

this tumor. Conversely, continuous passage in the mouse brain resulted in a loss of oncolytic activity. In other experiments the virus of Russian encephalitis was changed by

continuous passage in the Wagner osteogenic sarcoma so that it caused destruction of this hitherto resistant tumor.

Received March 8, 1951. P.S.E.B.M., 1951, v76.

Delay of the Early Inflammatory Response by Cortisone.* (18620)

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Experimental and clinical observations(1) have shown that cortisone and ACTH alter the course of bacterial infections, usually having an adverse effect on the host. The inhibitory effect of these substances on the development of granulation tissue(2) has suggested to some that disruption of this phase of tissue reaction might explain these observations. However, since granulation tissue containing its new blood vessels, fibroblasts, and ground substance develops late in the sequence of body defense against infection, it was thought advisable to explore the effects of cortisone on the earliest tissue phases of the acute inflammatory reaction. Croton oil was used as an irritant to incite a cutaneous inflammatory reaction similar to that produced by many bacteria.

Materials and methods. White New Zealand rabbits weighing 2 kg were used. The skin of the abdomen was prepared with fine-tooth, animal clippers 24 hours before the experiment was commenced. Cortisone was given in single daily doses of 12.5 mg intramuscularly, beginning 24 hours before the inflammation was produced. Two drops of croton oil were placed on each of 6 separate

sites on the shaved skin of the abdomen. Four longitudinal and 4 horizontal scratch marks, each approximately 2 cm in length, were made with a cutting needle through the oil; the scarified area was then rubbed with a glass rod. Paired biopsies of control and of cortisone-treated animals were made at frequent intervals under intravenous nembutal anesthesia. The sections were fixed in Zenker's solution and stained with phloxine methylene blue. The observations reported here are based on four lesions on each of 16 animals, 8 of which received cortisone.

Results. Because of the difficulty in producing uniform trauma at each site of scarification, the degree of the inflammatory response in the multiple areas of trauma of the same animal was slightly variable. There was also slight variation in response in different animals similarly treated. However, the inflammatory reaction in animals given cortisone was significantly and uniformly less intense than that in the controls.

Gross changes. In animals not given cortisone, the lesions became faintly erythematous within 20 minutes after application of the trauma. By 4 hours these had assumed an intense purplish coloration. Edema was marked by 8 hours. By 24 hours necrosis was obvious, and eschar formation had begun. On the other hand, in the animals given cortisone, the erythema could not be detected until at least 2 hours following scarification through croton oil. In these animals, the purplish discoloration appeared only after 12 to 18 hours and then was confined to the scratch marks. Edema was less than in the controls,

* Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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TABLE I. Graphic Representation of Tissue Sequences in Both Groups of Animals. Intensity of each reaction is graded from 0 to 4+, 4+ being of greatest severity. Each grading represents the average of multiple sections from each biopsy site in at least 2 animals.

		Time after stimulus										
		Minutes					Hours					
		5	10	20	30	45	1	2	4	8	12	24
Capillary dilatation	Control "E"	2+	3+	4+	4+	4+	4+	4+	4+	4+	4+	4+
		+	2+	3+	3+	3+	3+	3+	4+	4+	4+	4+
Leukocytes	Margination	Control "E"		+	2+	3+	4+	3+	2+	+		
				+	2+	2+	2+	2+	2+	+	+	+
	Migration	Control "E"				+	+	3+	4+	+		
								+	+	2+	2+	+
Infiltration of corium	Control "E"							+	2+	3+	4+	4+
									2+	2+	3+	3+
Edema	Control "E"						±	+	2+	3+	4+	4+
									+	2+	3+	3+
Necrosis	Control "E"									2+	2+	4+
										+	+	2+
Fibrin	Control "E"									2+	2+	2+
										+	+	+

and little necrosis appeared.

Microscopically, all of the histologic components of the inflammatory reaction were delayed in rabbits treated with cortisone (Table I). Some aspects of inflammation, such as margination of leukocytes in blood vessels, were never as striking as those seen in the control animals. At 24 hours in the control animals many mononuclear cells, primarily macrophages and mast cells, were seen in addition to numerous polymorphonuclear leukocytes. Only a very few mononuclear cells were seen in cortisone-treated animals at 24 hours (Fig. 1).

