Medication Errors

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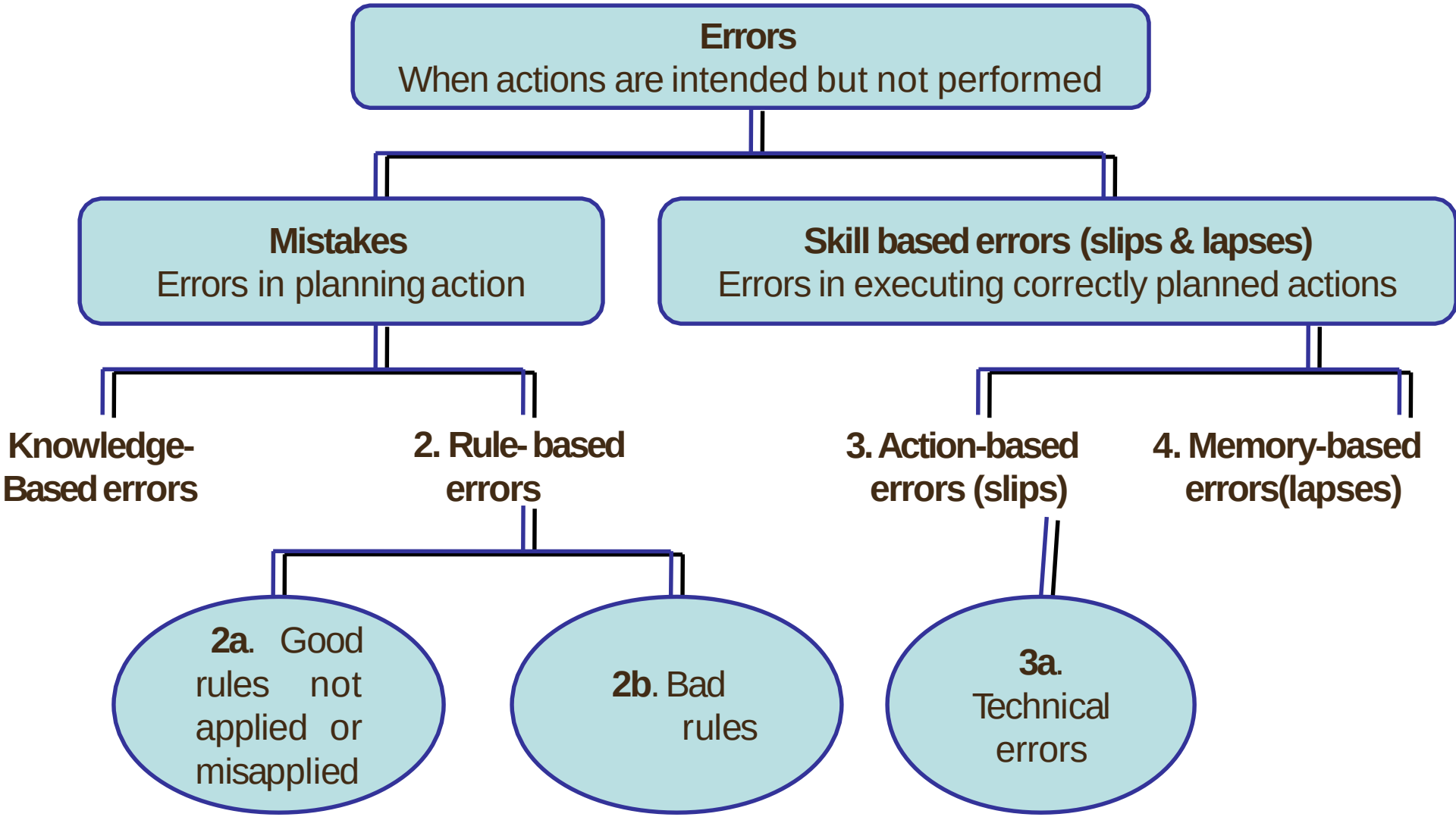
Epidemiology

- Interesting but horrifying fact-
  - More people in USA die in a given year as a result of medical errors than from motor vehicle accidents, breast cancers, or AIDS

- Majority are medication errors

- Indian study of paediatric intensive care unit reported 68.5% of all errors were medication errors

Classification



WHICH PATIENTS ARE MOST AT RISK OF MEDICATION ERROR?

