used to destroy bacteria in plasma are given in the sixth column of Table I. It appears that the treatments used to destroy bacteria directly influenced the metabolism of plasma, as was indicated by the fact that the effects characteristic of given compounds appeared even when bacteria were not present in the samples, for example, those indicated in the first, third, and fourth data-lines of Table I. Since the changes in plasma metabolism following bactericidal treatments appear to be independent of effects attributable to bacteria, but characteristic of the treatments employed, it seems logical to conclude that the quantity of oxygen consumed by those bacteria present was too small to be measured by our method, and therefore completely negligible. The data given in Table I deal with the second hour after ejaculation. Some of these measurements were continued through the sixth hour after ejaculation, but the results indicate that possible errors due to bacteria were negligible even during this longer period.

Conclusions. 1. Extra-cellular respiration was exhibited by seminal plasma of the boar. Oxygen consumption of seminal plasma ranged from 5 to 22% of that of the whole semen. The R.Q. was unity. After the plasma had been held for 5 minutes at 100°C respiration at reduced intensity was observed. Respiration was not exhibited by that fraction of the seminal plasma which passed through a porcelain filter. 2. The metabolic rate of the ejaculate of a cryptorchid boar was of the same order as that of seminal plasma. 3. No errors in measurement of oxygen consumption were detected which could be attributed to the presence of bacteria.

12028

Intraperitoneal Administration of Sulfanilamide; Concentration in Peripheral Blood in Dogs.

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The reports of encouraging results following the use of sulfanilamide administered subcutaneously in the treatment of peritonitis of appendiceal origin[1, 2] have prompted the use of this drug in

[1] Ravdin, I., Rhoads, J. E., and Lockwood, J. S., *Ann. Surg.*, 1940, **111**, 53.

[2] Corry, D. C., Brewer, A. C., and Nicol, C., *Brit. M. J.*, 1939, **2**, 561.

peritonitis due to rupture or inflammation at other levels of the gastrointestinal tract.[3, 4] Sulfanilamide has also been used as a prophylactic preoperative measure in surgery of the colon and rectum.[4, 5] More recently sulfanilamide in dry form has been sprinkled about the area of peritonitis disclosed at operation for the removal of a diseased appendix or for the closure of a ruptured peptic ulcer.[6, 7] Since no report concerning the blood levels of sulfanilamide following its introduction into the normal peritoneal cavity was found in the literature, the following experiments were performed to make such determinations.

Normal healthy mongrel dogs weighing from 4.6 to 8 kg were used. There was no restriction of food, drink, or activities during the 48 hours before and after the intraperitoneal injection. After obtaining a control sample of blood from a jugular vein, a suspension of sulfanilamide crystals* in distilled water was injected into the peritoneal cavity through the upper portion of the left rectus muscle. Five animals received .3 g per kg, 2 animals received .6 g per kg, and 3 animals received 1 g per kg of the drug. Subsequent blood samples, also from the jugular vein, were obtained 15 minutes after the injection and at 2-hour intervals up to 12 hours. In some of the animals 24- and 48-hour specimens were obtained. The samples were placed in tubes containing sodium oxalate and the sulfanilamide concentration was determined by the method of Marshall.[8]

TABLE I.

Blood Concentrations of Sulfanilamide in Relation to Dosage and Intervals Following Intraperitoneal Administration.

Dog		A	B	C	D	E	F	G	H	I	J
Sex		F	F	F	F	F	F	F	F	F	F
Weight, kg		6	8	6.8	5.5	4.6	6.2	6.8	5.9	5.5	6
Dose		.3 g per kg					.6 g per kg		1 g per kg		
Blood Level of Sulfanilamide in mg% Interval after inj'n	Control	0	0	0	0	0	0	0	0	0	0
	15 min.	0.66	0.84	2.1	2.21	4.2	3.9	3.51	7.5	0.2	4.26
	2 hr	3.6	3.75	3.6	4.9	6.3	6.9	5.1	16.7	3.0	6.0
	4 "	2.7	2.49	4.5	6.6	4.6	5.7	4.5	18	5.4	7.2
	6 "	2.25	2.13	3.0	6.0	4.08	5.1	4.2	15	6.9	8.58
	8 "	1.98	1.8	—	—	—	4.2	2.85	—	7.8	6.6
	10 "	1.32	1.05	1.92	4.5	3.06	3.0	2.7	6.9	9.9	—
	12 "	1.05	0.99	1.41	3.0	2.88	1.8	2.28	6.3	4.9	6.4
	24 "	—	—	1.08	2.2	1.5	0.81	0.84	5.7	3.75	1.8
	48 "	—	—	—	—	0.16	—	—	1.11	3.0	—

