

Vergleichsprodukt (DCA) ein 9 α -Fluorrest, der die mineralcorticoide Aktivität anregen könnte, und gegen welche der 16 α -Methylrest eine intramolekulare gegenseitige Wirkung ausüben könnte.

Da nun das 16 α -Methyl-DCA keine nennenswerte glykocorticoide Wirkung auf die Leberglykogenablage bei der Ratte zeigt, glauben wir bewiesen zu haben, dass der 16 α -Methylrest als solcher kein «Träger» der glykocorticoiden Aktivität beim Dexamethason, 16 α -Methylprednisolon und weiteren 16 α -Methyl-Sterolen sein kann.

Nachschrift: Nachdem die Arbeit zum Druck geschickt worden war, haben auch V. PETROW und D. M. WILLIAMSON, J. Chem. Soc. 1959, 3595, über die Herstellung durch andere Verfahren des 16 α -Methyl-desoxycorticosteron-acetats referiert.

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Summary

The introduction of a 16 α -methyl group in desoxycorticosterone acetate, a typical mineral-corticoid hormone, abolishes the sodium retention activity of desoxycorticosterone acetate. Since the same effect of 16 α -methylation had been previously noted by other authors in 9 α -fluoroprednisolone, our results further support the hypothesis that the 16 α -methyl group is responsible for this specific change of metabolic activity in steroids.

Studies on Wound Healing:

1. Metabolism of ^{35}S in 'Repair Tissue' of Skin Wounds during the various Phases of Healing¹

It is well known that 95% of ^{35}S parenterally injected in the form of $\text{Na}_2\text{S}^{35}\text{O}_4$ is rapidly eliminated through feces and urines (DZIEWIATKOWSKI²); the remaining 5% is distributed in the various organs according to a tropism which differs greatly from tissue to tissue (DZIEWIATKOWSKI³, CAMPBELL *et al.*⁴, BOSTRÖM⁵, JORPES *et al.*⁶, ASBOE-HANSEN⁷, BOSTRÖM *et al.*⁸).

The maximal amount of ^{35}S stored by the organism is taken up by the bone tissue, bone marrow, and cartilage, chiefly in the form of chondroitinsulphuric acid (DZIEWIATKOWSKI *et al.*^{9,10}).

BOSTRÖM¹¹ demonstrated that the dermis is also capable of taking up ^{35}S , though in much smaller quantity than the above-mentioned tissues, incorporating it almost

entirely into the chondroitinsulfuric acid of the ground substance.

It was observed by LAYTON¹² that embryonic tissues, especially granulation tissues, have a property of taking up much larger amounts of ^{35}S than the corresponding normal adult tissues.

He observed also that the uptake of ^{35}S is influenced by some hormones: thus cortisone, for instance, reduces considerably such ability.

The present investigations aim at studying the metabolism of ^{35}S in 'repair tissue' of skin wounds experimentally produced in laboratory animals.

Materials and Methods. 7 guinea pigs of both sexes weighing from 220 to 295 g were used in these experiments. Throughout the investigation, the animals were fed on a diet containing sufficient amounts of proteins and vitamins to cover the organism requirements.

After back-shaving and skin-disinfection, each guinea pig was inflicted a quadrangular wound of 2 cm side in the intrascapular region. The wounds, involving both skin and underlying subcutaneous tissue, were inflicted so that at a given moment the animals presented at the same time differently dated wounds, therefore different stages of repair tissue.

Two days before the animals were sacrificed, each guinea pig was intravenously injected with 5.678 μC of ^{35}S (in the form of $\text{Na}_2\text{S}^{35}\text{O}_4$ in aqueous solution)/1 g body weight. The wound-covering tissue, as well as a sheet of normal skin and subcutaneous tissue (taken as control), were excised, carefully weighed, then mineralized for 18 h with H_2SO_4 at 95–96% in 50 ml Kieldahl flasks. Each solution was then vaporized until a dry residue was obtained, which was diluted into 10 ml distilled boiling water and, after cooling, was put into a Geyger-Müller

¹ For 'repair tissue' we mean that tissue (first granulation, then scar tissue) which fills up and repairs any loss of substance in the soft tissues of the animal organism.

² D. D. DZIEWIATKOWSKI, J. biol. Chem. 178, 197 (1949).

³ D. D. DZIEWIATKOWSKI, J. exp. Med. 93, 451 (1951).

⁴ D. CAMPBELL and H. PERSSON, Exper. 7, 304 (1951).

⁵ H. BOSTRÖM, On the Sulphate Exchange of Sulpho-mucopolysaccharides, in *Connective Tissue in Health and Disease* (Munksgaard ed., Copenhagen 1954), p. 97.

⁶ E. JORPES, E. ODEBLAD, and H. BOSTRÖM, Acta haemat. 9, 273 (1953).

⁷ G. ASBOE-HANSEN, Cancer Res. 13, 587 (1953).

⁸ H. BOSTRÖM and S. AQVIST, Acta chem. scand. 6, 1551 (1953).

⁹ D. D. DZIEWIATKOWSKI, J. biol. Chem. 189, 187 (1951).

¹⁰ D. D. DZIEWIATKOWSKI, R. E. BENESCH, and R. BENESCH, J. biol. Chem. 178, 931 (1949).

