



PROGRAM MATERIALS
Program #3292
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Medication Misadventures

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Medication Misadventures: Medical Malpractice From a Toxicologist's Perspective



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Learning Objectives

Identify **“red flags”** in a medical record that harm may have been done to a patient due to a medication

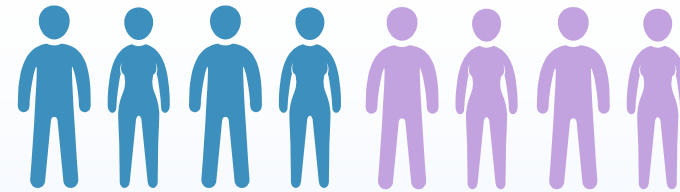
Cite **2 reasons** why safe dosages of a medication vary among patients

List **3 resources** for reliable, user-friendly drug information

Some Prescription Statistics...



50%



of adults in the US have taken at least one prescription drug in the past 30 days²

Top 3: analgesics, antidepressants, antihyperlipidemic agents²

Some Prescription Statistics...



According to the FDA,
up to

1.3 million
patients

each year are harmed by preventable
medication errors

MEDICATION MISADVENTURES: WHEN DO THEY OCCUR?

When the medication is...

- Ordered
- Verified
- Dispensed
- Administered

Possibly resulting in...

- Drug overdose
- Drug interactions
- Harm due to patient receiving the wrong drug
- Harm from medications during surgery

1. Limitations of the Medical Chart



Chart documentation...only part of the story

- Many medication errors go undocumented and unreported
- What about the “just-cause” safety culture?

1. Limitations of the Medical Chart

A bit more detective work...

- Patient compliance. Was the patient taking the medication as prescribed?
- Do we have all the records?
Multiple pharmacies?



2. Right Medication...Right Patient?



- To start with, was the patient given the right drug?
- Were there medical conditions that could make a drug less tolerable or worsen a pre-existing disease?

2. Right Medication...Right Patient?

Were there clinically significant drug-drug interactions?

-----DRUG INTERACTIONS-----

- Co-administration of ZEPATIER with moderate CYP3A inducers is not recommended as they may decrease the plasma concentration of ZEPATIER. (7)
- Co-administration of ZEPATIER with certain strong CYP3A inhibitors is not recommended as they may increase the plasma concentration of ZEPATIER. (7)
- Consult the full prescribing information prior to and during treatment for potential drug interactions. (4, 5.3, 7, 12.3)

2. Right Medication...Right Patient?

Drugs that should be red flags for potential drug interactions:

- *Antiseizure drugs* (eg, phenytoin, carbamazepine, valproic acid)
- *Warfarin*
- *Fluoroquinolone antibiotics*
- *NSAIDs* (non-steroidal anti-inflammatory drugs)
- *Selective serotonin reuptake inhibitors* (SSRIs) (eg, fluoxetine, paroxetine, sertraline)
- *Lithium*

3. Right Dose?

How dose is determined for an individual patient:



Kidney function



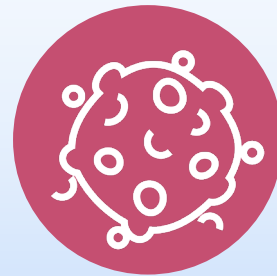
Liver function



Weight



Other drugs



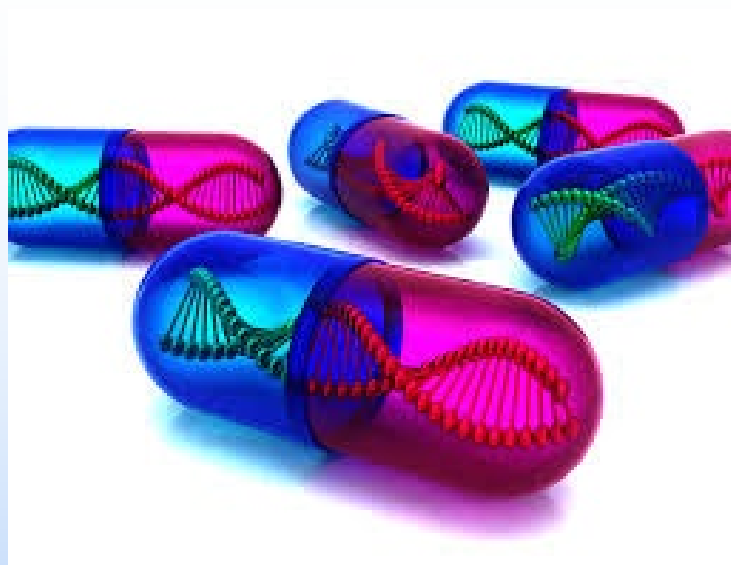
Disease states



Genetic factors

Pharmacogenomics: Risk for Drug Toxicity

- Genetic factors – which drugs do we have these data for?
- Some genetic conditions interfere with the body's ability to break down certain types of drugs



