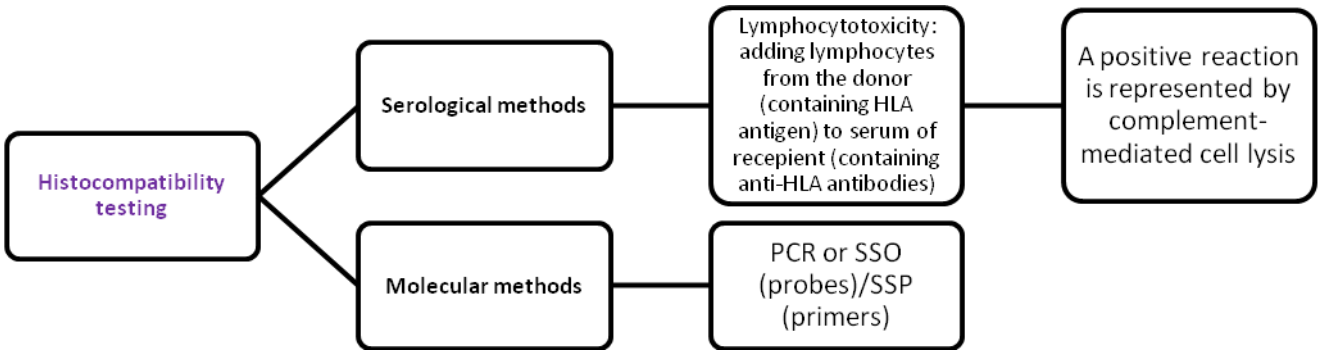
Pre-transplant (before transplantation)	Post-transplant (after transplantation)
HLA-typing	Immunological rejection
Crossmatching (showing if the recipient has antibodies to the donor or not)	
PRA (Panel Reactive Antibody screen)	

- **Human Leukocyte Antigen (HLA) = Major Histocompatibility Complex (MHC)**
  - **What is it?** cluster of genes which are important in:
    - ✓ Immune recognition.
    - ✓ Signaling between cells of the immune system.
  - **Discovery**: HLA was discovered in 1950s when they found antibodies to leukocytes in the sera of:
    - ✓ Multiple-transfused patients.
    - ✓ Multi-parous females.

    In 1973, they discovered that there is an association of HLA antigens with specific diseases.
  - **There are two classes of MHC (both presenting on short arm of chromosome 6): notice that the mode of inheritance of MHC is haplotype (which means that 50% is inherited from each parent):**

MHC class-I	MHC class-II
✓ It is present in all nucleated cells of the body ✓ Sub-classified to: A, B and C ✓ Function: cytosol-derived antigen recognition by cytotoxic T-cells (CD8+)	✓ Antigen-presenting cells (macrophages, B-lymphocytes and dendritic cells). ✓ Sub-classified to: D, DR, DQ and DP ✓ Function: processing vesicle-derived antigen to helper T-cells (CD4+)

    Notes:
    - ✓ Each of HLA-A, HLA-B, HLA-C and HLA-DR is a separate genetic locus.
    - ✓ The extensive range of HLA antigens which can be expressed by individuals at each of these loci is known as MHC polymorphism.
    - ✓ *Homozygousity*: refers to the inheritance of two same alleles (from each parent) for the same locus.
    - ✓ *Heterozygous*: refers to the inheritance of two different alleles (from each parent) for the same locus.
- **Organ transplantation rejection:**
  - Cytotoxic T-cells (CD8+) of the recipient recognize foreign MHC class-I antigens of the donor.
- **Bone marrow transplant rejection = graft versus host disease**
  - Donor's T-cells attack recipient's MHC class-II antigens.
- **HLA-typing:**
  - **Function:**
    - ✓ Paternity testing (فحص الأبوّة).
    - ✓ Prior to transplantation to select donor.
    - ✓ Disease association.



- **Crossmatching:**
  - Potential donor cells (lymphocytes: which express HLA antigens) will be added to serum of the recipient (which might contain anti-HLA antibodies). Then, you will look for the reaction by:
    - ✓ Complement-dependent cytotoxicity (CDC).
    - ✓ Flow cytometry crossmatch (FCXM) using immunofluorescence (this is an alternative method to CDC). This method has many advantages:
      - ❖ Detecting non-complement mediated antibodies.
      - ❖ Faster turn around time.
      - ❖ Lower incidence of ambiguous results (نتائج غامضة وملتبسة) due to poor cell viability.
      - ❖ Direct detection of IgG antibodies, thus avoiding false positive reactions caused by IgM autoantibodies.
  - A negative crossmatching result is required to proceed with the procedure of transplantation.
- **Panel Reactive Antibody Screen (PRA):**
  - Only the recipient is needed to be tested if he has anti-HLA antibodies or not.
  - **Methods:**
    - ✓ Complement-dependent cytotoxicity (CDC).
    - ✓ ELISA
    - ✓ Flow cytometry.
- **HLA-matching: graft survival**
  - **One year graft survival rate is:**
    - ✓ 94% in recipient of two haplotype match (HLA identical). Patient lives for 26.9 years!
    - ✓ 89% and 90% when one haplotype match parent or sibling. Patient lives for 12.2 years.
- **Generation of allograft rejection response: there are three mechanisms of rejection**
  - Cytotoxic T-cells (CD8+).
  - Delayed type hypersensitivity mediated by helper T-cells (CD4+).
  - Antibodies produced by plasma cells.