Practical Aspects of Immunosuppression

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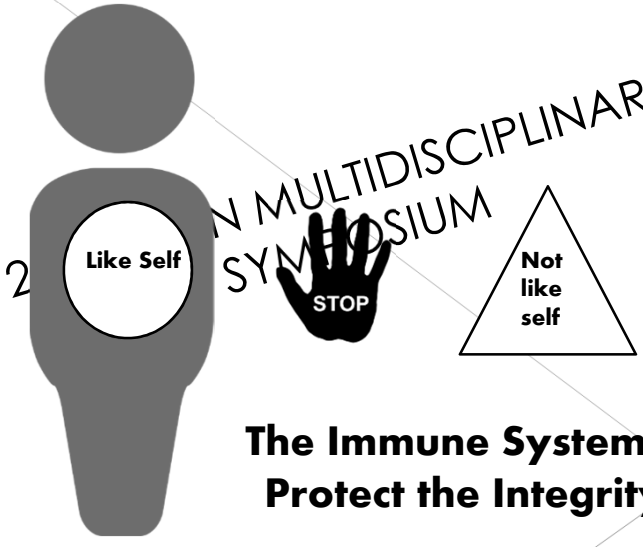
Goal:

- Enhance understanding of the common primary maintenance immunosuppressants, including monitoring, side effects, drug interactions and relevant clinical issues of significance.

Objectives:

- Identify the common "first line" maintenance immunosuppressant's and alternative medications.
- Recognize clinical issues related to specific immunosuppressant's and potential side effects for patients.

Immune Recognition



The Immune System Exists to Protect the Integrity of Self

Immunology in Kidney Transplants

- Immune system defends body against foreign substances (protects integrity of self)
  - Bacteria
  - Viruses
  - Transplanted tissues
- Goal with immunosuppression
  - Need to control body's immune system
  - Key component in promoting short and long term graft survival

Immunology in Kidney Transplants

- Immunosuppressive agents target different steps in rejection cascade.
  - Blocking T cell response
  - Activate other immunologic pathways
- Combing agents offers maximum protection

Overview of Immunosuppression

- Immunosuppressive agents
  - Induction
  - Desensitization
  - Primary immunosuppression

Induction Immunosuppression

- Strong medications – used immediately post transplant or in the setting of acute rejection
  - Alemtuzumab (Campath ®)
  - Anti-thymoctye globulin (rabbit) (Thymoglobulin®)
  - Basiliximab (Simulect ®)
  - Methylprednisolone (Solumedrol ®)

