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Prevention by Succinyl Sulfathiazole of Ulcerative Cecitis in Rats.

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In a previous note[1] we reported that inclusion of sulfaguanidine in the normal ration prevented the development of ulcerative cecitis in a rat colony in which the disease was occurring in most of the untreated animals. It seemed of interest, therefore, to study the prophylactic value of the new drug succinyl sulfathiazole* which has already been shown to be highly effective in eliminating various organisms from the intestinal tract. Succinyl sulfathiazole acts, as Poth[2] has shown, by breakdown in the bowel with liberation of sulfathiazole which is the effective agent.

Ulcerative cecitis of rats has been well described recently by various observers and in order to save repetition the reader is referred to these papers.[3] Suffice it to say that the main features are superficial ulceration of the mucosa of the cecum associated with inflammatory thickening of the bowel wall, marked pericecitis and regional adenitis. There is considerable superficial resemblance to so-called regional enteritis in man. Although paratyphoid bacilli are intimately associated with rat cecitis we have shown[4] that these organisms are probably not the primary cause (which at present remains unidentified) although there can be little doubt that the disease is an infection.

Experiments. Twelve normal male rats, 64 days old, were placed on the stock diet of the laboratory† in which 1% of succinyl sulfathiazole was incorporated. As each rat eats 10 to 15 g of the ration daily he ingests 0.1 g of the drug, which would correspond in a 60 kg man with a daily dose of 30 g. Eight litter mate rats were placed on the stock diet without the drug as controls. The animals all throve and there was no essential difference in the weight of the two groups. After 110 days on the drug (174 days old) the rats were exsanguinated under ether anesthesia.

All the animals looked well, and no lesions of any sort were found in the rats which had received succinyl sulfathiazole. The cecums were large and contained bulky, soft masses of feces, slightly lighter in color and with less odor than in the controls. No ulceration was found in the cecum and there was no enlargement of regional lymph nodes. Among the untreated litter mate controls, on the other hand, 38% showed typical lesions of ulcerative cecitis.

In addition to this group of litter mate

TABLE I.
Incidence of Ulcerative Cecitis in Rats Receiving Succinyl Sulfathiazole and in Controls.

	No.	Cecitis present	% showing cecitis
Rats receiving Succinyl sulfathiazole	12	0	0
Untreated litter mate controls	8	3	38
Other control groups of same age	18	8	
	13	7	
	12	7	
	12	4	48
	8	5	
	8	4	
	8	3	
	6	3	
	85	41	

† Casein 10, corn meal 73, linseed cake meal 10, sardine oil 3, alfalfa 2, bone ash 1.5, and NaCl 0.5 parts.

1 Bloomfield, A. L., and Lew, W., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 363.

* We are indebted to Sharp and Dohme, Inc., for the succinyl sulfathiazole used in these experiments.

2 Poth, E. J., Knotts, F. L., Lee, J. T., and Innui, F., *Arch. Surg.*, 1942, **44**, 187.

3 Stewart, H. L., and Jones, B. F., *Arch. Path.*, 1941, **31**, 37.

4 Bloomfield, A. L., and Lew, W., to be published.

controls we have records of the incidence of cecitis in other groups of normal rats of approximately the same size raised on the stock diet. These findings are summarized in Table I.

Pooled serum from the rats receiving succinyl sulfathiazole was tested for its sulfonamide content which was 0.8 mg %.

Conclusion. Succinyl sulfathiazole incorporated in the stock ration completely prevented the development of ulcerative cecitis in rats.

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No Demonstrable Substance Causing Increased Capillary Permeability in Lymph from an Injured Area.

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The possibility that the hypothetical "toxic" factor responsible for traumatic shock was present in lymph was considered by Dragstedt and Mead.[1] Since they found that lymph obtained from the thoracic duct of a dog after intestinal trauma did not cause a fall in blood pressure when injected intravenously into a test animal, they concluded that no "toxic" substance was present in this lymph. It seemed possible, however, by using increased capillary permeability as a criterion of shock rather than depression of blood pressure, that the presence of a "toxic" substance in the lymph might be demonstrable.

Technic. Large, mongrel dogs were used. Under spinal anesthesia, a cannula was tied into a collecting lymphatic trunk between the femoral artery and vein. Lymph was collected by gentle intermittent pressure upon the tissues of the extremity and was stored in chilled tubes. After several control samples of lymph had been obtained, the extremity was injured either by heat or by trauma. An immediate increase in the flow of lymph was observed. Within 5 min the lymph became turbid and soon thereafter became blood tinged. Samples of lymph were collected at intervals for 3 hr. A tourniquet was then tightly applied about the traumatized extremity and 3 mg per kg of the blue dye T-1824 were injected intravenously.

Two-tenths of a cm^3 of each lymph sample was injected intracutaneously into the abdominal wall of the dog from which the lymph had been obtained. An equal amount of each sample was injected into another dog which had previously received the same amount per kg of the blue dye. At the end of 15 min the degree of staining of the area where the lymph had been injected was noted. When the lymph contained a factor

TABLE I.

Changes in Capillary Permeability Indicated by Diffusion of Blue Dye into Area Injected with Lymph Obtained from Femoral Region Before and After Trauma.

Time lymph sample obtained	Dog A "Donor"	Dog B "Recipient"
10:45	0	+
10:53	0	0
11:00	0	0
11:12	0	0
Trauma to leg		
11:18	0	++
11:37	0	+
11:50	0	0
12:50	0	++
2:00	0	++++
2:27	0	+++
Donor Serum		
Arterial	0	+++
Venous	0	+++
Recipient Serum		
Arterial	++++	0
Venous	++++	0

[1] Dragstedt, C. A., and Mead, F. B., *J. Am. Med. Assn.*, 1937, **108**, 95.