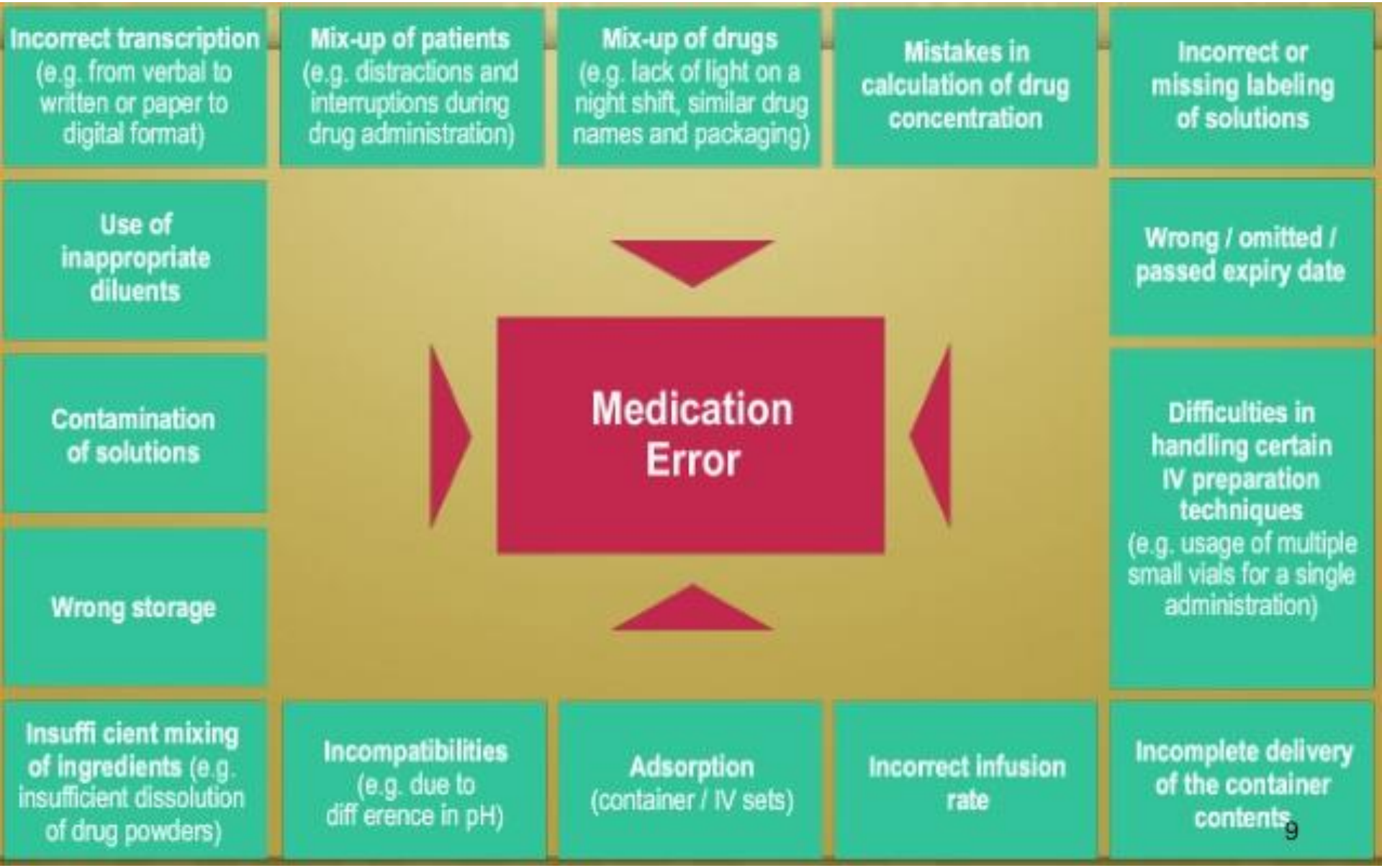
- Patients on multiple medications
- Patients with another condition, e.g. renal impairment, pregnancy
- Patients who cannot communicate well
- Patients who have more than one doctor
- Patients who do not take an active role in their own medication use
- Children and babies (dose calculations required)

World Health Organization WHO, Patient Safety Curriculum Guide

- Errors occur from-
  - Lack of knowledge
  - Unclear or erroneous labeling of drug
  - Misidentification of patient
  - Mental lapses or
  - Verification errors

- Errors committed by both experienced & inexperienced staff

Sources of Errors



Drug Compatibility

✓ Compatible (at Y-site only) | X Incompatible | ? Unknown

Numbers below refer to references. Symbols are explained immediately below the table.

