# Drug Interactions Post-transplant

# Objectives

- Explain the importance of identifying drug-drug interactions in caring for a transplanted organ
- Describe common types of drug-drug interactions
- Identify how some common drug-drug interactions may be managed

# Example Drug Interaction Screening

**Drugs in this analysis:** Bactrim; Fluconazole; Mycophenolate; NIFEdipine; OxyCODONE; Pantoprazole; PredniSONE; Tacrolimus (Systemic); Valcyte

**Drug-Drug Interactions**

- D Fluconazole – Tacrolimus (Systemic) *Depends on Dose and Route*
- C Bactrim (CYP2C9 Substrates) – Fluconazole (CYP2C9 Inhibitors (Moderate))
- C Fluconazole – NIFEdipine (Calcium Channel Blockers)
- C Fluconazole – Pantoprazole (Proton Pump Inhibitors)
- C Fluconazole – PredniSONE
- C Fluconazole (CYP3A4 Inhibitors (Moderate)) – OxyCODONE
- C Mycophenolate – Pantoprazole (Proton Pump Inhibitors) *Depends on Brand Name*
- C Mycophenolate – Valcyte (Ganciclovir-Valganciclovir)
- C NIFEdipine (Calcium Channel Blockers (Dihydropyridine)) – Tacrolimus (Systemic)
- B Bactrim (QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying)) – Tacrolimus (Systemic) (QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying))

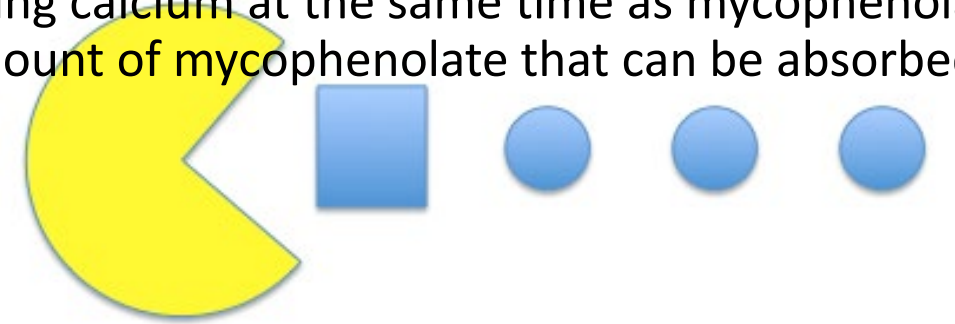
# Impact of Drug-Drug Interactions

- Highly dependent on medications involved and the severity of interaction
  - “Narrow therapeutic window”
- Can be serious, up to and including graft loss or death
- Many interactions do not impact a patient’s health

# Types of Drug-Drug Interactions

- Altered absorption


  - One medication lowers the body's ability to absorb another medication
    - Two medications are in the stomach/intestines at the same time and react with each other, making one less effective
    - Lowered acid levels in stomach make some medications harder to absorb

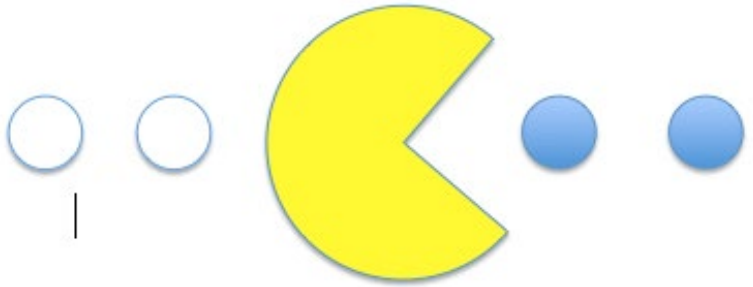



  - Example: taking calcium at the same time as mycophenolate (Cellcept) may lower the amount of mycophenolate that can be absorbed

