THE LEUKEMIA-PRODUCING ACTIVITY OF CELL-FREE FILTRATES
 OF HUMAN LEUKEMIC TISSUE

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(Received November 29, 1957. Presented by Active Member Acad. Med. Sci. USSR, A. D. Timofeevskii)

The ability to pass through a semipermeable membrane is a characteristic property of the so-called filtrable
viruses. By the use of special filters it is possible to isolate from a tissue extract a virus component, leaving un-
damaged cells and bacterial microorganisms on the filter [2]. If injection of the filtrate into an animal causes
the appearance of a disease, this implies that the filtrate contains a virus.

The possibility of transmission of a tumor from an affected animal to a healthy one by means of a filtrate
is the main factor in support of the virus etiology of these tumors. Tumors of this sort include carcinoma of the
breast and leukemia in mice, papilloma and fibroma in rabbits, fibroma in deer, sarcoma and leukemia in fowl
and so on.

There are no indications in the literature of the possibility of transmission of leukemia in man by means
of cell-free filtrates. We have produced leukemia in mice by injecting them with centrifuged extracts of human
leukemic tissue in which the presence of whole cells was practically impossible. However, the objection that
isolated undamaged cells may still be left in the extract persists.

For this reason it was essential to attempt to produce leukemia in mice by means of cell-free filtrates of
human leukemic tissue. In the present paper we give the results of experiments undertaken in this direction.

EXPERIMENTAL METHOD

We prepared cell-free filtrates from tissue from lymphatic glands, blood, brain and tumor-like leukemia
infiltrations from 4 human patients suffering or dying from acute leukemias (hemocytoblastoses). In control ex-
periments we used extracts of donated blood and of brain tissue from a patient dying from vascular disease. We
had studied previously the biological activity of extracts of "normal" lymphatic glands; the extracts possessed
no leukemia-producing activity [1]. In the same report the findings are given of the leukemia-producing activity
of extracts of human sarcoma (as a control of tumor-like leukemia infiltration).
The filtrates were prepared as follows: the tissue was ground up in a blender in the cold with physiological saline in a proportion of 1:5; the suspension was strained through gauze and then centrifuged at 2500-3000 rpm for 10-15 min. The supernatant fluid was filtered through a Seltz apparatus at a negative pressure (off pump) with a two-layer asbestos filter. The filtrates were tested for sterility.

In one case, after preparation of filtrates from brain tissue and a tumor-like leukemic infiltration from a patient dying from acute hemocytoblastosis (chloroma) we changed the method of obtaining the filtrate: the suspension contained 10% of 96% alcohol and before centrifuging it was allowed to stand at 4° for 20 hrs. It was then filtered through a No. 3 Rublevskii filter (diameter of pores 700 mμ).

The filtrates were injected into mice of the low leukemic strains C77 and C87A and impure strains, directly into the tissue of the spleen (adult mice) or subcutaneously (newborn). Altogether 309 mice were used in the experiments. Animals injected with filtrates of leukemic brain tissue and tumor-like infiltrates were given 5 mg of cortisone one month later (in 4 doses at intervals of 2-3 days). Blood from these mice was inoculated in nutrient media in order to detect paratyphoid infection which may give severe leukemoid reactions. No paratyphoid bacteria were discovered.

The diagnosis of true leukemia was made on the basis of the careful histological and cytological study of organs of the experimental animals. Where necessary the true malignant nature of the lesion was confirmed by transplantation into other mice of the same strain.

**EXPERIMENTAL RESULTS**

Essential details of the experimental results are shown in the summarized table.

<table>
<thead>
<tr>
<th>Extract</th>
<th>Age of mice</th>
<th>Method of Injection of extract</th>
<th>No. of mice used in the experiment</th>
<th>Time of first appearance of leukemia</th>
<th>No. of mice with appearance of leukemia</th>
<th>Average latent period of development of leukemia in months</th>
<th>No. of leukemic mice</th>
<th>No. of leukemoid reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtrate of leukemic brain</td>
<td>1.5 month</td>
<td>Intraperitoneal</td>
<td>21</td>
<td>3</td>
<td>19</td>
<td>4.7</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>7 days</td>
<td>The same</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>The same, in 10% aqueous alcohol</td>
<td>1.5 month</td>
<td>Into spleen</td>
<td>41</td>
<td>1.5</td>
<td>22</td>
<td>2.3</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>1-6 days</td>
<td>Subcutaneous</td>
<td>28</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Filtrate of normal brain in 10% aqueous solution</td>
<td>1 month</td>
<td>Into spleen</td>
<td>40</td>
<td>2.5</td>
<td>25</td>
<td>2.5</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>3-14 days</td>
<td>Subcutaneous</td>
<td>21</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Filtrate of leukemic tumor</td>
<td>1.5 month</td>
<td>Into spleen</td>
<td>19</td>
<td>2.5</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Filtrate of leukemic blood</td>
<td>5-14 days</td>
<td>Subcutaneous</td>
<td>23</td>
<td>1</td>
<td>14</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>5 days</td>
<td>&quot;</td>
<td>33</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Whole donated blood</td>
<td>1 month</td>
<td>Into spleen</td>
<td>26</td>
<td>-</td>
<td>20</td>
<td>-</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Filtrate of leukemic lymphatic glands</td>
<td>1 month</td>
<td>Into spleen</td>
<td>9</td>
<td>1</td>
<td>8</td>
<td>1.5</td>
<td>2</td>
<td>1</td>
</tr>
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