weight and an increase in blood sugar; these changes are more marked than they were on the balanced diet; the level of the drug in the blood is higher. The decrease in liver glycogen is of the same order as on the balanced diet.

In conclusion, it appears that a high protein diet decreases the effect of sodium sulfapyridine on liver glycogen, while a high fat diet does not appear to increase the susceptibility of the liver to the action of sodium sulfathiazole.

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Sulfonamides and the Blood pH.*

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In a previous paper (Wertenberger[1]) on the effect of single doses of some of the sulfonamide preparations upon blood pH, it was shown that intraperitoneal injections of the sodium salts of sulfapyridine (sodium 2-para-amino-benzene-sulfonamido pyridine) and sulfathiazole (sodium 2-para-amino-benzene-sulfonamido-thiazole) produced a marked rise in blood pH, while sulfadiazine (2-sulfanil-amido-pyrimidine) showed only a slight rise.

Since the sulfonamides are most frequently given by mouth, this study was extended to include a comparison of the effects produced by oral and intraperitoneal administration.

Method. Albino male rats from a standard strain of approximately the same age and weighing between 100 and 150 g were used. The animals were kept on a standard diet (Purina Dog Chow Checkers) for one week before treatment. All rats were fasted for 18 hours before the experiment.

The blood pH was determined electrometrically with the glass electrode using the Behrmann-Fay[2] blood chamber as previously described (Wertenberger[1]).

Drug concentrations in the blood were determined by the method of Bratton and Marshall[3] using the photoelectric colorimeter.

A sufficient amount of blood was withdrawn at one time for both the pH and drug concentration determinations in all of the experiments except two.

Results and Discussion. A total of 147 rats was used for this study and the data are summarized in Table I. Sodium sulfapyridine and sodium sulfathiazole produce a marked rise in blood pH when given intraperitoneally and the blood level is high.

This shift does not occur, however, when the drugs are given orally and the blood level is much lower. In the series run 6 hours after treatment, there was a slight rise in the blood pH with sulfapyridine but none with sulfathiazole even though the concentration in the blood had risen to about one-third of the concentration observed after intraperitoneal injection.

The effect of sulfathiazole is not quite as marked, however, and the blood levels are lower and show the least conjugation. This latter fact was observed by Van Dyke and co-workers[4] who found that sulfathiazole is more rapidly metabolized and undergoes less conjugation than sulfapyridine.

Sodium sulfadiazine by intraperitoneal injection was studied in a series comparable to those previously run on sulfapyridine and

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1 Wertenberger, Grace E., *Medical Times*, 1941, **69**, 471.

2 Behrmann, V., and Fay, M., *Science*, 1939, **90**, 187.

3 Bratton, A. C., and Marshall, E. K., Jr., *J. Biol. Chem.*, 1939, **128**, 537.

4 Van Dyke, H. B., Greep, R. O., Rake, G., and McKee, C. M., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 410.

TABLE I.
Comparison of Effect of Oral and Intraperitoneal Administration of Sulfonamides upon Blood pH.

Compound	Dose 1 cc/100 g rat %	No. rats	Route	Observation period, hr	Avg pH			Blood levels of drug mg/100 cc blood		
					Initial	After drug	Change	Free	Total	Combined
Controls	—	10	—	3	7.51	7.50	—.01	.58	.58	0
	—	4	—	6	7.49	7.50	+.01	1.30	1.30	0
Sodium Sulfapyridine	10	13	Intraperit.	3	7.51	7.59	+.08	59.88	67.94	8.06
	10	16	Oral	3	7.48	7.48	.0	12.52	14.97	2.45
	10	11	"	6	7.47	7.50	+.03	18.79	22.14	3.35
Sodium Sulfadiazine	10	28	Intraperit.	3	7.516	7.53	+.014	—	—	—
	10	6	"	3	7.50	7.49	—.01	139.67	154.06	14.39
	10	11	Oral	3	7.50	7.50	.0	—	—	—
	10	7	"	6	7.49	7.49	.0	68.44	80.56	12.12
	1	6	Intraperit.	3	7.476	7.49	+.014	13.49	15.02	1.53
Sodium Sulfathiazole	10	14	"	3	7.51	7.58	+.07	54.63	62.49	7.86
	10	9	Oral	3	7.48	7.49	+.01	—	—	—
	10	6	"	6	7.48	7.48	.0	14.56	16.88	2.32
	1	6	Intraperit.	3	7.49	7.49	.0	4.89	6.11	1.22

sulfathiazole. It is evident that it does not produce the marked effect on the blood pH shown by the other preparations, even though the blood levels were much higher. However, there is some individual variation in the effect of the drug for 8 (about 25%) of the animals showed an increase of .04 unit or more in blood pH. The majority, however, showed no change. No evidence of toxicity was observed and no animals died during the experimental period.

It is evident that in the case of sulfapyridine and sulfathiazole single doses given intraperitoneally, if sufficiently concentrated, by their rapid absorption and sudden rise in the blood stream affect the buffer capacity of the body and give rise to an alkalosis. When the blood level rises more slowly as with oral administration and slow absorption, the buffer capacity of the body is not embarrassed and the normal blood pH is maintained.

Sulfadiazine, however, does not have this effect.

Summary. Single doses of the sodium salts of sulfapyridine and sulfathiazole cause a marked rise in the blood pH which is greatest in the case of sulfapyridine when they are given by intraperitoneal injection. This rise does not occur when they are administered orally even when the observation period is doubled and the blood level of the drug has risen somewhat higher, though it is markedly lower than the level observed three hours after intraperitoneal injection.

Sodium sulfadiazine, on the other hand, does not have this marked effect upon blood pH when administered intraperitoneally or orally even though the blood level is more than twice that observed in either of the other preparations.

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