

PATHOLOGY

Neoplasm Transplantation Inhibition by Uninvolved Lymph Tissue

HETEROLOGOUS transplantation of human neoplasms into the cheek pouch of the syrian hamster (*Mesocricetus auratus*) was first reported in 1951 (ref. 1). The uniqueness of the pouch as a site for transplantation results from the alymphatic structure and the very slow diffusion of large molecules out of the pouch area². The large mass of loose connective tissue which comprises most of the pouch may be responsible for limiting the diffusion of transplantation antigens. Its selection as a favourable site for tumour transplantation has been based not only on its immunological responses, but also on its simplified structure, the ease with which transplants vascularize, the accuracy with which growth rates and regressions can be measured, and the fact that repeated eversion of the pouch for observation of transplants creates little or no trauma to host tissue or transplant.

The present investigation was designed to determine the effects of uninvolved lymph tissue on the ability of normally invasive human tumour tissue to be successfully transplanted into the cheek pouch. The method was a modification of that used by Handler³. Tumour tissue from female patients undergoing radical mastectomy was obtained at the time of operation and its malignant nature was affirmed by a pathologist. Uninvolved lymph tissue was taken from the axillary region, and microscopic examination attested to its non-involvement. Permanent mounts of both tumour and node were made for further investigation and confirmation of involvement. Within 1 h after removal the tissue had been transplanted as follows.

Hamsters of both sexes of weight 55–85 g were anaesthetized with 8 mg of 'Nembutal'/100 g of body weight, administered intraperitoneally. The peripheral portions of the tumour were excised and small pieces were placed in a loose fitting hand homogenizer. These clumps were minced until there remained only small clumps of cells which were drawn into a size eighteen needle. Cell counts were made and clumps containing fifty to a hundred cells were most easily placed. After eversion of the pouch, the crude homogenate and fragments were inserted into the loose connective tissue at a point near the junction of two blood vessels to assure a good blood supply. Cells were transplanted into the caudal half of the pouch or portion where thin bands of muscle fibres seem to provide a more suitable medium for transplantation. Intra-peritoneally, 2.5 mg of cortisone acetate was administered on the day of the operation and on every fourth day thereafter to diminish the immunological response of the host by lowering the lymphocyte count in the circulating blood⁴. In a second group, the same procedure was followed except that uninvolved lymph tissue was added to the hand homogenizer before the crude homogenate was prepared; an approximate 1 : 1 ratio of node to tumour was prepared. Any dilution effect of the neoplasm was tested by using, in a separate pilot experiment, a 1 : 1 ratio of tumour to adipose tissue from the same patient. In all cases the effects of dilution alone were of no significance in the alteration of the ability of the neoplasm to be transplanted successfully.

The results clearly show inhibition of invasion of the neoplasm when uninvolved lymph tissue and tumour cells were injected together. Thirty-eight hamsters received tumours alone, and eleven of them (29 per cent) had observable growing transplants after 5 days. In the experimental group receiving tumour and lymph node, only one of the twenty-six animals showed even a trace of implant, and this slight growth was rejected by the tenth day after transplantation. Examinations were made on all animals at intervals of 5 days and in each case the host rejected the tumour after 30 days.

A smaller scale investigation was carried out with both human melanotic tumour cells and carcinoma of the lung. Results, based on these few cases, indicate that the same relationship of tumour and lymph node may hold for these neoplasms also. Five out of eight transplants were successful for at least 25 days in animals receiving tumour alone, whereas in five animals injected with tumour and lymph node no implant was detectable after 5 days.

Further investigations are in progress to test the relationship of these tissues. The implication that tumour invasion is blocked by uninvolved lymph tissue is of great significance in attempts at a definition of normal mechanisms of defence against the invasion process of neoplastic tissues.

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¹ Patt, D. I., Handler, A. H., and Lutz, B. R., *Anat. Rec.*, **111**, 170 (1951).

² Shepro, D., Kula, N., and Halkett, J., *J. Exp. Med.*, **117**, 749 (1963).

³ Handler, A. H., *Ann. N. Y. Acad. Sci.*, **76**, 775 (1958).

⁴ Handler, A. H., Patt, D. I., and Lutz, B. R., *Anat. Rec.*, **112**, 449 (1952).

ANTHROPOLOGY

Canine "Field" in Sexual Dimorphism of Tooth Size

AMONG primates, sexual dimorphism in the size of permanent teeth is usually greatest for the canine tooth, that of the male exceeding that of the female by 3–7 per cent in *Hylobates agilis* and *Homo sapiens* and by nearly as much as 80 per cent in *Papio anubis*. Such dimorphism raises the theoretical question of whether the canine itself is exclusively involved, or whether the degree of sexual dimorphism spills over to adjacent teeth in the form of a "field".

Table 1. PERCENTAGE SEXUAL DIMORPHISM IN PERMANENT TOOTH SIZE FOR EIGHT PRIMATES

	Maxilla					Mandible				
	I ¹	I ²	C	P ¹	P ²	I ₁	I ₂	C	P ₁	P ₂
<i>Hylobates agilis</i> ¹	0.0	5.0	7.1	6.4	2.4	5.9	2.5	3.0	9.4	4.2
<i>Homo sapiens</i> ²	3.3	3.9	6.2	3.6	3.3	1.3	2.9	6.4	3.9	3.3
<i>Symphalangus syndactylus</i> ¹	0.0	6.4	16.9	6.5	6.3	2.6	4.5	13.0	9.9	10.8
<i>Cercocebus albigena</i> ²	11.1	10.0	31.6	10.6	7.0	9.6	7.0	23.7	27.3	2.0
<i>Cercopithecus ascanius</i> ²	1.9	0.0	23.4	0.0	5.4	—	0.0	26.8	16.7	0.0
<i>Pan troglodytes</i> ⁴	0.0	4.3	40.0	1.2	2.7	0.0	3.4	29.7	—	1.2
<i>Papio ursinus</i> ⁵	11.7	15.4	65.6	32.8	13.7	19.4	32.1	52.0	144.4	16.9
<i>Papio anubis</i> ²	11.7	18.6	78.9	16.1	5.8	7.1	11.7	55.4	112.4	12.3

Published and unpublished data on various primate genera, including *Cercocebus*, *Cercopithecus*, *Homo*, *Hylobates*, *Papio*, *Pan* and *Symphalangus*, provide considerable evidence for a canine-centered field of sexual dimorphism. For the maxilla, percentage dimorphism is usually greater for the second incisor than the first, except for *Cercopithecus ascanius*. Similarly, the first premolar shows a greater percentage of sexual dimorphism than the second, again with the exception noted (see Table 1). The same tendency holds in the mandible, though less completely, with I₁ exceeding I₂ in percentage sexual dimorphism and P₂ exceeding P₁ in the same respect. Thus, teeth once removed from the canine tend to show relatively more