Heterotransplantation of Human Cancer

II. Hamster Cheek Pouch*

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A technic developed by Lutz, Handler, and associates (1-4) employed the cheek pouch of the hamster (Mesocricetus auratus) as a site for transplantation of tissues, including animal and human cancers. Through the courtesy of these workers, we learned their method and employed it in experiments on the heterologous transplantation of human cancers.

Sixty-five human neoplasms were so implanted, with successful growth in 30 (46 per cent).

METHODS

Hamsters of either sex, 1½-8 months old and weighing 40-100 gm., were used.

Two technics of transplantation were used—that of Lutz (4) and a modification—with comparable results.

For stretching the everted cheek pouch, a simple animal holder was used as originally described by Lutz. In the modified technic, the hamster was anesthetized with ether and the cheek pouch simply everted over one finger. A fragment of human tumor, selected and treated as described in the preceding communication, was implanted beneath the mucosa with a No. 18 trocar. Care was taken to avoid extrusion of the fragment through the wound of introduction, by working it away from this site. Refrigeration of the tumor for 48 hours did not appreciably alter its viability.

After implantation the hamster was observed for tumor growth by everting the cheek pouch approximately every 4 days. When the nodule showed peripheral hemorrhage or edema, its vascularity decreased, or it became softened, the tissue was removed for histologic examination or further transplantation.

Usually the tumor was implanted in one pouch of each of six hamsters. Occasionally, after negative results, the same pouches were used for further transplants.

RESULTS

In general, after about 4 days an enlarged nodule was evident beneath the cheek pouch mucosa. It was gray-pink, spherical, and smooth-surfaced. Vascularization was not always evident at this time. With certain tumors, the nodules became softened, shrank, and were generally absorbed within 10-20 days. No generalized effects on the hamsters were observed.

Measurement of changes in the size of the nodules was not successful as an index of cancer growth. Peripherally, granuloma formation closely simulated cancer, and it was not possible grossly to distinguish accurately the margin between implanted tumors and reactive host tissues.

In Table 1 are listed the results of 65 transplants of human cancer. “Positive” results refer to survival or growth of cancer, “negative” to complete degeneration or absence of cancer, and “questionable” to presence of a few doubtful cancer cells. As noted in irradiated rats, there is not sufficient evidence as yet to predict whether any particular type of neoplasm would or would not grow heterologously. Fortunate or unfortunate choice of the fragment for implantation was the one factor of most importance.

The survival of all implants was confirmed by microscopic examination. Vascularization was more prominent grossly than microscopically, and the margin of cancer tissue often appeared confined histologically by leukocytic infiltration. The hamster responded by exuberant histiocytic granulomatous response to the foreign tissue. The cancer cells appeared healthy, with or lacking mitoses, although signs of degeneration were occasionally present. No changes in growth characteristics or type of cancer were noted.

Second-generation transplantation was attempted, employing twenty neoplasms (Table 2). As with animal neoplasms (5), the relative proportion of successes was increased. Third-generation transplants succeeded with one of three carcinoma simplex tissues and two of two epidermoid carcinomas tested and failed with one leiomyosarcoma. In these positive implants, proliferative growth rather than mere persistence was observed.

In another series, twelve hamsters were irrad-
ated with 300–600 r total body x-ray doses before implantation with twelve human neoplasms. The irradiation factors were 200 kvp, 2 mm. Cu, 10 m. amp., t.s.d. 36.5, and 60 cm. with exposure times 1–4 minutes, according to dose. Fifty-eight per cent of these tumors were successfully grown in both the irradiated and unirradiated control animals. Transplantation of thirteen neoplasms was successful in hamsters treated with stilbestrol and in untreated control hamsters (15 per cent), and with four neoplasms in hamsters given aureomycin and in their untreated controls (75 per cent). No evidence of more favorable effects was obtained from these additional procedures.

**DISCUSSION**

In our experience, employment of hamster cheek pouches for heterologous cancer implants of human origin has appeared to be of great potential value. It has the advantages of ease of implantation and of observation. Vascularization may be studied by reflected or transmitted light, and the tumor may be easily photographed. Changes in tumor consistency and color are readily observed beneath the thin mucosa.

With experience in the proper choice of tissue fragments, an increased proportion of successes is anticipated, comparable to the results of the originators of this method. Furthermore, this makes possible the employment of the gross measurement of tumor implants as an index of their growth.

The technic has developed to a point where intensive study of selected types of cancer is now feasible. Further extension to different neoplasms is also contemplated.

**SUMMARY**

In the hamster cheek pouch, 30 of 65 human neoplasms persisted after heterologous transplantation (46 per cent). Second-generation transplantations were successful with eleven of twenty cancers, and third-generation growth in three of six cases. The method is relatively simple and appears...
to be of great potential value in growth studies of human cancer tissue. Treating host animals with stilbestrol or aureomycin or x-ray did not affect transplant survival.

REFERENCES


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