The course of the inflammatory reaction and subsequent granulation tissue and healing corresponded closely to that previously described(3).

Discussion. From these observations, it would appear that cortisone has altered the inflammation provoked by a combination of croton oil and trauma in the following manner. The earliest changes of margination of leukocytes, migration of leukocytes, and formation of edema and fibrin are strikingly delayed and quantitatively reduced. Furthermore, the ultimate development of tissue necrosis was diminished in the cortisone-treated animals as compared with the controls. Dougherty

and Schneebeli(4) report analogous results in studies of an allergic inflammatory reaction in mice using a tissue spread technic. They found that the percentage of polymorphonuclear leukocytes in all preparations, taken from 1 to 24 hours, was significantly lower in cortisone-treated mice when compared with controls. Moreover, the total number of cells was apparently reduced in the cortisone-treated group. Where cellular defenses are important early in the course of an infection, it is believed that this delay in the earliest inflammatory response might be partly responsible for the spreading of certain bacterial infections noted under the influence of cortisone and ACTH.

Summary. The effect of cortisone on the earliest tissue phases of the inflammatory reaction in the skin of rabbits was studied. A combination of croton oil and scarification was used as the inflammatory stimulus. In animals given cortisone, all of the tissue components of the inflammatory reaction were delayed, and some were quantitatively reduced. Vascular margination of leukocytes, migration of leukocytes from blood vessels, and the formation of fibrin and edema were strikingly altered. The ultimate development of necrosis was diminished. The relationship

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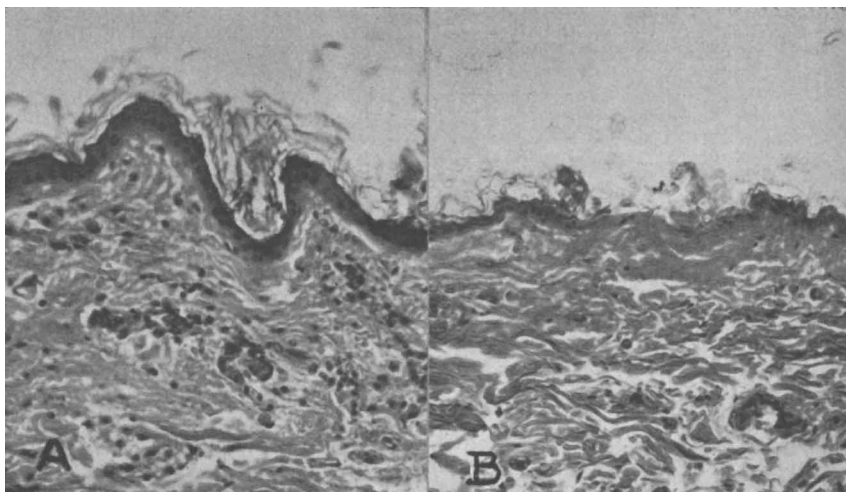


FIG. 1a.

Two hr (control): Margination and beginning migration of leukocytes.

FIG. 1b.

Two hr (cortisone): Area of necrosis in upper corium representing needle scratch. Minimal margination of leukocytes.

of these observed facts to the enhancing effect of cortisone and ACTH on certain bacterial infections is suggested.

Received March 9, 1951. P.S.E.B.M., 1951, v76.

The Plasma Potassium Level in the Newborn.* (18621)

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High serum potassium levels during the early weeks of infant life have been reported by several observers. Data from the literature are summarized in Table I. The values recorded are well above the normal adult level of 4.41 meq./liter, $\sigma = 0.36$ meq./liter (5). The erythrocytes contain a considerable amount of potassium which may diffuse out

of the cells under certain circumstances or which may be released by hemolysis. Either of these circumstances could produce erroneously high plasma or serum potassium levels. The problem, therefore, has been reinvestigated.

Methods. Placental blood was obtained immediately after the infant was born and before the cord was severed. Blood was withdrawn through a needle inserted in the umbilical vein. Blood was obtained from young infants from the femoral vein or the superior longitudinal sinus. Dried heparin was used to prevent clotting. The blood sample was immediately centrifuged and the

* This work was supported in part by the Life Insurance Medical Research Fund.

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