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Growth Stimulation of Spinal and Sympathetic Ganglia of the Chick after Transplantation of Mouse Sarcomas*

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Mouse sarcomas (37,180) when transplanted to the limb fields of 2½-day chicks were found to grow and at 8-15 days of total incubation were filled with an abundance of peripheral nerves. Spinal and sympathetic ganglia with nerves related to the tumor were enlarged and viscera which normally have a poor nerve supply were flooded with post-ganglionic sympathetic fibers. Stimulation of nerve growth was also observed with allantoic grafts and in vitro techniques (Levi-Montalcini '53). To know the distribution of this growth factor in various transplantable and transmissible tumors becomes increasingly important. In this study mouse sarcomas (A274, T241 Lewis, MCI, S637, S635, MA387, Ds2, Ds3, Ds4, and Patterson's lymphosarcoma), mouse carcinomas (CA-15, C954) and human sarcoma (Toolan's Hs#1) were investigated.

Methods and Results

Tumors were removed from the host, placed in sterile Petri dishes and cut into small pieces. Rectangular openings were cut in the shell of 2½ and 4-day incubated eggs. Tumors were grafted in the somatopleure or on the allantois. Openings were sealed with adhesive tape. Animals were sacrificed at 4-17 days of incubation and prepared with DeCastro's modification of Cajal's technique and Wenger's hematoxylin.

From 686 transplant experiments 302 specimens were obtained. Mouse sarcomas A274, T241 Lewis, S653, MCI, and MA387 produced striking growth effects in adjacent spinal and sympathetic ganglia. Sensory ganglia were 1.3x-3.4x, sympathetic 1.3x-3.8x, larger than corresponding control ganglia. Nerve cell hypertrophy and hyperplasia were observed in enlarged ganglia. Grafts were invaded with peripheral nerves. These growth effects were very similar to those observed with Sarcomas 1,37,180. An abnormal nerve supply was also found in the viscera of cases with grafts of A274, T241 Lewis, and MCI. Allantoic grafts of sarcoma A274 produced an overgrowth of sympathetic fibers in the mesonephros and adrenals; similar to that obtained with grafted sarcomas 180 or 37. Sympathetic centers which served as centers for the overgrowth were hyperplastic and hypertrophied.

Most of the sarcomas which gave a maximum response may be classified as the pleomorphic, undifferentiated, or anaplastic type. Spindle cell sarcomas Ds2 and Ds3 were negative or at best produced a slight enlargement in adjacent ganglia. Human sarcoma (Toolan's Hs#1) which had been transmitted for twelve generations in cortisone treated animals

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(rats, hamsters) was negative. This tumor grows strikingly in the chick. Silver preparations show only few nerves in the graft. Mouse carcinomas (CA-15, C-954) actually block nerve outgrowth. Adjacent ganglia were smaller than corresponding ganglia.

With the exception of Patterson's lymphosarcoma all tumor grafts used in this study showed conspicuous growth at 10-17 days of incubation. Present results indicate that nerve growth stimulating effects observed in sensory and sympathetic ganglia are probably associated with a large number of transplantable mouse sarcomas.

Excretion in the Lobster, *Homarus*: II.

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Single injections of inulin, 10-20 mg., followed up to 28 hrs., gave U/P ratios of approximately 1, with both urine and plasma concentrations falling with the same slope. Inulin is not secreted in the lobster as reported for the crayfish (Maluf '41).

Phloridzin produced glucosuria and blocks glucose retention (Burger '52).

Blood-urine NPNs showed no constant relationship to each other, each ranging from 5-32 mg. %. Volatile ammonia and urea were undetectable in the urine (less than 1 mg.%) in analyses kindly made by Xenia Boysen and Claus Brunn. Following injection of urea into lobsters with occluded nephridiopores, blood-sea water values (2-3 liters of sea water) became about equal in 1 hour, indicating a rapid loss of urea through the gills. The NPN values indicate the loss through the nephridia of non-urea, non-volatile nitrogen.

Further investigation with sulphate showed the body and gills were relatively impermeable to this ion, as Krogh found for the crab (*Carcinus*). Sulphate placed in the stomach resulted in elevated blood and urinary sulphate, indicating that this ion is absorbed with feeding and drinking (Burger '52).

Following the injection of centrifuged, hemolyzed dogfish (*Squalus acanthius*) blood a pink protein appeared in the urine. The nephridia seem permeable therefore to very large molecules, but not to the animal's own hemocyanin. Our data add nothing to the problem of how urine is formed. The very thin delicate nature of the bladder would indicate that water and other substances can diffuse directly from the blood to the urine, and vice versa, although small particles such as sulphate, urea, and the larger phenol red are held by the bladder at very unequal concentrations.