Organ Donation, Transplantation and the Immune Response

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Surgical Foundations
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Disclaimer

- Presenter Profile
  - Conflicts of interest
    - None
  - Level of expertise
    - Quite low
  - Level of enthusiasm
    - Quite high
  - Goal of presentation
    - Familiarity with basics
    - Ability to understand main challenges of transplantation
    - Enough detail to field questions on major concepts
Outline

- Immune system overview
- Organ donation
- Compatibility principles
- Rejection
- Immunosuppression
- Challenges for post-transplant patients

  ▫ Practice Qs throughout – stay awake!
The Immune System
Broad overview

- Immune System
  - Innate
    - Anatomic
    - Physiologic
    - Phagocytic
  - Adaptive
    - Inflammatory
    - Humoral
    - Cell-mediated
Innate vs Adaptive Immunity

- **Innate**
  - Early response (0-12h), but same speed each time
  - Takes advantage of a set number of common *pathogen-associated molecular patterns* (doesn’t learn new ones)
  - Phagocytes, natural killer cells, complement, cytokines

- **Adaptive**
  - Response takes 24h+, faster, stronger response if past exposure
  - Takes advantage of genetic recombination to create ++diversity
  - Sequence of events leading to targeted destruction
    - Antigen recognition
    - Lymphocyte activation, differentiation, proliferation
    - Cytokine release and activation of effector cells against the antigen
<table>
<thead>
<tr>
<th><strong>Specificity</strong></th>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>For structures shared by classes of microbes (&quot;molecular patterns&quot;)</td>
<td>For structural detail of microbial molecules (antigens); may recognize nonmicrobial antigens</td>
</tr>
<tr>
<td><img src="image1" alt="Diagram" /></td>
<td><img src="image2" alt="Diagram" /></td>
<td><img src="image3" alt="Diagram" /></td>
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<table>
<thead>
<tr>
<th><strong>Receptors</strong></th>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
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<tbody>
<tr>
<td></td>
<td>Encoded in germline; limited diversity</td>
<td>Encoded by genes produced by somatic recombination of gene segments; greater diversity</td>
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<tr>
<td><img src="image4" alt="Diagram" /></td>
<td><img src="image5" alt="Diagram" /></td>
<td><img src="image6" alt="Diagram" /></td>
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<table>
<thead>
<tr>
<th><strong>Distribution of receptors</strong></th>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonclonal: identical receptors on all cells of the same lineage</td>
<td>Clonal: clones of lymphocytes with distinct specificities express different receptors</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th><strong>Discrimination of self and nonself</strong></th>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
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<tbody>
<tr>
<td>Yes; host cells are not recognized or they may express molecules that prevent innate immune reactions</td>
<td>Yes; based on selection against self-reactive lymphocytes; may be imperfect (giving rise to autoimmunity)</td>
<td></td>
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</tbody>
</table>
Question

• Which of the following statements about the immune system is correct?
  ▫ 1) The immune system is genetically set and does not change during an individual’s lifetime
  ▫ 2) The innate component of the immune system responds more quickly to a pathogen the second time it is encountered
  ▫ 3) Autoimmune disease can result from flaws in adaptive immunity
  ▫ 4) None of the above statements are correct
Innate Immunity

- **Anatomic**
  - Skin, mucous membranes
  - Sebum: pH 3-5 inhibits microorganism growth
  - Mucous, tears, saliva: irrigation/flushing

- **Physiologic**
  - Temperature, acidity (gastric acid)
  - Toll-Like-Receptors: recognize molecules not found on multi-cellular organisms (e.g. LPS, mannose) and tag them for destruction
  - Complement (participates in both innate and adaptive immunity)

- **Phagocytic**
  - Foreign bacteria phagocytosed, digest by coupling phagosome with lysosome

- **Inflammatory**
  - Influx of immune cells & fluid to area
Phagocytosis

1. Chemotaxis and adherence of microbe to phagocyte.
2. Ingestion of microbe by phagocyte.
3. Formation of a phagosome.
4. Fusion of the phagosome with a lysosome to form a phagolysosome.
5. Digestion of ingested microbe by enzymes.
6. Formation of residual body containing indigestible material.

