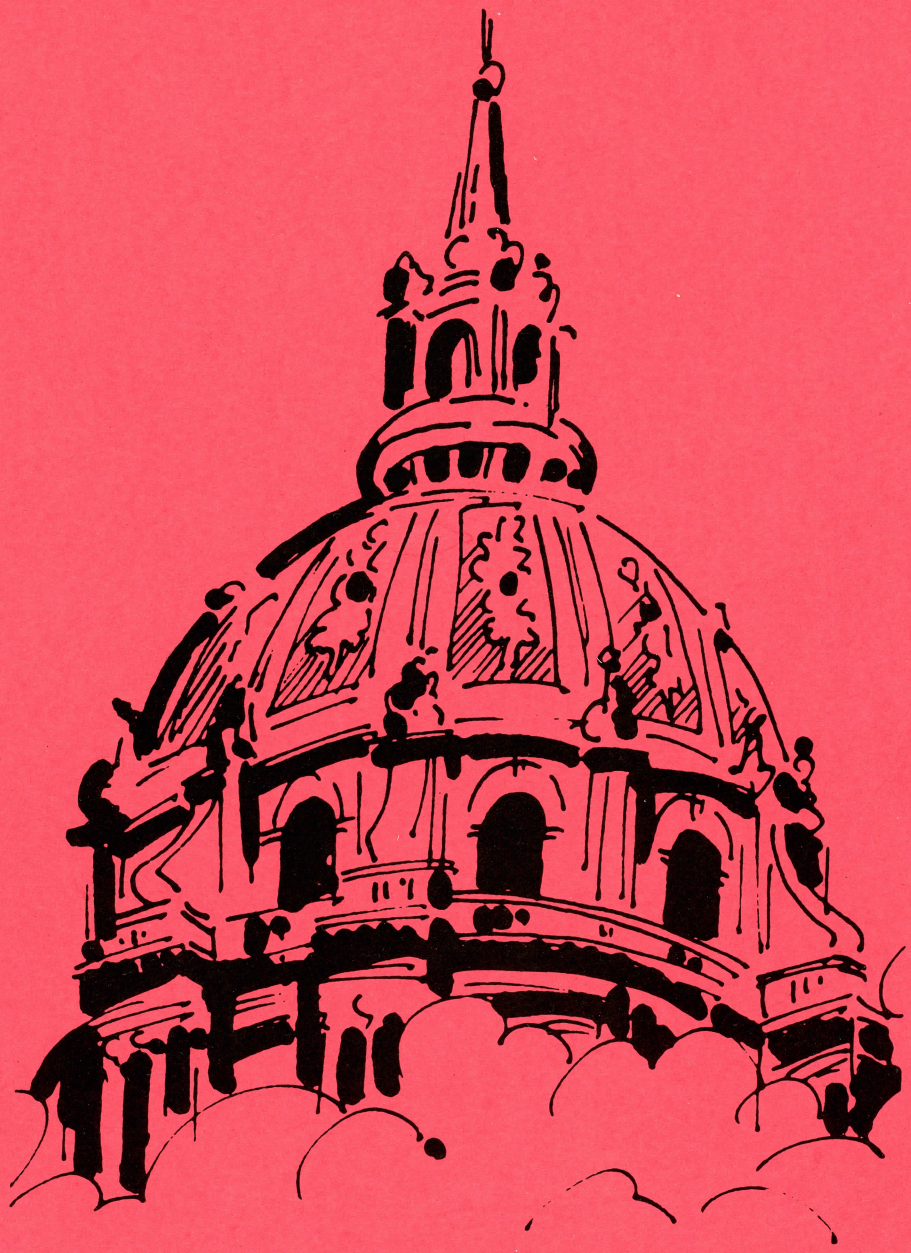
III[rd] International Symposium on SMALL BOWEL TRANSPLANTATION



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BOOK OF ABSTRACTS

- ORAL COMMUNICATIONS
- POSTERS

SEQUENTIAL PATHOLOGY OF COLON REJECTION : A COMPARISON WITH ULCERATIVE COLITIS.

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We have recently shown that transplantation of the ascending colon improves the function of a small bowel isograft in the rat. Herein, we report the clinical and histopathologically findings after ileocolic allotransplantation in the rat.

