

zweite ins Netz gereicht wurde. Durch Vertauschen der Faktoren konnte gezeigt werden, dass der Geschmack den auslösenden Reiz bildet. Wenn hingegen geschmacklose Glasperlen mit den Tönen kombiniert wurden, richteten sich die Spinnen in ihrem Verhalten nach der Schwingungsfrequenz. Diese Ergebnisse zeigen die Fähigkeit der Spinnen, sowohl zwischen verschiedenen Schwin-

gungsfrequenzen zu unterscheiden, als auch ihr Verhalten der Erfahrung anzupassen.

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Effects of 4-Hydroxy-17- α -Methyltestosterone and Prednisolone on Wound Healing

On the basis of available evidence, the action of anabolic steroids on wound healing appears to consist in promoting reparative processes¹. This aspect, however, has not been thoroughly investigated, whereas the anti-inflammatory action² of cortisone and its congenerous compounds, as well as their inhibitory action on formation of granulation tissue^{2,3}, has been sufficiently documented.

The present investigation was undertaken to study the effect of an orally active anabolic steroid, 4-hydroxy-17- α -methyltestosterone (Oranabol), on wound healing, and to find out to what extent such action might modify the inhibitory influence of a glucocorticoid compound, Prednisolone.

Sixty eight male mice from Swiss strain, weighing from 40 to 45 g, kept on Rockland diet and fed *ad libitum*, were employed. Under ether anaesthesia a fragment of skin from the dorsal region, of the same size

in all animals (5 per 10 mm), was excised. The animals, divided into six groups, received, by *gavage* for a period of ten days, Oranabol and/or Prednisolone⁴, according to the following scheme: 1st group, normal saline 0.25 cm³; 2nd Oranabol 0.5 mg; 3rd, Oranabol 1.0 mg; 4th, Prednisolone 0.5 mg; 5th, Oranabol 0.5 mg and Prednisolone 0.5 mg; 6th, Oranabol 1.0 mg and Prednisolone 0.5 mg. The doses of the compounds were dissolved in normal saline 0.25 cm³.

At the end of this treatment, all the animals were sacrificed by ether, and the area of skin including the wound was removed, fixed in neutral formaline 10% and

¹ L. LODDI and L. MOGGI, *Acta chir. patav.* 9, 607 (1953). – C. W. PEARCE, N. C. FOOT, C. L. JORDAN, S. W. LAW, and C. E. WANTZ, *Surg. Gynec. Obst.* 111, 274 (1960).
² C. CAVALLERO, *Rev. Canad. Biol.* 12, 189 (1953).
³ G. ASBOE-HANSEN, *Connective Tissues*. Trans. 5th Conf. J. Macy Found (1954), p. 23. – K. KOWALSKY, *Endocrinology* 62, 493 (1958).
⁴ Oranabol and Prednisolone were kindly supplied by Farmitalia, S.p.A., Milano (Italy).

Summary of microscopic features											Remarks
Group		Edithelization	Cornification	Fibroblasts	Reticulum	Collagen	Capillaries	Mastzellen	PAS-Positivity	Inflammatory changes	
I	Saline, 0.25 cm ³ (16 animals)	2+	1+	2+	2+	2+	2-3+	1+	2-3+	2-3+	Wounds repaired: 3 (19%) Good evidence of inflammatory changes
II	Oranabol, 0.5 mg (10 animals)	2-3+	1+	3+	2-3+	1+	2-3+	1+	2-3+	0-1+	Wounds repaired: 5 (50%) More intense repair activity Reduction of phlogistic pattern
III	Oranabol, 1.0 mg (10 animals)	0-1+	0-1+	0-1+	1+	0-1+	1+	1+	1-2+	2+	Wound repaired: 0 Healing response very poor and limited to the marginal zone
IV	Prednisolone, 0.5 mg (10 animals)	0-1+	1+	0-1+	1+	1+	1-2+	1+	1-2+	0	Wound repaired: 0 Healing response and inflammatory changes almost absent
V	Oranabol, 0.5 mg + Prednisolone, 0.5 mg (11 animals)	2+	1+	2+	1-2+	1+	2+	1+	2+	0	Wounds repaired: 2 (18%) Good healing activity, often more marked at the marginal zone
VI	Oranabol, 1.0 mg + Prednisolone, 0.5 mg (11 animals)	2+	1+	1-2+	1-2+	1+	2+	1+	2+	0	Wounds repaired: 2 (18%) Good healing activity, often more marked at the marginal zone

0 = none; 1+ = slight; 2+ = moderate; 3+ = advanced

embedded in paraffin. The following methods of staining were used: hematoxylin-eosin, Hotchkiss-McManus, aqueous toluidine blue (0.5%/₀₀), Verohof-Van Gieson for elastic fibres, Gomori for reticulum, Azan-Heidenhein. Histological observation was directed to the possible modification of fibrillary reticulum, elastic fibres⁵, vascular and inflammatory components, collagen formation and epidermization, as well as to the quantitative and qualitative response to metachromasia and PAS-positivity.

The results are summarized in the Table. Oranabol, at the dose of 0.5 mg, induced a more intense proliferative activity with a higher percentage of wounds repaired (50%), as compared with the controls (19%); the inflammatory component was very low. In this group the persistence of features characteristic of newly formed tissues (higher cellularity, more dense fibrillary reticulum, comparatively less marked increase of collagen fibres), suggested an evolutive rather than a maturative process.