(a) Phases of phagocytosis

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Complement

- **Four mechanisms of attack**
  - **Lysis of target cell**
    - Complement can poke holes in the enemy cell membrane, like shooting holes in the hull of a ship to sink it
  - **Opsonization**
    - Opsonins stick to their target and promote phagocytosis, like coating the enemy with honey in front of a pack of bees
  - **Activation of inflammatory response**
    - Complement triggers pro-inflammatory cytokine signals, like calling 911 and getting police/firefighters/ambulance
  - **Clearance of immune complexes**
    - Complement can stick to immune complexes and tag them for clearance by T-cells, like marking an ‘X’ on the trees to be cut down
Complement

- **C1** binds to antigen-antibody complex (adaptive immunity)
  - This binding activates C1 and becomes an enzyme that starts a cascade
  - Multiple molecules cleaved into active enzymes (C2-4)
  - Ultimately forms the Membrane Attack Complex (C5-9)
- **C3** spontaneously binds to random membranes (innate immunity)
  - Human cells have sialic acid levels that inactivate it
  - Yeast & bacteria lack sialic acid, so C3 remains active and carries out enzymatic reactions ultimately forming the Membrane Attack Complex
Membrane Attack Complex

CLASSICAL PATHWAY

Artigen-antibody

C1 → C1a → C2 → C2a → C4 → C4b → C4b2a (C3 convertase) → C4b2a3b (C5 convertase) → C3a → C3b → C5 → C5a

ALTERNATIVE PATHWAY

C3 → C3b (C3 convertase) → C3bBb (C5 convertase)

Factor D

Biomaterial Surface

C3a

Inrushing fluids

Complement proteins

Cytoplasm

Phospholipid bilayer

K and Cl ions

Water and Na ions
Natural Killer Cells

• NK cells kill stressed cells, viral-infected cells, cancer cells

• How?
  ▫ Recognize stress signals expressed on cell surface
    • Bind to stressed cells and prepare to destroy unless a counter-signal is present
  ▫ A normal cell will express MHC at the surface with self-peptide
    • This counter-signal will inactivate the NK cell
  ▫ Stress, viruses and cancer interfere with cell’s ability to express MHC with a self-peptide
    • If the NK cell doesn’t sense an MHC molecule, destruction of that cell ensues

• Just like complement, NK cells are part of both innate and adaptive immunity
Question

- Which of the following is NOT a component of the innate immune system?
  - 1) The Membrane Attack Complex (MAC)
  - 2) Erythrocytes
  - 3) Macrophages
  - 4) The epithelium
Immune System
  - Innate
    - Anatomic
    - Physiologic
    - Phagocytic
    - Inflammatory
  - Adaptive
    - Humoral
    - Cell-mediated
Adaptive Immunity

- Two types
  - **Humoral immunity**
    - Main players: B-cells and antibodies
  - **Cell-mediated immunity**
    - Main players: T cells
B-cell Development

- B-cells mature in the bone marrow
  - Through genetic recombination of the DNA responsible for the antigen-binding portion of the antibody, B cells form antibodies with a unique antigenic specificity
  - If they bind self in the bone marrow, they either...
    - Undergo ‘receptor editing’ (try a new recombination)
      or
    - Undergo apoptosis
Adaptive Immunity: Humoral

- B cells lurk in the shade of lymphatic tissue, waiting for an antigen to bind the antibodies sitting poised on their cell membranes
- Clonal selection = antigen binding
  - The B cell becomes activated
- Clonal expansion = B cell proliferation
  - Helper T cells produce cytokines to promote clonal expansion
- B cell transforms into a plasma cell
  - Specialized for mass production of antibodies
- Memory B cells eventually form, and are left behind, remaining dormant, ready to strike stronger and faster the next time that same antigen shows up
Illustration

- Link to a demonstration of humoral immunity
T-cell Development

- Diversity built-in as T-cells are matured
  - Pre-T cells proliferate in the thymus; all have different molecular affinities
- T-cells are destroyed unless they can play nicely with antigen-presenting cells and don’t have self-destructive tendencies
  - Negative selection: T cells that react to self-antigens in the thymus are destroyed
    - Remaining T cells will not attack host cells
    - Imperfect system – some T cells that react to a self-antigen slip through, resulting in auto-immune disease
  - Positive selection: T cells that can attach with a good affinity to self–MHC are spared
    - Remaining T cells will recognize antigen-presenting cells
Lymphocyte Circulation