	Aminophylline pH 8.8-10.0	Caffeine pH 2.0-3.0	Dobutamine pH 2.5-5.5	Dopamine pH 2.5-4.5	Fentanyl pH 4.0-7.55	Heparin pH 5.5-8.0	Indomethacin pH 6.0-7.5	Morphine pH 2.5-6.0	Prostaglandin E1	$NaHCO_3$ pH 7.0-8.5	IVN pH 5.5-6.5	Intralipid pH 5.5
Aminophylline pH 8.8-10.0		?	X 1	✓ 1	?	✓ +++ 1	?	✓ 12	✓ ++ 10 +	?	X 21	X 13
Caffeine pH 2.0-3.0	?		?	?	?	?	X 2	?	?	?	X 4	X
Dobutamine pH 2.5-5.5	X 1	?		✓ 1	?	? ***	X 11	✓ 5	?	X 1	✓ 20	?
Dopamine pH 2.5-4.5	✓ 1	?	✓ 1		?	✓ 1	X 11	✓ 1	✓ + 10	X 1, 3	✓ 20	?
Fentanyl pH 4.0-7.55	?	?	?	?		✓ 1	?	?	?	?	✓ 20	?
Heparin pH 5.5-8.0	✓ +++ 1	?	?	✓ 1	✓ 1		?	✓ * 6	✓ + 10	?	?	✓ # 1
Indomethacin pH 6.0-7.5	?	X 2	X 11	X 11	?	?		X 8, 9	?	X 11	X 11	X 8, 9
Morphine pH 2.5-6.0	✓ 12	?	✓ 5	✓ 1	?	✓ * 6	X 8, 9		✓ + 10	✓ 1, 18	✓ 20	? ** 15
Prostaglandin E1	✓ ++ 10 +	?	?	✓ + 10	?	✓ + 10	?	✓ + 10		?	?	X 7
$NaHCO_3$ pH 7.0-8.5	?	?	X 1	X 1, 3	?	?	X 11	✓ 1, 18	?		?	X
IVN pH 5.5-6.5	X 21	X 4	✓ 20	✓ 20	✓ 20	?	X 11	✓ 20	?	?		?
Intralipid pH 5.5	X 13	X	?	?	?	✓ # 1	X 8, 9	? ** 15	X 7	X	?	