[3] Lockwood, J. S., and Rhoads, J. E., *S. Clin. North America*, 1939, **19**, 1457.

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[5] Garlock, J. H., and Seley, G. P., *Surgery*, 1939, **5**, 787.

[6] O'Neil, L. J., personal communication.

[7] Mueller, R. S., *J. A. M. A.* (Correspondence), 1941, **116**, 329.

* P-aminobenzenesulfonamide, manufactured by Eastman Kodak Co.

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

Fig 1

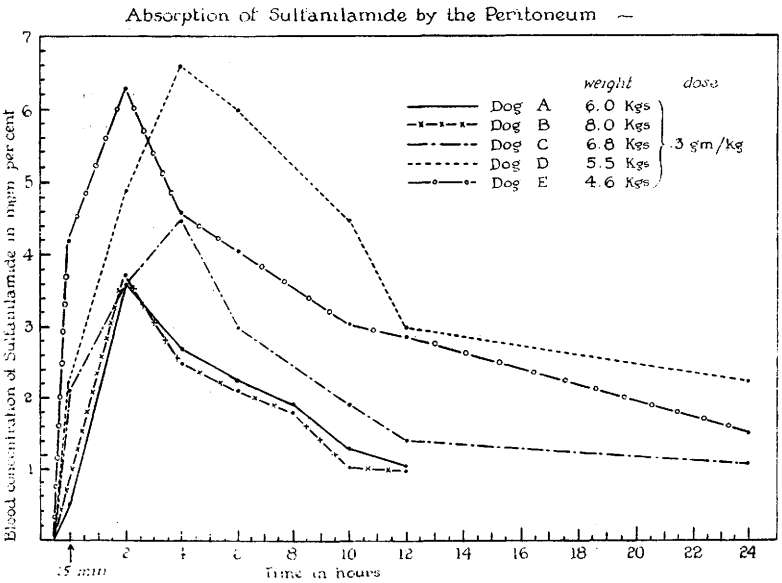
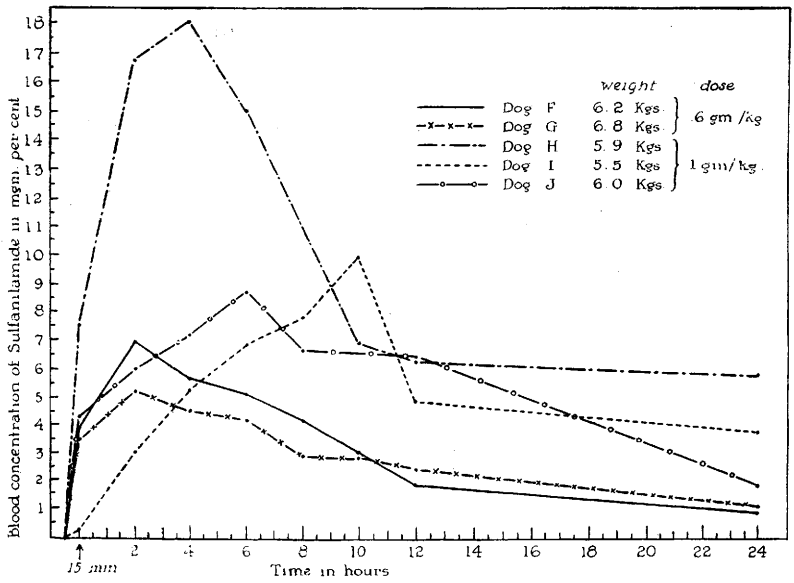


Fig 2



The results are shown in Table I and the trends of the values are presented in Figs. 1 and 2. All blood samples obtained 15 minutes after the injection contained sulfanilamide, the concentration varying

from .66 to 7.5 mg % and averaging 2.6 mg %. The higher values were associated with the larger doses.

