

crude oils contains a substance or substances which will cause epidermoid carcinomas when applied externally to the skin of C-57 black mice and sarcomas when injected subcutaneously into the same strain.

We are grateful to Dr. Raymond L. Teplitz who rendered important service by microscopic examina-

tion of specimens.

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2. Am. Soc. for Testing Materials. Standard D8 (Quoted from (1) above)

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Studies in Wound Healing. III. Contraction in Vit. C Deficiency. (24907)

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The closure of full thickness skin defects in mammals by spontaneous approximation of the wound edges—wound contraction—has been demonstrated to result from forces localized in the wound margins(4,8). Although the site of origin of the contraction process has been clearly identified, the mechanism remains obscure. Histologic study of the wound margin in the guinea pig has revealed an inactive dermis but a highly cellular area of proliferation of loose subdermal connective tissue (unpublished data), suggesting that the latter is the active layer within the margin. While our studies indicated that the collagen fibers composing the central mass of wound granulations were unrelated to the contraction process(4,8), they did not clarify the roles of individual components of the new forming connective tissue in the marginal area, nor did they exclude a possible function for new formed collagen fibers in this region. Experimental scurvy offers a method for partial dissection of components of connective tissue by inhibition of collagen formation(5,7,10). Abercrombie, Flint and James(1) stated that the contraction occurring in skin defects in scorbutic guinea pigs in the first 10 days after

wounding did not differ significantly from that in normal animals. Woessner(9), on the other hand, concluded that "contraction took place normally in wounds of animals on ascorbic acid supplemented diets, but in scorbutic animals very little contraction took place." Edwards and Dunphy commented on conflicting reports of contraction in scurvy(3). This point is of obvious importance in determining relative roles of cells and fibers in the "picture frame" mechanism; we report here the results of systematic study of contraction in skin wounds in scorbutic guinea pigs.

Methods. Male guinea pigs weighing 300-400 g were used. The control animals were placed either on a standard laboratory diet of Purina pellets or on a MacDonald #5 Scorbogenic Diet(2),‡ receiving supplementary Vit. A, B complex, D, and, in addition, ascorbic acid. Experimental animals were placed on the same diet omitting ascorbic acid for 7 and 12 days prior to wounding. Wounds 2 cm square were made on each side of the back through skin and panniculus carnosus. Wound outlines were traced initially and at intervals of one to 3 days. Areas were determined by planimetry. *Wounds without dressings.* For the control series of guinea pigs with undressed wounds and intact scabs, our previously published data(4) were used. In a second control series scabs were removed at

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‡ Dr. W. VanB. Robertson, Coll. of Med., Univ. of Vermont, made available generous supply of this diet.

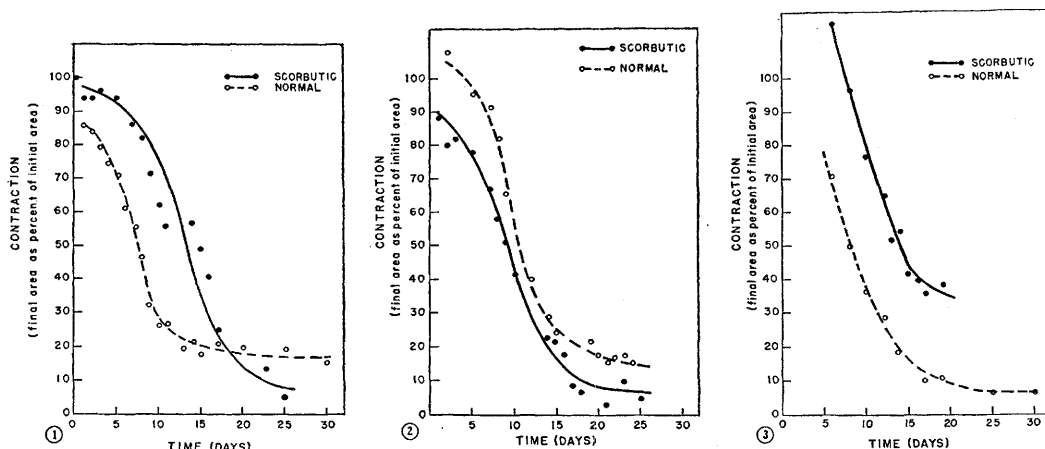


FIG. 1. Contraction with time, undressed wounds, with scabs intact, in scorbutic and in normal guinea pigs as indicated. Points represent averaged measurements.