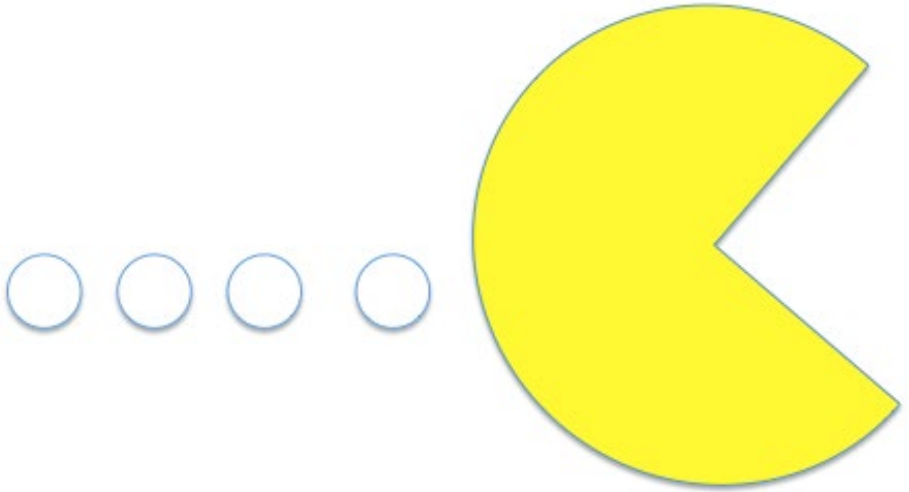
# Types of Drug-Drug Interactions

- Induction
  - One medication increases how quickly the body gets rid of another by increasing enzyme activity
  - Example: taking rifampin makes the body process tacrolimus (Prograf) more quickly, potentially lowering tacrolimus (Prograf) levels and causing rejection

Normal



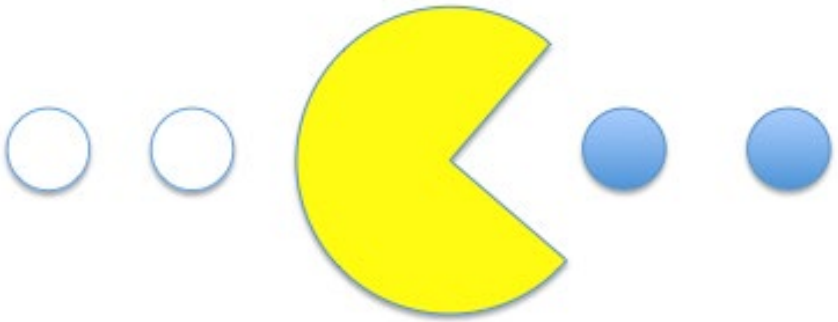
Induction



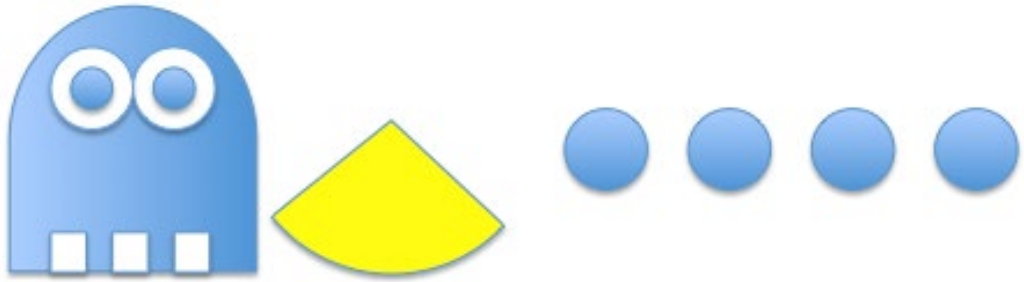
# Types of Drug-Drug Interactions

- Inhibition
  - One medication slows down how quickly the body gets rid of another, usually by competing for the same enzyme
  - Example: starting voriconazole (Vfend) while taking cyclosporine (Neoral, Gengraf) can greatly increase cyclosporine levels

Normal



Inhibition



# Example Drug Interaction Screening

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# Common Interaction Examples

- Fluconazole (Diflucan) and tacrolimus (Prograf)
  - Type: inhibition
  - Affected medication: tacrolimus
  - Potential impact: increased tacrolimus levels, possibility of toxicity
  - How to minimize impact: monitor tacrolimus levels, adjust dose of tacrolimus if needed

# Common Interaction Examples

- Fluconazole (Diflucan) and nifedipine (Procardia, Adalat)
  - Type: inhibition
  - Affected medication: nifedipine
  - Potential impact: increased nifedipine efficacy, possibility of developing low blood pressure, which could lead to dizziness or fainting
  - How to minimize impact: monitor blood pressure/symptoms, adjust dose of nifedipine if needed

# Common Interaction Examples

- Mycophenolate (Cellcept) and pantoprazole (Protonix)
  - Type: altered absorption
  - Affected medication: mycophenolate
  - Potential impact: lower mycophenolic acid levels, possibility of rejection
  - How to minimize impact: no dose adjustment usually necessary, monitor for signs and symptoms of rejection (varies based on organ)
    - Could also stop pantoprazole if not absolutely needed

