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Chimerism: The Glue of Transplantation Immunology

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The Concept of Microchimerism in Organ Recipients

CHIMERISM: THE GLUE OF TRANSPLANTATION IMMUNOLOGY

by

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Further real growth of transplant immunology comes from those from disparate species. This is the mechanism of organ allograft acceptance and chimerism (1,2). The following thought experiment, which will be debated in the future, illustrates the concept.

THE HISTORY OF TRANSPLANTATION

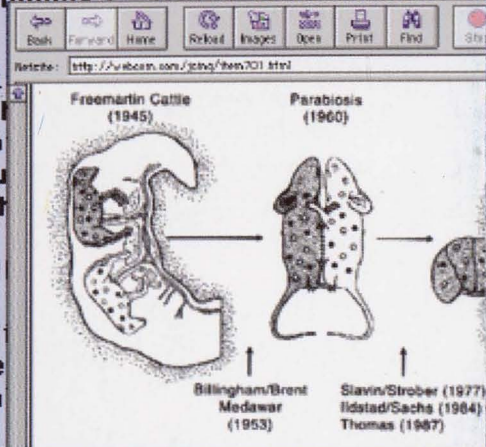
Until 1992, and ever since Medawar's definition of organ allograft was envisioned as a defense mechanism first seen as unrealistic, even after total body transplantation in 1950 to be immunosuppressive.

The Billingham, Brent, and Medawar Class

This grim pessimism was lightened in 1960 by the discovery of acquired tolerance in immunologically naive recipients of hematopoietic donor cells, and with the development of transplantation, a natural extension of the immune system, made possible by simulation of the neonatal model. As with Medawar's experiments (graft versus host disease), organ allografts.

The Enigma of Organ Transplantation

The resulting one-way paradigm in which the immune reaction appeared to explain the



Xenotransplantation

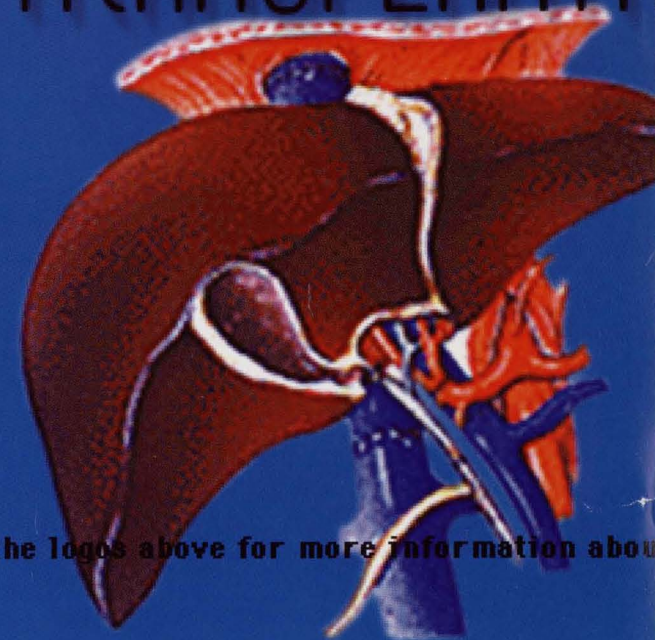
Strategies for xenotransplantation will follow the same principles as those for allogeneic transplantation, of course, a straightforward attention to barrier, focused on avoiding humoral rejection. A historic alternative is to develop xenotransplantation, however, is how to maintain co-existence of the animal and the undoubtedly long period necessary for their stable maintenance. This implies an active reciprocal "defensive" mechanism (HVG) which appears to be particularly important in the population is outnumbered and if there is severe MHC disparity. The xenotransplant stonewall has been suggested by reports from the University of Nevada (16). Using a modification of the Billingham model, sheep embryos were inoculated intraperitoneally with human stem cells purified from adult bone marrow at the 4-month gestational period. A handful of these fetuses have lived and have mixed chimerism 6 to 7 years later. The chimerism is successfully used to inoculate other fetuses, an adoptive model potentially practical importance. However, our assumption of tolerance (if it develops at all) will require protracted monitoring. The critical question is if humoral immunity in Zengani's humanized sheep, antihuman endothelial antibody after 6 years of stable chimerism. However, the critical question could not be attempted and will have to await testing in xenotransplant experiments.

