The Immunogenicity of Peripheral Nerve Allografts is Related to the Cellular Components

Leslie Boxer, BA, Jack H. van der Meulen, PhD, Robert G. Dennis, PhD, William M. Kuzon, Jr., MD, PhD, Paul S. Cederna, MD

University of Michigan Department of Plastic and Reconstructive Surgery, Ann Arbor, MI

Purpose. Peripheral nerve allografts have been shown to support axonal regeneration over short and long distances but are limited in their clinical utility due to the need for immunosuppression to prevent allograft rejection. We hypothesize that the immunogenicity of peripheral nerve allografts is directly related to the cellular components of peripheral nerves, and that nerves stripped of their cellular components will be non-immunogenic.

Methods. In adult Lewis (RTI[1], Charles River) and ACI (RTI[a], Harlan Sprague-Dawley) rats, peroneal nerves were harvested and transplanted either as allografts or autografts into the subcutaneous space. These two strains were chosen because they differ at a major histocompatibility locus with active rejection of allogeneic tissue transplanted across this barrier. Fourteen of the peripheral nerve grafts underwent a chemical process that removes all cellular elements from the graft (Acell group). Fourteen additional peripheral nerve grafts were transplanted as standard allografts and autografts to function as positive and negative controls (Cell group). Nerve grafts were harvested either seven days (acute group) or 21 days (chronic group) post-operatively. All specimens were paraffin embedded, stained, and evaluated by histomorphometry. Cellular infiltrates were classified by cell type and quantified via inflammatory cell counts.

Results. Nerve autografts elicited an inflammatory reaction consistent with surgical wounding (Data in table). Nerve allografts were surrounded by, and infiltrated with, significantly more inflammatory cells than autografts, presumably as a result of a cellular immune response to the allotransplant. The acellular nerve grafts elicited a local immunologic cellular response that was significantly less robust than either autografts or allografts. These observations were consistent at both time points studied.

Inflammatory Cell Counts/High Power Field

	7 days post transplant		21 days post transplant	
	Autograft	Allograft	Autograft	Allograft
Cellular	55±20	131±30	67±20	84±30
Acellular	21±10*	43±20*	20±10*	15±10*

*denotes statistical significance related to cellular counterparts ($p < 0.05$)

Conclusion. These data support our hypothesis that the immunogenicity of peripheral nerve allografts is directly related to the cellular components in the graft. We have previously demonstrated that acellular nerve *autografts* can support axonal regeneration over short gaps. Because of their non-immunogenic nature, acellular peripheral nerve *allografts* may have potential for the reconstruction of clinical peripheral nerve gaps.