A total of 18 fully allogeneic grafts (Brown-Norway --> Lewis rats) were transplanted orthotopically. Isografts served as controls. Daily clinical follow-up included: body weight, serum protein levels and intestinal transit time. The animals were sacrificed at POD 3, 5, 7 and 10. Full autopsies were performed. Samples from colon (graft and recipient's) and small intestine were processed and stained with Hematoxylin-Phloxin-Saffranin. The slides were read blindly by a pathologist. The following diagnostic features (criteria) were scored on a scale of 0 to 2. (O: absent, 1: present, 2: striking presence):
a) regeneration (mitosis, crypt disorganization), b) inflammatory changes (inflammatory gap, cryptitis, lymphoid infiltration, PMN's infiltration, vasculitis), and c) destructive/reparative changes (goblet cell loss, ulceration, sloughing, crypt dilatation and fibrosis).

The small intestine and colon rejected synchronously. In both sets of specimens there were regenerative, inflammatory and destructive changes as the rejection progressed over time. Significant differences between small intestine and colonic rejection included: 1) the degree of lymphoid infiltration, cryptitis, crypt dilatation, arteritis and venulitis was more severe in the colon, and 2) in the colon the submucosa was actively involved in both the inflammatory and the reparative processes (including fibrosis), as opposed to a relatively unaffected submucosa in the small intestine. Many of the rejecting colon grafts had the histopathologic features classically seen in biopsies of patients suffering from active chronic ulcerative colitis including cryptitis, crypt dilatation, crypt disorganization, mitotic atypia, mucin loss, "inflammatory gap", submucosal inflammation and fibrosis. "Villi" were found in the long term (over 30 days) colon isografts.

Conclusion. Colon rejection has some of the features of ulcerative colitis, suggesting that both conditions share common pathogenic mechanisms. Villous formation occurs in long-term colon allografts suggesting adaptation to the new environment.

P30

MORPHOLOGY OF ACUTE REJECTION AND OBSERVATION OF LYMPHOPROLIFERATIVE HYPERPLASTIC REACTION IN FK 506 TREATED PIGS AFTER SMALL BOWEL TRANSPLANTATION

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Small bowel transplantation (SBT) has become a clinical reality after the introduction of FK 506 immunosuppresion. However, acute cellular rejection (ACR) continues to be a major problem. This study was undertaken to evaluate histologic changes after SBT in FK 506 immunosopressed pigs.

Twenty outbread pigs (mean weight 29.2±2.3 kg) underwent orthotopic, in continuity, SBT; 15 of them entered this study. A 10-cm segments of graft proximal jejunum was exteriorized, as a jejunostomy, for visual monitoring and postoperative mucosal biopsies (MB). The animals were divided in four groups, according to FK 506 dosage. Group 1 (n=2) received no immunosuppression (controls); group 2 (n=4) animals were treated with 0.1 mg/kg day, group 3 (n=4) with 0.15 mg/kg day and group 4 (n=5) with 0.2÷0.4 mg/kg day. Samples obtained from stomal biopsies (performed after reperfusion and in 7th, 14th, 21, 28th postoperative days) or at post-mortem examination (PME) were fixed with 10% buffered formaline and stained with hematoxylin-eosin and Movat pentacrome.

Mean survival time was 12 days in group 1, 12.3 days in group 2, 18.3 days in group 3 and 27.2 days in group 4. In all groups histological findings after reperfusion showed oedema with lacteal enlargement and focal epitelial cell loss at the villus tips. Three histological grades of ACR were identified according with previous clinical and experimental studies. Severe ACR was characterized by diffuse hemorragic necrosis of the mucosa. Moderate ACR was identified by short and broad villi, focal epithelial denudation, significant cellular infiltration, lacteals enlargement. Mild ACR was defined by mild edema, some dilated lacteals, few slighty shortened villi and initial cellular infiltration. The incidence of the different grades of ACR in each group at PMB and PME are summarized in the following table.

Grade of ACR	GROUP 1		GROUP 2		GROUP 3		GROUP 4	
	MB	PME	MB	PME	MB	PME	MB	PME
Absent	-	-	-	-	-	-	40%	80%
Mild	-	-	-	-	50%	50%	60%	-
Moderate	50%	-	100%	75%	50%	50%	-	20%
Severe	50%	100%	-	25%	-	-	-	-

In group 4 a lymphoproliferative hyperplastic reaction suspicious for a post-transplant limphoproliferative disease (PTLD) was present in three cases (60%) at PME. No hystopathological signs of graft versus host disease (GVHD) were detected in all groups.
In conclusion, FK506 at daily doses grater than 0.2 mg/kg IM prevents occurrence of rejection in small bowel grafts but can predispose to dangerous PTLD. Lower doses of FK506 are unable to control rejection reactions, which occurr with similar findings as described in other large animal models.