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Homoplastic Transplantation of Suprarenal Glands of Rat into the Anterior Chamber of Eye.

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It has been established that functional suprarenal grafts consist only of cortical tissue, the medullary part of the gland seldom persisting. It is known that the interior of the transplants degenerates after the blood supply is interrupted and that the new cortex is restored by proliferation from a peripheral layer of glomerulosa or by the differentiation of unspecialized cells in the capsule.¹ Incorporation of the cortex does not occur subsequent to the removal of the capsule.^{1, 2} Previous workers have reported that neither autoplasmic nor homoplastic suprarenal transplants in intramuscular and intraperitoneal positions persist in hosts possessing both or one of the intact suprarenal glands.^{1, 3}

The present experiments were begun in order to analyze the factors which regulate the incorporation and persistence of suprarenal transplants. It was thought that the anterior chamber of the eye should be a more favorable transplantation site than those which had been previously employed. Whole glands from young donors, ranging in age from birth to 32 days, were transplanted unilaterally and bilaterally to the eyes of adult hosts. A total of 387 glands were introduced into the eyes of 245 hosts. The grafts were removed at intervals ranging from 12 hours to 5 months after insertion and studied histologically and cytologically.

Among normal hosts, a total of 51% of the bilaterally transplanted glands incorporated and contained cortical tissue at the time of removal; 64% of the unilaterally transplanted glands persisted under the same conditions (Table I a). While cortical proliferation was not so extensive in grafts from normal hosts as in those from doubly suprarenalectomized animals, these experiments are sufficient to demonstrate conclusively that cortical restoration does occur in intra-ocular grafts in rats possessing both intact suprarenal glands. A significantly higher percentage of transplants persisted in suprarenalectomized hosts than in normal hosts (Table I a, b). By reference to Table I it may be seen that the unilateral grafts

¹ Ingle, D. J., and Higgins, G. M., *Endocrinology*, 1938, **22**, 458.

² Wyman, L. C., and Walker, B. S., *Am. J. Physiol.*, 1929, **89**, 215.

³ Wyman, L. C., and tum Suden, C., *Am. J. Physiol.*, 1932, **101**, 662.

TABLE I.
Summary of Incorporated Suprarenal Transplants.*

Bilateral Transplantation				Unilateral Transplantation			
Type of transplan- host	No. of tations	No. of grafts in- corporated	% incor- porated	Type of transplan- host	No. of tations	No. of grafts in- corporated	% incor- porated
a. Entire glands to normal hosts.							
♀	56	30	53.6	♀	27	18	66.7
♂	40	19	47.5	♂	12	7	58.3
total	96	49	51.0	total	39	25	64.1
b. Entire glands to doubly suprarenalectomized hosts.							
♀	24	22	91.7	♀	12	12	100.0
♂	88	78	88.6	♂	36	33	91.7
total	112	100	89.3	total	48	45	93.7
c. Entire glands to normal hosts plus pituitary implants.							
♀	30	22	73.3	♂	2	2	100.0
d. Capsules of suprarenal glands to suprarenalectomized hosts.							
♀	16	11	68.7	♂	4	4	100.0
e. Medullæ to normal hosts.							
♀	22	6	27.3	♀	5	0	0

* Fibrotic or calcified nodules were not counted as incorporated grafts. The transplants removed during the first 10 days after insertion into the eye are not included in the table.

persisted better than the bilateral ones. Histological studies indicated that there was more extensive cortical proliferation in the grafts from suprarenalectomized hosts than in those from normal hosts, and also that there was more extensive cortical restoration when the glands were transplanted unilaterally. The percentage of incorporated grafts recovered from normal hosts receiving pituitary homo-implants was greater than that recovered from comparable hosts which were not implanted (Table I a, c). The size of the grafts from implanted hosts, as well as the degree of cortical regeneration, did not equal that of grafts persisting in doubly suprarenalectomized hosts but was much in excess of that characteristic for normal untreated hosts. No pronounced sex difference in the capacity to regenerate cortical tissue, as reported by Wyman and tum Suden,³ was observed in the intra-ocular grafts.

After preparing the glands according to the technic of Ingle and Higgins,¹ enucleated capsules (*i. e.*, capsular investment separated from cortical and medullary tissue) were transplanted to the anterior eye chamber and recovered after persistence for approximately 2 months. The results are summarized in Table I d. Medullary tissue was expressed from the glands of 20-day-old donors and, while the glands were in Ringer's solution, the adherent cortex was further teased away under a dissecting microscope. The medullæ were transplanted to normal adult hosts and 27% of them were recovered and found to contain histologically normal medullary cells after persisting for 20 days (Table I e).

Summary. Homoplastic suprarenal cortices may incorporate and persist for as long as 5 months in the eyes of normal hosts. The extent of cortical regeneration in suprarenal grafts as well as the frequency of persistence is augmented by suprarenalectomy and by homopituitary implantation. The evidence seems to indicate that differentiation in cortical transplants is conditioned by the cortico-adrenotropic principle of the anterior hypophysis. The medullary tissue is relatively specialized but it may persist in homoplastic grafts if the period of nutritional interruption is minimized.

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Effect of Beta-methylcholine-urethane on Normal and on Reflexly Inhibited Intestine.*

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Although acetylcholine produces marked stimulation of the isolated intestine,¹ it is not suitable for increasing the motility of the intestine *in situ* because of its rapid hydrolysis by the cholinesterase of the blood,² its severe blood-pressure lowering effect, and its indiscriminate stimulation of autonomic ganglia (nicotinic action). Protecting acetylcholine from hydrolysis by the use of physostigmine potentiates and prolongs the intestinal effects of acetylcholine³ but the other two objections are still applicable. Acetyl-beta-methylcholine lacks the nicotinic action⁴ and is somewhat more stable in blood, but it also has severe blood pressure effects due to cardiac slowing especially when given parenterally.⁵ A sharp fall in blood pressure causes reflex production of adrenine and sympathin, both of which are inhibitors of the intestine. These compensatory responses occur

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¹ Dale, H. H., *J. Pharm. and Exp. Therap.*, 1914, **6**, 147.

² Matthes, J. *Physiol.*, 1930, **70**, 338.

³ Zimmerman, L. M., Frank, R., and Neeheles, H., *Arch. Surgery*, 1936, **33**, 187.

⁴ Simonart et Simonart, *Arch. internat. de Pharm. et de Therap.*, 1935, **51**, 76.

⁵ Starr, I., *Trans. Assn. Am. Physicians*, 1936, **51**, 326.