

Ansteigen der Werte um etwa 10% infolge des Holmes-Effektes, wie es bei einer Schnittdicke von 20  $\mu$  für zylindrische Objekte vom Durchmesser der Plazentazotten (50–80  $\mu$ ) zu erwarten wäre, wird damit wieder kompensiert und kommt im Messergebnis nicht zum Ausdruck. Entsprechende Überlegungen gelten auch für die Messung der Oberfläche.

**Summary.** In stereological measurements of volume and surface of human placental villi systematic overestimation due to section thickness (Holmes-effect) was

not observed, probably because it is compensated by overlapping of sections of villi.

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## The Effect of Abdominal Wounding on the Rate of Tissue Regeneration

It has been demonstrated that the rate of tissue regeneration is higher in male rabbits than it is in females<sup>1</sup> and it has been proposed that the higher androgen level in males is concerned in producing this effect<sup>2</sup>. The reduction of the androgen level in males by orchidectomy does not cause a simple lowering of their regeneration rate as might be expected. Instead a significant reduction in regeneration rate only occurs if there is a considerable delay between castration and the excision of ear tissue. Where castration is followed by immediate excision of ear tissue the amount of regenerative growth achieved by 49 days after excision (when measurements ceased) is similar to that found in control males. In all the groups of castrated males there is an initial acceleration of growth, inversely proportional to the delay between castration and the excision of ear tissue, followed by a reduction in the rate of regeneration<sup>3</sup>. One possible explanation for the initial increase is that the stress produced by the castration procedure temporarily stimulates regeneration so that the predicted inhibitory effect of decreased testicular androgen supply is masked. The present communication describes some experiments performed to investigate this possibility.

**Method.** Under i.v. pentobarbitone anaesthesia a mid-line abdominal incision, 3 cm long and ending 3 cm above the symphysis pubis, through the whole thickness of the abdominal wall, was made in each of a series of rabbits, of

mixed stock and over 6 months old. The wound was sutured in 2 layers, one for the peritoneum and muscle and one for the skin, with continuous sutures of silk. In one group of males and one of females, 1 cm<sup>2</sup> of tissue was excised through the full thickness of the pinna of the ears immediately after abdominal wounding. In a further 2 groups of rabbits the ear tissue was excised 14 days after the abdominal operation. Wounds were made in both ears of each rabbit but the growth of the regenerate was only measured, by a photographic procedure, in one. The growth of the ear regenerates of the 4 groups of abdominally wounded animals was compared with that of a series of controls without abdominal wounds.

**Results and discussion.** The effect of abdominal wounding on the growth of the ear blastemata is shown in Figures 1 and 2 and Tables I and II. The presence of an abdominal wound stimulated regeneration, for there was significantly more growth in the ear regenerates of all 4 groups of abdominally wounded rabbits by 14 days after ear tissue excision than there was in their respective controls ( $P < 0.005$  in all cases). In females the regeneration rate was maintained at a high level so that at 49 days,

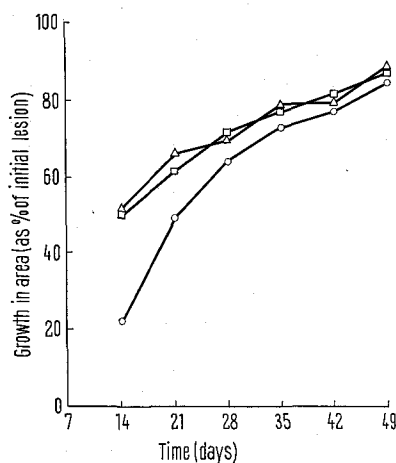


Fig. 1. The effect of abdominal wounding on the rate of regeneration of ear tissue in males.  $\Delta$ , Abdominal wound made at the time of ear tissue excision;  $\square$ , abdominal wound made 14 days before ear tissue excision;  $\circ$ , control males without abdominal wounds.

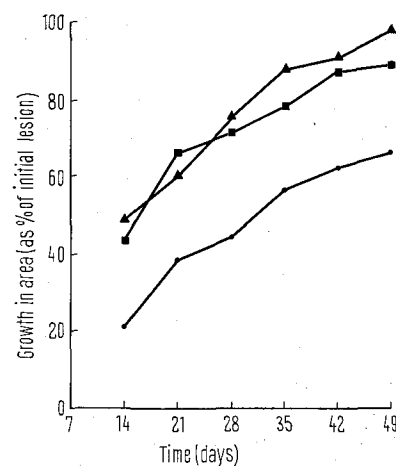


Fig. 2. The effect of abdominal wounding on the rate of regeneration of ear tissue in females.  $\blacktriangle$ , Abdominal wound made at the time of ear tissue excision;  $\blacksquare$ , abdominal wound made 14 days before ear tissue excision;  $\bullet$ , control females without abdominal wounds.

<sup>1</sup> J. JOSEPH and M. DYSON, *Nature* 208, 599 (1965).

<sup>2</sup> J. JOSEPH and M. DYSON, *Br. J. Surg.* 53, 372 (1966).