-----DOSAGE AND ADMINISTRATION-----

	Initial Dose	Recommended Dose	Maximum Dose
Schizophrenia – adults (2.1)	10-15 mg/day	10-15 mg/day	30 mg/day
Schizophrenia – adolescents (2.1)	2 mg/day	10 mg/day	30 mg/day
Bipolar mania – adults: monotherapy (2.2)	15 mg/day	15 mg/day	30 mg/day
Bipolar mania – adults: adjunct to lithium or valproate (2.2)	10-15 mg/day	15 mg/day	30 mg/day
Bipolar mania – pediatric patients: monotherapy or as an adjunct to lithium or valproate (2.2)	2 mg/day	10 mg/day	30 mg/day
Major Depressive Disorder – Adults adjunct to antidepressants (2.3)	2-5 mg/day	5-10 mg/day	15 mg/day
Irritability associated with autistic disorder – pediatric patients (2.4)	2 mg/day	5-10 mg/day	15 mg/day
Tourette's disorder – (2.5)	Patients <50 kg	2 mg/day	5 mg/day
	Patients ≥50 kg	2 mg/day	10 mg/day
Agitation associated with schizophrenia or bipolar mania – adults (2.6)	9.75 mg/1.3 mL injected IM		30 mg/day injected IM

- Oral formulations: Administer once daily without regard to meals (2)
- IM injection: Wait at least 2 hours between doses. Maximum daily dose 30 mg (2.5)
- Known CYP2D6 poor metabolizers: Half of the usual dose (2.7)

3. Right Dose?

- Drugs with very “narrow therapeutic indexes”

What does this mean and which drugs have this	
• <i>Carbamazepine</i>	• <i>Lithium</i>
• <i>Cyclosporine</i>	• <i>Phenytoin</i>
• <i>Digoxin</i>	• <i>Warfarin</i>

4. Antidotes: Why are They in the Chart?

- Purpose of an antidote
 - Adverse drug reaction
 - Overdose



4. Antidotes: Why are They in the Chart?

Examples of antidotes (and what drugs they target)

- *Naloxone – opioid narcotics*
- *Flumazenil – benzodiazepines*
- *Glucagon – beta blockers, calcium channel blockers**
- *Glucose – insulin**
- *Leucovorin – methotrexate*

