purified to constant radioactivity by recrystallization from hot water using Norit.‖ The original histamine solution was assayed by adding the same amount used for injecting the mice to the usual amount of carrier (40 mg) then preparing and counting the dipicrate. For example 1.00 μg C^{14}-histamine added to 40 mg carrier, after conversion to the dipicrate, produced 500 counts per minute when counted at infinite thickness and corrected for background only. When 1.00 μg C^{14}-histamine was injected into a mouse the isolated histamine dipicrate produced 200 counts per minute at infinite thickness and corrected for background only. Therefore, the percentage of histamine remaining in the entire mouse is $200/500 \times 100 = 40\%$. All counts were made on 4.5 square cm plates in flow counters with background about 20 c.p.m.

Results. The data of Tables I and II show that although there are often marked differences between individual mice treated identically, there is no significant difference in the rate of histamine destruction between adrenalectomized and sham-operated mice. This discrepancy with the findings of Rose and Browne may be due to differences in histamine concentrations administered, species differences, or variations in experimental procedure. In any event the results suggest that the participation of the adrenal cortex in histamine inactivation under physiological conditions is questionable and that the matter requires further clarification.

Summary. No significant difference was found between adrenalectomized and sham-operated mice in the ability to destroy minute quantities of injected C^{14}-histamine.

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Effect of Epidermal Damage upon Serum Polysaccharides. (19896)

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(Introduced by A. A. Hellbaum.)

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Elevations of serum polysaccharides have previously been reported by Shetlar, *et al.*(1), to occur in dogs following production of sterile turpentine abscesses, of bacterial abscesses and of talc granulomas, the injection of turpentine intrapleurally, and experimental surgery. The cause and mechanism of these elevations is of considerable interest. Seibert *et al.*(2), have suggested that the elevation noted in malignancies, tuberculosis, and other pathological conditions is related to tissue destruction. Shetlar *et al.*(1) have suggested that this phenomenon may just as logically be correlated with tissue proliferation and repair. Since a number of carbohydrate rich protein fractions occur in serum, it also seems likely that they may vary differentially. Shetlar *et al.*(3) using a sodium sulfate fractionation procedure, noted that the distribution of polysaccharide among different serum protein fractions varied in different diseases. In the course of a study of treatment of thermal injury in dogs the opportunity to study this problem further presented itself. If the source of the serum polysaccharides, which rise after injury, is the injured tissue itself, one would expect the lymph polysaccharides to rise after injury at a more rapid rate than those of the serum. Consequently, the experiment was designed to allow polysaccharide studies of lymph samples from dogs at various times after burning.

Methods. In this study nonglucosamine

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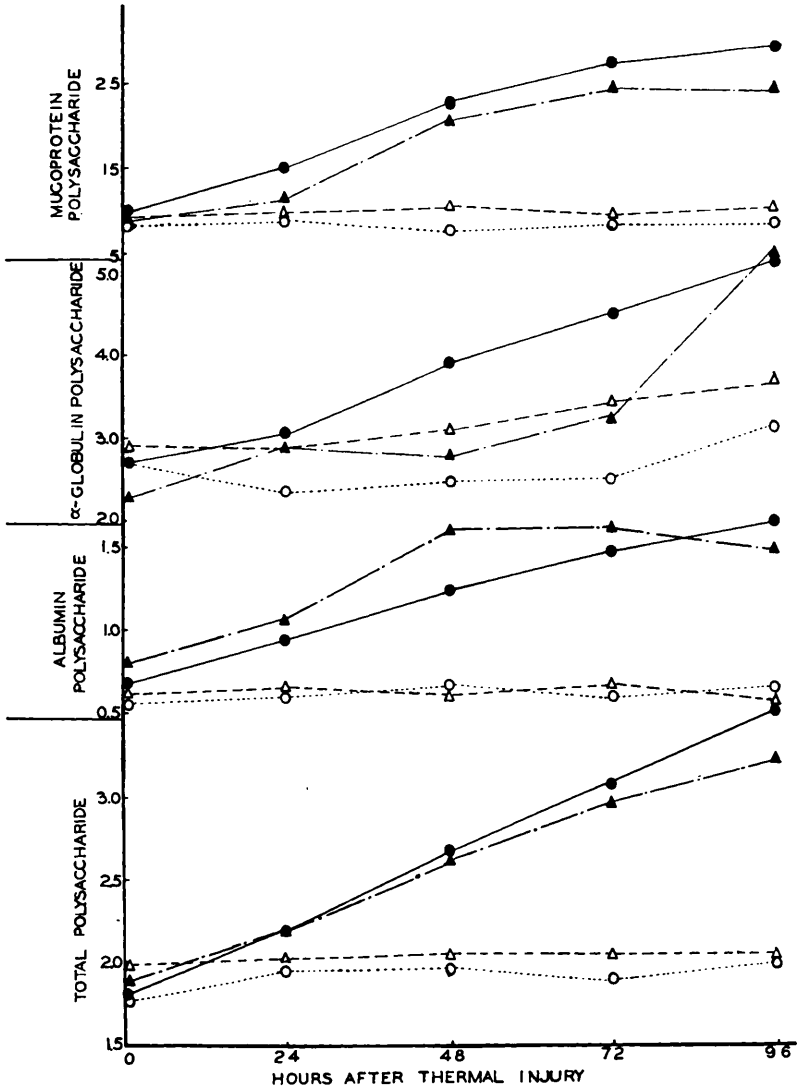