¹¹ H. BOSTRÖM, Arch. Kemi 6, 43 (1954).

¹² L. L. LAYTON, Proc. Soc. exp. Biol. Med., N. Y. 73, 718 (1950).

counter for fluids (Twentieth-Century-Electronics, Type M. 6) in order to dosage the radiations emitted by the ³⁵S contained in the various tissue extracts.

Values obtained in the various estimations have been worked out so as to express the 'concentration index', that is the relationship between the relative specific activity (R. S. A.) of repair tissue and that of normal skin and subcutaneous tissue.

Results. Values obtained through the present experiments are reported in the Table and in the Figure.

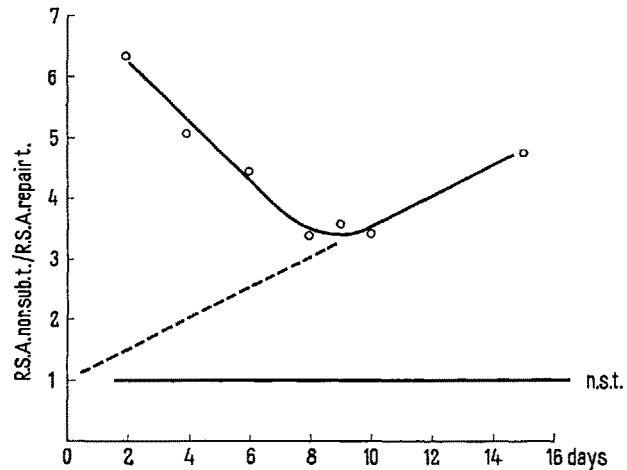
Discussion. The ability of repair tissue to take up a larger amount of ³⁵S that is done by normal skin and subcutaneous tissue (these data being in perfect agreement with those of LAYTON¹³) points a considerably increased metabolism of ³⁵S in the repair tissue.

The very high initial values might find a logical explanation by admitting that ³⁵S in repair tissue is not at first incorporated in the SO₄-group of chondroitinsulphuric acid, since the mechanism of its incorporation surely requires a comparatively long time, but bound to some substance or group of substances present in the tissue, which would take it up in considerable quantities and in a relatively labile way. It is probably only with time, probably in relation to the changes observed by several authors both in the fibrocellular part (DUMPHY *et al.*¹⁴, SYLVÉN¹⁵ etc.) and in the ground substance (SYLVÉN¹⁶, CAMPANI *et al.*¹⁷ etc.) of repair tissue, that ³⁵S pass from 'uptake' to 'incorporation'.

Relative specific activity (R. S. A.) of normal cutaneous and subcutaneous, and of repair tissue of skin wounds at various stages of the healing process.

Guinea pig No.	Tissue type	R. S. A.		Concentration index
		Normal cutaneous tissue	Repair tissue	
1	2-days rep. t.	0.0432825	0.2732230	6.31
2	4-days rep. t.	0.0171934	0.0874926	5.08
3	6-days rep. t.	0.0202942	0.0903792	4.45
4	8-days rep. t.	0.0783679	0.2672030	3.40
5	9-days rep. t.	0.0163303	0.0582180	3.56
6	10-days rep. t.	0.0221658	0.0758071	3.42
7	15-days rep. t.	0.0164203	0.0778325	4.74

$$R.S.A. = \frac{\mu c \text{ observed}}{\text{sample weight}} \cdot \frac{\text{body weight}}{\mu c \text{ injected}}$$



Behaviour of the ³⁵S content in the repair tissue of cutaneous wounds

The lowest values of ³⁵S found between the sixth and tenth day are perhaps the expression of the metabolism cycle of chondroitinsulphuric acid of repair tissue.

The amount of ³⁵S incorporated into the chondroitinsulphuric acid of wound repair tissue might probably be expressed as a straight line which, starting from very low values, joins the curve of the Figure by the eighteenth day and, from that point on, follows it. The large amount of ³⁵S found in the early days might in fact be the result of the ³⁵S uptake plus incorporation, since the method used in these experiments does not allow such differentiation.

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Riassunto

- 1) Il «tessuto di riparazione» delle ferite cutanee ha la proprietà di «fissare» una quantità di S³⁵ notevolmente più grande di quella captata dal connettivo sottocutaneo.
- 2) La quantità di S³⁵ fissata varia durante le diverse fasi del processo di guarigione delle ferite: è molto alta nei primi giorni; scende quindi sino al sesto-decimo giorno, epoca nella quale raggiunge i valori più bassi, e risale poi gradualmente sino al quindicesimo giorno (ultimo giorno preso in considerazione nelle presenti ricerche).

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Queen Recognition by Worker Honeybees (Apis mellifera L.)

Introduction. The sight, sound and scent of a queen honeybee do not inhibit either queen rearing by worker bees¹⁻³ or the development of their ovaries⁴⁻¹⁰. Inhibition occurs only when the bees can touch their queen and obtain 'queen substance' from her^{3,10}.

Many beekeepers believe that a queen has an odour attractive to workers. If this true it would be important because the odour would help workers to find the queen and get queen substance, but the only experimental evidence even suggestive of a queen odour seems to be that provided by LECOMTE¹¹, VOOGD¹², and PAIN¹³.

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