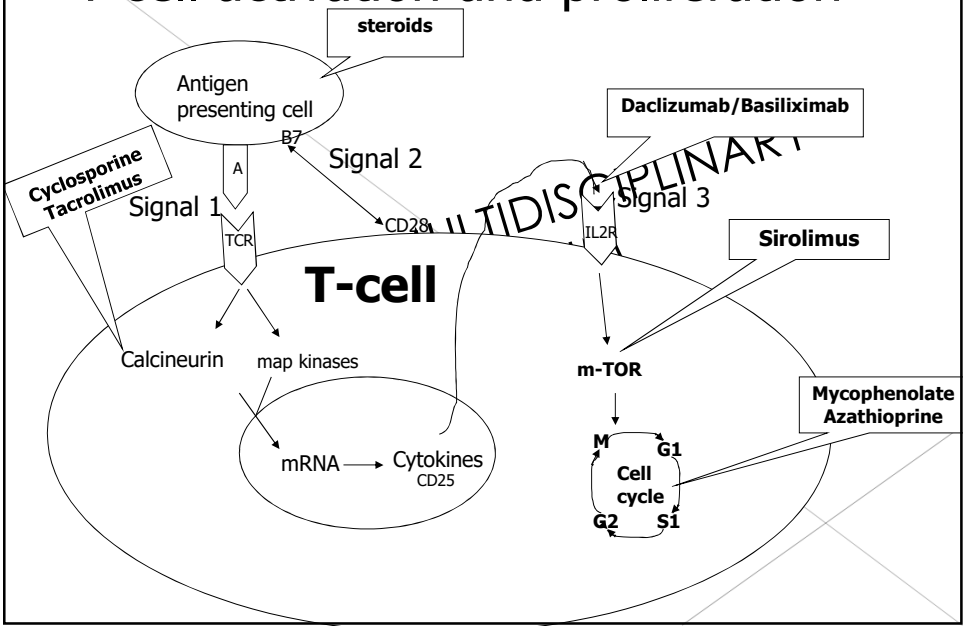
Desensitization

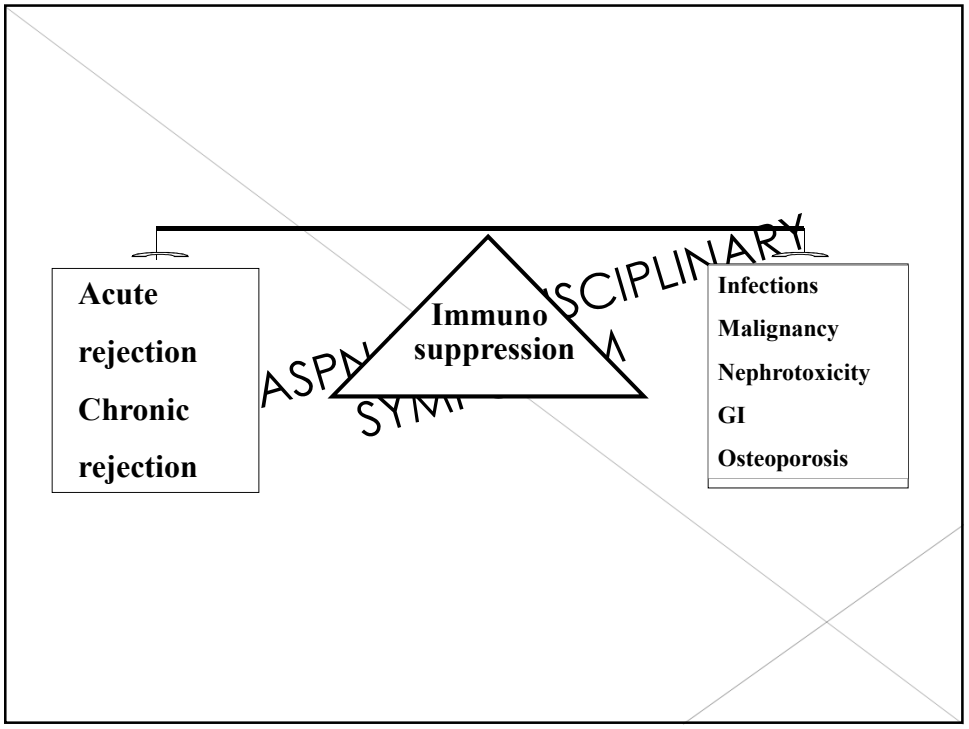
- Allows high risk patients more successful outcomes
  - IVIG monthly

