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Role of Hemoconcentration in Production of Gastric and Duodenal Ulcer Following Experimental Burns.*

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The occurrence of hemoconcentration following extensive burns in man, first noted by Baraduc,[1] is well known. Hemoconcentration was suggested by Kapsinow as the mechanism of the production of Curling's Ulcer.[2] The role of sepsis in the mechanism of the occurrence of gastric and/or duodenal ulceration following experimental burns has been studied by Hartman.[3]

The purpose of this study is (1) to evaluate the role of hemoconcentration in the production of ulceration of the gastro-intestinal tract following burns, and (2) to correlate the incidence of hemoconcentration to the incidence of ulceration in dogs subjected to extensive superficial burns, with and without accompanying administration of histamine-in-beeswax mixture, with and without treatment directed to the prevention of hemoconcentration.

When daily intra-muscular injections of histamine-in-beeswax mixture are given to normal dogs, 40 days (or an average of 23 days) are necessary to produce ulcer with regularity.[4]

Method. Healthy dogs, weighing 15 to 36 pounds, anesthetized by intravenous injection of sodium pentobarbital (15 mg per pound), were subjected to 40%, third degree burns by immersion into water at 100°C for 10 to 15 seconds. No evidence of pain or discomfort to the animal was noted. The hair was closely clipped prior to scalding. Blood studies were carried out on all dogs, 3 determinations before the burn for the average of normal values, and serial determinations after the burn. The following determinations were made: Hemoglobin (alkaline hematin method), Hematocrit (Wintrobe method), Erythrocyte Count, Specific Gravity of whole blood and plasma (copper sulfate method of Phillips, Van Slyke, *et al.*), BUN (Karr's urea nitrogen method), Plasma and Blood Volumes (Gibson and Evan's method), and Rectal Temperatures. Blood for these determinations was obtained under oil from the femoral vein before the burn and from the heart following the burn. A number of the dogs received, in addition, daily intramuscular injections of histamine-in-beeswax mixture (30 mg base) prepared after the method of Code and Varco,[5] the first injection being given 30 minutes prior to the burn. No restriction of food intake was made, except that dogs were fasted for 18 hours before each experiment. Water intake was allowed up to 250 cc per day in all dogs. In some of the animals an attempt was made to prevent the hemoconcentration following burns by slow intravenous administration of human dried plasma into an antecubital vein, regulation of the rate of drip being determined by serial blood studies. Blood pressure determinations were made in 3 dogs by serial or continuous recordings on a kymograph, the carotid artery being cannulated. Dogs were sacrificed 4 hours to 6 days following the burn. Animals in Series II were sacrificed when death was impending or allowed to die. Sections of the stomach, duodenum, liver, lung, brain, kidney, and adrenals were obtained for microscopic studies.

Experiments. Studies were carried out on 30 dogs in 3 series of experiments:

Series I. Fourteen dogs were subjected to 40%, third degree burns accompanied by

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1 Harkins, H. N., *The Treatment of Burns*, Springfield, Illinois, Charles C. Thomas, publisher, 1942.

2 Kapsinow, R., *Southern Med. J.*, 1934, **27**, 500.

3 Hartman, F. W., *Gastroenterology*, 1946, **6**, 130.

4 Hay, L. J., Varco, R. L., Code, C. F., and Wangensteen, O. H., *Surg., Gyn. and Obst.*, 1942, **75**, 170.

5 Code, C. F., and Varco, R. L., *Am. J. Physiol.*, 1942, **137**, 225.

TABLE I.

Dogs Subjected to 40% Burn Accompanied by Daily Administration of Histamine-in-Beeswax (30 mg Base), Not Treated with Intravenous Infusion.