- B and T cells hang out all over
  - Blood stream
  - Lymph nodes
  - Lymph nodules in skin, gut, respiratory tract
  - Spleen
Adaptive Immunity: Cell-mediated

- **Antigen-presenting cells (capture of antigens)**
  - Dendritic cells and macrophages are the main APCs
  - Phagocytose and display the antigen on surface
  - Present antigens to lymphocytes

- **Lymphocytes (recognition of antigens)**
  - Responsible for specificity of human immune response
  - Recognize foreign antigens; distinguish foreign from self
  - Release cytokines once activated by foreign antigen

- **Effector cells (elimination of antigens)**
  - Cytotoxic T cells (CD8+), macrophages, NK cells are activated by cytokines
Antigen-Presenting Cells

Only CD4+ Helper T cells will recognize MHC II

Start here with an external antigen

MHC I for internal antigens (virus, tumor protein)

MHC II for external antigens
Activated T Cells

- **Helper T Cells (CD4+ T Cells)**
  - Activated by binding to antigen presented on MHC II
    - External antigens (bacteria, yeast)
  - Secrete cytokines to orchestrate effector cells
  - Proliferate

- **Cytotoxic T Cells (CD8+ T Cells)**
  - Activated by binding to antigen presented on MHC I
    - Viral antigens, bacterial proteins, mutant tumor proteins
  - Kills the cell by creating pores in its membranes, and releasing enzymes that trigger apoptosis
Apoptosis

- Regulated (orderly and sequenced) cell death
  - Nucleus condenses, fragments
  - Proteases destroy proteins and DNA
  - Plasma membrane vesiculates
  - Cell gets phagocytosed
    - No inflammation, no spillage
Apoptosis Triggers

- **Fas**
  - Fas is a “death receptor” located on the cell surface
  - High **IL-2** levels lead to Fas ligand (FasL) production by T-cells
  - When FasL binds Fas, apoptosis results

- **Tumor Necrosis Factor (TNF)**
  - Macrophages produce TNF
  - TNF binds to receptor TNF-R1 on cells, and apoptosis results
  - TNF is also a major inflammatory cytokine
Cell-Mediated & Humoral Immunity

Cytokines to know

• IL-1
  ▫ T and B cell proliferation
  ▫ fever, inflammation
  ▫ endothelial cell activation

• IL-2 ★
  ▫ T cell growth factor
  ▫ B cell prolif/differentiation
  ▫ NK cell growth/activation

• IL-4
  ▫ Similar to IL-2

• IL-5
  ▫ Stimulates eosinophils

• IL-6
  ▫ Similar to IL-2
  ▫ Fever, inflammation
Cytokines to know

- **TNF-alpha & beta**
  - NK cells and T cells secrete this to cause B cell proliferation, enhanced T cell function and neutrophil/macrophage activation

- **IFN-alpha and beta**
  - Cause class I MHC expression to be increased
  - Lead to NK cell activation

- **IFN-gamma**
  - Class I + II MHC expression increased
  - Antiviral
  - Activates macrophages, endothelial cells
  - Augments NK cell activity
FIGURE 12-5 Interaction of antigen with macrophages and the subsequent activation of resting T H cells leads to release of numerous cytokines (blue arrows), generating a complex network of interactions among various immune cells.
Question

• Interleukin-2 (IL-2) is...
  ▫ 1) involved in the adaptive immune response
  ▫ 2) a cytokine secreted by helper T cells
  ▫ 3) a stimulus for B cell proliferation, T cell growth and NK cell activation
  ▫ 4) all of the above
What is a transplant?

- **Transplant:** the transfer of an organ or tissue from one part of the body to another
  - **Autograft:** tissue for transplant from a patient’s own body
  - **Isograft:** tissue for transplant from a genetically identical individual
  - **Allograft:** tissue for transplant from a genetically unrelated donor (of same species)
  - **Xenograft:** tissue for transplant from a different species
- **Implant:** surgically embedded object or device
  - Prosthesis, stent, cardiac valve, lens, mesh

http://www.thefreedictionary.com/transplant
Organ Donation Types

- Live donation
- Deceased donors
  - Established brain death
    - Irreversible coma
    - Absence of brain stem reflexes (pupillary, corneal, gag, vestibulo-ocular)
    - Apnea test
  - Consent from family
  - PMHx screening
- Donation after cardiac death (DCD)
  - Brain death not established, but withdrawal of life support planned given no long-term prognosis of recovery
  - Life support d/c’d in OR; harvest shortly after asystole

