Possible induction by blood transfusion of immunological tolerance against growth of transplanted tumors in mice.

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Abstract

That blood transfusions aid kidney graft survival is well known. Our data show that blood transfusions, except for the red blood cell component, promote growth of transplanted tumors in mice. These clinical and experimental observations suggest that blood transfusions may induce some immunological tolerance.

KEYWORDS: blood transfusion, immunological tolerance, growth of transplanted tumors (in mice), blood component

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--- BRIEF NOTE ---

POSSIBLE INDUCTION BY BLOOD TRANSFUSION OF IMMUNOLOGICAL TOLERANCE AGAINST GROWTH OF TRANSPLANTED TUMORS IN MICE

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Abstract. That blood transfusions aid kidney graft survival is well known. Our data show that blood transfusions, except for the red blood cell component, promote growth of transplanted tumors in mice. These clinical and experimental observations suggest that blood transfusions may induce some immunological tolerance.

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In the field of kidney transplantation, it has become an established fact that pre-transplant blood transfusions have a beneficial effect on the kidney graft and increase the graft survival rate (1, 2). However, the mechanism of such transfusions is still unclear, though it is conjectured that some immunological tolerance is induced (3). With this possibility in mind, the following experiment was undertaken to determine whether blood transfusions have any effect on transplanted tumors in mice.

The mice, H-2 complex, tumors and combination of blood transfusions in our experiment are shown in Table 1. Two weeks after a 0.3 ml blood transfusion, tumor cells (1 × 10⁶ in 0.3 ml RPMI medium) were transplanted by subcutaneous injection into the back of mice. The control group mice were injected with saline or RPMI medium.

Assessment of the blood transfusions was calculated on the basis of the size of the transplanted tumor. The comparison of mean values between the various groups were performed by Student’s t-test.

When examining the effect of a transfusion of C3H (H-2k)-, AKR (H-2k)- and (C57/BL × DBA/2) F₁ (BDF₁) (H-2₅)₆ mouse whole blood against tumor (MH 134) growth in C3H mouse, transfusions of C3H- and AKR-mouse blood did not

*This work was presented in part at the 18th Japanese Congress of Transplantation, September, 1982.
### Table 1. Materials and Methods

<table>
<thead>
<tr>
<th>TSF donor mouse</th>
<th>H-2 component</th>
<th>Recipient mouse</th>
<th>H-2 #</th>
<th>Graft tumor</th>
<th>H-2</th>
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<tbody>
<tr>
<td>(C57BL/6 × DBA/2)F₁</td>
<td>b, d</td>
<td>Whole blood</td>
<td>C₃H</td>
<td>k</td>
<td>9</td>
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<tr>
<td>C₃H</td>
<td>k</td>
<td>Whole blood saline</td>
<td>C₃H</td>
<td>k</td>
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<tr>
<td></td>
<td></td>
<td>saline</td>
<td>C₃H</td>
<td>k</td>
<td>9</td>
</tr>
<tr>
<td>AKR</td>
<td>k</td>
<td>Whole blood saline</td>
<td>C₃H</td>
<td>k</td>
<td>6</td>
</tr>
<tr>
<td>AKR</td>
<td>k</td>
<td>Whole blood (C57BL/6 × DBA/2)F₁ b, d</td>
<td>5</td>
<td>LLC</td>
<td>b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>saline (C57BL/6 × DBA/2)F₁ b, d</td>
<td>4</td>
<td>LLC</td>
<td>b</td>
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<tr>
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<td>k</td>
<td>Red cell (C57BL/6 × DBA/2)F₁ b, d</td>
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<td>LLC</td>
<td>b</td>
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<tr>
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<td>B-cell (C57BL/6 × DBA/2)F₁ b, d</td>
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<td>LLC</td>
<td>b</td>
</tr>
<tr>
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<td>k</td>
<td>T-cell (C57BL/6 × DBA/2)F₁ b, d</td>
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<td>LLC</td>
<td>b</td>
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<tr>
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<td>k</td>
<td>RPMI (C57BL/6 × DBA/2)F₁ b, d</td>
<td>5</td>
<td>LLC</td>
<td>b</td>
</tr>
</tbody>
</table>

![Graph](image)

Fig. 1. Transfusions of BDF₁-mouse whole blood into C₃H mice have a beneficial effect on tumor growth which peaked at the 12th day, while transfusions of C₃H-mouse whole blood into C₃H mice do not in comparison with heparin or saline injected controls.

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Fig. 2. Transfusions of AKR-mouse whole blood into BDF₁ mice promote tumor growth compared with controls.

Enhance tumor growth (data unshown), though transfusions of BDF₁-mouse blood did, that is, in the latter case there was clear acceleration of tumor growth which peaked 12th days after tumor transplantation (p < 0.01) (Fig. 1). The whole blood transfusion of AKR-mouse blood into BDF₁ mice also promoted tumor (LLC) growth (Fig. 2).

Components of AKR-mouse blood was transfused into BDF₁ mice in the next experiment (Fig. 3). The red blood cell (red cell) only component did not accelerated tumor growth in BDF₁ mice, however transfusions of T-cell, thymus cell, and B-cell components greatly enhanced tumor growth compared with transfusions of the red cell only component (p < 0.05). Interestingly, plasma transfusions accelerated tumor growth the most, with a statistically significant difference when compared to transfusions of lymphoid cells. When compared to red cell only transfusions, plasma transfusions had a remarkable effect on tumor growth, which was statistically significant from the 5th day (p < 0.01).

It is evident from the above results that whole blood transfusions involving different H-2 antigens, especially lymphoid cell or plasma transfusions, promote
Fig. 3. Transfusions of the red blood cell only component promoted tumor growth the least while plasma or thymus cell transfusions had a remarkable effect on tumor growth.

tumor growth, while transfusions of red blood cells only do not have such an effect.

From these results, it seems that consideration of various factors may be in order when performing major surgical operations requiring massive blood transfusions or when using component blood transfusions for cancer patients. Though blood transfusions are the best therapy for anemia, we think that red cell only transfusions should be given to cancer patients, and transfusions including many lymphoid cells should be avoided as much as possible. However, it cannot be denied that the results of this experiment are different from clinical cases involving human cancer patients in that transplanted tumors were studied.

It has been reported that normal allogeneic blood transfusions have an antitumor effect in rats (4). This contradiction with the results of this study can be explained by assuming that the animals and tumors used were different. Furthermore, the immunological mechanism of blood transfusions itself remains unclear.

Still, that certain kinds of blood transfusions may induce an immunological
tolerance comes from the many clinical reports on kidney transplantations as well as the results of the present experiment, though there are many unknown factors involved in blood transfusion. Further study of blood transfusion is necessary, especially since transfusion is so important clinically.

REFERENCES