Dog No.	Wt in lb	Burn		No. of hist. injections	Hematocrit change		Results	Remarks
		%	sec		Initial	Final		
23	29	40	10	4	40	41	No congestion, erosion, or ulcer	Died—anorexia
24	32	40	10	5	44	55	Congestion; duodenal ulcers, one perforated	Died—peritonitis
25	22	40	10	3	42	53	Congestion; pyloric and duodenal ulcers	Died the third day
36	17	40	15	1	49	56	Congestion; small pyloric ulcer; many bleeding points	Sacrificed, 24 hr
37	22	40	15	2	43	65	Congestion; bleeding pyloric ulcer; two large duodenal ulcers	" 48 "
38	24	40	15	2	50	61	Congestion; pyloric-duodenal ulcer; bleeding small fundic ulcers	Died second day—melena
39	22	40	15	2	30	41	Congestion; large duodenal ulcers, one perforated; fundic ulcers	Died—peritonitis
40	24	40	15	2	50	55	Congestion; three large duodenal ulcers; one large gastric ulcer; many small bleeding ulcers	Sacrificed—melena
42	15	40	15	1	40	57	Congestion; marked bleeding in stomach and duodenum	" 18 hr
44	20	40	15	1	49	72	Intense congestion	" 4 "
45	26	40	15	3	47	56	Congestion; bleeding antral ulcer	Died third day
50	22	40	10	1	42	42	No congestion, erosion, or ulcer	Sacrificed, 24 hr
51	36	40	10	1	49	54	Congestion only	" 6 "
52	31	40	15	1	45	53	Congestion; large duodenal ulcer; many petechial gastric ulcers	" 24 "

histamine-in-beeswax administration. Blood determinations were carried out in all animals.

Series II. Five dogs were subjected to 40%, third degree burns alone, blood determinations being carried out in all dogs.

Series III. Six dogs were subjected to 40%, third degree burns accompanied by histamine-in-beeswax administration, and attempts to prevent the hemoconcentration were carried out by intravenous infusion of plasma. One dog (No. 41) received, in addition, 5% glucose in normal saline, and another dog (No. 49) received 5% glucose in normal saline alone. As an additional control, one dog (No. 48), not subjected to a burn, received histamine-in-beeswax, was anesthetized, and received a comparable amount of plasma by intravenous infusion. Four additional dogs received daily intramuscular injections of histamine-in-beeswax for 5 successive days, and were sacrificed at the end of this period.

Results. Series I. (See Table I). Twelve of the 14 dogs subjected to 40% burns accompanied by histamine administration developed increased concentration of the blood. All 12 dogs demonstrated marked congestion of the mucous membrane of the stomach and duodenum. Nine of these 12 dogs were sacrificed 24 hours or more after the burn and showed definitive ulcers, 5 bleeding and 2 perforated. Three of the 12 dogs were sacrificed at 4, 6, and 18 hours after the burn, the latter showing in addition to the congestion, marked diffuse bleeding from the surface of the gastric and duodenal mucosa. The 2 dogs which failed to develop increased concentration of the blood demonstrated no gastric or duodenal pathology in one and 4 days.

Series II. (See Table II). Four of the 5 dogs subjected to 40% burns without administration of histamine-in-beeswax developed increased concentration of the blood and demonstrated congestion of the gastrointestinal mucosa in 2 to 6 days. Two of these dogs showed, in addition to congestion, bleeding petechial gastric ulcers, and antral bleeding points with hemorrhagic gastritis and duodenitis. One dog failed to develop increased concentration of the blood and demonstrated no gastric or duodenal pathology in 4 days.

TABLE II.

Dogs Subjected to 40% Burn—No Histamine Administration—Not Treated with Intravenous Infusion.

Dog No.	Wt in lb	Burn %	Burn sec	No. of hist. injections	Hematocrit change Initial	Hematocrit change Final	Results	Remarks
26	26	40	10	0	50	56	Bleeding petechial gastric ulcers; congestion	Sacrificed 6th day
27	31	40	10	0	45	57	Hemorrhagic gastritis duodenitis; antral bleeding pts.	Died 2nd day
							Marked congestion	" 4th "
28	15	40	10	0	59	60	Essentially negative	Sacrificed 5th day
29	24	40	15	0	48	59	Congestion only	Died 5th day
30	30	40	15	0	45	56	"	

TABLE III.

Dogs Subjected to 40% Burn, Accompanied by Histamine-in-Beeswax Administration, Treated by Intravenous Infusion.