Drug Shortages Cause Treatment Delays

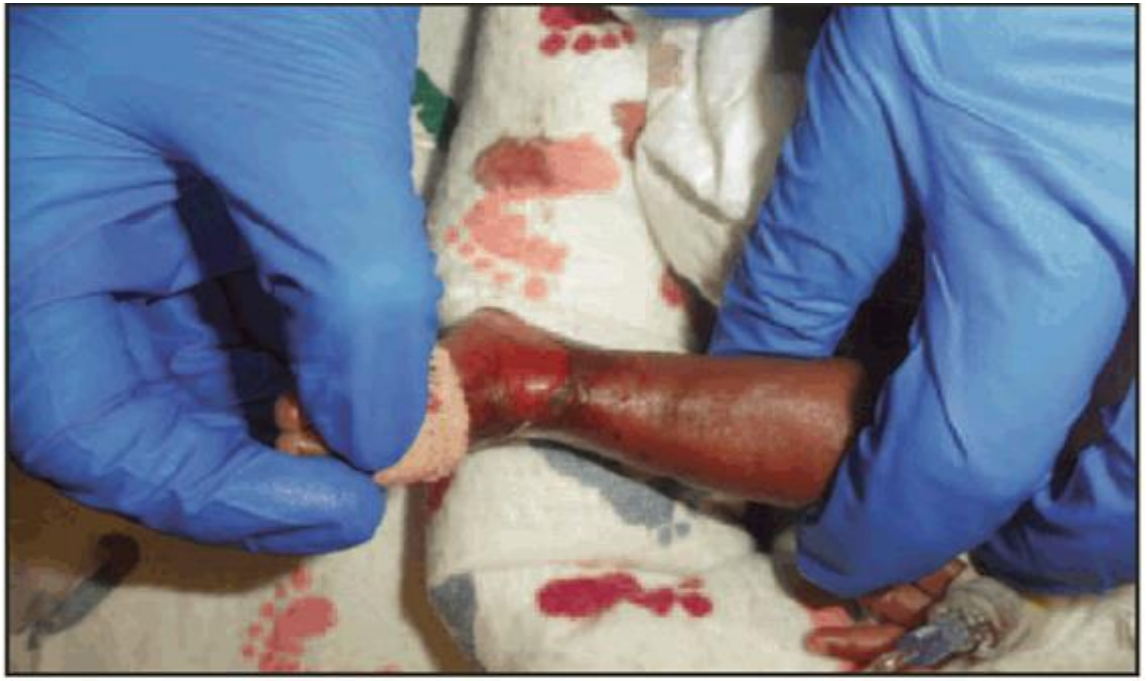
- Missed opportunities to immunize
- Delays for antimicrobials may be life-threatening
- Clinical trial enrollment delays – standard of care not available
- Treatment delays – survey of oncology practitioners in US – 83% say drug of choice not available, 75% had to switch patients to a potentially less effective agent.

J Natl Cancer Inst. 2012;104(12):891-892
AJHP. 2013;70(7):609-617
Clin Infect Dis. 2012;54(5):684-691
NEJM 2013;369(25):2463-2464

Drug Shortages Cause Adverse Patient Outcomes

Zinc shortage results in dermatitis for premature infants.

Children’s National Hospital, United States



Photo/S.A. Norton, Children's National Medical Center

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6207a5.htm

Case #1

LF is a 63 yom with a h/o asthma, DM, HTN, HLD, and PVD who presents with unstable angina and is going to go for PCI with probable stent placement. He started on antiplatelet before the PCI and was discharged without antiplatelet.

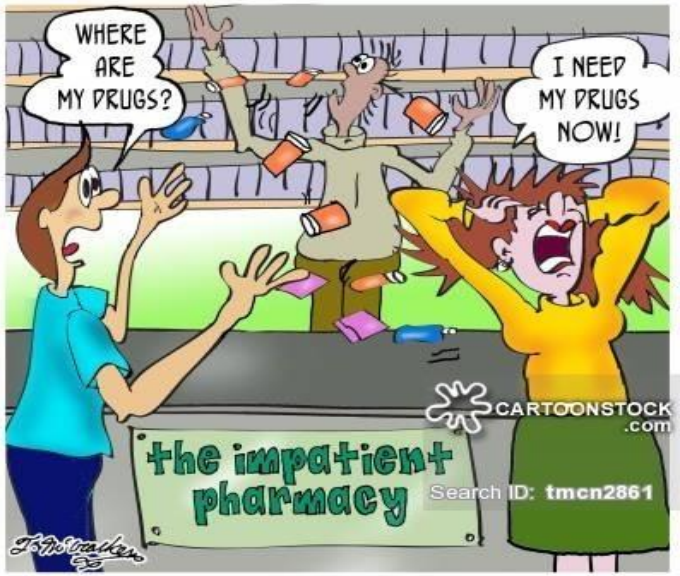
The patient died after 1 week of discharge

HOW CAN PRESCRIBING GO WRONG?