# Common Interaction Examples

- Nifedipine (Procardia, Adalat) and tacrolimus (Prograf)
  - Type: inhibition
  - Affected medication: tacrolimus
  - Potential impact: increased tacrolimus levels, possibility of toxicity
  - How to minimize impact: monitor tacrolimus levels, adjust dose if needed
    - Usually, no adjustment is needed

# What about other medications?

- Some medication classes are generally more likely to cause important interactions:
  - Antibiotics
  - Some blood pressure medications
  - Antacids and acid reducers
  - Anti-seizure medications
  - Non-steroidal anti-inflammatory medicaitons (NSAIDs)
    - Examples: ibuprofen (Motrin, Advil), naproxen (Aleve)

# Drug-Drug Interactions: Take-away messages

- Notify your physician or pharmacist **before** making any medication changes
  - Make sure there is a healthcare professional who knows every medication you take
  - This includes over-the-counter medications and herbals!
- If interactions exist, impact can be lowered by dose adjustment or monitoring of drug levels/other measurements

# Food and Herbal Interactions



# Objectives

- Discuss common food interactions and strategies to manage
- Discuss common herbal interactions and strategies to manage
- Explain why food and herbal interactions differ from drug interactions

# Foods can interact?

- Fruits and vegetables can interact with transplant medications
- Some herbal products may also have similar interactions
- An interaction is considered significant if it alters the therapeutic response
  - ❖Potential to put new organ at risk for rejection
  - ❖Toxic drug levels

# How Does Food Impact Medications?

- Drug-food interactions with medications can be similar to drug-drug interactions

- Transplant Recipients
  - Most frequent interactions affect the immune response

  - Some affect the ability of the drug to enter or exit the blood

# What Foods To Avoid?

- Some fruits and juices may interact with your immunosuppression
  - ❖Grapefruit and grapefruit juice
  - ❖Pomegranate and pomegranate juice
  - ❖Seville Oranges

# All in Moderation:

Grapes

Cranberries

Tangerines

Cauliflower

Broccoli

# Food-Drug Considerations

- **These are general recommendations. Follow any specific instructions from your doctor.**

- **Corticosteroids: prednisone, methylprednisolone**
  - To prevent retaining water
    - ❖Read food labels to pick the products lowest in salt
  - Limit the amount of processed foods
    - ❖Frozen dinners, packaged entrees, canned soups
    - ❖Restrict salted or smoked meat or fish
  - Avoid luncheon meats, bratwurst, and bacon

# Food-Drug Considerations

- **Corticosteroids: prednisone, methylprednisolone**
  - Increase your calcium intake
    - Milk and milk products are the best sources of calcium
  - Eat enough protein
    - Milk, meats, eggs, peanut butter and dried beans or peas
    - 2-3 protein servings a day

# Food-Drug Considerations

- Cyclosporine (Neoral®) and Tacrolimus (Prograf®)

  - These medicines can be taken with or without food
  - Do not eat grapefruit or drink grapefruit juice
  - Do not take extra potassium or use salt substitutes that contain potassium while taking this drug
  - Try to avoid taking with calcium, magnesium, antacids or supplements

# Food-Drug Considerations

- Sirolimus (Rapamune®) or Everolimus (Zortress®)
  - Either take with food or without food consistently
  - Do not eat grapefruit or drink grapefruit juice

# Food-Drug Considerations

- Mycophenolate (Myfortic®) (Cellcept®)
  - Take it with food to prevent stomach upset
  - Do not take with calcium, magnesium, antacids, or supplements

# Herbal Products

- St. John’s Wort
- Vitamin C
- Echinacea


# Herbal Products

## Ginseng


## Feverfew

# Herbal Products

- Herbal teas
  - Green tea – generally OK
  - Chamomile – possibly OK
  - Peppermint – possibly OK
  - Dandelion – possibly OK

# Avoiding Potential Interactions

- Monitoring of medication blood levels
  - Allows for a timely discovery of the interactions
  - Organ-saving interventions

- Keep your healthcare team informed
  - Talk with team before discontinuing or starting an over the counter supplement
  - Discuss any major changes in diet

# Foods and Herbals vs. Drugs – What's Different?

- Drugs
  - Well-studied in clinical trials
  - Purity and effectiveness requirements and control
  - Interaction data comes from high quality studies and many patients

- Foods and Herbals
  - Almost never studied in clinical trials
  - Herbals an generally be sold to consumers with minimal government oversight
  - Interaction data comes from  small sample sizes and might not be from human data

# Take Home Points

- Understanding possible food and herbal interactions are important
- Ask to speak with a dietician during your inpatient stay to learn about any necessary nutritional supplements
- Speak with your transplant pharmacist about specifics with your medication regimen
- Check with your transplant team before beginning any herbal supplements