induced melanotic tumours in the skin of the hamster. These authors find that the tumours contain many Schwann cells and nerve fibres. Also within the tumour, pigmented cells are found in the sheaths of small dermal nerves and in lamellar structures that resemble nerve endings. In parts of the tumour near the epithelium of the follicle, Nakai and Rappaport demonstrated many nerve fibres enveloped by Schwann cells. These are probably the nerve endings that surround the neck of the tylotrich follicle.

Considering the findings of Ghadially and Barker[1], of Nakai and Rappaport[5], and of the work presented here, there are two distinct hypotheses that can explain in part the histogenesis of these carcinogen-induced melanotic tumours. The tumour may arise from dermal melanocytes of the tylotrich follicle, then invade and envelop the adjacent neural elements, or melanotic neural components of this richly innervated hair follicle may undergo carcinogenesis directly.

On account of its large pilosebaceous structure, abundant nerve endings, and numerous pigmented cells, the tylotrich follicle may have a unique significance in skin carcinogenesis.

This work was partially supported by grant *E*–282 from the American Cancer Society.

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Inhibition of the Growth of Implanted Mouse Carcinoma by an Irradiated Bacterial Culture

Concerning Prof. C. A. Pannett's communication[1], under the above title, confirming, and the further elucidation of the observation made by me[2], his essential findings can conveniently be resumed schematically thus:

'Oxoid' or nutrient broth —bacteria (*E. coli*)→ y —X-rays→ tumour-growth-inhibitory substance, x

This schema, which distinguishes the relative roles of bacteria and irradiation in the phenomenon, indicates that peptone, or other substance, present in the bacterial culture-medium, becomes changed, under the influence of the growth of an 'effective' *E. coli*, as distinct from a 'non-effective' one[2], into the hypothetical substance y, which in turn, when irradiated by X-rays, is changed into the tumour-growth-inhibitory substance x.

Bacteria would thus be envisaged as not necessary in the actual irradiation, but they are necessary before the irradiation; and this, in order to change some constituent of the culture-medium into the intermediate product y, essential for the irradiation to act upon, so as to produce the growth-inhibitory substance sought, x.

Points in which the Pannett technique differs from my own, and which may, or may not, constitute improvements, concern mainly the use by him of : (1) initially smaller tumour-grafts; (2) 48 h. instead of 24 h. broth cultures for the irradiation; (3) larger irradiation dosage: 150,000 r. as against 50,000 r.; (4) 'Oxoid' culture-medium, as against nutrient broth; (5) subcutaneous injection of irradiated culture-medium freed from bacteria either before or after the irradiation, as against feeding to the mice irradiated culture-medium in which the bacteria are included.

My original observation being thus confirmed, new investigations are obviously called for, to determine the conditions for the maximum production of the hypothetical substances y and x (Pannett), with the view of their isolation, particularly of x—the necessity for the isolation of which in the pure state I have previously amply stressed.

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Choriocarcinoma: Growth Patterns in Hamster Tissues

Choriocarcinoma is a highly invasive tumour that retains some of the peculiar properties of normal immature human trophoblast[1]. In order to study the manner in which it invades tissues, we inoculated small fragments of transplantable human choriocarcinoma into the following sites in 19 young (70–90 g) female Syrian hamsters (Dennen): uterine broad ligament, peritoneal cavity, lung, liver, brain, thigh muscle, vena cava, hepatic portal vein, and internal jugular vein. Testicular inoculation was carried out in one male hamster. The tumour used was the Greene choriocarcinoma (kindly supplied by Dr. Roy Hertz), originally isolated in 1960 by Roy Hertz, carried by serial passage in the hamster cheek pouch, and similar in behaviour to the *WO* strain described by Hertz[2]. Although cortisone is not needed to maintain growth of the Greene choriocarcinoma in the cheek pouch we gave it to 15 of the 19 hamsters in this preliminary work with the hope of ensuring tumour growth at the various inoculated sites[3]. For direct implantation into organs, two–ten 3-mm tumour fragments were inoculated into each site by cannula (Lundy–Irving caudal needle). For intravenous inoculation, the tumour was minced with Bard Parker knives into fragments less than 1 mm in diameter. About 50 of these tiny fragments were suspended in 0·1 ml. or less of Gey's balanced salt solution, and slowly injected with a tuberculin syringe through a 21-gauge hypodermic needle. All hamsters were autopsied within 7–16 days.

In all cortisonized hamsters, the tumour fragments grew actively, invaded the surrounding tissue, and displayed the characteristic hæmorrhagic nature of choriocarcinoma. Tumour hæmorrhage and necrosis resulted from extreme dilatation of blood spaces, with subsequent breakdown of partitions between them. Many tumour blood channels were devoid of an endothelial lining, a finding typical of choriocarcinoma and normal trophoblast[1]. Further details are as follows:

Implantation of broad ligament (3 *hamsters*). Tumour fragments were inoculated into the broad ligament where it adjoins the uterus. In two hamsters receiving intracutaneous cortone (0·05 ml. twice weekly), the growing tumour nodules after 7 and 11 days, respectively, invaded the uterine wall and also engulfed peritoneal fat cells. One tumour fragment became secondarily implanted on the abdominal wall, where it penetrated the overlying striated muscle so actively that individual engulfed muscle fibres were literally drawn into the tumour. In the hamster killed at 11 days, there was free blood in the peritoneal cavity. In the remaining non-cortisonized hamster, the inoculated tumour fragments regressed.

Implantation of the peritoneal cavity (3 *hamsters*). In two cortisonized hamsters after 8 and 16 days, respectively, there was free blood in the peritoneal cavity, and there were several tumour nodules randomly implanted on the peritoneal surfaces. In one non-cortisonized hamster, after 16 days there was one actively growing tumour nodule and one regressing nodule.

Implantation of the lung (1 *hamster, cortisonized*). After 13 days, most of the inoculated right lung was hæmorrhagic, necrotic, and largely replaced by tumour.