CONCLUSIONS

The assumption for the last third of a century that stem cell transplantation was irrelevant to successful transplantation is now being questioned by recent studies.

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Foreword by Thomas E. Starzl M.D., Ph.D.

Foreword

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Professor of Surgery

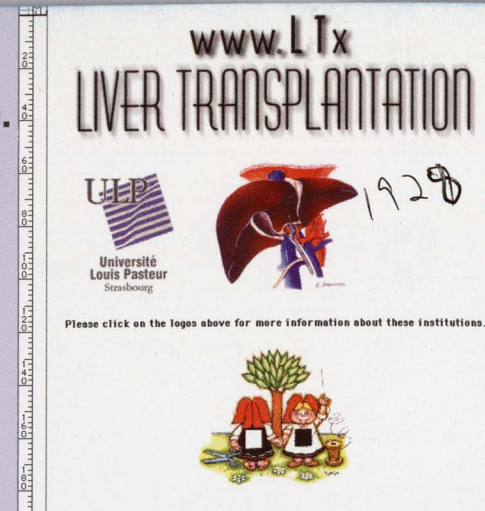
Director, Thomas E. Starzl Transplantation Institute

The idea (and now the reality) of a continuously updated electronic textbook of liver transplantation goes to the heart of a more general problem in science and medicine. The exponential growth of professional journals and the material published in them has long since outstripped the ability of interested parties to keep up.

Even for the diligent reader, the reward may not match the effort. For one thing, the delays engendered by the review, publication, and distribution process conspire to make journal articles obsolete by the time they see the light of day. Consequently, many journals have become no more than renewable incomplete textbooks, which are skimmed to see if familiar concepts are confirmed (almost invariably the case), or challenged sufficiently to warrant looking at the evidence in detail.

The gestational period of textbooks is even more protracted, sometimes lasting so long that the central theme at insemination has disintegrated by the time the finished product appears in the book stores. The best books are, however, more enduring than journals because they provide for their given subject a broader and more even account of the historical experience upon which future progress can be mounted.

No one has suggested that journals or books will disappear from the scene. However, the University of Strasbourg surgical faculty has taken a step that could shorten the time gap between discoveries and observations and their dissemination. This is particularly important for a field like



liver transplantation which is undergoing constant change. Instead of organization by classical chapters, the format is based on 160 (or more) recurring questions, problems, or topics. The selection of appropriate subjects requires the dedicated input of people with extensive personal exposure to liver transplantation. The Strasbourg team is well qualified by virtue of their decade's work in the clinical trenches of liver transplantation, and their even longer deep interest in liver disease. It has been said, sometimes critically, that surgeons compete amongst themselves more remorselessly than in any other area of life science. Such remarks betray an ignorance of history. The tradition of surgeons throughout the centuries has been to report triumphs promptly, but there has been an equal emphasis on complications and mistakes. Most importantly, surgeons and those who work with them have ennobled the profession by prompt open disclosure of discoveries and innovations. Advances that might have driven others to secrecy, or to the patent office, have been freely shared with peers. Because the Strasbourg initiative has the core objective of informing and bringing together colleagues internationally, it has a bright future.

How Did This Idea Evolve?

Jacques Cinqualbre M.D.

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Can we envision another approach? Definitely we can by using new communications pathways. Here is the world wide web, a marvelous toy for adults, an increasingly efficient tool for commercial purposes, and probably the most important development for the future of mass or individual education. This is how the idea of submitting a project to the transplant community on the Internet came into being: a collaborative, on-line, truly "non-definitive", continuously in-progress book, devoted to liver transplantation.

At its best, this book will also fulfill the prophecy: **"knowledge is the only wealth that increases when it is being shared"**, which appears to be a fair illustration of the web concept (...).

web server:

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contact D. Jaeck M.D.

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November 11, 1996

Surgical Anatomy of the Liver

Daniel Jaeck
Renée Wolfram
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The Morphological Aspect of the Liver

Surgical Anatomy of the Liver

by
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Renée Wolfram
Philippe Bachellier

List of Items as of 07/17/96

Key to Items
■ Open Items ■ Fulfilled Items

425 Orthotopic auxiliary transplantation K. Boudjema M.D.
518 Graft-versus-host disease
702 Xenotransplantation of the liver P. Wolf M.D.