FIG. 2. Contraction with time, undressed wounds, where scabs have been repeatedly removed, in scorbutic and in normal guinea pigs. There is no significant difference between these 2 curves. Hence apparent reversal of scorbutic and normal curves when compared with Fig. 1, where scorbutic contraction was delayed, is not significant.

FIG. 3. Contraction with time, dressed wounds, scorbutic and normal animals.

frequent intervals from 8 wounds, care being taken not to disrupt the wound margins. In scorbutic test animals 7 wounds with scabs intact, and 11 wounds with scabs removed at intervals of 2 or 3 days were followed. *Wounds with dressings.* Sterile vaseline gauze dressings were held in place by light plaster jackets. Four normal animals, 4 animals on a scorbutigenic diet for 7 days prior to wounding and 5 on the diet for 12 days prior to wounding were studied. Body weight was followed as an index of general condition. No infection occurred in these animals.

Results. Criteria of scurvy. A state of total scurvy was established by histologic examination of the incisor tooth roots as described by Crampton(2) at times ranging from 7 days on the Vit. C deficient diet. Further criteria of the scorbutic state were obtained by demonstrating histologic absence (VanGieson's stain) of collagen in the scorbutic wounds at times when it was clearly demonstrable in the normal. Chemical analysis of the scorbutic granulation tissue for hydroxyproline content(6) revealed 1.4 γ per mg of dry tissue at 9 days, and 1.0 γ per mg at 12 days as compared with 25 γ per mg at 9 days and 35 γ per mg at 12 days in the normal.

Wounds without dressings. Characteristic

thick scabs formed in scorbutic wounds and remained in place several days longer than normally if undisturbed. The curve of contraction when the scab was left intact (Fig. 1) showed a delay in contraction in the first 5 days in contrast with the prompt decrease in wound area occurring in the normal. However, once contraction began, its rate was identical with that of the control. We have previously noted that repeated removal of scabs from normal wounds did not significantly alter the contraction pattern(8). This is again demonstrated by comparing the curves of normal wound contraction (Figs. 1 and 2) where the scabs have been left intact and where they have been removed. When scabs were repeatedly removed from scorbutic wounds, the contraction curve varied little from the normal (Fig. 2).

Wounds with dressings. Further confirmation of the ability of the scorbutic wound to contract actively was obtained by measurements on wounds kept moist by dressings which prevented drying and crusting which causes scab formation. Again, (Fig. 3) the slope of the contraction curve in scurvy is much the same as the normal. At 6 days (the earliest feasible period for observing this type of wound) the area was enlarged as compared with the normal; again contraction was

delayed 5 or 6 days. The behavior of wounds in animals on the scorbutogenic diet for 7 and 12 days prior to wounding was very similar. It is important to record the observation that the contracting scorbutic wound margin at any time could be readily detached from the base, causing immediate distraction. The wound margin was much more firmly bound in the normal.

Discussion. It must be emphasized that the term "wound contraction" is used here to describe that early phase of closure of tissue defects characterized by the movement of preformed tissues, and does not describe the late changes in scar tissue shortening. This latter process is probably different in origin and dependent on collagen fibers of the new formed connective tissue (although direct evidence is presently lacking).

The fact that contraction, except for an initial delay, proceeds in an almost normal manner in scorbutus is consistent with the hypothesis that the actual movement inward of the wound edge is dependent upon directed cell migration as originally suggested by Abercrombie, Flint and James(1), and by Grillo, Watts and Gross(4,8). The markedly different strength of attachment of the wound margins in normal and scorbutic wounds suggests that the role of collagen in this process, if any, is to produce a temporary and continually remodelled tethering of the wound margin to the base. Thus, as the margin progresses inward, collagen fibers might be laid

down in advance and removed or detached as the wound edges pass overhead, a phenomenon suggested by our previous observation(4) that normally firm attachment was found only at the wound margin and relatively little collagen could be demonstrated peripheral to the margin beneath the advancing skin.

Summary. Full thickness skin wounds in scorbutic guinea pigs contract at same rate during the first 2 weeks of healing as do those in normal animals. There appears to be a delay in initiation of contraction. Significance of these observations is discussed.

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Interference Between Certain Neurotropic Viruses in Tissue Culture.* (24908)

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Interference between Col SK virus and poliomyelitis virus, which occurs in monkeys, guinea pigs or in hamsters upon infection with both viruses, has previously been described (1-6). More recently, tissue culture methods have been employed in quantitative studies of

interference reactions between related or unrelated viruses(7-13). Since several strains of the Col SK virus group can be propagated on certain cell lines with definite cytopathogenic effects(14), it became of interest to study interference phenomena between these agents and other neurotropic viruses on suit-

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