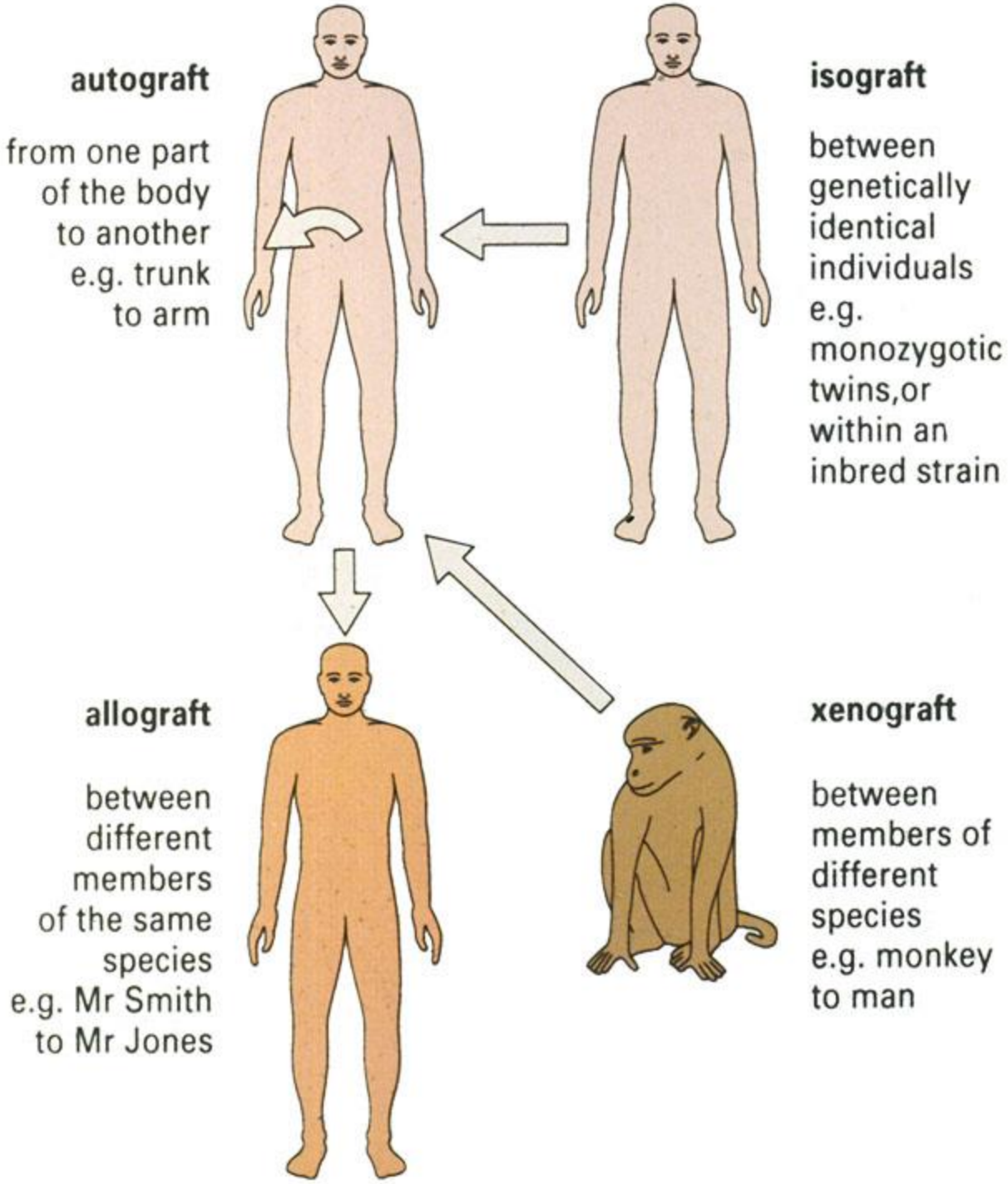
Immunology of transplantation

Types of transplantation

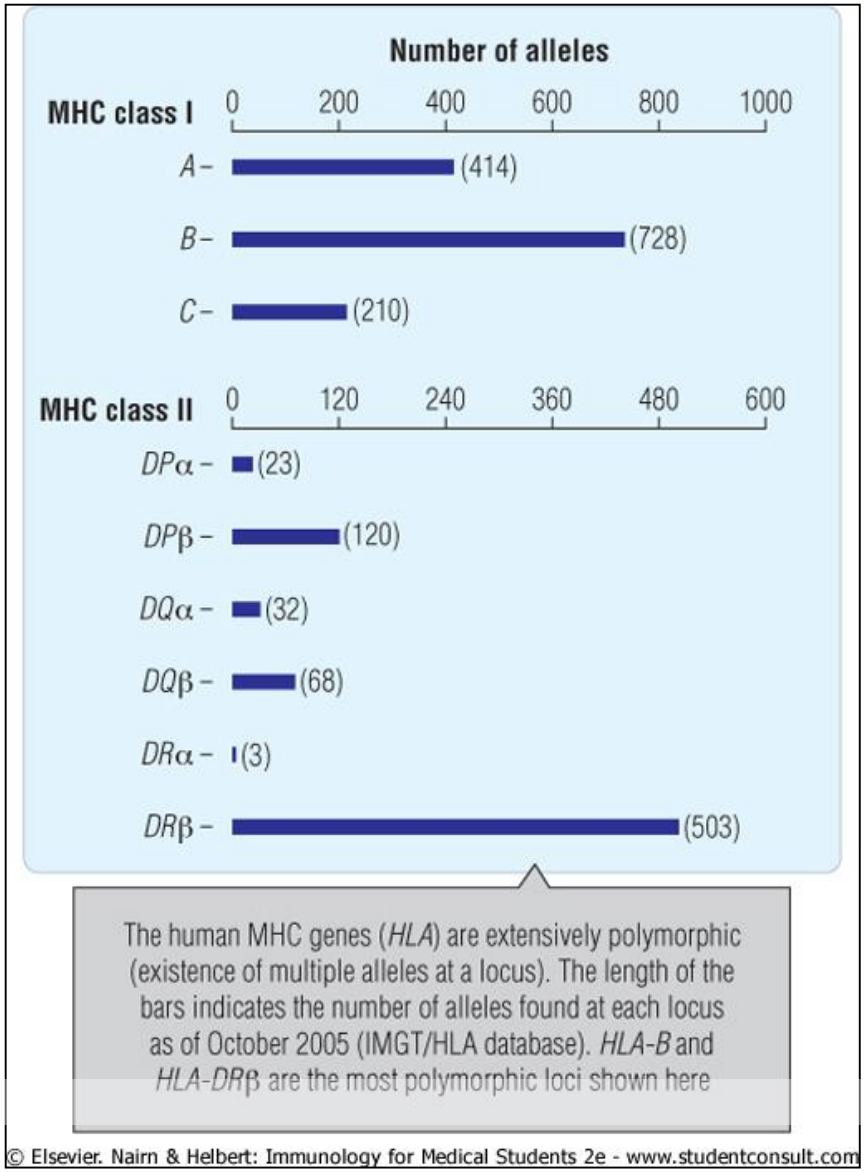
- Autotransplantation –within one organism
- Allotransplantation- between one species
- Xenotransplantation- between two different species


autograft
from one part of the body to another e.g. trunk to arm
isograft
between genetically identical individuals e.g. monozygotic twins,or within an inbred strain
allograft
between different members of the same species e.g. Mr Smith to Mr Jones
xenograft
between members of different species e.g. monkey to man

