#### Thyroid-pituitary System of the Dogfish Pup, Squalus acanthias

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Four types of studies were made of the dogfish thyroid-pituitary system. 1) To determine the length of time that the "candles" with young embryonic stages could be kept alive in plastic bags through which slowly circulated running sea water. There is reason to believe that with care they could be maintained and developing in this environment for long periods of time. Possibly the sole contribution of the female to the uterine young is protection. 2) The uptake of I<sup>131</sup> by the thyroid of the pup was reexamined with tracer doses of the isotope injected intraperitoneally. The pups were also exposed to constant light, constant darkness, or diurnally varying illumination (normal summer day-night). Activity of the thyroid at this stage of development, is comparable quantitatively to that of the adult gland, and it is not readily modified by the factors experimentally tested. 3) Thyroid activity of adult nonpregnant females and females with small embryo (candle) or pup stages of development was compared following the subcutaneous injection (at the base of the pectoral appendage) of 20-30 microcuries of 1131. 4) Pups were implanted subcutaneously with carbowax pellets containing dl-thyroxin, or proylthiouracil, or triodothyroacetic acid, or whole pituitary powder and they were subsequently maintained in screened glass dishes in running seawater aquaria for 6-9 days under three conditions: constant illumination. constant darkness, and diurnal cyclic conditions at laboratory temperatures. Twenty-four hours before sacrifice they were injected with 1<sup>131</sup>. Animals were sacrificed at the 6th or 9th day. The hypothalamic-pituitary territory was preserved for study of the neurosecretory system and thyroid activity determined under these experimental conditions. Uptake of the thyroid was compared with that of certain other tissues and organs, including the whole intestine, whole stomach, tail muscle, and the area from which the thyroid was taken.

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#### Analysis of Homograft Reaction in (Fundulus Heteroclitus)

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Homotransplantation of pigmented scales in *Fundulus* is normally followed by an inevitable immunological response by the host against the grafts. Manifested by the microscopically visible destruction of melanophores in the foreign scales, this temperature dependent reaction occurs in 3 days at 28°C, 5 to 6 days at 21°C, and 14 to 16 days at 14°C. It is not adversely influenced by splenectomy or hypophysectomy of the host, nor by daily injections of 0.1 ml of 1% trypan blue.

Investigations of the effects of anti-mitotic agents on the homograft reaction were conducted on fishes to which ventral autografts and homografts of pigmented scales were made on either side of the linea alba. At 28°C the homografts of control fishes invariably exhibited extensive or complete melanocyte breakdown on the 3rd day after operation. Autografts survived indefinitely. Daily intraperitoneal injections (1-2 mg in 0.1 ml distilled water) of antagonists of nucleic acid synthesis (5-fluorouracil, 5-deoxyribofluorouridine and 6-mercaptopurine) prolonged survival of homografts up to 7 days by which time the fishes had died of the lethal effects of the drugs. Injections of 2 mg of 6-fluorohydrocortisone acetate and delta-1-hydrocortisone sodium succinate likewise enhanced survival of homografts, but only until the 4th to 5th days. Two antibiotics which were tested also had the effect of postponing the homograft destruction usually occurring on the 3rd day Chloramphenicol, in doses of 10 mg per fish per day, resulted in survival of homograft pigment cells until the 5th day. Tetracycline hydrochloride (1 mg) permitted survival of some grafts until the 7th day. Administration of amino acid analogues was considerably less effective in protecting homografts from destruction. Daily injections of 5 mg of 5 different serine and phenylalanine analogues slightly prolonged homograft survival (to the 4th day), while ethionine. given in a dose of 3.3 mg per day, delayed the homograft reaction until the 5th day. These doses, however, were frequently lethal.

These results indicate that antibody production depends upon nucleic acid synthesis, where it is most vulnerable to analogue interference. Inhibition of protein synthesis by adrenal cortical hormones or antibiotics is somewhat less effectual. Administration of amino acid analogues was least effective in preventing antibody synthesis. Treatment with nearlethal doses of colchicine (0.005 mg) failed to preclude homograft breakdown, indicating that cellular proliferation is far less important in the process of antibody production than is the biosynthesis of nucleic acids and proteins.

# Importance of Molecular Synthesis vs. Mitosis in Immunological Reactions

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The clonal selection theory of acquired immunity, as postulated by Burnet and augmented by Lederberg, contends that each immunologically competent cell in the mature animal is endowed with hypermutable genes each of which controls the synthesis of a particular kind of antibody. Upon exposure to antigens, certain of these cells are stimulated to multiply into clones which in turn manufacture correspondingly appropriate antibodies. It would follow that inhibition of proliferation by anti-mitotic agents might be expected to block the synthesis of specific protein antibodies.

Accordingly, adult teleosts (Fundulus heteroclitus) were treated