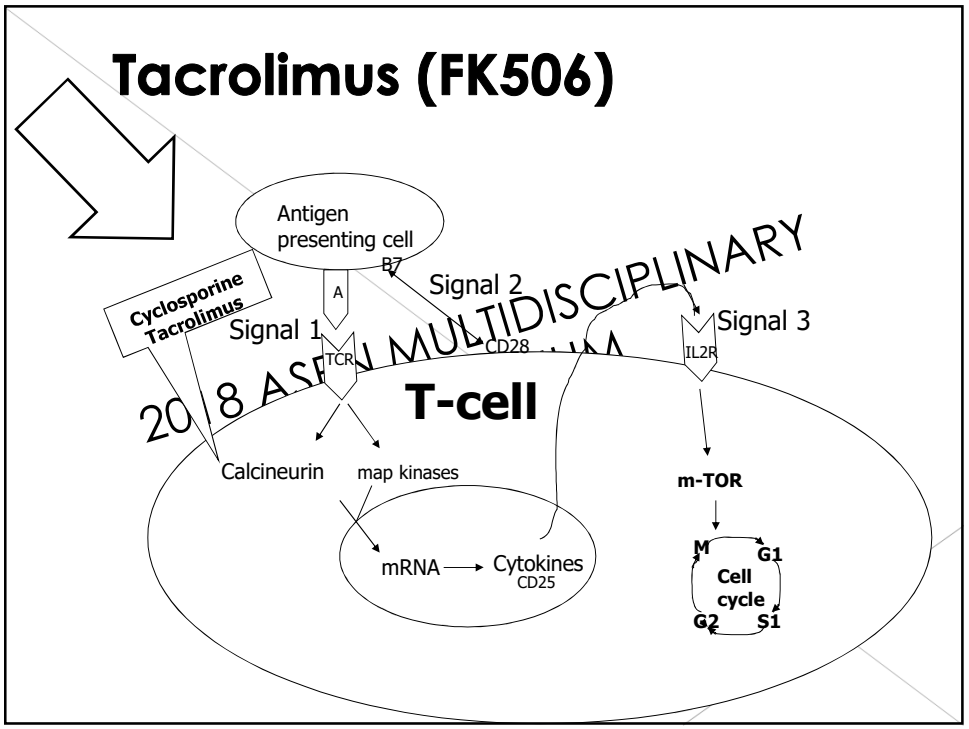
Primary (Maintenance) Immunosuppression

- Key to preventing rejection over the life of the transplant
- They are medications which will be used daily for the rest of an individual's life to prevent rejection
- Current approach typically utilizes tacrolimus for clinical protocols.
- Immediately following transplant immunosuppression levels are high to prevent rejection and reduced overt time as the graft stabilizes

T-cell activation and proliferation




Acute rejection
Chronic rejection
Immuno suppression
Infections
Malignancy
Nephrotoxicity
GI
Osteoporosis


Tacrolimus (FK506)
Antigen presenting cell
B7
A
Signal 2
Cyclosporine Tacrolimus
Signal 1
Signal 3
TCR
CD28
IL2R
T-cell
Calcineurin
map kinases
m-TOR
mRNA
Cytokines
CD25
M
G1
Cell cycle
G2
S1

Tacrolimus (FK506) (Prograf®, Hecoria®, Astagraf XL®, Sandoz®)

- Calcineurin Inhibitor
- Needs to be given at the same time every day (typically 12 hours, sometimes 8 hours for small children)
- Give the same way every day (with or without food)
- Monitor the brand of tacrolimus