Success rate of transplantation in humans

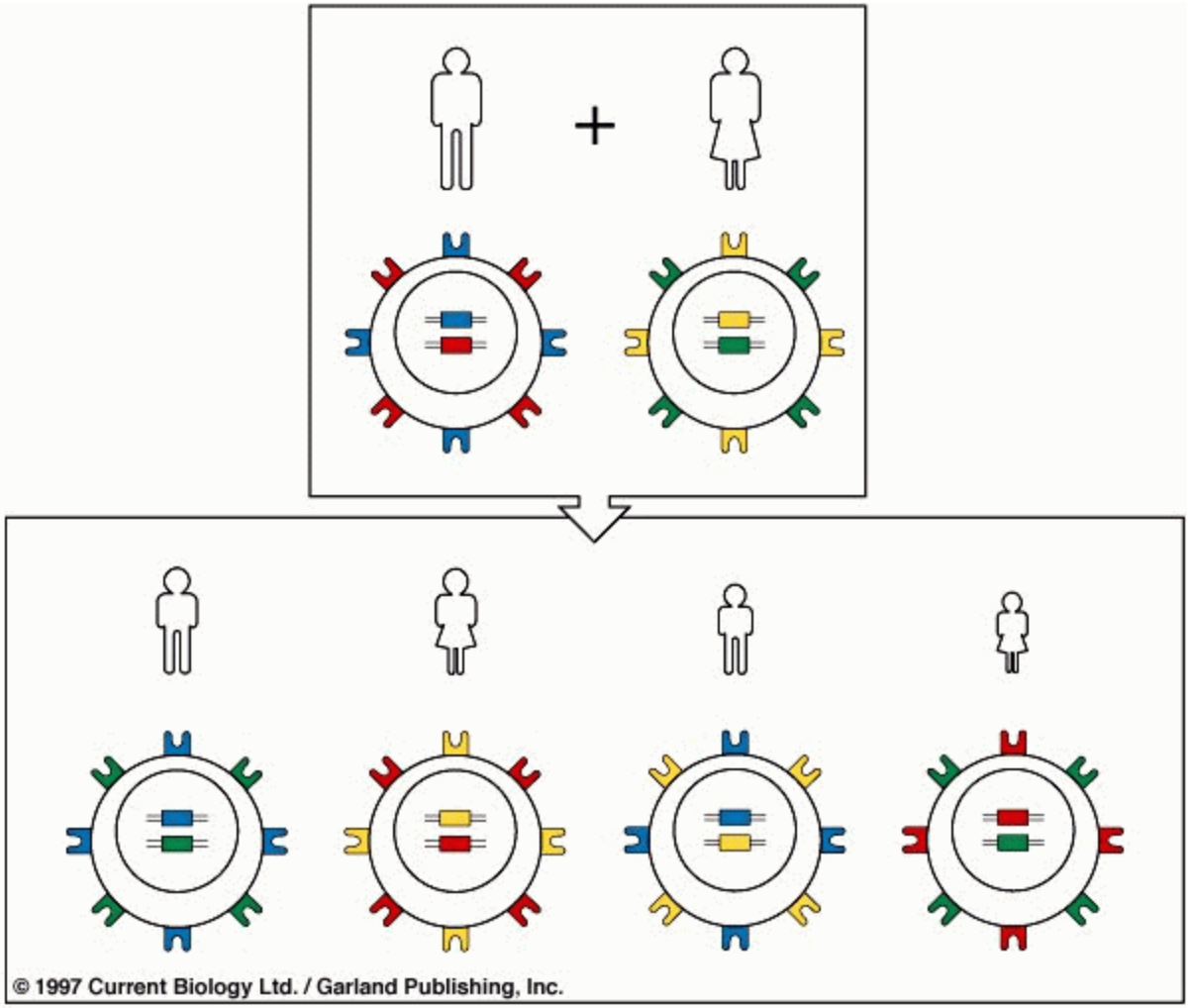
Tissue transplanted	5-year graft survival*	No. of grafts in USA (1999)
Kidney	80–90%	13,429 (12,483)
Liver	40–50%	4698
Heart	70%	2234 (2185)
Lung	30–40%	934 (885)
Cornea	~70%	~40,000†
Bone marrow	80%	23,500‡

