10) but after that rose to 8 and 9, at which it was being maintained at the time of this report, 2 months after parturition. This raises the question: Whence comes the hormone conditioning the sex color? One thinks of the placenta as substituting for the ovary during pregnancy, but during lactation we must look elsewhere for the source of "ovarian" hormones. As a matter of fact the monkey sex skin may be experimentally reddened by all the estrogens, by androgens, by deoxycorticosterone⁶ and even by progesterone⁷ alone. It is quite possible that adrenotropic hormone of the hypophysis is involved, stimulated in pregnancy by placental hormones, in lactation by the act of suckling. Other facts also point to extragonadal, synergistic factors in the maintenance of the sex color of the Rhesus monkey. This problem will be discussed in another place.

Summary. Theoretical considerations predicted and the experiment here recorded have proved that in the rhesus monkey the ovaries are not necessary from the twenty-fifth day of pregnancy on for normal gestation, parturition at term, postpartum involution of the uterus and lactation. Surprisingly, the bright red color of the sex skin was maintained, in the absence of the ovaries, not only during gestation but also during lactation.

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Absorption of Sulfathiazole from the Gastrointestinal Tract, Pleura, and Peritoneum of Dogs.

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The recent literature contains many reports describing the use of sulfonamide drugs locally, particularly in the treatment of traumatic and operative wounds. Since these drugs have also been used locally in such highly absorptive areas as the pleural and peri-

⁶ Speert, H., *Bull. Johns Hopkins Hosp.*, 1940, **67**, 189.

⁷ Hartman, Carl G., and Speert, H., in press.

toneal cavities,¹⁻⁶ it appears important to establish experimentally the extents to which they are absorbed from these surfaces in order that safe doses may be approximated.

Hudson, Smith, and Selbie⁶ applied sulfanilamide to the peritoneum of rabbits and noted the time necessary for complete absorption. Keeley⁷ injected a suspension of this drug into the peritoneal cavity of dogs and determined the sulfanilamide content of the blood.

Experiments from this laboratory on sulfanilamide,⁸ and the present experiments on sulfathiazole, were designed to simulate the local use of these drugs after thoracic and abdominal surgery, and to compare the degree of absorption from the pleura and peritoneum with that from the gastrointestinal tract.

Experimental. Four dogs were used for each of the 3 methods of administration, the procedure being identical with that previously described.⁸ Determinations for sulfathiazole were made on blood taken immediately before and at regular intervals after the drug administration. The method of analysis was that of Marshall and Litchfield,⁹ using sulfathiazole as the standard. In all cases the dose was 100 mg per kg. For the oral administration the drug was suspended in water and given by stomach tube after withholding food for 14 hours. For the intrapleural and intraperitoneal administrations the dogs were etherized, operated on under sterile conditions, and the powdered drug deposited into the pleural space, or on the intestines beneath the greater omentum. The incisions were closed and the dogs allowed to recover.

Results. The accompanying graph presents the sulfathiazole values found in the blood after the oral, intrapleural, and intraperitoneal administration of the drug. Each point represents the average of the determinations on 4 dogs. Statistical analysis* of our data showed that for every point, except one, there was no significant

1 Herrell, W. E., and Brown, A. E., *Proc. Staff Meet. Mayo Clinic*, 1940, **15**, 611.

2 Dees, J. G., *Mississippi Doctor*, 1940, **18**, 215.

3 Barondes, R. deR., *Clin. Med. Surg.*, 1940, **47**, 292.

4 Adams, H. D., *Lahey Clin. Bull.*, 1940, **1**, 13.

5 Rosenburg, S., and Wall, N. M., *Surg. Gyn. Obs.*, 1941, **72**, 568.

6 Hudson, R. V., Smith, R., and Selbie, F. R., *Lancet*, 1941, **1**, 438.

7 Keeley, J. L., *Proc. Soc. Exp. Biol. and Med.*, 1941, **46**, 458.

8 Haag, H. B., Spealman, C. R., and McCue, H. M., *Surgery*, in press.

9 Marshall, E. K., Jr., and Litchfield, J. T., *Science*, 1938, **88**, 85.

* According to Fischer's method for small samples.¹⁰

¹⁰ Baten, W. D., *Elementary Mathematical Statistics*, John Wiley and Sons, Inc., N. Y., 1938, p. 271.

difference in the blood levels of sulfathiazole after absorption from the gastrointestinal tract, pleura, and peritoneum. The exception is at the 2-hour point in comparing absorption by the oral and intrapleural routes. At this point the *t*-value (3.87 for 6 degrees of freedom) was somewhat elevated. This would seem to indicate at this one point a significantly higher blood level after pleural than after oral administration.