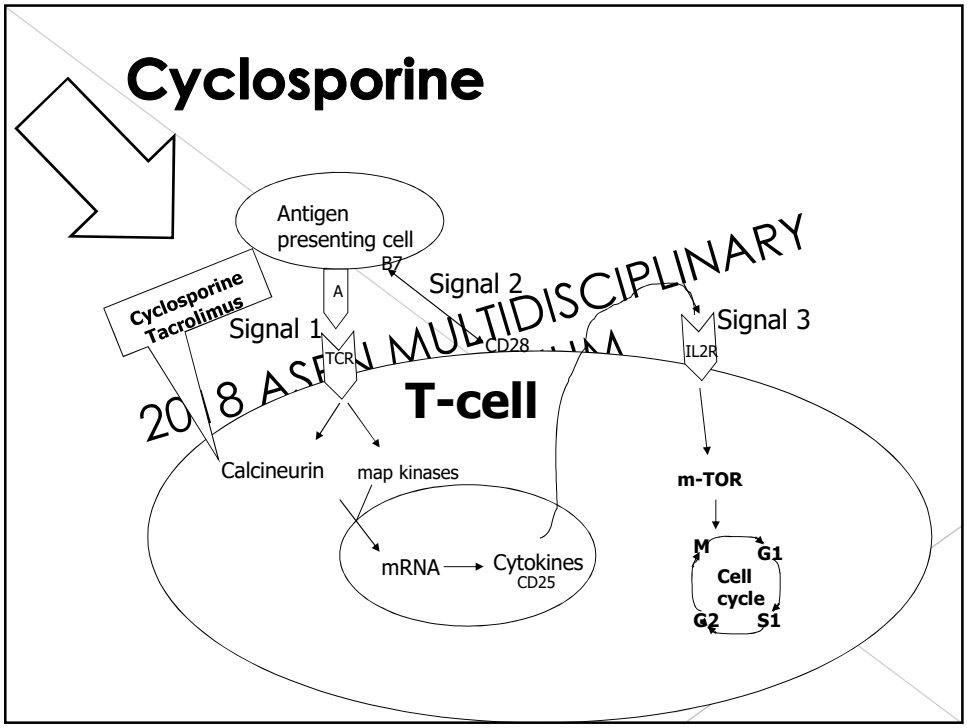
Tacrolimus

Side Effects

- Decreased magnesium levels
- Increased potassium
- Increased glucose
- Increase blood pressure
- Nephrotoxic
- Tremors
- Leg cramps
- Hair loss

Important Notes

- Agitate compound tacrolimus (must shake prior to each dose)
- NEVER give grapefruit or juices with grapefruit
- NEVER give fruit related to grapefruit
  - Pomelos
  - Tangelos



Cyclosporine (Gengraf®, Neoral ®, Sandimmune®)

- Calcineurin inhibitor
- Needs to be given at the same time every day (typically 12 hours, sometimes 8 hours for small children)
- Give the same way every day (with or without food)
- Monitor the brand of tacrolimus
- Neoral and Sandimmune are different drugs. **NEVER SWAP**

Cyclosporine

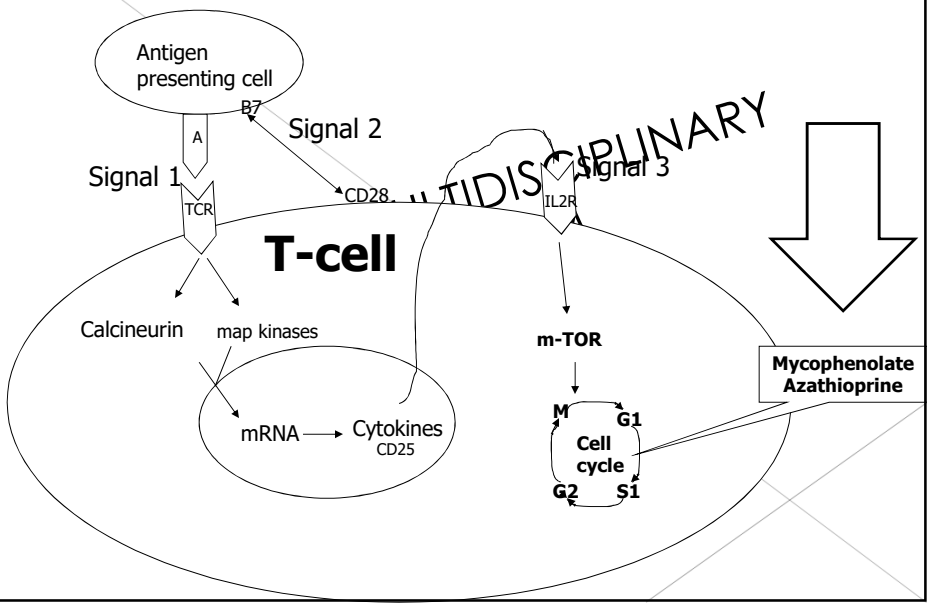
Side Effects

- Decrease magnesium levels
- Increased potassium levels
- Increase blood pressure
- Increased glucose
- Nephrotoxic
- Headaches
- Tremors
- Body hair growth
- Swollen gums

