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Histamine Forming Capacity of Human Wound Tissue.* (29448)

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(Introduced by G. Kahlson)
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During the last decade evidence has accumulated to show that there is a relationship between histamine forming capacity and rapid tissue growth(1,2). For example, in experimental studies on rats(3) it was found that excised wound tissue and granulation tissue grown into subcutaneously implanted polyvinyl sponges develop a high histamine forming capacity. Moreover, it was shown that the rate of repair of skin incisions determined by wound tensile strength could be influenced by altering experimentally the histamine forming capacity of the tissue of the wound. It has been suggested that a relationship exists between wound healing and histamine formation also in man(4). The present experiments were designed to investigate this problem further by studying histamine formation in normal skin and in tissue removed in the state of wound healing.

Material and methods. Wound tissue was obtained from 9 patients operated on for bilateral varicose veins under general anaesthesia (Fluothane). The patients were subjected to ligation of the long saphenous vein in the groin and stripping of the vessels in a 2-stage procedure in which the operation was performed on one leg at a time. At the first operation a portion of skin was excised from the leg just below the inguinal ligament and used for determination of histidine-decarboxylase activity. At the second operation performed at various intervals after the first one (1-11 days) normal skin was taken from a similar site of the other leg, the first wound was excised and resutured and histidine decarboxylase activity was determined in both specimens. In this way studies could be made of 1) normal skin (skin I) 2) normal skin after a previous operation (skin II) and 3) excised wound tissue.

The tissues were minced, suspended in phosphate buffer and incubated with ^{14}C-histidine and the amount of ^{14}C-histamine formed was measured by isotope dilution. The procedures used have been fully reported (5,6). Blank values were obtained by adding semicarbazide (10^{-2}M) to the incubation mixture.

Results. The results are listed in Table I where the amount of ^{14}C-histamine formed is expressed in counts per minute per gram tissue exceeding blank specimens. Normal skin only exceptionally showed any histamine forming capacity while wound tissue regularly had a high histamine forming capacity. This enzymic change seemed to reach a peak on the second and third day after the incision.

TABLE I

Age of patient	Sex	Wound age, days	Histamine forming capacity		
			Skin I	Skin II	Wound
53	♂	1	11.3	0	0
55	♀	1	0	5.6	27.5
39	♀	2	0	0	30.3
56	♂	2	30.4	15.3	65.8
67	♀	3	0	0	73.5
39	♂	3	0	0	48.5
61	♂	4	0	4.8	42.3
39	♂	4	0	0	15.3
69	♂	11	1.6	0	14.6

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Discussion. The present study has shown that human wound tissue has a high histamine forming capacity whereas uninjured skin only exceptionally has any measurable histamine forming capacity. From experimental studies on rats(3) it has been suggested that the histamine forming capacity is an essential factor in initiating and sustaining rapid tissue growth in healing wounds. The present results indicate that the same mechanism may be operative in human wound healing. The present findings are in accordance with those previously reported(4) for histamine forming capacity of wound tissue in man.

In the present experiments normal skin from the groin in man only exceptionally formed ^{14}C-histamine from ^{14}C-histidine *in vitro,* whereas such formation has been demonstrated by other workers(4,7). This apparent discrepancy may be explained by methodological differences, e.g. relative substrate concentration, or may reflect a real difference in the histamine forming capacity of skin in different body regions or experimental conditions.

The present study included determinations on uninjured skin taken 1-11 days after a previous minor operation. This was done because an increased histamine content has been found in uninjured skin after operation in rats(8). The present observations indicate that a corresponding increase in histamine formation does not occur after a minor operation in man.

Summary. The histamine forming capacity of human wound tissue has been studied. It was found that whereas uninjured human skin only rarely showed a measurable histamine forming capacity, human wound tissue regularly showed a high histamine forming capacity.

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Antiandrogenic Activity of Tetra-N-Butyllead in a Mouse Assay.* (29449)

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Various steroids, a tricyclic compound (2-acetyl-7-oxo-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydrophenanthrene), and 5-fluorouracil(1) have been shown to inhibit the action of testosterone on the seminal vesicles of the castrated mouse(2). This activity has been observed for tetra-n-butyllead and is the subject of this report.

Methods and material. Swiss albino mice were castrated at 21 to 23 days of age. On the day of operation and once daily for a total of 7 consecutive days, testosterone dissolved in 0.1 ml of sesame oil was injected subcutaneously. The total dose of androgen was 0.8 mg. The test material, in an aqueous suspending medium, was injected once daily for 7 days also, starting on the day of operation. This medium consists of sodium chloride (0.9%), polysorbate 80 (0.4%), carboxymethyl cellulose (0.5%) and benzyl alcohol (0.9%). Twenty-four hours after the last injections, the body, prostate, and seminal vesicle weights were determined. The results were expressed as tissue ratios de-

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