parent as soon as the polymorphonuclear cells appear in the infected areas; 4) as the inflammatory process subsides, macrophages, which herald the onset of the repair process, become the predominant cell in the involved areas; and 5) fibrin formation does not occur.

In contrast to Smith and Wood's observations with type I pneumococci, the following features were noted in this study: 1) there is destruction of nodal architecture by the infectious process with formation of frank abscesses;** and 2) streptococci persist in the involved nodes for many hours. It should be pointed out that in these regards type III pneumococcal infections bear more similarity to group A streptococcal infections than do those produced by type I pneumococci (11,17).

That the infection was confined initially to the lymph nodes was evidenced by the fact that bacteremia usually did not occur until 18 or more hours after the animals were inoculated. Terminally blood stream invasion was encountered in all instances. Examination of contiguous structures and of the lungs failed to show streptococci outside the involved nodes, even in the most fulminating infections. This finding contrasts with that report by Sonkin when group C streptococci were used. With the latter organism, under the conditions employed, cellulitis of the areas surrounding the involved nodes was common.

Summary and conclusions. The study described herewith affords a demonstration of the fact that a small laboratory animal can be infected via the upper respiratory tract with group A streptococci by a simple reproducible method. The lymphadenitis resulting from group A streptococcal infection bears significant resemblance in its histologic pattern to that produced by pneumococci, particularly by type III strains.

** The necrotizing property of group A streptococci(16), a property not common to pneumococcus, probably explains this particular difference.

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Adrenal Weight and Ascorbic Acid Concentration in Alloxan-Injected Rats. (20033)

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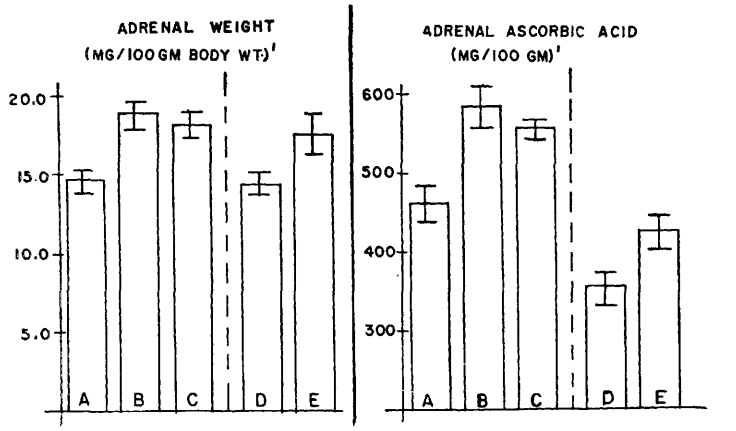
A reduction in adrenal ascorbic acid concentration and/or an increase in wet or dry weight of the adrenal glands are commonly regarded as a good index of increased adrenocortical activity. However, the relationship of adrenal ascorbic acid concentration to adrenal steroid production is still a controversial subject(1-3). Though the literature intimates



EXPERIMENTAL GROUP		PLASMA GLUCOSE (MG %)[4]
NORM. INTACT (14)	A	87±6
" + ALLOXAN, (14)	B[2]	121±10
" + ALLOXAN, (11)	C[3]	144±9
NORM. INTACT, GLUCOSE I.V. (7)	D	87±5
NORM. + ALLOXAN, GLUCOSE I.V. (6)	E	193±24

STATISTICAL ANALYSES OF DATA[5]

GROUPS	ADR. WT.	ADR. ASCB. AC.	PL. GLUC.
A–B	<.01	<.01	< 01
C–A	<.01	<.01	<.01
B–C	>.05	>.05	>.05
A–D	>.05	<.01	>..05
B–E	>.05	>.01	<.01

