In order to determine whether the same relationship between specific gravity and protein concentration exists in rabbit plasma as in human and dog plasma, blood from 20 normal rabbits fed on Purina chow and later from the same animals suspended by their ears until they became unconscious from peripheral circulatory deficiency ("gravity shock")[6] has been studied. The plasma of arterial heart blood was analyzed for protein by the micro-Kjeldahl method, for glucose by the Folin-Wu method as modified by Andes and Northup,[7] and the specific gravity was determined by the falling drop method.

In Fig. 1 plasma protein before and during gravity shock is plotted against plasma specific gravity. The data for normal animals are well described by the line drawn through the open circles having the equation: $P = 375\ (G_p - 1.0064)$, which is of the same order of magnitude as the equation reported for human[1] and dog[2] plasma. For rabbits in gravity shock, however, the constant relation between specific gravity and protein concentration did not hold, as indicated by the solid circles, showing even greater divergencies than those found by Moore and Van Slyke[1] in human nephritic patients. The greatest differences below the line occurred in animals with high plasma glucose, as might be expected from the work of Simeone and Sarris.[8] More data are needed to determine why the discrepancies exist, although there is indication that increased glucose and non-protein nitrogen are involved.

It is concluded that the linear relationship between protein concentration and specific gravity of normal rabbit plasma is essentially the same as that for human and dog plasma. For rabbits in gravity shock, however, the correlation of protein concentration and specific gravity is low. A similar low correlation may be found for other animals showing shock symptoms.

[6] Allison, J. B., Cole, W. H., Leathem, J. H., Nastuk, W. L., and Anderson, J. A., *J. Biol. Chem.*, 1943, **147**, 255.

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Pharmacology of Sodium Sulfanilylsulfanilate.*

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Sodium sulfanilylsulfanilate, a derivative of sulfanilamide, was first used therapeutically by Dochez and Slanetz[1] against a fatal infection in ferrets supposed to be due to and resembling dog distemper. MacIntyre and Montgomerie[2] in England employed this drug unsuccessfully in infections due to the distemper virus described by Carre-Laidlaw-Durkin. Oakley[3] used it without benefit in experimental influenza. Coggeshall[4] tested sodium sulfanilylsulfanilate in avian malaria. Hebb, Sullivan, and Felton[5] recommended

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† Deceased November 9, 1943.

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[3] Oakley, G. L., *Brit. Med. J.*, 1938, **1**, 895.

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TABLE I.
Fate of a 5-g Oral Dose of Sodium Sulfanilylsulfanilate.

Blood:
Blood was drawn 5 min, 1 hr, 6 hr and 24 hr after administration.
Blood contained only traces of the drug.

Urine and Feces:
Sulfanilylsulfanilate in mg; Output in Urine and Feces.

	4 hr	6 hr	24 hr	48 hr	72 hr	Total recovery	% recovery
Urine:							
Free	114	38	14	trace		166	3.3
Conjugated	27	21	11	"		59	1.2
Total	141	59	25			225	4.5
Feces:							
Free			1200	7	41	1248	24.9
Conjugated			700	2	31	733	14.6
Total			1900	9	72	1981	39.5

Percent recovery combined—44.0.

sodium sulfanilylsulfanilate and sodium sulfanilate for the treatment of lymphopathia venereum. This report deals with the pharmacology and toxicity of sodium sulfanilylsulfanilate.

Sodium sulfanilylsulfanilate was determined by the Marshall[6] method using alpha dimethylnaphthylamine in alcoholic solution as the coupling component. Determinations were made on whole blood, urine, and fecal discharges. The fate of single and repeated doses were studied in some normal subjects and in patients, following oral and intravenous administration.

Six subjects were given single 5 g doses of sodium sulfanilylsulfanilate. In all 6 cases only traces were observed in the blood. The drug, however, may be recovered in the urine and feces. As shown in Table I, only 4.5% of the total ingested was excreted in the urine while the fecal excretion was 39.5%. In 10 patients repeated oral doses of 5 g statim and 1 g every 4 hours yielded only traces in the systemic circulation. In 2 subjects 10 g 3 times daily resulted in systemic blood levels of 1.0 mg % per 100 ml or less.

When 50 ml of a 10% solution of sodium sulfanilylsulfanilate was administered intravenously immediate high blood concentrations were observed. However, as is usual with intravenous sulfonamide therapy, though the rise in concentration is rapid, the fall is equally fast. It will be noted in Chart II that 15 minutes following a 5 g intravenous administration the concentration in the blood was 12 mg per 100 ml. Five hours afterwards, it was only 1.0 mg per 100 ml of blood. This rapid fall was also observed by Dochez and Slanetz.[1] After intravenous administration most of the drug is recovered from the urine and only small amounts are present in the feces and is completely excreted in 24 to 48 hours. From 75 to 83% was recovered from the urine and feces. The urine alone accounted for 70 to 80% of the recovery. From 15% to 35% of the administered drug was conjugated.