Important Notes

- NEVER give grapefruit or juice with grapefruit
- NEVER give fruit related to grapefruit
  - Pomelos
  - Tangelos

Azathioprine



Azathioprine (Imuran®)

- Antiproliferative agent
- Given once a day at the same time
- May be given with or without food –be consistent – may affect absorption
- When given with food may lessen GI symptoms

Azathioprine

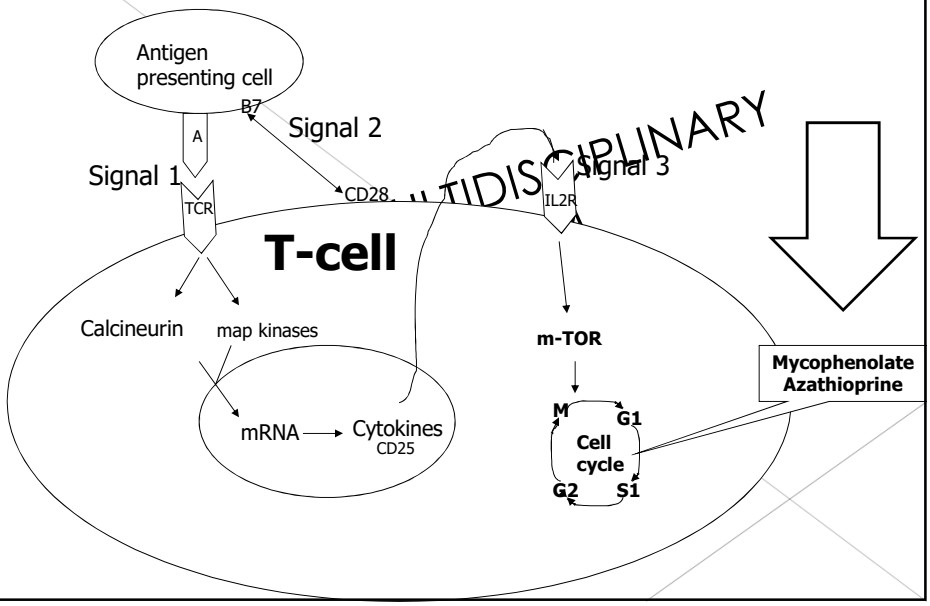
Side Effects

- Nausea, vomiting
- Decreased appetite
- Low platelet count
- Low WBC
- Low RBC
- Headaches
- Dizziness
- Hair loss
- Rash

Important Notes

- Often used when patients do not tolerate MMF due to diarrhea.

Mycophenolate



Mycophenolate (Cellcept®, Myfortic®)

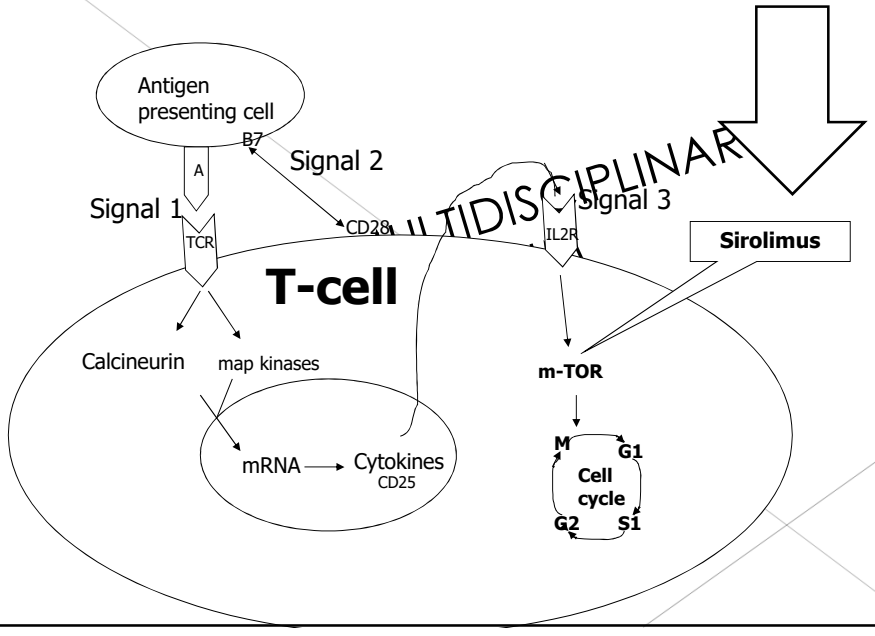
- Antiproliferative agent
- Give medication at the same time every day, 12 hours apart
- May be given with or without food. Be consistent – give the same way every day.
- Mycophenolate mofetil (Cellcept)and Mycophenolate sodium (Myfortic) **are DIFFERENT DRUGS – DO NOT SWAP**