*also many non-toxicology uses

4. Antidotes: Why are They in the Chart?

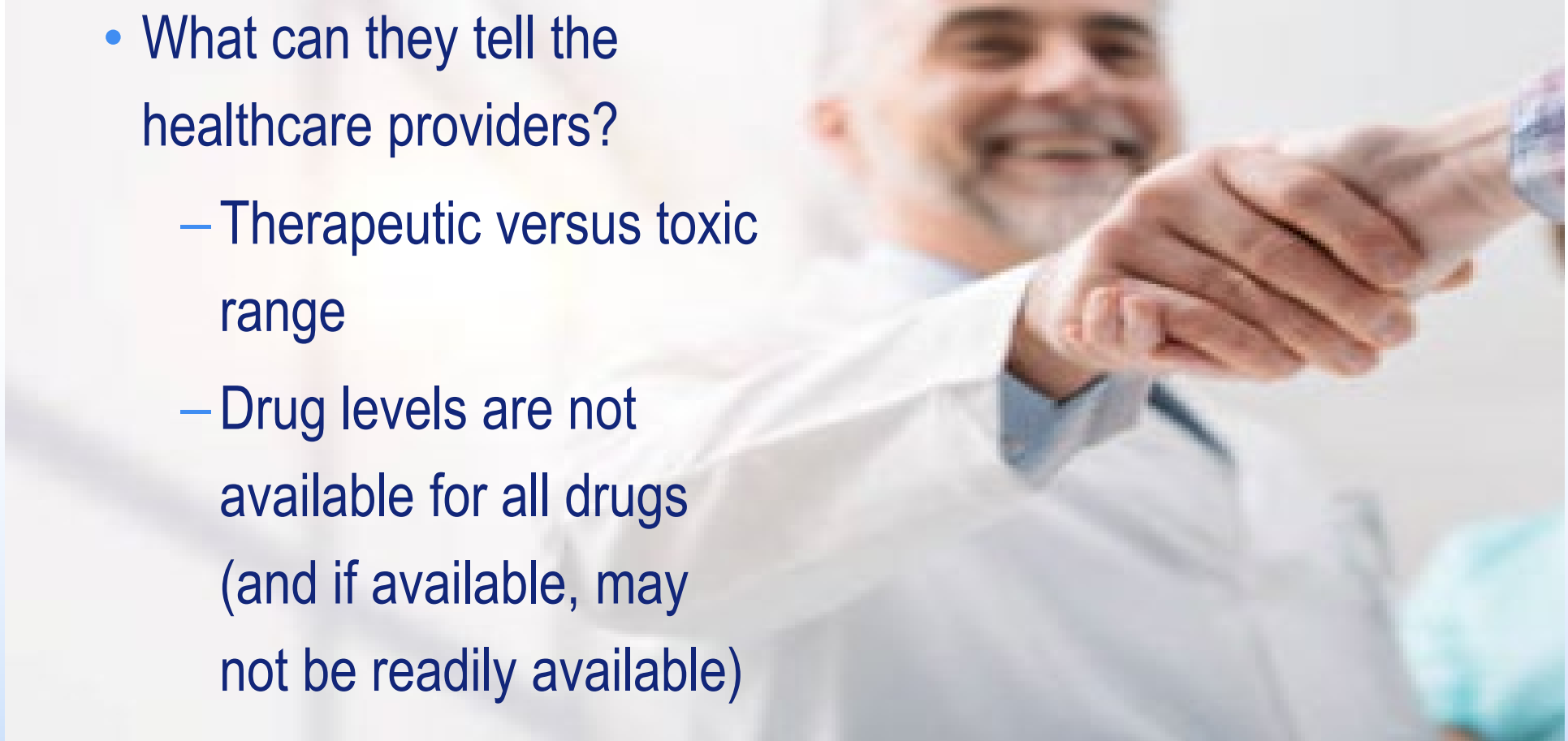
Examples of antidotes (and what drugs they target)

- *Vitamin K and fresh frozen plasma – warfarin*
- *Protamine sulfate – heparin*
- *Sodium bicarbonate – tricyclic antidepressants**
- *N-acetylcysteine – acetaminophen*
- *DigiFab® – Digoxin*

*also many non-toxicology uses

5. Drug Levels

- What can they tell the healthcare providers?
 - Therapeutic versus toxic range
 - Drug levels are not available for all drugs (and if available, may not be readily available)



5. Drug Levels



- Pitfalls when interpreting drug levels
 - “Normal range” is not necessarily “normal”

6. Older Adults and Medications: Safety

- High risk population (≥ 65 years old) for medication adverse events
- “BEERS list” from the American Geriatric Society: medications that are potentially inappropriate for older adults
(geriatricscareonline.org)



7. Check the Prescribing Information

- What is prescribing information?
- How can I find it?
 - Manufacturer's website
 - DailyMed.com (National Library of Medicine)
 - FDA.gov

7. Check the Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use KENGREAL safely and effectively. See full prescribing information for KENGREAL.

KENGREAL™ (cangrelor) for injection, for intravenous use
Initial U.S. Approval: 2015

INDICATIONS AND USAGE

KENGREAL is a P2Y₁₂ platelet inhibitor indicated as an adjunct to percutaneous coronary intervention (PCI) for reducing the risk of periprocedural myocardial infarction (MI), repeat coronary revascularization, and stent thrombosis (ST) in patients in who have not been treated with a P2Y₁₂ platelet inhibitor and are not being given a glycoprotein IIb/IIIa inhibitor (1)