<sup>3</sup> M. DYSON and J. JOSEPH, *J. Anat.* 103, 491 (1968).

when the last measurements were made, the mean areas of the ear regenerates in both abdominally operated groups were significantly higher than the controls ( $P < 0.010$  in both cases). In males the growth rate fell

Table I. Effect of abdominal wounding on regenerative growth in males

Group	Treatment	Days after excision	N	Mean area of regenerate as % of initial lesion	Standard error of mean
1	Abdominal wound made at the time of ear tissue excision	14	5	50.7	$\pm 5.3$
		21	5	66.4	$\pm 6.1$
		28	5	70.3	$\pm 4.3$
		35	5	78.6	$\pm 5.1$
		42	5	79.2	$\pm 5.9$
		49	5	88.3	$\pm 4.6$
2	Abdominal wound made 14 days before ear tissue excision	14	6	50.5	$\pm 3.7$
		21	6	61.7	$\pm 5.4$
		28	6	71.6	$\pm 6.3$
		35	6	77.8	$\pm 6.6$
		42	6	81.1	$\pm 6.9$
		49	6	86.8	$\pm 6.0$
3	Control males without abdominal wounds	14	18	22.3	$\pm 3.5$
		21	18	49.1	$\pm 2.4$
		28	18	63.9	$\pm 2.8$
		35	18	72.8	$\pm 2.6$
		42	18	77.0	$\pm 2.8$
		49	18	85.2	$\pm 2.6$

Table II. Effect of abdominal wounding on regenerative growth in females

Group	Treatment	Days after excision	N	Mean area of regenerate as % of initial lesion	Standard error of mean
4	Abdominal wound made at the time of ear tissue excision	14	8	48.7	$\pm 2.7$
		21	8	61.2	$\pm 3.5$
		28	7	75.9	$\pm 5.4$
		35	8	88.0	$\pm 4.2$
		42	7	91.0	$\pm 3.5$
		49	7	97.6	$\pm 3.2$
5	Abdominal wound made 14 days before ear tissue excision	14	6	44.1	$\pm 2.9$
		21	6	67.2	$\pm 4.4$
		28	6	72.4	$\pm 2.9$
		35	6	78.9	$\pm 4.6$
		42	6	88.5	$\pm 2.3$
		49	6	89.6	$\pm 3.8$
6	Control females without abdominal wounds	14	11	21.6	$\pm 4.1$
		21	11	38.9	$\pm 5.0$
		28	12	45.3	$\pm 5.6$
		35	12	57.1	$\pm 5.6$
		42	12	63.2	$\pm 5.5$
		49	12	67.2	$\pm 4.9$

progressively after the initial acceleration. It would thus appear that surgery can affect the regeneration rate at a distant site, and that the effect is greater and lasts longer in females than in males.

The mechanism by which operative procedures affect distant regeneration has not been established. Although the possible release of a wound hormone from the abdominal wounds cannot be discounted, it may be that changes in the hormonal environment in response to stress are concerned. Such changes do occur<sup>4,5</sup>, particularly in response to surgical stress<sup>6</sup>. Since the hormonal environments of males and females are different, it could also account for the different responses in growth rate found in males and females towards the end of the regenerative process. Provided that the nerve supply to the injured part is intact<sup>7</sup> there is a pituitary-adrenocortical response to surgical stress resulting in an increased level of ACTH in the blood and an increased output of glucocorticosteroids<sup>8</sup>. The latter may help to initiate the regenerative process by intensifying protein metabolism and making amino acids and nucleoprotein available for use in the later, anabolic, phase of repair. Since ACTH stimulates adrenal androgen production<sup>9</sup> and many androgens are anabolic agents, these may also stimulate regeneration. It has been demonstrated that the adrenal glands are larger, and the plasma concentrations of adrenal hormones higher, in female rats than in males<sup>10</sup>. This may explain, if it is also true for rabbits, why the stimulation of regenerative rate was greater in females after surgical stress than in males, and why it persisted longer in females<sup>11,12</sup>.

*Zusammenfassung.* Verwundung induziert Regeneration in entfernten Stellen bei männlichen und weiblichen Kaninchen. Dies gilt für frühe Regenerationsstadien bei männlichen Tieren, während bei Weibchen die Regenerationswirkung mindestens 49 Tage anhält. Es wird vermutet, dass es sich um hormonale Einwirkungen infolge Stress handelt.

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<sup>4</sup> H. SELYE, *Stress* (Acta Inc., Montreal 1950).

<sup>5</sup> H. SELYE, *Science* 122, 625 (1955).

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<sup>7</sup> D. M. HUME and R. H. EGDAHL, *Ann. Surg.* 150, 697 (1959).

<sup>8</sup> C. E. COOPER and D. H. NELSON, *J. clin. Invest.* 41, 1599 (1962).

<sup>9</sup> A. PRADER, CIBA Foundation Study Group 27, 29 (1967).

<sup>10</sup> E. SAKIZ, C. r. hebdomadaire Séances Acad. Sci. Paris 251, 2237 (1960).

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## Lymphostatic Retinal Haemangiopathy

A prelymphatic-lymphatic pathway has been described in the wall of cerebral blood vessels, leading protein and tissue fluid to the cervical lymphatics. Blockage of this system results in oedematous alterations in cerebral blood vessels; the term 'Lymphostatic Cerebral Haemangiopathy' was coined for this new entity of angiological pathology<sup>1-3</sup>.

Further studies revealed the fact that – although *there are no lymph vessels in the retina* – blockage of the cervical lymphatic system results in a Retinal Lymphostatic Haemangiopathy too.

Albino rats were subjected to a cervical lymph blockage and to a sham operation, respectively. On the 5th post-operative day, the animals were anaesthetized with