Different effects were observed in the group of mice treated with Oranabol 1.0 mg: a remarkable reduction of the repair processes as compared with the controls was found, with evidence of phlogistic changes, no wounds being completely repaired. The different results obtained by varying the dose of the steroid, though apparently discordant, may be ascribed to toxicity through overdosage, depression of pituitary activity being the possible mechanism⁶. This point deserves further investigations.

The administration of Prednisolone 0.5 mg resulted in a very low degree of formation of granulation tissue and repair activity (no wounds repaired), with marked

reduction of the inflammatory response. This is in accordance with the results obtained by other authors⁷, concerning the effect of cortisone and derivatives on granulation tissue.

Oranabol and Prednisolone, administered simultaneously, induced effects similar to those observed in the control animals (18% of wounds repaired) with a good formation of granulation tissue and very few inflammatory changes. Such results suggest that the inhibitory effect exerted by cortisone on wound healing can be partially prevented by the simultaneous administration of anabolic steroids.

Riassunto. Il trattamento associato di 4-idrossi-17- α -metiltestosterone (Oranabol) e Prednisolone ha determinato sui processi di guarigione delle ferite cutanee del topo una risposta riparativa che lascia intravedere la possibilità di una neutralizzazione da parte degli steroidi anabolizzanti dell'azione inibente dei cortisonici.

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⁵ Elastic fibres were always absent within the healing area, both in control and treated animals.

⁶ M. TAUBENHAUS and G. D. ANROMIN, *J. lab. clin. Med.*, **36**, 7 (1950).

⁷ A. D. BANGHAM, *Brit. J. exp. Path.*, **32**, 77 (1951). - G. ASBOE-HANSEN, in *Inflammation and Diseases of Connective Tissue*, Hane-mann Symp. (Saunders 1961), p. 38.

Störung der Atemmotorik durch Parasympathicomimetica, verglichen mit der Wirkung von Reizstoffen

Reflexogene Reizgifte, wie Aconitin, Veratrin, Veratrum- und Delphiniumalkaloide und Andromedotoxin oder Inhalation örtlich reizender Gase bewirken bei Mäusen, Ratten und Meerschweinchen eine periodisch auftretende charakteristische Störung der Atemmotorik (Respirationszeichen, RZ). Diese besteht in einer krampfartigen Bewegung des Rumpfes, wobei der Kopf nach vorne geneigt wird. Bei dieser etwa 1-2 sec dauernden steifen Verbeugung macht das Tier den Eindruck, als wolle es sich erbrechen. Das Zeichen wiederholt sich in Abständen von $\frac{1}{2}$ bis mehreren Minuten über einen Zeitraum bis zu 1 h und auch darüber¹⁻³. Tiefe Narkose hebt das Phänomen auf.

In einer früheren Mitteilung² haben wir das RZ als Reflexbewegung gedeutet, die ihrerseits durch einen kurzdauernden reflektorischen Bronchialverschluss ausgelöst wird. Von dieser Deutung ausgehend wurde in den hier mitgeteilten Versuchen geprüft, ob sich das Phänomen auch durch Gifte hervorrufen lässt, die nicht reflektorisch, sondern parasympathicomimetisch oder myotrop bronchokonstriktorisch wirken. Es konnte nicht vorausgesagt werden, ob es möglich ist, durch geeignete Dosen dieser Stoffe Bronchialverschlüsse von so kurzer Dauer zu erzeugen, wie es für die Entstehung des RZ erforderlich ist. Anhaltend starke Bronchokonstriktion muss das Phänomen durch schwere Atemstörung verdecken oder verhindern.

Versuche. Es gelang uns nicht, am Meerschweinchen mit Histamin und an Mäusen mit Pilocarpin das RZ zu erzeugen. Dagegen konnte das Phänomen bei Mäusen beobachtet werden nach Injektion von 1 μ g/20 g Pro-

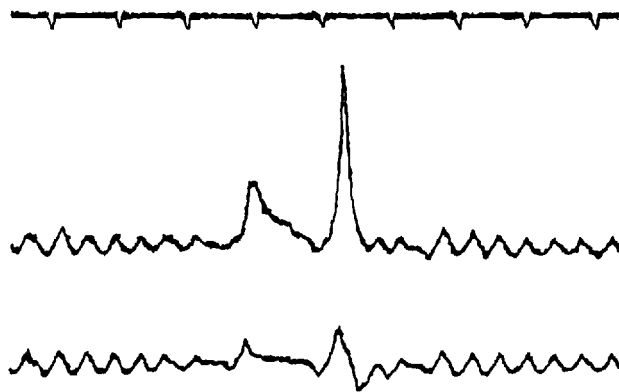


Fig. 1. Atemstörung (RZ) nach 10 μ g/20 g Physostigmin s.c. Bei insgesamt verlangsamerter Atmung Stillstand der Luftbewegung für etwa 1 sec bei verstärkter inspiratorischer Thoraxbewegung; danach tiefer Atemzug.

¹ P. PULEWKA und H. GREVENER, *Arch. exp. Path. Pharmacol.*, **177**, 74 (1934).

² P. PULEWKA, M. BÜHLER und B. KLUMPP, *Arzn.-Forsch.*, **10**, 953 (1960).

³ P. PULEWKA, *Bull. Fac. Med. Istanbul*, **12**, 275 (1949).