Mycophenolate

Side Effects
- Stomach cramps, diarrhea
- Nausea, vomiting or heartburn
- Low platelet count
- Low WBC
- Low RBC
- Headaches
- Birth defects to unborn fetus (Need two forms of birth control)

Important Notes
- Given with food helps prevent GI upset
- If patient is experiencing diarrhea switch drug to Myfortic (enteric coating- less GI irritation)
- REMS education

Sirolimus



Sirolimus (Rapamune®)

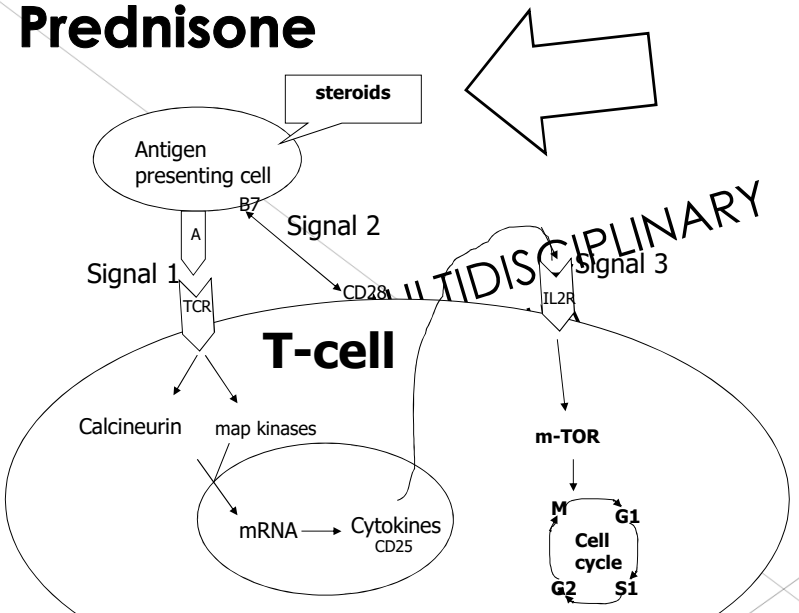
- Antiproliferative agent
- Typically given once a day; however, some individuals may require BID dosing
- May be given with or without food. Be consistent – give the same way every day.

Sirolimus

Side Effects
- Upset stomach, vomiting or diarrhea
- Headaches
- High cholesterol/triglycerids
- Low WBC
- Mouth sores or ulcers
- Low RBC
- Low platelet count
- Delayed wound healing
- Ance
- Swelling
- Proteinuria
- Leg cramps

Important Notes
- NEVER give grapefruit or juices with grapefruit
- NEVER give fruit related to grapefruit
  - Pomelos
  - Tangelos

Prednisone



Prednisone/Prednisolone (Deltasone®, Orapred®, Pediapred®)

- Corticosteroid
- Typically given once a day
- Steroid withdrawal protocols

Prednisone

Side Effects
- Increased blood pressure
- Higher blood sugar
- Upset stomach
- Hunger
- Weight gain
- Edema
- Mood swings, irritability
- Difficulty sleeping
- Headache
- Acne
- Stretch marks

Important Notes
- Long term use may cause weaker bones, slower growth, cataracts

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