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## Histopathologic Changes of Antibody-Mediated Small Bowel Graft Rejection in Blood-Transfused Recipients

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**W**E PREVIOUSLY reported that early (less than 3 days) small bowel graft failure occurred in preoperatively blood-transfused rat recipients who had developed antibodies reactive to non-MHC-related antigens on the small bowel graft.<sup>1</sup> This study describes the histologic changes seen in these failing small bowel grafts and a detailed analysis of the responsible antibodies.

### MATERIALS AND METHODS

Orthotopic small bowel transplantation (SBT) was performed from PVG (RT1<sup>c</sup>) to ACI (RT1<sup>a</sup>) rats with a procedure described previously.<sup>2</sup> Donor-specific or third-party LEW (RT1<sup>l</sup>) heparinized whole blood (1.0 mL) was given 7 days before transplantation. In this experimental series, six of eight donor blood-transfused recipients and one of six third-party blood-transfused recipients died within 3 days after SBT. This early graft failure was not seen in untransfused ACI recipients of PVG grafts, and the animals survived for 9 to 13 days.<sup>1</sup>

A section of ileum obtained 30 minutes after SBT was divided and one portion was fixed in formalin, embedded in paraffin, and stained with H&E. The other was snap frozen, and cryostat sections were incubated with FITC-conjugated goat anti-rat IgG or IgM (1:100, Accurate Chemical and Scientific Corp) to detect immunoglobulin depositions.

### RESULTS

Histopathologic examination of small bowel grafts 30 minutes after revascularization showed sloughing of the villi and marked congestion of the capillaries with diffuse hemorrhage at the base of the villi and in the lymphoid tissues (Peyer's patches and graft mesenteric lymph nodes). Neutrophilic margination of the small vessels with mild endothelial hypertrophy and platelet thrombi was also noted. These findings were seen in the small bowel grafts of both donor and third-party blood-transfused recipients, and suggested antibody-mediated graft damage.

In addition, direct immunofluorescence study of the small bowel grafts in the donor blood-transfused recipients revealed intense IgM > IgG deposits on the vessels at the base of the villi, and weak IgM = IgG deposits on the vessels at the top of the villi. In the graft transplanted into a third-party blood-transfused recipient, IgM, but not IgG, deposition was seen at a slightly lower intensity.

### DISCUSSION

Although numerous studies have described the beneficial effects of preoperative blood transfusion on subsequently transplanted allograft survivals, our previous study demonstrated that this procedure caused early graft failure in

SBT.<sup>1</sup> The present study shows histopathologic evidence that early graft failure was based on antibody-mediated damage, which was mediated by IgM > IgG deposits on the graft vessels in the lamina propria and the lymphoid tissues. Antibody-mediated damage was histopathologically demonstrated in small bowel grafts transplanted into both donor and third-party blood-transfused recipients.

These findings suggest that early small bowel graft damage in blood-transfused recipients is caused by antibodies which may be reactive to non-MHC-related antigens shared by lymphocytes and special endothelial cells in the small intestine. The small bowel graft contains a special type of venule, high-endothelial venules (HEV), in the lymphoid tissues of the mesenteric lymph nodes and Peyer's patches.<sup>3</sup> Lymphocytes specifically migrate from the blood circulation into the extravascular compartment of the intestine by the specific cell-to-cell recognition system between lymphocytes and the specialized endothelial cells of HEV, which may become a site of intense immune reactivity early after transplantation. Although the deposition of immunoglobulin on HEV was not clear in this study because of heavy IgM and IgG deposits on B cells in lymphoid tissues, the deposition was evident on the endothelial cells of small blood vessels at the base of the villi. These small vessels are also HEV-like blood venules, through which lymphocytes migrate from the blood into the lamina propria of the gut.<sup>4</sup> The antibodies produced after blood transfusion may have a cross reactivity to these special endothelial cells in the small bowel through their specified recognition system of lymphocytes.

### REFERENCES

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