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Gaseous Distention in the Obstructed Small Intestine of Cats.

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In a previous paper[1] we demonstrated that sulfathalidine and sulfamethazine exert an inhibiting effect on gas production in the obstructed small intestine of the cat. This report concerns similar studies of other sulfonamides and of penicillin and streptomycin.

The following drugs were investigated: Sulfadiazine, sulfamerazine, sulfathiazole, sulfasuccidine, penicillin and streptomycin. Phthalic acid and succinic acid were tested because they are hydrolytic products of sulfathalidine and sulfasuccidine.[2] Additional experiments with sulfathalidine and sulfamethazine in smaller doses were carried out and are compared with the previously reported results with the larger doses.

Method. The experimental method is identical with that used previously. Cats weighing 1½-3 kg, which had been deprived of food and water for 24 hours, were subjected to laparotomy with the usual sterile precautions. A heavy cotton ligature was used to completely occlude the esophagus at the cardio-esophageal junction. A similar ligature was applied to the ileum just proximal to the ileocecal junction, thus producing a closed loop. Although the stomach was free of solids or liquids, gas up to 30 cc was present occasionally. This was aspirated prior to injection of the material to be studied. Two teaspoonfuls of powdered malted milk* in 100 cc of milk, with or without the drug to be tested, was injected into the stomach. The dose of sulfonamide was 1.5 g/kilo in most experiments; in the remaining ones, 0.5 g/kilo. The dose of penicillin was 30,000 U/kilo and of streptomycin 60,000 U/kilo. After 22-26 hours the animals were sacrificed by etherization and the amount of gas and liquid or semisolid contained in the closed loop was measured.

A total of 178 cats were studied. Six cats, not included in the results, were found dead after 24 hours. Most of these had received no drug. They showed enormous gaseous distention as the probable cause of death.

Results. Table I lists the average amounts of gas found and also the greatest and smallest amounts, to demonstrate the range of effectiveness of the various drugs used. No relation whatever was apparent between the amount of gas and the amount of solid and liquid material.

The data show that sulfadiazine, sulfamerazine, sulfamethazine, sulfathiazole and sulfathalidine are equally efficacious in depressing gas formation from malted milk in a closed loop. Doses of 0.5 g/kilo are just as effective as the larger dose. Both doses are large compared to amounts used clinically. Sulfasuccidine is definitely less effective, though significantly better than the controls. Succinic and phthalic acid have no effect whatever on gas production. Of the drugs studied, penicillin proved to be the most powerful inhibitor of gas formation. Streptomycin, on the whole, showed a good depressing effect, but the amounts of gas varied over a wide range.

Discussion. Since the sulfonamides in general exert their action on the gram negative bacteria of the intestinal tract (coli-aerogenes group) and on the clostridia normally present there, it is not surprising that these drugs work very much alike in depressing gas formation.

Of the 2 conjugated sulfonamides studied sulfathalidine exerts a definite antibacterial action *in vitro* and in the gut[2,3] while sulfa-

1 Segel, A., Schweinburg, F., and Fine, J., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 17.

2 Poth, E. J., and Ross, C. A., *Texas Reports on Biol. and Med.*, 1943, **1**, 345.

* Wander Powdered Malted Milk.

TABLE I.

Drug	Dose, g/k	No. of cats	cc gas		
			Max.	Min.	Avg
Sulfadiazine	1.5	10	35	4	14.3
"	.5	10	32	6	16.9
Sulfamerazine	1.5	10	30	1	12.8
Sulfamethazine	1.5	10	30	0	12.0
"	.5	4	14	8	10.0
Sulfathiazole	1.5	6	22	7	12.0
"	.5	12	25	1	11.1
Sulfathalidine	1.5	20	60	0	17.5
"	.5	4	31	5	15.2
Phthalic acid	.6	5	210	87	155.0
Sulfasuccidine	1.5	12	175	13	44.0
Succinic acid	.5	5	164	62	101
Penicillin	30.0 U/kg	10	38	0	8.5
Streptomycin	60.0 U/kg	29	225	0	33
Controls	—	31	215	55	117

succidine does not act *in vitro* but acts in the gut only after hydrolysis.[4] This fact explains the less effective action of sulfasuccidine. Phthalic and succinic acid exert no inhibitory action.

Since penicillin has no effect, except in excessive doses, on gram negative bacilli, it acts presumably by suppressing the clostridia which are present in the gut.

Since coliform bacteria predominate and clostridia are relatively few, one would expect gas formation to be suppressed to a lesser degree by penicillin than by those drugs which work on both clostridia and gram negative bacilli. This is not the case, however, since it works best of all the drugs studied.

The results with streptomycin are difficult to explain. The range of gas production is fairly narrow for all drugs except streptomycin. Of 29 cats treated with streptomycin, 16 had either no gas or less than 5 cc; 6 had less than 25 cc; 3 showed amounts of gas between 25 and 100 cc and 4 had 110, 150, 195, and 225 cc of gas respectively. The last of these is a little more than the highest amount of gas found in the controls, or with phthalic and succinic acid, which may also be considered controls. We are not able to explain these observations.

A study of the chemical composition of the gas and the associated changes in the bacterial flora of the small intestine of dogs brought about by these drugs is proceeding.

Conclusions. Gas formation from malted milk in milk in a closed loop, comprising the stomach and the entire small intestine, is markedly depressed by sulfadiazine, sulfamerazine, sulfamethazine, sulfathiazole and sulfathalidine. There is a definitely less, but still significant depression by sulfasuccidine. Phthalic and succinic acid have no inhibitory effect on gas production. Streptomycin works well in the majority of the experiments, but is a complete failure in others. Penicillin works best of all the drugs tested.

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[3] Schweinburg, F. B., and Yetwin, I. J., *J. Bact.*, 1945, **49**, 193.

[4] Poth, E. J., and Knotts, F. L., *Arch. Surg.*, 1942, **44**, 208.