

isopropylhydrazine showed greater brain than liver MAO inhibiting properties. Substitution on terminal hydrazine with an isonicotinyl group reversed the brain-liver MAO inhibiting relationship. Compounds lacking the benzene ring as in methyl-, ethyl-, and isopropylhydrazine also showed greater liver than brain MAO inhibiting effects. It is concluded that the benzene ring of the unsubstituted aryl-alkylhydrazines may aid in their passage into the brain.

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Influence of Local Hypothermia on Absorption from Isolated Intestinal Segments.* (25661)

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The transport of substances from the lumen of the small bowel to the blood stream under varying environmental conditions has always represented a fascinating physiologic problem. Some effects previously recorded are: interference with vascularity of an isolated loop of bowel slows absorption of strychnine(1); anoxemia increases absorption of water(2); drug-induced decrease of motility of the bowel impedes absorption of radiosodium and heavy water(4), vagotomy which reduces intestinal motility decreases glucose absorption from isolated jejunal loops, while sympathectomy has the opposite effect(5). The reduced intestinal motility(6) attending hypothermia suggested that the effect of hypothermia upon venous return and absorption from isolated canine intestinal loops should be assessed.

Methods and materials. The effect of hypothermia was determined on 1) venous outflow from closed jejunal and ileal loops, 2) strychnine absorption, and 3) removal of radioactive iodine (I^{131}) and radioactive iodi-

nated serum albumin from isolated intestinal loops. Adult mongrel dogs weighing 6-10 kg, anesthetized with intravenous nembutal (30 mg/kg) were used in the study. Through a midline abdominal incision, a loop of ileum or jejunum was delivered through the wound. A 15 to 20 cm segment was isolated between 2 ties of umbilical tape. In the blood flow studies a Y cannula was placed in the mesenteric vein which drained the vascular arcades coming from the obstructed loop. The dogs were given heparin, 1.5 mg/kg. By placing clamps at appropriate sites, the flow could continue into the portal system without obstruction except when interrupted during timed periods (2 minutes) for measuring venous return. In the absorption studies, a polyethylene catheter was placed into the isolated segment through a small enterostomy opening for introduction of materials to be absorbed. When measurement of radioactivity in portal blood was needed, a catheter was threaded through the splenic vein into the portal vein, and 4 cc samples taken at appropriate intervals. In the normothermic (38.5°C) dogs, similar procedures were performed and the segment allowed to remain in

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TABLE I. Small Bowel Blood Flow (ml/Min./kg of Body Wt). 6 dogs.

Bowel wall temp., °C	Jejunum	Ileum
38.5	Mean 2.2 Range 1.5-3.2	Mean 1.7 Range 1.2-2.1
14	Mean .72 Range .4-1.4	Mean .47 Range .4-.6

the abdominal cavity. Local hypothermia was accomplished by surrounding the isolated intestinal loop with extremely flaccid balloons through which a coolant solution could be circulated at varying temperatures. A thermistor was placed within the wall of the isolated loop to permit instantaneous recording of its temperature. Body temperature of the animals with local cooling of isolated intestinal segments was maintained at 38.5°C by external heating. In assessing strychnine absorption, 50 or 75 mg of strychnine was placed intraluminally immediately at conclusion of the operation in the normothermic control animals. Strychnine placement in the hypothermic animals was made when temperature of the bowel wall had been reduced to 15°C in some experiments and to 10° in others. In the studies on absorption of the radioactive iodine, 10 μ C of RISA or I¹³¹ were placed intraluminally as in the strychnine experiments. After obtaining a portal blood

TABLE II. Time on Appearance of Convulsions Following Intraluminal Introduction of Strychnine (Jejunum 15-20 cm).

Bowel wall temp., °C	No. dogs	Dose strychnine (mg)	Onset of convulsions (min.)	Animal survival
38.5	4	50	Mean 6 Range 3-8	0
15-20	3	50	Mean 42 Range 35-55	2
10	3	50	No convulsions	
38.5	3	75	Mean 7 Range 3-12	0
15-20	2	75	Mean 38 Range 31-44	0
10	5*	75	Mean 31 Range 18-45	0
25-30†	3	75	Mean 14 Range 5-24	0

* 1 dog did not convulse while the loop was cold.
† Systemic hypothermia.

