Serial Passage of Choriocarcinoma of Women in the Hamster Cheek-Pouch

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GREENE (1952) initially described the survival and growth of human malignant tissue in the anterior chamber of the guinea pig's eye. These pioneer studies provided the basic experimental background for the observations to be reported here.

Subsequently, TOOLAN (1953) and SOMMERS et al. (1952) introduced the use of the hamster cheek-pouch as a site for such heterologous tumor transfer. They also found that the frequency of tumor takes could be very much increased by prior suppression of the immune response of the host animal. This was accomplished through x-irradiation or cortisone administration or through a combination of both of these procedures.

PIERCE et al. (1957) showed that certain human testicular tumors could be maintained as heterologous grafts by serial passage through similarly conditioned hamsters. They found that such tumors continued to produce the chorionic type of gonadotropin even after prolonged maintenance in the foreign host.

This report will describe the growth characteristics and hormonal behavior of seven strains of human uterine choriocarcinoma derived from metastatic tumor masses of seven women. The respective responses of these transplanted tumors to various chemotherapeutic agents will be compared with the response to these same agents previously observed in the individual donor patient. Certain immunological phenomena will also be described.

Materials and methods

Tumor tissue was initially obtained under aseptic conditions within one to seven hours after surgical excision or necropsy (Table).

Female golden hamsters of the NIH strain varying from one to three months in age were employed. Purina checkers were fed as a basal diet and a daily ration of kale, apples, and carrots was provided.

Under Nembutal anesthesia, each hamster received by direct inoculation into the cheek-pouch a piece of freshly excised tissue about 0.05 cu. cm. in volume. Recipient hamsters were either left totally untreated or they received 3 mgm of cortisone acetate in aqueous suspension at the time of inoculation and every third day for the ensuing two weeks. Repeated inspection of the everted cheek-pouch revealed the course of growth of the tumor inocula and this was recorded by a free-hand sketch of the size and shape of the growing tumor mass. Histological studies were performed on certain speci-
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mens by fixation in Bouin's solution and staining with hematoxylin and eosin. Hamster plasma was prepared from heparinized blood drawn from the abdominal aorta under Nembutal anesthesia just prior to autopsy. Detailed observations were recorded at autopsy concerning the size and form of the tumors of treated and untreated control animals provided an estimate of the extent of inhibitory effects obtained (Fig. 1).

Upon discontinuing serial passage of each strain, portions of tumor were preserved in 50% saline and 50% glycerol.

### Table. Seven strains of human choriocarcinoma in hamster cheek-pouch

<table>
<thead>
<tr>
<th>Strain</th>
<th>Date started</th>
<th>Source</th>
<th>Generation</th>
<th>Patient's clinical status</th>
</tr>
</thead>
<tbody>
<tr>
<td>BO</td>
<td>7/22/57</td>
<td>Metastasis to breast (S)</td>
<td>132</td>
<td>Patient had incomplete remission on MTX; cerebral hemorrhage while off therapy; strain requires cortisone</td>
</tr>
<tr>
<td>WO</td>
<td>10/24/58</td>
<td>Brain metastasis (A)</td>
<td>216</td>
<td>Resistant to MTX after initial response.</td>
</tr>
<tr>
<td>MA</td>
<td>11/12/58</td>
<td>Lung metastasis (A)</td>
<td>140</td>
<td>Resistant to MTX after initial response.</td>
</tr>
<tr>
<td>JO</td>
<td>11/11/59</td>
<td>Lung metastasis (A)</td>
<td>118</td>
<td>Resistant to MTX after initial response; then no response to VLB or Cytoxan.</td>
</tr>
<tr>
<td>RE</td>
<td>1/21/60</td>
<td>Metastasis to cervix (S)</td>
<td>126</td>
<td>No chemotherapy before tissue obtained; subsequently had complete remission on MTX followed by Actinomycin D although still potentially responsive to MTX.</td>
</tr>
<tr>
<td>GR</td>
<td>11/2/60</td>
<td>Brain metastasis (A)</td>
<td>99</td>
<td>Limited response to MTX and VLB. Followed by resistance to both drugs.</td>
</tr>
<tr>
<td>CA</td>
<td>9/26/61</td>
<td>Lung metastasis (A)</td>
<td>46</td>
<td>No initial response to MTX or Actinomycin D.</td>
</tr>
</tbody>
</table>

(A) = Autopsy; (S) = Surgical specimen.

1 As of Oct. 1, 1964 or prior to storage in liquid nitrogen and discontinuation of passage.

All hamsters treated daily subcutaneously for 4 to 6 days beginning on day 7 after transplantation; effective doses were: (MTX) methotrexate — 50.0 mgm/kg; (VLB) Vinblastine — 0.75 mgm/kg; Actinomycin D — 50 gamma/kg.

Concerning the qualitative and quantitative effects of the tumor transplant on various endocrine organs.

All chemotherapeutic agents were administered daily subcutaneously in the form and dosage indicated in the legend of the Table. The drugs were started on the 6th day after transplantation when initial growth of the transplant could be clearly observed. Repeated sketches of the under liquid nitrogen refrigeration. The frozen tissue from each strain was subsequently successfully reinoculated into untreated hamsters whenever required for further study.

**Results and discussion**

The seven successfully established strains of choriocarcinoma resulted from a total of thirty attempts. Five of these