FIG. 1. Legend. 1—Bars represent mean ± S.E. 2—Members of this group received subcut. inj. of alloxan at dose of 150 mg/kg body wt. 3—Members of this group received intrav. inj. of alloxan at dose of 40 mg/kg body wt. 4—Mean ± S.E. 5—The probability of greater error occurring by chance of the difference between the means of the indicated groups. Figures in parentheses are the number of rats in each group.

that ascorbic acid depletion in the adrenal glands is a gauge of adrenocortical activity, this is probably true only in acute conditions. The relationship of gland content of hormone or precursor substance(s) to the factors of syntheses and discharge is still an unresolved problem which has been discussed in some detail by Sayers and Cheng(4). Since the functional relationship of adrenal ascorbic acid concentration to hormonal secretion is still unknown, experimental evidence of conditions in which adrenal ascorbic acid is increased is particularly noteworthy. Evidence will be presented here of an increase in both adrenal gland weight and adrenal ascorbic acid concentration in rats following alloxan administration.

Materials and methods. The data were obtained from the following experimental groups of male Wistar rats weighing 250-275 g: (A) Normal intact; (B) Normal rats approximately 65 hours after the subcutaneous injection of alloxan (5% solution of Alloxan monohydrate, Eastman No. 1722, 150 mg/kg body weight); (C) Normal rats approximately 65 hours after intravenous injection of alloxan (5% solution, 40 mg/kg body weight: (D) Normal intact 60 minutes after intravenous administration of 208 mg glucose; and (E) same as group B but 60 minutes after intravenous administration of 208 mg glucose. The glucose was administered as an 8% solution prepared in M/15 sodium phosphate buffer, pH 7.4. The rats were anesthetized with EVIPAL (n-methylcyclo-hexenyl-methyl barbituric acid) in preparation for either subcutaneous or intravenous injection of the different materials. The intravenous injections were done directly into an exposed saphenous vein. The adrenals were obtained from rats after an overnight fast. Adrenal ascorbic acid concentration was determined by the method of Roe and Keuther(5). Cardiac blood obtained by direct puncture was used in the determination of plasma glucose by the method of Kingsley and Reinhold(6).

Results. The mean ± S. E. adrenal weight

(mg/100 g body weight) and the mean ± S. E. adrenal ascorbic acid concentration (mg/100 g fresh adrenal) of the several groups of rats are presented in Fig. 1. The probability of greater error occurring by chance of the difference between the means as determined from Fisher's "t" test for plasma glucose, adrenal weight, and adrenal ascorbic acid concentration are presented for the indicated groups below the bar graph. It is evident from an inspection of these data that the mean adrenal weight and ascorbic acid concentration of the two groups of alloxan-injected rats were significantly greater than the respective mean values of the normal intact group. Also, it is apparent that the mean adrenal weight and ascorbic acid concentration were not different in the two alloxan-injected groups although the route of administration of this substance was different.

The data for Groups D and E were obtained from analyses of adrenals of the normal intact and alloxan-injected (subcutaneous) rats 60 minutes after an infusion of 208 mg glucose in order to determine the comparative effect of an acutely stressful condition upon ascorbic acid depletion. Application of the Fisher's "t" test to the difference between the means of Groups A-D and Groups B-E show that there was no difference in the mean adrenal weight of these groups; but there was a significant depletion of adrenal ascorbic acid concentration after the glucose infusion in both the intact group (D) and the alloxan-injected group (E). It is noteworthy that the per cent of ascorbic acid depletion in both groups after intravenous glucose was relatively the same, 28% and 33% respectively.

Discussion. The data presented in Fig. 1 illustrate the acuteness of the problem of whether the concentration of adrenal ascorbic acid may be considered a reliable guide of the hyper- or hypo-activity of the adrenal cortex insofar as steroidal hormone secretion is concerned. The increased weight of the adrenal glands in the alloxan-injected groups indicate an adjustment to increased adrenocortical requirements in these rats since it is an established fact that the C-11 oxysteroids of the adrenal are in the main physiologically responsible for the maintenance of the increased blood sugar level in depancreatized and alloxan-diabetic animals. That the heightened concentration of adrenal ascorbic acid in the alloxan-injected groups in this study is not possibly the resultant of a decreased ability to release (discharge or synthetic incorporation) of this material is indicated by the fall in concentration of the ascorbic acid in Groups D and E after glucose infusion. The change in adrenal ascorbic acid concentration in these two groups was in accord with the accepted pattern of ascorbic acid depletion in response to an acutely stressful condition.