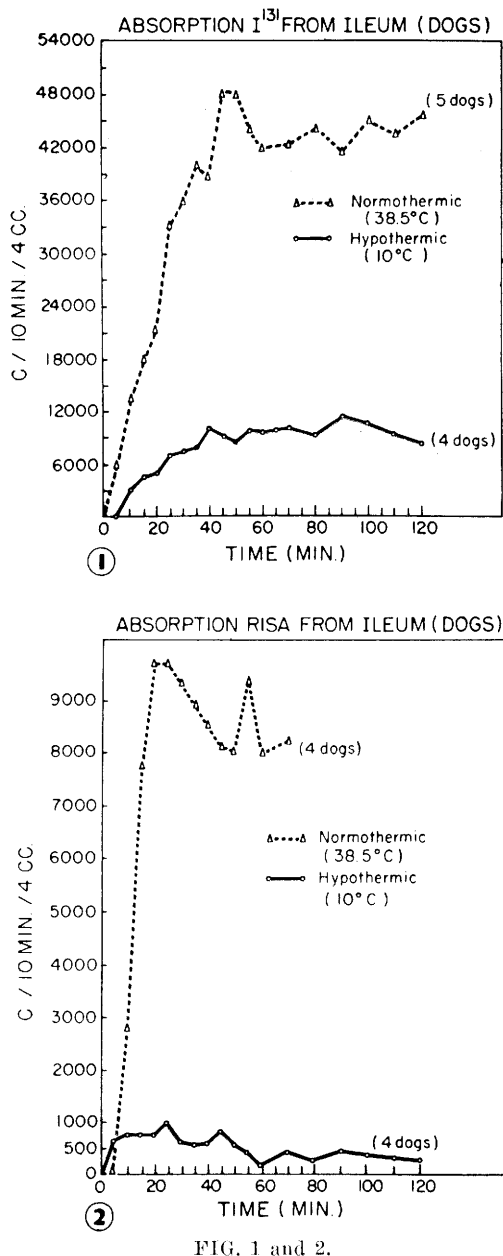


FIG. 1 and 2.

sample for background counts, collections were begun 5 minutes after the iodine had been placed within the lumen of the bowel and were continued at 5-minute intervals over the first hour, and at 10-minute intervals over the second hour.

Results. Venous outflow: Lowering the temperature of the jejunum from 38.5°C to a level of 14°C (Table I) is followed by a drop

in venous outflow in all animals. Mean reduction in similar lengths of jejunum and ileum was 72% and 66% respectively. The difference in mean flow under normothermic conditions may be accounted for by the heavier weight of similar jejunal segments.

Strychnine absorption. Placement of 50 mg of strychnine into a closed jejunal loop at 10°C was not attended by spontaneous convulsions during cooling, but when the normothermic situation was restored, fatal convulsions supervened, (Table II). In contrast, a bowel wall temperature of 15-20°C, while not abolishing convulsions, did permit an occasional survivor. At a dosage of 75 mg, there were no survivors. A jejunal temperature of 10°C prevented spontaneous convulsions in only one dog but quadrupled the time for development of spontaneous convulsions in the others. Systemic hypothermia at the 25-30°C level increases the time period for convulsions to appear, but does not prevent death of the animals.

The 2 factors of decreased venous return and hypomotility during hypothermia probably account for this decreased transport of strychnine. Hypothermic paralysis of cellular enzyme function also may play a part. Experiments using monoiodo-acetamide, a dehydrogenating system poison, in various combinations with strychnine, however, failed to demonstrate any protection from reduced cellular enzyme function.

Iodine and RISA absorption. From Fig. 1 and 2, it is quite evident there is a marked decrease in absorption of I^{131} or radioactive iodinated albumin (RISA) from isolated hypothermic intestinal loops. It is significant that in the normothermic state total absorp-

tion of iodine as a free ion is greater than the RISA ($p = <.01$). This indicates some decrease in absorption when the iodine is attached to a semi-permeable molecule, as has been shown to be true for sodium(3). The more effective inhibition of RISA than I^{131} during hypothermia indicates that the absorptive mechanism responsible for the disparity in absorption of free and bound iodine at 38.5°C is markedly affected by cooling.

Conclusions. Our results indicate that hypothermia reduced net transport of substances from gut lumen to blood stream. In strychnine absorption, systemic hypothermia (25-30°C), at clinically feasible levels is not as effective in delaying transport as local hypothermia (10°C). Neither protects the animals from fatal outcome when large doses are used. Hypothermia reduced absorption of RISA approximately ninefold, ($p = .005$) while it reduced absorption of I^{131} only 5-fold ($p = <.01$). Venous return in hypothermic intestinal loops is reduced 72 and 66% in closed jejunal and ileal segments.

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