

THE EFFECT OF HORMONES AND ANTIBIOTICS ON THE REGENERATION OF CORNEAL EPITHELIUM IN RABBITS

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The purpose of the present investigation has been to study the effect of various pharmacological agents on tissue regeneration [1].

Of the hormones we used testosterone and desoxycorticosterone. Published reports on their effect on regeneration are contradictory [6, 9, 10, 12, 13, 15].

Of the antibiotics we used penicillin and biomycin. Several reports have been published to the effect that local application of high concentrations of antibiotics restrains proliferation in the region of the wound, while in low concentrations it has a stimulant effect [2, 3, 4, 8, 14]. We found no reports on the resorptive effect of antibiotics on regeneration.

METHOD

The experiments were carried out on adult male rabbits. We used the method of Ponomareva-Astrakhantseva [5], which consists of scarifying the corneal epithelium, staining it with fluorescein, and measuring the extent of the damaged area.

To start with we measured the average time required for the corneal epithelium to regenerate after a scratch 4-5 mm long had been made in it (and a subcutaneous injection of isotonic saline was given). This time we found to be 6.42 ± 0.64 hours.

After this we found the effect on regeneration of the substances to be investigated when injections of them were given 20 minutes before or 2 and 4 hours after making the wound. The dose to be given was calculated from the mean therapeutic dose for a human adult. This was calculated from the formula: $\text{dose/kg weight} \times \sqrt[3]{\text{the body weight}} = \text{Constant}$, [7, 11].

RESULTS

Experiments with Testosterone. This was injected in doses of 0.001 and 0.005 g per kg weight.

A dose of 0.001 g/kg, corresponding to a single dose for man of 0.005 g/kg of testosterone had no definite effect on the time taken for the corneal epithelium to regenerate. A dose of 0.005 g/kg was therefore tried. This dose is equivalent to one for man of 0.05 g/kg.

When the 0.005 g/kg injection was given before causing the damage, the repair time was shortened by 0.72 hours, when given 2 and 4 hours after the damage, the reduction was 0.59 and 1.08 hours respectively.

Experiments with Desoxycorticosterone. Desoxycorticosterone acetate, supplied by the firm Organon, was given as a subcutaneous injection of 0.00025 g/kg. When the injection was given before inflicting the damage the

repair time was shortened by 0.86 hours, and when injected 2 and 4 hours after the damage the reduction was 1.14 and 1.09 hours respectively.

Thus, in our experiments, testosterone in doses of 0.005 g/kg and desoxycorticosterone in doses of 0.00025 g/kg increased the rate of regeneration of the corneal epithelium (Table 1).

TABLE 1

Increase in Rate of Regeneration of the Cornea Caused by Sex Hormones (in hours)

Substance	Regeneration when hormone was injected		
	Before damage	2 hours after damage	4 hours after damage
Testosterone	0.72	0.59	1.08
Desoxycorticosterone	0.86	1.14	1.09

Experiments with Penicillin. We investigated the effect of both amorphous and crystalline penicillin. Injections of 6,000 units/kg of both preparations were given intramuscularly.

When the injections were given before the damage, the amorphous penicillin advanced regeneration by 1.15 hours, and the crystalline by 1.09 hours. When given 2 hours after damage, the reduction in time resulting from the amorphous penicillin was 2.13 hours, and that from the crystalline, 2.15 hours.

Experiments with Biomycin. 10,000 units/kg were injected into the stomach. When given before damage healing time was reduced by 0.47 hours, and when given after 2 hours - by 0.72 hours.

Thus, in these experiments, both penicillin and biomycin stimulated regeneration of the corneal epithelium of the rabbit. This effect was greatest in the case of penicillin. Both amorphous and crystalline varieties had the same effect (Table 2).

TABLE 2

Increase in Rate of Regeneration of the Cornea Caused by Antibiotics

Substance	Regeneration time (in hours) when injections given	
	Before damage	2 hours after damage
Amorphous penicillin	1.15	2.13
Crystalline penicillin	1.09	2.15
Biomycin	0.47	0.72

The published reports on the effect of antibiotics on the growth of young animals and on metabolic rates, and our results, suggest that the therapeutic effect of antibiotics on wound healing is not only due to their bacterial action but also to their effect on the body itself.

In these experiments both hormones and antibiotics accelerate regeneration of rabbit corneal epithelium.

SUMMARY

Testosterone (0.005 per kilogram of body weight), desoxycorticosterone (0.00025 per kg), penicillin (6,000 units per kg) and biomycin (10,000 units per kg) were the preparations administered in this experiment. Their stimulating effect on the healing of the corneal defects in rabbits was established. The preparation was introduced before the injury was inflicted, or directly after it (in 2 to 4 hours).

LITERATURE CITED

[1] G. S. Alekseeva, Effect of Various Pharmacological Agents on Regeneration of Rabbit Corneal Epithelium,* Dissertation, 1956.

* In Russian.

[2] G. R. Dambite, Clinical and experimental observations on the healing of Ulcus Serpens Corneae by Sulfanilamide Preparations and by Penicillin,* Author's abstract of Dissertation, 1951.

[3] G. K. Mironich, Voenno-med. zhurn. 3, 27-32 (1953).

[4] E. A. Timofeevskaya, Bull. Eksptl. Biol. i Med. 10, 313-315 (1951).

[5] L. Z. Ponomareva-Astrakhantseva, Farmakol. i Toksikol. 13, 4, 54-55 (1950).

[6] N. A. Shereshevskii, Nov. med. 12, 3-5 (1949).

[7] H. C. Bazett and W. H. Erb, J. Pharm. Exp. Therap. 1933, Vol. 49, No. 3, pp. 352-360.

[8] O. Bucher, Schweiz. Med. Wchschr. 1946, Vol. 76, pp. 16-17, 375-378.

[9] C. Covallero, et. al., Arch. internat. pharmacodyn. 1951, Vol. 86, pp. 43-51.

[10] R. L. Howes, J. internat. chir. Brux. 1953, No. 13, 2, pp. 127-133.

[11] H. J. Klarc, Handbuch der exper. Pharmac. 1937, No. 4, pp. 166-167.

[12] C. L. Pirani, et. al., J. Exper. Med. 1951, 93, 3, 217-218.

[13] U. Principe and G. Bellucci, Sperimentale, 1952, 102, 8, 9, 10.

[14] G. K. Smelser, Am. J. ophth. 1946, Vol. 29, No. 5, pp. 541-551.

[15] M. Taubenhaus and G. D. Amromin, Endocrinology 1949, Vol. 44, No. 4, pp. 359-367.

* In Russian.