The low recovery from the urine and the high fecal value, when the drug is given orally, might indicate that little of the drug is absorbed from the gastrointestinal tract. We administered orally to 6 rabbits 1 g per kilo body weight of this compound. Two of these rabbits received 1 g of sodium sulfanilylsulfanilate per kilo body weight for 4 days and 2 g for 2 subsequent days. Daily bloods drawn from the ear showed only traces of the drug. At the completion of the drug administration these animals were operated and specimens of venous blood, portal blood, and gall bladder bile were taken for analyses. The venous blood yielded only traces of the drug. The concentrations of the bloods obtained from the portal veins were 1.8 mg % and 2.0 mg % per 100 ml and from the bile the concentrations were 2.9 mg % and 7.2 mg % per 100 ml in 2 rabbits. Drains were inserted into the gall bladders and the ob-

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

TABLE AND CHART II.
SULFANILYLSULFANILATE IN BLOOD, URINE AND FECES

[MGS.] SULFANILYLSULFANILATE OUTPUT IN URINE						RECOVERY	
HOURS	2	4	24	48	72	TOTAL	PER-CENT
FREE	1947	570	58	103	48	2726	54.5
CONJUGATED	973	330	11	20	12	1346	26.9
TOTAL	2920	900	69	123	60	4072	81.4

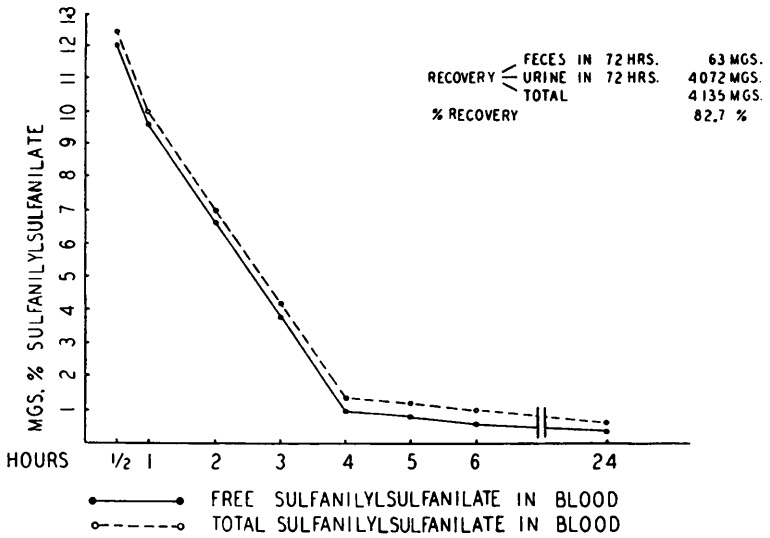

TABLE III.
Mg of Sulfanilylsulfanilate per 100 g of Material.

Rabbit No.	Ear blood	Portal vein blood	Bile	Stomach contents	Duodenal contents	Large gut contents
1	trace	2.0	7.8	22.6	1.0	
2	0.6	1.1	4.6	36.5	14.0	320.0
3	1.6	1.6	4.8	27.0	10.7	240.0
4	trace	2.1	5.9	39.1	9.4	290.0

servations were continued. Twenty-four hours after the drains were inserted ear blood showed traces and the drained bile 1.0 mg % per 100 ml of the drug. At this time the rabbits were given 1 g of sodium sulfanilylsulfanilate and 24 hours after the concentrations in the ear blood were 0.5 mg % per 100 ml and 0.6 mg % per 100 ml. For the bile the concentrations were 3.2 mg % per 100 ml and 4.3 mg % per 100 ml. Four rabbits were fed sodium sulfanilylsulfanilate and were sacrificed. Contents of various organs were analyzed for the drug (Table III). The greatest concentrations were found in the bile obtained from the gall bladder. This suggests that most absorption occurs by the portal system and may account for high concentrations in the feces as well as for its beneficial effect on lesions in the bowel as reported elsewhere.[7]

Discussion. Only traces of sodium sulfanilylsulfanilate were found in the blood when 0.5 to 5.0 g were administered orally. After 10 g 3 times daily the systemic blood levels were low. High systemic blood concentrations may be noted when the drug is given intravenously, however, the concentrations thus obtained fall very rapidly. In rabbits high concentrations were noted in the bile indicating portal absorption and excretion into the gastrointestinal tract.

[7] Levy, J., Holder, E., and Bullowa, J. G. M., *Am. J. Dig. Dis.*, 1942, **9**, 237.