- Inadequate knowledge about drug indications and contraindications
- Not considering individual patient factors, such as allergies, pregnancy, co-morbidities, other medications
- Wrong patient, wrong dose, wrong time, wrong drug, wrong route
- Inadequate communication (written, verbal)
- Documentation - illegible, incomplete, ambiguous
- Mathematical error when calculating dosage
- Incorrect data entry when using computerized prescribing e.g. duplication, omission, wrong number

Dispensing errors

- Receipt of the prescription → supply of a dispensed medicine to patient
- Occurs primarily with drugs having similar name or appearance
- Example :lasix® (frusemide) and losec®(omeprazole)
- Other potential dispensing errors include
  - wrong dose P
  - wrong drug M
  - wrong patient



At the Impatient Pharmacy


NDC 50111-326-01
HydrALAzine Hydrochloride Tablets, USP
50 mg
Rx only
100 Tablets
Sidmak
NDC 50111-307-01
HydrOXYzine HCl Tablets, USP
10 mg
Rx only
100 Tablets
Sidmak


PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
cefTAZIDIME 2g
Sandoz®
ceftazidime powder for injection 2g
1 vial
CAREFUL!
CHECK
FOR MEDICINES WITH SIMILAR NAMES
I.V.
Each vial contains 2g ceftazidime (as ceftazidime pentahydrate).
AUST R 90916
SANDOZ
PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
cefEPIME 2g
Sandoz®
cefepime powder for injection 2g
1 vial
CAREFUL!
CHECK
FOR MEDICINES WITH SIMILAR NAMES
I.M. / I.V.
Each vial contains 2.0g cefepime (as hydrochloride)
AUST R 171734
SANDOZ


NDC 0093-7173-01
GABAPENTIN Tablets
600 mg
New Tablet Appearance
Each tablet contains: Gabapentin 600 mg
℞ only
100 TABLETS
TEVA
NDC 0093-0670-06
GEMFIBROZIL Tablets, USP
600 mg
Each tablet contains: Gemfibrozil, USP 600 mg
℞ only
60 TABLETS
TEVA

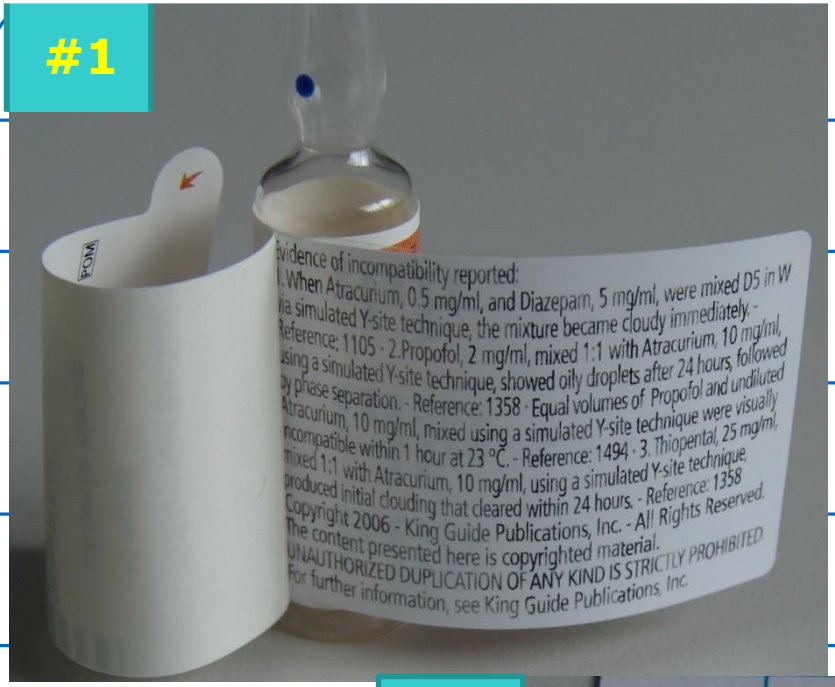

BAUSCH & LOMB
BAUSCH & LOMB
BAUSCH & LOMB
Cyclopentolate Hydrochloride Ophthalmic Solution USP 1%
Phenylephrine Hydrochloride Ophthalmic Solution USP 2.5%
Tropicamide Ophthalmic Solution USP 0.5%

HOW CAN ADMINISTRATION GO WRONG?

