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Reaction to Chilling as an Index of Tolerance for Ingested Sulfonamide, in the Rabbit.

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Massive doses of sulfanilamide produce a depression in ability to recover body temperature after chilling,[1] in the rabbit, equivalent to that produced by morphine in toxic dosage.[2] The effect is examined, in this report, for relation to quantity fed, blood level reached, percent weight loss induced and percent fatality. Comparative examination is made of sulfapyridine and sulfathiazole.

The ability to recover body temperature after chilling is appraised from observation of the number of minutes required to accomplish a rise from 96 to 99°F after chilling to a point between 95 and 96°F as described in reference 2. The number of minutes so measured is reported as the warming time. Warming times between 28 and 40 are within the normal range. Serious impairment in capacity for temperature recovery after chilling is indicated by values substantially longer than 45.[2]

TABLE I.

Effect of Ingested Sulfonamide on Warming Time as Related to Amount Fed, Blood Level Reached, Per Cent Weight Loss and Mortality.

Drug	Amt given g/kg	Blood level at time of test, mg %* range	Blood level at time of test, mg %* avg	No. of rabbits	% with a warming time lengthening of >16%	% with a warming time lengthening of >60%	% with total wt losses of >5% or per diem losses of >3%	% deaths
SA	.10-.15ad	4- 8	5	6	33	0	17	0
	.26-.36de	12-40	20	7	100	57	100	14
SP	.14-.29ad	1- 7	4	4	25	0	25	0
	.30-.55abd	2-27	11	8	75	25	75	13
ST	.15-.36adf	3-16	7	10	10	0	0	0
	.48-.72de	4-32	15	7	72	29	43	14
none†				295	14	0.3	5	0

Abbreviations: SA, sulfanilamide; SP, sulfapyridine; ST, sulfathiazole.

a: given once only. b, c, d, e, f: given 3 times daily for 1, 2, 3, 4 and 8 days, respectively. The dosage was progressively increased from rabbit to rabbit, in each group, but was held at a constant level for each individual rabbit compared.

*Free, non-conjugated substance.

†Rabbits comparably observed, over a period of 3 to 8 days, for range of spontaneous change in warming time and weight.

[1] Locke, A., and Main, E. R., *J. Immunol.*, 1939, **36**, 173.

[2] Locke, A., *J. Infect. Dis.*, 1937, **60**, 106; *J. Immunol.*, 1939, **36**, 159

Table I compares the effect of sulfanilamide (SA), sulfapyridine (SP) and sulfathiazole (ST) on the warming time following feedings in the indicated amounts over the indicated number of days. The rabbits used were New Zealand White males averaging 3 kg in weight. They had not been losing weight before the experiment was begun and had normal rectal temperatures. The average warming time before the drug feedings was 35. The drugs were given in tablet form with water.* The blood level estimations[3] were made on samples drawn from the marginal vein of the ear 2 to 3 hours after the final drug feeding and immediately before the test for degree of warming time lengthening induced.

The lengthenings observed did not persist following discontinuance of the drug feedings.

Summary. Sulfanilamide, sulfapyridine and sulfathiazole produced a lengthening of the warming time, in the rabbit, roughly proportional to the amount fed and the blood level reached. Serious (>60%) lengthening occurred to an extent paralleling the incidence of rapid weight loss and death.

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Stability of Prothrombin in the Presence of Thrombin.

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In earlier numbers of these PROCEEDINGS, Mertz, Seegers and Smith[1, 2] allege that thrombin can inactivate its precursor prothrombin. We have published evidence[3] that a trypsin-like enzyme is not only a thromboplastic agent[4] but also a *progressive* antithrom-

* The tablets were pushed through the side of the mouth, and as far back as possible, with the right forefinger. The mouth was kept moist and the finger held against the disintegrating material until swallowing was complete.

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

1 Mertz, E. T., Seegers, W. H., and Smith, H. P., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 657.

2 Mertz, E. T., Seegers, W. H., and Smith, H. P., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 604.

3 Ferguson, J. H., and Erickson, B. Nims, PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 625.

4 Ferguson, J. H., and Erickson, B. Nims, *Am. J. Physiol.*, 1939, **126**, 661.