Dog No.	Wt in lb	Burn %	Burn sec	No. of hist. injections	Concentration of blood	Results	Remarks
43	21	40	15	1	Maintained at normal values	No congestion, erosion, or ulcer	Sacrificed after 18 hr
49	32	40	15	1	" " " "	" " " "	" " 24 "
53	35	40	15	1	" " " "	" " " "	" " 24 "
46	18	40	15	2	Normal except for 18 hr of hemoconcentration	Congestion, lesser curvature ulcers	" " 54 "
47	19	40	15	2	Normal except for 18 hr of hemoconcentration	Congestion, perforated duodenal ulcers	Died, peritonitis, 54 hr
41	22	40	15	1	Overtreated—hemodilution	Pallor, submucosal and mucosal hemorrhage and erosion of stomach	Died 16 hr

Series III. (See Table III). Of the 6 dogs subjected to 40% burns accompanied by histamine-in-beeswax administration in which an attempt at prevention of the hemoconcentration in burns was made, 3 dogs were well controlled throughout the entire duration of the experiment; 2 dogs, partially controlled; and one dog, overtreated. The 3 dogs in which blood concentration values were maintained at normal levels demonstrated no gastric or duodenal pathology when sacrificed in 18 to 24 hours. The 2 dogs in which normal blood concentration values were maintained except for a period of 18 hours out of a total duration of 54 hours, demonstrated gastro-intestinal congestion, with lesser curvature ulcers and perforated duodenal ulcer, respectively. One dog was overtreated in the first few hours of the experiment so that marked hemodilution occurred. Death occurred in this animal in 16 hours, presenting pallor of the stomach with several areas of mucosal and submucosal hemorrhage and erosions.

Microscopic examination of the viscera of the animals developing hemoconcentration showed marked vascular congestion; of the animals in which hemoconcentration did not take place or was prevented, no significant findings were noted.

Four dogs receiving daily intramuscular injections of histamine-in-beeswax for 5 days developed no hemoconcentration and no gastro-intestinal abnormality.

Discussion. It is apparent that there exists a close correlation between increased concentration of the blood and gastro-intestinal abnormality following burns. That hemoconcentration, with its resultant congestion, renders the gastro-duodenal mucosa more susceptible to the action of gastric acid-peptic juice is evident in the marked increase in the incidence of ulceration when histamine-in-beeswax administration accompanies the burn. It is shown, in addition, that prevention of the occurrence of hemoconcentration following severe burns portends a normal gastro-intestinal tract, even when histamine-in-beeswax is administered and animals are sacrificed in less than 5 days. Failure of 3 dogs in Series I and II to develop hemoconcen-

tration and mucosal pathology following the burns may be attributable to the fact that those animals received a 40% 10-second burn, a less severe burn than the majority of the animals in this study received. Serial blood pressure determinations were made in 3 burned dogs, continuously anesthetized, which developed hemoconcentration, and no readings of shock level were observed. Animals were usually awake and moving about after 4 hours following the burn.

It is interesting to note that superficial necrosis of the gastric mucosa was present upon microscopic examination in 2 dogs, both sacrificed, one after marked hemodilution due to overtreatment, the other after marked hemoconcentration and congestion of the mucosa. Microscopically, the vascular spaces of the mucosa of the overtreated animal were conspicuously devoid of blood, while those of the untreated animal were markedly dilated and engorged with blood with extravasation and necrosis. Both conditions result in mucosal ischemia, susceptible to the erosive action of gastric acid-peptic secretions.

Conclusions. Evidence is presented to show that increased concentration of the blood following burns is an important factor in the occurrence of gastro-duodenal ulcer after experimental burns. (The occurrence of gastro-intestinal congestion, erosion and/or ulcer in burns is directly related to the occurrence of hemoconcentration).

Moreover, gastro-intestinal abnormality following burns, even when accompanied by histamine administration, may be prevented by avoidance of the hemoconcentration of burns by proper therapy.

The incidence of gastric and/or duodenal ulceration provoked by hemoconcentration in burns is markedly increased when histamine-in-beeswax administration accompanies the burn.

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Comparative Utilization of Raw and Autoclaved Soy Bean Protein by the Human.

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Osborne and Mendel[1] in 1917 noted that rats fed raw soy bean flour grew more slowly than a control group which received the same flour after it had been autoclaved. Hayward, Steenbock and Bohstedt[2] confirmed these investigations and suggested that this effect was not due to a difference in palatability but to a deficiency in the raw flour. Later investigations by Hayward and Hafner,[3] Almquist, Mecchi, Kratzer and Grau[4] and Johnson, Parsons, Steenboch[5] suggested that this increase in biological activity produced by autoclaving raw soy bean flour was due to a rise in the level or increase in the availability of sulfur bearing amino acids.

That the autoclaved soy bean protein has a high biological value similar to egg white and liver protein has been shown by Cahill, Schroeder and Smith[6] from a study of ni-

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