The peak blood concentrations occurred 2 to 3 hours after administration. These values of 4.24, 4.56, and 5.54 mg per 100 cc of blood for the oral, peritoneal, and pleural routes respectively, are somewhat lower than those obtained in similar experiments from this laboratory using the same dose of sulfanilamide.⁸ In the latter experiments the peak values found (in the same order) were 7.1, 8.2, and 8.2 mg per 100 cc of blood. Goodwin and Findlay¹¹ also found the blood level of sulfathiazole lower than that of sulfanilamide after application to uninfected wounds on the hind legs of rabbits.

Summary. With one exception (as discussed) no significant difference was found in the absorption of sulfathiazole as judged

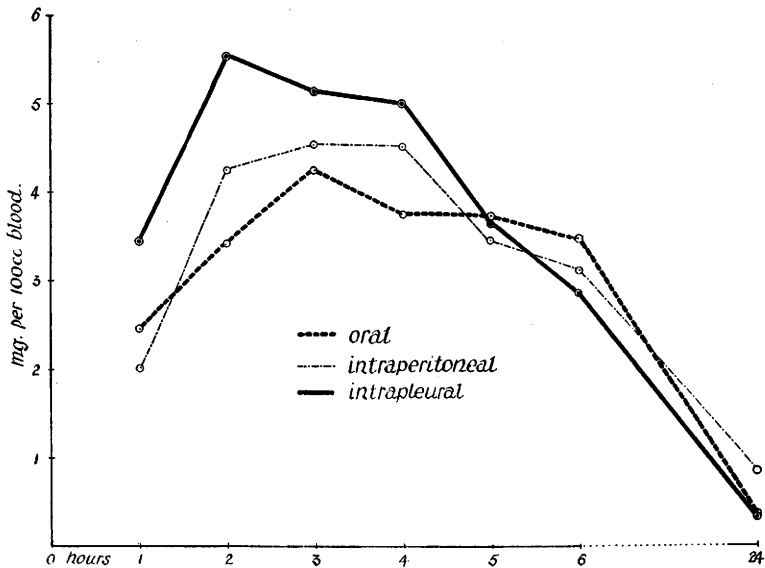


FIG. 1.
Comparative absorption rate of sulfathiazole in dogs following various routes of administration. Dose of sulfathiazole, 100 mg per kg.

¹¹ Goodwin, L. G., and Findlay, G. M., *Lancet*, 1941, 1, 691.

from studies of blood concentration, after oral, intrapleural, and intraperitoneal administration to dogs. Although these experiments are not directly comparable to the clinical use of sulfathiazole, they may well serve as a guide in the matter of dosage in the local application of the drug to the pleural and peritoneal cavities.

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Experimental Production of Tumors by Tars from Various Foods.

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In view of the successful production of tumors by crude coal tar¹⁴ and its derivatives with known chemical composition,¹⁻⁴ interest has been directed to the question whether tars prepared from substances which we eat or smoke are also carcinogenic. Fukida and Kinoshita⁵ found that tar from rice bran is carcinogenic to the skin of mice. Kenneway⁶ produced cancers and papillomas by human skin tar and yeast tar. Shibata¹¹ reported on the carcinogenic action of the tar from sugar. Roffo⁸ found tumor growths in the stomach, liver, and cecum of rats fed on bread and milk to which was added animal fat or olive oil that had been heated to 350°C for half an hour. Widmark¹³ succeeded in obtaining adenocarcinomas of breast with alcohol or petroleum-ether extract of roasted horse muscle, coffee and brown butter. Lü,⁷ Taki,¹² and Sugiura,¹⁰ etc., produced tumors on mice by tobacco tar. Roffo⁹ was able to identify

¹ Cook, J. W., Haslewood, G. A. D., Hewett, C. L., Hieger, I., Kenneway, E. L., and Mayneord, W. V., *Am. J. Cancer*, 1937, **29**, 219.

² Cook, J. W., and Kenneway, E. L., *Am. J. Cancer*, 1938, **33**, 50.

³ Cook, J. W., and Kenneway, E. L., *Am. J. Cancer*, 1940, **39**, 381.

⁴ Cook, J. W., *Nature*, 1940, **145**, 335.

⁵ Fukida, T., and Kinoshita, R., *Transact. Jap. Path. Soc.*, 1923, **13**, 636.

⁶ Kenneway, E. L., *B. M. J.*, 1925, **2**, 1.

⁷ Lü, Fu-hwa, *Frankf. Z. Path.*, 1934, **46**, 513.

⁸ Roffo, A. H., *Bull. de l'Ass. franc. l'etude du cancer*, 1939, **28**, 556.

⁹ Roffo, A. H., *Z. f. Krebsforsch.*, 1939, **49**, 588.

¹⁰ Sugiura, K., *Am. J. Cancer*, 1940, **38**, 41.

¹¹ Shibata, S., *Higu, Kiyo.*, 1928, **12**, 298.

¹² Taki, S., *Osaka Igaku Z.*, 1937, **36**, 483.

¹³ Widmark, E. M. P., *Nature*, 1939, **143**, 984.

¹⁴ Yamagiwa, K., and Ichikawa, K., *Verhandl. d. jap. path. Gesell.*, 1915, **5**, 142.