DOSAGE AND ADMINISTRATION

- KENGREAL is intended for administration via a dedicated IV line, only after reconstitution and dilution. (2.3)
- Administer 30 µg/kg intravenous (IV) bolus prior to PCI followed immediately by a 4 µg/kg/min IV infusion for at least 2 hours or duration of procedure, whichever is longer. (2.1)
- To maintain platelet inhibition after discontinuation of KENGREAL infusion, an oral P2Y₁₂ platelet inhibitor should be administered. (2.2)

DOSAGE FORMS AND STRENGTHS

Single-use 10 mL vial containing 50 mg KENGREAL as a lyophilized powder for reconstitution (3.0)

CONTRAINDICATIONS

- Significant active bleeding (4.1)
- Hypersensitivity to KENGREAL or any component of the product (4.2)

WARNINGS AND PRECAUTIONS

- Bleeding: Like other drugs that inhibit platelet P2Y₁₂ function, KENGREAL can increase the risk of bleeding (5.1)

ADVERSE REACTIONS

The most common adverse reaction is bleeding (5.1, 6.1)

To report SUSPECTED ADVERSE REACTIONS, contact The Medicines Company at 1-888-977-6326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Clopidogrel: Do not administer during KENGREAL infusion. (7.1)
- Prasugrel: Do not administer during KENGREAL infusion. (7.1)

Revised: 6/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Recommended Dosing
- 2.2 Transitioning Patients to Oral P2Y₁₂ Therapy
- 2.3 Preparation and Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

- 4.1 Significant Active Bleeding
- 4.2 Hypersensitivity

5 WARNINGS AND PRECAUTIONS

- 5.1 Bleeding

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

7 DRUG INTERACTIONS

- 7.1 Thienopyridines

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use

- 8.5 Geriatric Use

- 8.6 Renal Impairment

- 8.7 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

- 14.1 CHAMPION PHOENIX Trial
- 14.2 CHAMPION PCI and PLATFORM Trials

16 HOW SUPPLIED/STORAGE AND HANDLING

*Sections or subsections omitted from the full prescribing information are not listed.

8. Some Drugs Have Rare Toxicities

- Premarketing safety trials: take a look at the prescribing information for some prescription drugs
 - Most have 3,000 or less short-term patient exposures (and even less long-term ones)
- Just because a side effect isn't listed in the prescribing information as “common”, doesn't mean you should stop there

9. Drug Info Resources

- You will easily find sources of general drug information involving the drug in question via medical information websites, law firm websites, and professional resources
- Know the reputation of the source



9. Drug Info Resources

Requires subscription



TRUVEN HEALTH ANALYTICS 
MICROMEDEX SOLUTIONS

Free sources

Drug Information Portal (U.S. National Library of
Medicine): <http://druginfo.nlm.nih.gov/>

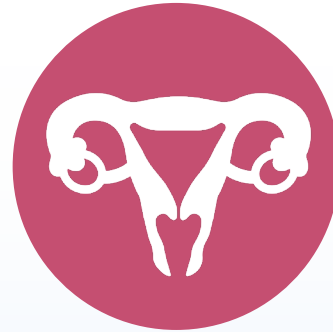
Medscape : <http://reference.medscape.com/>

10. Toxicologists: The Differences

Types of toxicologists



Clinical/Medical



Reproductive



Forensic

10. Toxicologists: Narrowing it Down



10. Finding a Toxicologist

How to find a toxicologist



Professional organizations for toxicologists
(American Academy of Clinical Toxicology, American College of Medical Toxicology)

Case Example #1

- 46 year-old woman stopped for erratic driving.
- Failed field sobriety test, low breath ethanol reading.
- Toxicology testing at the ER reveals:
 - blood ethanol: 0.04 g/dL
 - tramadol 0.27 mg/L
 - trazodone 0.49 mg/L



Case Example #2

- 26 year-old man on lithium presents to a clinic with nausea, vomiting, diarrhea of 3 days' duration.
- He is seen in the local ER the following day with tremor, confusion, and ataxia.
- A lithium level is drawn and hemodialysis is started.
- His lithium level is "low" but his neurological symptoms persist.



Case Example #3

- An woman is treated with fentanyl patches for pain following a workplace accident. She takes numerous antidepressants and alprazolam for anxiety.
- Her daughter calls EMS after not hearing from her for 2 days.



Case Example #4

- A 68 year-old woman is hospitalized for kidney stones.
- She receives morphine during her first 3 hospital days.
- You notice she received naloxone on day 4.





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