Approaching Families

• Trillium Gift of Life Network
  ▫ One donor can save up to 8 lives
  ▫ Donation does not interfere with open casket funeral, but heart valve/MSK tissue may alter choice of clothing for burial
  ▫ Donation is completely non-profit: no money gained for patient or for organization

• Trained Trillium representative always available to speak to family about donation

www.giftoflife.on.ca
“GIFT” Criteria for Referral to Trillium

- Grave prognosis or GCS 3
- Injured brain or non-recoverable injury/illness
- Family-initiated discussion of donation/withdrawal of life support
- Therapy-limited, de-escalation of care, withdrawal of life support planned
Types of Tissues Sought

- Organs
  - Lungs, heart, liver, pancreas, kidneys, bowel
- Tissues
  - Eye, skin, heart valves, bone, tendons, ligaments
Eligibility

- Not eligible if active infection or malignancy
- Assessed on a case-by-case basis – always feel free to call Trillium and talk through the case

- Even patients with hepatitis may be eligible to donate (many Hep B/C + patients are on the transplant list)
- If a potential donor is a coroner’s case, coroner should be approached first (may determine some limitations on tissue donation, based on investigation required)
Ontario’s Transplant Wait List in 2012

<table>
<thead>
<tr>
<th>WAITING LIST YEAR TO DATE</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>LIVER</td>
<td>242</td>
</tr>
<tr>
<td>HEART</td>
<td>63</td>
</tr>
<tr>
<td>KIDNEY</td>
<td>1095</td>
</tr>
<tr>
<td>LUNG</td>
<td>66</td>
</tr>
<tr>
<td>HEART LUNG</td>
<td>1</td>
</tr>
<tr>
<td>PANCREAS</td>
<td>36</td>
</tr>
<tr>
<td>SMALL BOWEL</td>
<td>1</td>
</tr>
<tr>
<td>KIDNEY PANCREAS</td>
<td>48</td>
</tr>
<tr>
<td><strong>TOTAL ON WAITING LIST</strong></td>
<td><strong>1552</strong></td>
</tr>
</tbody>
</table>
Question

• Regarding organ donation in Ontario, which of the following statements is NOT correct?
  ▫ 1) If a potential donor is a victim of homicide, he or she is ineligible to donate
  ▫ 2) Kidneys are the organ in highest demand
  ▫ 3) The most common live organ donations are for kidney and liver transplants
  ▫ 4) Organs and tissues are harvested in a way that still allows for an open casket funeral
Transplant Team

- Example: Renal failure
  - Urologist
  - Nephrologist
  - Social worker
  - Transplant coordinator

- Pre-Op
  - Determining if patient is a candidate
  - FHx, PMHx (mental health, addictions, active cancer, etc)
  - Multidisciplinary evaluation committee decides whether or not patient is suitable for transplant list

Washington
Major Histocompatibility (MHC)

- Major Histocompatibility complex is a collection of genes
- HLA = human leukocyte antigen
  - Present on all nucleated cells
    - Class I MHC
      - Presents antigens from inside the cell to cytotoxic T cells
      - HLA-A and HLA-B are products of the MHC class I locus
    - Class II MHC
      - Presents antigens phagocytosed from outside the cell to helper T cells
      - HLA-DR is a product of the MHC class II locus
Compatibility

- Blood group and major histocompatibility antigens cause the most severe rejection reactions
- Blood group testing and HLA typing are used to check for any major incompatibility between donor and recipient

MHC Locus on chromosome 6 contains the HLA genes
Panel Reactive Antibodies (PRA)

- Once on transplant list, recipient’s blood is tested monthly for the PRA level
  - Similar to ABO test, patient’s blood is mixed with a panel of cells from random donors to check for antibodies against them
  - Most patients have a 0-5% PRA (no preformed anti-HLA antibodies)
    - If pt has autoimmune disease, previous transplant, pregnancy or transfusions, the PRA may be higher
More Compatibility Tests

- **Tissue typing**
  - Uses PCR to identify alleles of class I (HLA-A, HLA-B) and class II (HLA-DR) MHCs – 2 alleles from each HLA and 1 from each parent = 6 alleles in total
  - Best results are when match is 6/6
  - Even if ABO compatible and 6/6 alleles match, minor histocompatibility loci differences can result in graft rejection