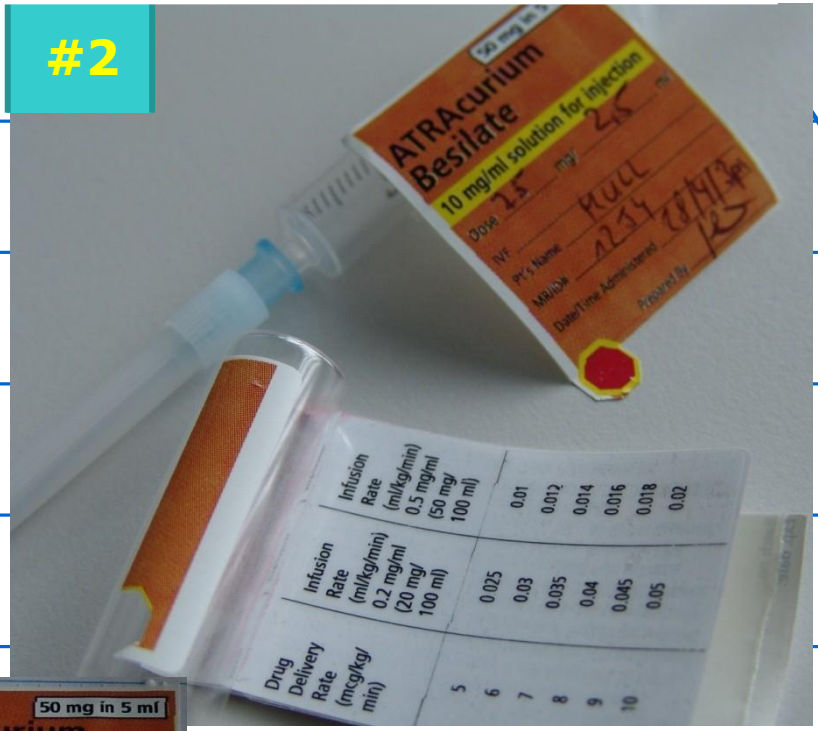
- Wrong patient
- Wrong route
- Wrong time
- Wrong dose
- Wrong drug
- Omission, failure to administer
- Inadequate documentation