FIG. 1. Effect of epidermal thermal injury on nonglucosamine polysaccharides of serum protein. The different groups are denoted graphically, (1) untreated injured ●——●; (2) untreated uninjured ○------○; (3) ACTH treated injured ▲——▲; (4) ACTH treated uninjured △——△. Total polysaccharide is denoted as % of the serum protein, "albumin" polysaccharide as % of the albumin protein, "α-globulin" polysaccharide as % of α-globulin, and mucoprotein polysaccharide as mg of hexose per 100 ml of serum.

polysaccharide was determined by the tryptophan method(4). Serum and lymph were fractionated as previously described(3) by precipitation with 21.6% and 26.0% sodium sulfate. As indicated by Gutman(5), the protein not precipitated by 26% sodium sulfate was assumed to be largely albumin and shall be designated in this paper as the albumin fraction, while that not precipitated by 21.6% was assumed to be combined albumin and pseudoglobulin (α-globulin). Figures obtained by subtracting the results of analyses of the 26% from the 21.6% sodium sulfate fraction were considered to be representative of pseudoglobulin and shall be designated hereafter in this paper as the α-globulin fraction. Mucoprotein polysaccharide was determined by the tryptophan method after isolation of the mucoprotein fraction by the method of Winzler and Smyth(6). Mongrel dogs weighing from

TABLE I. Comparative Changes of Nonglucosamine Polysaccharides of Lymph and Serum Following Experimental Epidermal Thermal Injury.

Hr after burning	Total protein[1]		α-globulin[2]		Albumin[3]		Mucoprotein[4]	
	Lymph	Serum	Lymph	Serum	Lymph	Serum	Lymph	Serum
0	1.51	1.76	2.56	2.37	.84	.56	6	8
0	1.98	2.03	2.44	3.22	1.51	.66	6	8
24	1.40	2.12	3.46	2.14	.98	.87	7	10
48	1.76		3.34		1.45		20	
72	2.84	2.80	6.66	4.30	1.47	1.66	22	26
72	2.52	2.48	6.55	4.05	1.17	1.07	12	14
72	2.58	3.19	5.19	5.90	1.85	1.64	39	34
96	2.80	3.69	5.06	3.69	1.71	1.25	22	25
96	2.64	3.58	4.75	5.26	2.37	1.91	28	33

Expressed as % of [1] the total serum protein, [2] α-globulin protein, [3] albumin protein, and [4] as mg/100 ml of serum.

10 to 20 kg were selected. After shaving the skin and under intravenous nembutal anesthesia, second and third degree burns were induced with electric cauterization. Burns were made over the medial and lateral surfaces of both legs, flanks and abdomen to the costal margin. No dressings were applied other than petroleum jelly. Under nembutal anesthesia a skin incision was made over the medial border of the lower one-half of the left sternocleidomastoid muscle. The left jugular vein was exposed and dissected free to its junction with the subclavian vein. The thoracic duct was identified at its termination at the venous angle. The external jugular vein, the innominate vein and all their tributaries were ligated above and below the venous angle. The external jugular vein was then cannulated with a polyethelene tube and the thoracic duct lymph collected in a small beaker and allowed to clot. The lymph sera were later separated by centrifugation.