Polymorphism of HLA antigens

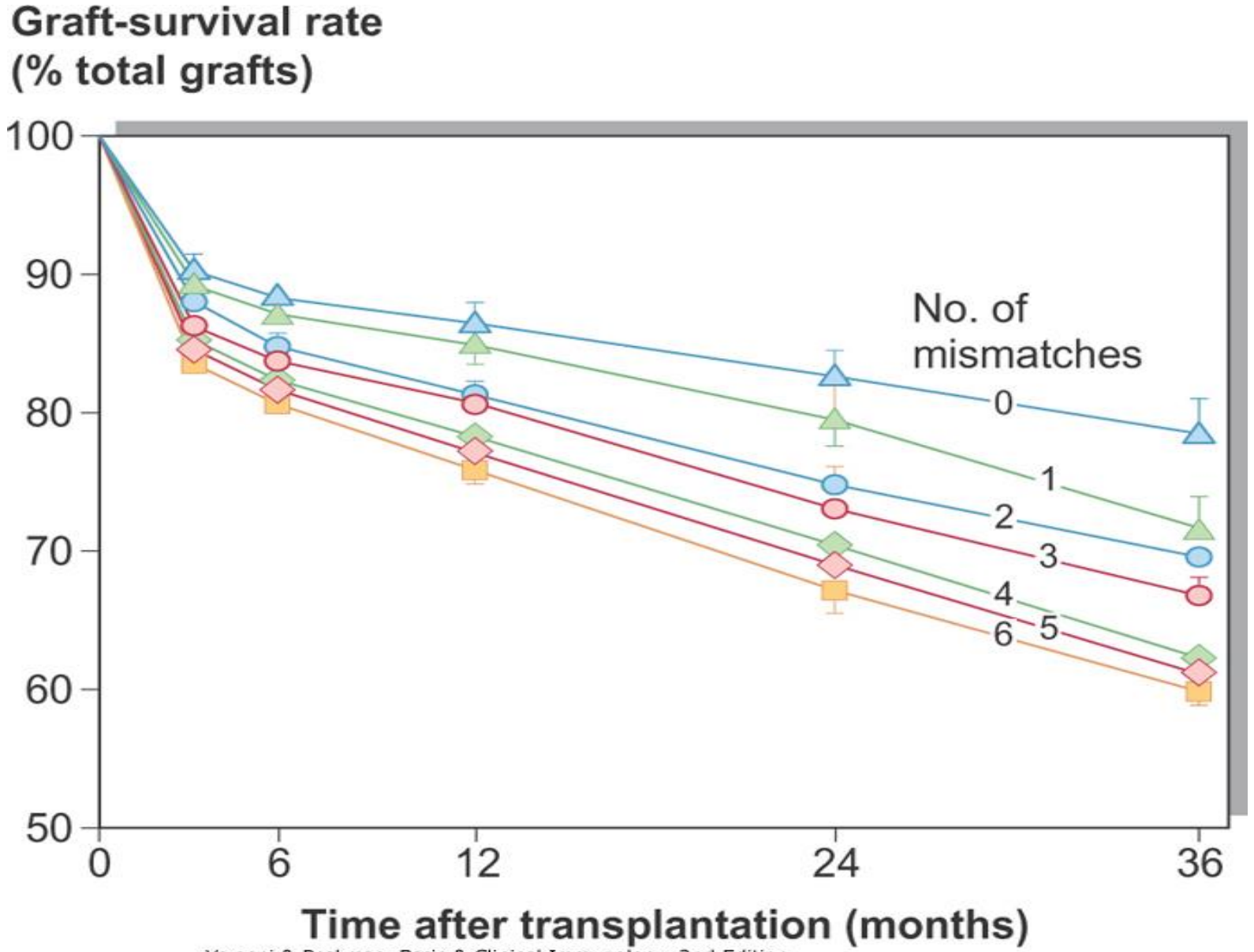


The human MHC genes (*HLA*) are extensively polymorphic (existence of multiple alleles at a locus). The length of the bars indicates the number of alleles found at each locus as of October 2005 (IMGT/HLA database). *HLA-B* and *HLA-DR*β are the most polymorphic loci shown here

Co-dominant expression of HLA genes



Effect of HLA-identity on kidney graft survival



Cross match test

- Used for detection of recipient´s antibodies against donor´s antigens (mainly HLA antigens)
- Donor´s leukocytes + patient´s plasma
- Positivite – antibodies bind to leukocytes – can be detected e.g. by flow cytometry
- Positivity contraindicates transplantation

Types of graft rejection

- Hyperacute - minutes to hours after transplantation. Caused by pre-formed recipient antibodies against HLA antigens of the donor. Irreversible.
- Acute -several days to months after transplantation. Mainly T-cell mediated. Usually reversible by aggressive immunosuppression.
- Chronic - years after transplantation. Continuous decrease in graft function. Irreversible. Mechanism unknown.

The most frequent types of organ transplantation

- Heart
- Kidney
- Liver
- Lungs
- Pancreas
- Cornea

Heamatopoietic stem cells transplantation

- Indications: malignancies, bone marrow failure, primary immunodeficiencies.
- “Whole“ bone marrow or separated CD34+ cells can be used.
- The most significant complication: graft-versus host reaction (GVHR).
- Optimal HLA-matched donor is required.

Graft-versus host reaction (GVHR)

- Immunological reaction of transplanted T-cells against recipients (HLA) antigens.
- Skin, liver, intestine predominantly affected.
- Milder forms can be treated by immunosuppression, severe forms may be fatal.
- Can be induced by transfusion of non-irradiated blood to immunodeficient patients (primary immunodeficiencies, leukemia…).

Systemic Immunosuppression

- High-dose steroids
- Purine antagonists: Azathioprin
- Alkylating agents: Cyclophosphamide
- Anti-pholates: Methotrexate
- Calcineurin antagonists: Cyclosporine A, Rapamycin, Tacrolymus
- Block of purins synthesis: Mycophenolate
- Monoclonal antibodies: anti-CD3, anti-CD20, anti-CD54