- **Cross-matching**
  - Serum from recipient is tested for preformed antibodies against donor cells
  - Ensures no hyperacute rejection
Purpose of Matching

• The better the match of HLA alleles between donor and recipient, the higher the rate of survival
• Higher risk for rejection with...
  ▫ High PRA
  ▫ Recipient pre-sensitized to the donor’s antigens
  ▫ ABO incompatibility
  ▫ HLA incompatibility
  ▫ Previous graft loss from rejection
  ▫ Young age in recipient
  ▫ Autoimmune comorbidities
Question

- What is the Panel Reactive Antibody level?
  - 1) A measure of the donor’s antibodies against recipients’ antigens
  - 2) A measure of the recipient’s antibodies against donors’ antigens
  - 3) A measure of the donor’s antibodies against a standard set of antigens
  - 4) A measure of the recipient’s antibodies against a standard set of antigens
Graft Rejection

• Attack on the graft by the host’s immune system
  ▫ Hyperacute rejection (within 24h)
    • Preformed antibodies react to graft endothelium, activate complement and cause thrombosis & necrosis of vessel wall
    • Massive inflammatory reaction, neutrophil influx into graft
  ▫ Acute rejection (first few weeks)
    • Acute vascular rejection: T cells attack endothelium
    • Acute cellular rejection: T cells attack parenchyma
  ▫ Chronic rejection (months to years)
    • T cells induce proliferation of smooth muscle cells leading to blockage of the vessel lumen
    • Characterized by scarring and fibrosis
## Rejection Summary

<table>
<thead>
<tr>
<th>Timing</th>
<th>Type of Rejection</th>
<th>Immune Response Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 24h</td>
<td>Hyperacute</td>
<td>Humoral: pre-formed antibodies (memory B cells)</td>
</tr>
<tr>
<td>First few weeks</td>
<td>Acute</td>
<td>Cell-mediated: T-cells</td>
</tr>
<tr>
<td>Months to years</td>
<td>Chronic</td>
<td>Cell-mediated &amp; humoral: B &amp; T-cells</td>
</tr>
</tbody>
</table>
Chronic Rejection Risk Factors

- Donor: older age, HTN
- Recipient: diabetes, HTN, post-transplant infections
- Organ preservation during transport, reperfusion injury
- Initial delayed graft function
- Subtherapeutic immunosuppression
- Hx of acute rejection episodes (the more severe and the more frequent, the higher the risk)
Question

Which of the following is unlikely to increase the risk of rejection in a transplant recipient?

- 1) Young age
- 2) Poor medication adherence
- 3) Post-operative wound infection
- 4) Use of corticosteroids within 3 months of transplant operation
Immunosuppression Phases

- **Induction**
  - Right after transplant, need high level of suppression
  - Also for acute rejection treatment

- **Early intense immunosuppression**
  - To try to prevent acute rejection

- **Maintenance phase**
  - Lower dose immunosuppressants
  - To combat chronic rejection
Immunosuppressive Agents

• Induction
  ▫ Antilymphocyte agents
  ▫ Antibodies against IL-2R
  ▫ Antibodies against CD3 (present on all T-cells)

• Maintenance
  ▫ Corticosteroids (prednisone)
  ▫ Antiproliferative agents (azathioprine, MMF, leflunomide)
  ▫ T-cell suppressants (cyclosporine, tacrolimus, sirolimus)
  ▫ Lymphocyte sequesterers (FTY720)
Corticosteroids

• Mechanism of action
  ▫ Inhibit cytokine and prostaglandin production
  ▫ Alter function of APCs

• Toxicity
  ▫ infection, poor wound healing, osteoporosis, avascular necrosis, HTN, DM, hyperlipidemia, obesity, Cushingoid facies

• Current use
  ▫ minimize dose, alternate day therapy
  ▫ early steroid withdrawal

Cyclosporine

- **Mechanism of Action**
  - inhibits calcineurin --> inhibits T-cell activation/IL-2 /IL-2R/IFN-gamma

- **Toxicity**
  - Nephrotoxicity, hypertension
  - Neurotoxicity (tremor, headache, direct CNS)
  - DM, hyperlipidemia, hirsutism, gingival hyperplasia

- **Current use**
  - Calcineurin inhibition: standard
  - Optimal monitoring using C₂ (peak level) not C₀ (trough levels)
  - Drug level affected by many common drugs (abx, anti-epileptics, etc.)