Results. Changes of serum polysaccharides. The results of experiments involving 5 untreated injured dogs, 2 injured dogs treated with adrenocorticotropic hormone, 2 untreated normal controls, and 2 controls injected with adrenocorticotropic hormone are presented graphically in Fig. 1. The total nonglucosamine serum polysaccharide was divided by the serum protein. The average results for each day after thermal injury was compared statistically with the data obtained before injury. The term "significantly" is used here to denote differences significant at the 1% level. A noticeable, but not statistically significant, elevation occurred in every case within 24 hours after burning. At 48 hours the total nonglucosamine serum polysaccharide was significantly elevated. Dogs treated with ACTH were not noticeably different from the untreated. The polysaccharide of the α-globulin fraction (Fig. 1) was also noticeably, but not significantly elevated within 24 hours after injury and significantly elevated at 48 hours. Elevation of this factor in the dogs treated with ACTH was apparently repressed for the first 72 hours. However, after this time, the level became as high as in the untreated dogs. The polysaccharide associated with the albumin fraction, as isolated by the precipitation of globulin with 26.0% sodium sulfate, was found to be significantly elevated 24 hours after injury and continued to rise until death as shown in Fig. 1. By this method of fractionation, the mucoprotein is found in the albumin fraction(7). The elevation of the polysaccharide of the albumin fraction was entirely explainable by the rise which occurred in the mucoprotein polysaccharide depicted in Fig. 1.

Changes in lymph polysaccharides. Due to the necessity of sacrificing the animal in order to obtain the lymph, serial determinations of lymph polysaccharides in the same animal were not possible. As considerable variation between animals was noted, care must be taken in interpreting the data obtained on lymph. A study involving more animals is indicated. However, the data, summarized in Table I, indicate that the total nonglucosamine polysaccharide increases in lymph after burning. Much of this increase is due to the increase of polysaccharide in the fraction precipitated by

26% but not by 21.6% sodium sulfate (α-globulin fraction). The polysaccharide found in the albumin fraction also appears to rise but the elevation is not so striking. The polysaccharide associated with the mucoprotein fraction is consistently elevated in the lymph following burns. It is noteworthy that the figures for each lymph sample and its corresponding serum sample are practically the same. It appears likely that mucoprotein passes freely back and forth between tissue fluids and blood.

Discussion. Thermal injury to experimental animals results in an elevation of serum polysaccharides. This response is probably no different than that previously noted in other injuries(1). As the animals in this study were either sacrificed or died as a result of the injury, data as to the maximum elevation were not obtained. In contrast to cancer patients or pregnant women, the polysaccharide of the albumin fraction after correction for mucoprotein polysaccharide was not elevated in these animals. It appears that the elevation of serum polysaccharide in burned animals is due largely to increases of the mucoprotein fraction and of a polysaccharide rich component which occurs in the α-globulin fraction as isolated by sodium sulfate fractionation. After completion of this work Keyser(8) reported a study on patients which included several burned cases, one of which was followed for some time serially. He estimated total serum nonglucosamine polysaccharide and mucoprotein polysaccharide. He reports an elevation of both total and mucoprotein polysaccharide. The rise of the total polysaccharide is not completely due to the mucoprotein elevation. Apparently in humans, as in canines, an elevation of both mucoprotein and another carbohydrate rich fraction occurs. Treatment of burned animals with ACTH may influence the elevation of the polysaccharide of the α-globulin fraction, but not that of the mucoprotein. Since the differences between the polysaccharide levels of the lymph and serum were not conclusive, the question as to whether the elevation of serum polysaccharide is derived from the injured tissue requires further study.

Summary and conclusions. Epidermal thermal injury in dogs resulted in an elevation of total polysaccharide in both lymph and serum and of the polysaccharide of both the albumin and α-globulin (pseudoglobulin) fractions isolated by salt precipitation methods. The elevation of the polysaccharide of the albumin fraction was shown to be due to an elevation of the mucoprotein polysaccharide. The mucoprotein content of the lymph and serum from the same animal were nearly the same indicating that this component may pass easily between tissue fluids and blood plasma. Preliminary studies of the effects of adrenocorticotropic hormone on animals with epidermal thermal injuries indicate that this substance has no effect on the elevation of mucoprotein, but may repress the elevation of α-globulin polysaccharide.

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