enzymes by stimulation of the pancreas cannot cause any change at this stage.

Summary. In 2 dogs separation of the pancreas from the duodenum with permanent occlusion of all pancreatic ducts was followed by a transient increase of blood amylase. No permanent increase of blood amylase was found as has been reported by others. The dogs showed no increase of blood lipase after the operation. One of these dogs had a secondary and tertiary rise of blood amylase as described by Gould and Carlson, and a transient rise of blood lipase coincident with the secondary rise of amylase.

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Sulfonamide Compounds in Treatment of Experimental *B. typhosus* (*Eberthella typhosus*) Infections of Rabbits.

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Buttle, Parish, McLeod and Stephenson[1] found that p-aminobenzenesulfonamide protects mice against multiple lethal doses of *B. typhosus* and *B. paratyphosus B.* Kolmer and Rule[2] also observed that sulfanilamide administered by subcutaneous and intraperitoneal injection was slightly effective in the treatment of mice inoculated intraperitoneally with *B. typhosus* but noted that sulfapyridine was less effective.

In the present investigation sulfanilamide, sulfapyridine and sulfathiazole were employed by oral administration in the treatment of rabbits inoculated intravenously with *B. typhosus.* The strain employed was of such virulence that the intravenous injection of 0.6 cc of 24-hour broth culture per kilo produced a rapidly fatal infection. Since it was desired to produce a prolonged infection for treatment purposes rabbits were given 0.2 cc of culture per kilo intravenously at daily intervals for 6 days. As a general rule 3 inoculations at daily intervals produced fatal infections with positive heart blood cultures and this amount was employed in order to avoid overwhelm-

[1] Buttle, G. A. H., Parish, H. J., McLeod, M., and Stephenson, D., *Lancet*, 1937, **1**, 681.

[2] Kolmer, J. A., and Rule, A. M., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 615.

ingly severe infections and to permit the administration of multiple doses of the compounds.

Each compound was given orally in doses of 0.1 and 0.2 g per kilo twice daily for 8 days to surviving animals. The first dose of each was administered 2 hours after the first inoculation of culture and the second 4 hours later, followed thereafter by 2 doses daily (10 a.m. and 3 p.m.). The subsequent daily inoculations with *B. typhosus* were 2 hours before the morning doses of compounds. Heart blood cultures were made daily.

The results are summarized in Table I. Of 16 untreated controls 4, or 25%, survived, indicating that the amount of culture employed was about the minimal lethal dose and therefore favorable for eliciting any therapeutic effects on the part of the compounds employed. It will be observed that of 12 rabbits given sulfanilamide in dose of 0.1 g per kilo 8, or 66.6%, survived while 4 (33.3%) survived with this dose of sulfapyridine and 4 (33.3%) with sulfathiazole. In other words, sulfanilamide was more effective than sulfapyridine as observed in our previous investigation employing mice.[2]

With sulfanilamide in dose of 0.2 g per kilo all of the animals survived; the same was observed with sulfapyridine but only 4 (33.3%) survived in the case of sulfathiazole. It would appear, therefore, that these sulfonamide compounds possess some therapeutic activity in the treatment of rabbits inoculated intravenously with virulent *B. typhosus* but that the effects are slight, as likewise found in the treatment of mice inoculated intraperitoneally. Of the 3 compounds employed sulfanilamide was found most effective, followed in order by sulfapyridine and sulfathiazole.

Apparently recovery of the surviving rabbits was aided by the rapid production of antibodies as the sera of all surviving animals,

TABLE I.

Sulfonamide Compounds in Treatment of Experimental *B. typhosus* Infections of Rabbits.*

Compounds†	Dose per kg (g)	No. animals	Survivals; Days								% survivals
			1	2	3	4	5	7	10	14	
Sulfan.	0.1	12	12	12	12	12	8	8	8	8	66.6
"	0.2	12	12	12	12	12	12	12	12	12	100
Sulfapyr.	0.1	12	12	12	12	8	4	4	4	4	33.3
"	0.2	12	12	12	12	12	12	12	12	12	100
Sulfathiazole	0.1	12	12	8	4	4	4	4	4	4	33.3
"	0.2	12	12	12	6	4	4	4	4	4	33.3
Controls	—	16	16	16	12	8	8	4	4	4	25

*Inoculated intravenously with 0.2 cc of 24-hr broth culture per kg daily for 6 days.

†Twice daily (10 a.m. and 3 p.m.) for 8 days in succession.

including the 2 controls, showed the presence of H agglutinins for the strain employed in final dilution ranging from 1:2560 to 1:5120 when tested about 2 weeks after the termination of the experiment. Agglutination of O antigen ranged from 1:10,240 to 1:40,960 with all of the sera tested.

Of the 16 untreated controls 12 showed positive blood cultures at daily intervals up to the time of death; blood cultures of the 4 surviving animals were negative throughout. Of the 72 treated animals positive blood cultures were observed at daily intervals up to the fourth day of treatment in 50 or 70%; thereafter they were sterile in the case of those that subsequently succumbed, as likewise in those surviving.

Summary. (1) Sulfanilamide, sulfapyridine and sulfathiazole were slightly effective in the treatment of *B. typhosus* septicemia of rabbits. (2) Sulfanilamide was found most effective followed in order by sulfapyridine and sulfathiazole. (3) Recovery was apparently aided by the rapid production of antibodies (agglutinins).

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Failure of Sulfonamide Compounds in Treatment of Experimental *B. diphtheriae* (*Corynebacterium diphtheriae*) Infections of Guinea Pigs.

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To the best of my knowledge the effects of the sulfonamide compounds in the treatment of experimental *Corynebacterium diphtheriae* infections have not been reported upon and no reports are available upon their use in the treatment of diphtheria of human beings. As herewith reported, neoprontosil, sulfanilamide, sulfapyridine and sulfathiazole by oral administration to guinea pigs inoculated with 1 to 2 minimal lethal doses of the virulent bacillus have proven ineffective insofar as mortality is concerned although it is reasonable to assume that their administration to human cases of diphtheria may be helpful in combatting secondary infections with hemolytic streptococci, pneumococci and *Staphylococcus aureus.*

The virulence of the strain of *Corynebacterium diphtheriae* selected was such that subcutaneous injection (abdominal) of 0.6 to 0.8 cc of a suspension carrying about 1000 million per cc harvested