Mycofenylate mofetil

• Advantages
  ▫ Inhibits lymphocyte proliferation
  ▫ More lymphocyte-specific than azathioprine
  ▫ no nephro- or neuro-toxicity
  ▫ reduced acute rejection

• Toxicity
  ▫ marrow, GI tract

• Current use
  ▫ primary “triple immunotherapy”
  ▫ add to cyclosporine or tacrolimus monotherapy following rejection or to reduce dose for calcineurin toxicity

Tacrolimus

• Advantages
  ▫ Calcineurin inhibitor, similar to cyclosporine
  ▫ lower incidence of acute rejection than cyclosporine?
  ▫ useful for refractory or chronic rejection
  ▫ less hyperlipidemia, hirsutism, gingival hypertrophy than cyclosporine

• Toxicity
  ▫ same as Cyclosporine A
  ▫ more DM

• Current use
  ▫ primary immunotherapy, esp those at high risk
  ▫ for steroid resistant or refractory rejection

Sirolimus

• Advantages
  ▫ No neurotoxicity
  ▫ Less nephrotoxicity
  ▫ synergistic with cyclosporine, tacrolimus
  ▫ ? effective without calcineurin inhibitor

• Toxicity
  ▫ Hyperlipidemia, thrombocytopenia, anemia
  ▫ Impaired wound healing, ulcers

• Current use
  ▫ “BLACK BOX WARNING” regarding HAT following liver transplantation
Azathioprine

- **Mechanism of action**
  - antimetabolite, inhibits lymphocyte proliferation (purine synthesis)
- **Toxicity**
  - marrow: esp neutropenia, thrombocytopenia
  - liver: cholestasis
- **Current use**
  - rarely used
  - added to reduce calcineurin inhibitor
  - added for rejection despite adequate calcineurin inhibitor levels

Polyclonal Antibodies

- Antibodies that bind to more than one specific target

- Examples:
  - Thymoglobulin

- Toxicity
  - Leukopenia, thrombocytopenia, fever

- Use
  - Induction, acute rejection tx
Monoclonal Antibodies

- Antibodies that bind a single, specific target

- Daclizumab, basiliximab
  - IL-2 receptor antagonist
  - Used in induction

- OKT-3
  - T-cell receptor antagonist; induces T-cell lysis
  - For severe, steroid-resistant rejection
  - Can cause fever, chills, resp distress, hypotension
Question

- Which of the following immunosuppressant medications does not cause nephrotoxicity?
  - 1) Corticosteroids
  - 2) Cyclosporine
  - 3) Tacrolimus
  - 4) Sirolimus
Risks of Immunosuppression

• Infection
  ▫ Environmental pathogens
    • EBV, candida, RSV, adenovirus, aspergillus, PCP, etc
  ▫ Reactivation of previously controlled pathogens
    • CMV

• Infection Prophylaxis
  ▫ Vaccines: pneumococcal vaccine, Hep B vaccine
  ▫ Antibiotics: Septra (against URTI/UTI)
  ▫ Antivirals: acyclovir or others (CMV)
  ▫ Antifungals: nystatin or others (fungal)
Risks of Immunosuppression

• Malignancy
  ▫ Most common: skin, cervix
  ▫ Higher risk of virus-related cancers
    • HPV: cervical cancer
    • Hep B/C: hepatoma
    • HHV8: Kaposi’s sarcoma
    • EBV: lymphoma (aka post-transplant lymphoproliferative disorders or PTLDs) – in this case, tx is usually only removing immunosuppression

• Toxicities (agent-specific)

http://www.thefreedictionary.com/transplant
The Post-Transplant Patient

- At risk of graft rejection
- At 10x risk of malignancy, compared to controls
- At risk of infection
- At higher risk of CAD (cyclosporine & steroids worsen atherosclerosis)

- Most common causes of death after 1st year
  - Graft loss from chronic rejection
  - CV disease, infection
Question

• Immunosuppression given to patients post-transplant increase the risk of developing certain malignancies EXCEPT
  ▫ 1) Lymphoma
  ▫ 2) Endometrial adenocarcinoma
  ▫ 3) Squamous cell carcinoma
  ▫ 4) Kaposi’s sarcoma
The End...

"Doc, I think I need more of those anti-rejection pills. I'm still having a problem getting dates."

...phew!