Of the 5 animals which received .3 g per kg, the maximum concentrations of sulfanilamide were found in the 2-hour samples in 3. These peak values varied from 3.6 to 6.6 mg % and averaged 4.99 mg %. The maximum concentrations in the 2 animals which received .6 g per kg were 6.9 and 5.1 mg %. They averaged 6 mg % and were found in the 2-hour samples. In the animals which received 1 g per kg of the drug, the maximum concentrations were higher and occurred later. Thus, values of 18, 8.5 and 9.9 mg % (average 12.1 mg %) were found 4, 6, and 10 hours after injection. These maximal concentrations were followed by decreases which were less rapid in the animals receiving the larger doses and which tended to become less marked after 12 hours as judged by the 24-hour levels.

Marshall, Emerson, and Cutting[9] found that a maximum concentration of from 10 to 15 mg % was present in 3 to 4 hours after the oral or subcutaneous administration of .1 g of sulfanilamide per kg of body weight in dogs. In the present series of experiments, the maximum concentration of sulfanilamide in the blood exceeded 10 mg % in one animal only, dog "H", which received 1 g/kg of body weight. It is possible that when sulfanilamide is given intraperitoneally it is incompletely absorbed or that it may leave the blood stream rapidly, either due to absorption by the tissues or to excretion by the kidneys, thus preventing high levels of the drug in the blood. These points remain for further study.

Signs of toxicity occurred in only 2 animals, dogs "H" and "J", both of which received 1 g/kg doses of sulfanilamide. Retching, weakness, and diarrhea appeared in these animals within 2 hours. At 6 hours they had convulsions and exhibited marked extensor rigidity. Partial narcosis followed. The most severe toxic manifestations were synchronous with maximal concentrations of the drug in the blood. The animals appeared to be completely recovered in approximately 12 hours after the most severe signs of toxicity. Marshall, Cutting and Emerson[10] found no observable symptoms of toxicity with blood concentrations under 30 mg % in dogs receiving single doses of the drug orally. They point out, however, that this level of blood concentration may have been maintained for

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

10 Marshall, E. K., Jr., Cutting, W. C., and Emerson, K., *J. A. M. A.*, 1938, **110**, 252.

only a short period of time. Concerning the relation of toxic symptoms to dosage, the same authors found that of 7 dogs receiving 1 g/kg of sulfanilamide in capsules by mouth 5 showed toxic symptoms but no mention was made of the concomitant blood levels in these animals.

Conclusions. Sulfanilamide is promptly absorbed from the peritoneal cavity in dogs. Following the intraperitoneal injection of sulfanilamide the levels of concentration of the drug in the peripheral blood are not as high as those reported by other investigators following the oral or subcutaneous administration of smaller doses.

12029

Catheterization of the Right Auricle in Man.

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Forssmann[1] first used catheterization of the right heart on himself, after exposure of a vein of the arm by a surgeon. Numerous other investigators since have used right heart catheterization for visualization of the right chamber of the heart and pulmonary vascular trees by means of contrast substance.[2-7] The introduction of the Robb and Steinberg method,[8] however, renders this method unnecessary for the latter purpose. Collection of right heart blood by catheterization of the right auricle for determining cardiac output in man[9] is mentioned by Grollman,[10] who discredits it because of the possible

*Supported by a grant from the Commonwealth Fund.

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8 Robb, G. P., and Steinberg, I., *J. Clin. Invest.*, 1938, **17**, 507.

9 Klein, O., *Muench. Med. Wchschr.*, 1930, **77**, 1311.

10 Grollman, A., *The Cardiac Output of Man in Health and Disease*, Monograph, Williams and Wilkins Co., Baltimore, 1932.