An explanation of the increased adrenal ascorbic acid concentration in the alloxan-injected groups can not be made from the data in this report. However there is evidence in the literature relating to the interrelationship between alloxan and glutathione on the one hand, and between ascorbic acid and glutathione which provide a promising speculative basis for an explanation of the results presented here. It has been shown that glutathione protects rats against alloxan diabetes(7). It also has been demonstrated (8-10) that following the injection of alloxan there is a fall in the glutathione content of tissues. The existence of an inverse relationship between ascorbic acid and glutathione is indicated by reports that ascorbic acid injection decreased the glutathione content of the blood(11) and the injection of glutathione decreased the ascorbic acid content of adrenals (12).

The relationship through glucose metabolism of the endocrine function of the pancreas and the adrenal glands is established. However, the effect of experimental diabetes on the function of the adrenal cortex and related constituents of this gland has not received the consideration that it deserves. Until further experiments along these lines are performed, the results presented here are of undoubted interest for investigators in this field.

Summary. The mean adrenal weight/100 g body weight, and the adrenal ascorbic acid concentration of groups of rats approximately 3 days after subcutaneous or intravenous injection of alloxan were shown to be significantly greater than the respective mean values in intact rats. The extent of adrenal ascorbic

acid depletion 60 minutes after subjection to an acutely stressful condition (208 mg glucose solution by intravenous administration) in intact and alloxan-injected groups was practically identical; and significantly lower concentration than control values were obtained. The results were discussed as further evidence of the problem whether adrenal ascorbic acid concentration may be considered a reliable guide of hyper- or hypofunction of the adrenal cortex. A tentative explanation of the increased ascorbic acid concentration in the alloxan-diabetic groups was also discussed.

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Effect of Vitamin C Deficiency on Healed Wounds.* (20034)

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The importance of vit. C in wound healing is well known. In advanced ascorbic acid deficiency wound healing is impaired(1-8). This impairment is characterized histologically by an abundant proliferation of fibroblasts which remain immature, by failure of formation of extracellular material, and by a marked reduction of histochemically detectable alkaline phosphatase. The small amount of extracellular material which may be produced in less severe cases does not become organized into collagen fibers, and argentaffine reticulum fibers (pre-collagen) persist. In addition, the new capillaries which form in this abnormal granulation tissue are defective, and lead to hemorrhages in the wound area. The tensile strength of the wounds is markedly reduced. The subject has been extensively reviewed by Bicknell and Prescott(8) and Levenson *et al.* (9). Vit. C has also been reported as essential for the maintenance of scar tissue even when this had formed many years previously. In Walter's account(10) of Lord Anson's voyage around the world (1769) it is stated that, "the scars of wounds which had been for many years healed were forced open again by this virulent distemper" (scurvy, editor). From this description it would appear that wound scar tissue is particularly susceptible to a prolonged ascorbic acid deficiency. Experimental proof of this susceptibility of scar tissue has been reported and commented upon briefly by Hunt(11) and Hartwell and Stone (12). On the other hand Robertson(13), in a recent study, measured chemically the amount of collagen present in healed wounds using the method of Lowry *et al.*, but failed to observe a significant reduction of its concentration in scorbutic guinea pigs.

It is the purpose of this study to present and discuss the nature of the gross and histologic changes taking place in healed wounds during ascorbic acid deficiency. The altera-

* The opinions expressed in this paper are those of the authors and do not necessarily represent the official views of any governmental agency.