“POINT OF USE” LABEL

#1

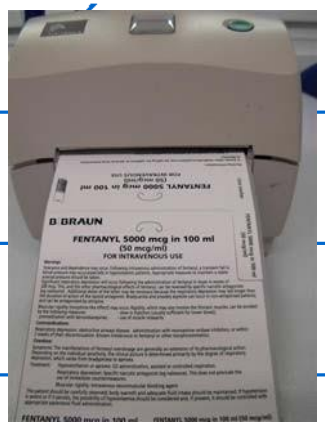


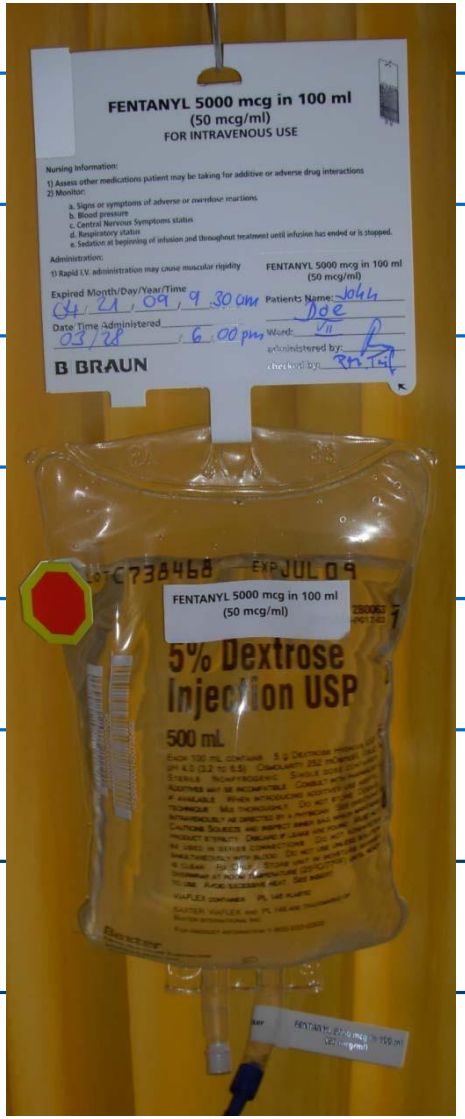
#2

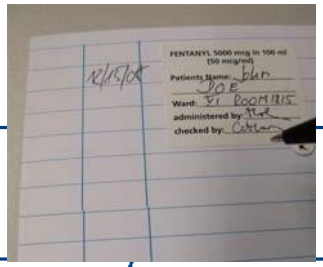


#3

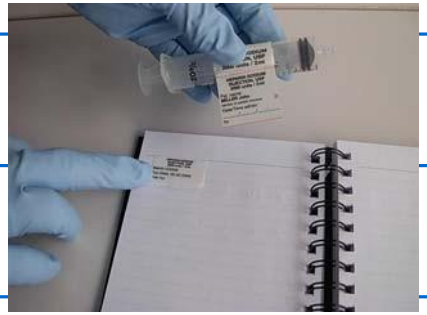
IV Compound Bag Label

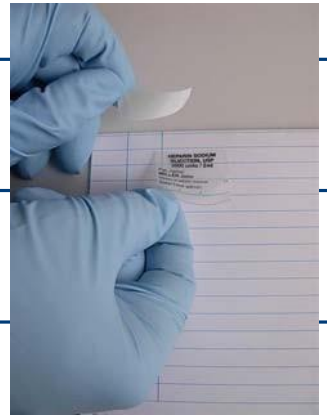






Compound Label for Syringe





IN WHAT SITUATIONS ARE STAFF MOST LIKELY TO CONTRIBUTE TO A MEDICATION ERROR?

- Inexperience
- Rushing, doing two things at once
- Interruptions
- Fatigue, boredom, being on “automatic pilot” leading to failure to check and double-check
- Lack of checking and double checking (including two-person checking) habits
- Poor teamwork and/or communication between colleagues
- Reluctance to use memory aids

World Health Organization WHO, Patient Safety Curriculum Guide

Anaphylaxis

- Acute, life-threatening allergic reactions involving multiple organ systems
  - Dermatologic
  - Respiratory
  - Gastrointestinal
  - Cardiovascular
- Accounts for 1500 deaths per year in the US
- Occurs within 30 minutes of exposure
- Monitor for late phase reaction for 12 hours

Case #2

AP is a 72 yof with a history of Chronic Fatigue, CHF, HTN and Fibromylagia.
Her medication allergies include asprin allergy. When asked she says it causes rash.

The ER physician gave her Ketrolac IV, she was discharged and after 45 minutes she had passed away.

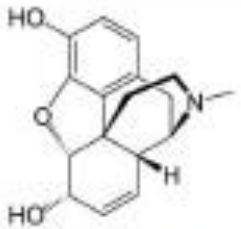
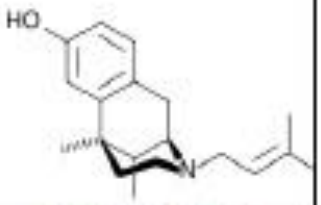
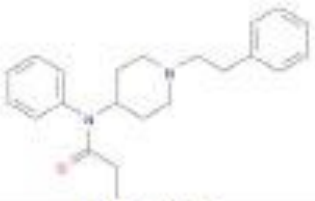
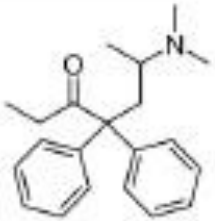
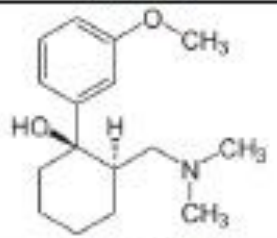
Table 2

Commonly Used NSAIDs by Chemical Structure

Chemical Class	Medications	Comments
Salicylic acid derivatives	Aspirin	Strong COX-1 inhibition
Propionic acid derivatives	Ibuprofen, naproxen, ketoprofen, oxaprozin	Strong COX-1 inhibition
Acetic acid derivatives	Indomethacin, sulindac, etodolac, ketorolac, diclofenac, nabumetone	Strong COX-1 inhibition
Para-aminophenol derivatives	Acetaminophen	Weak COX-1 inhibition
Enolic acid derivatives	Meloxicam, piroxicam	COX-2 inhibition > COX-1 inhibition
Selective COX-2 inhibitors	Celecoxib	Highly selective COX-2 inhibition

COX-1: cyclooxygenase-1; COX-2: cyclooxygenase-2; NSAID: nonsteroidal anti-inflammatory drug.
Source: Reference 2.

Chemical Classes of Opioids

PHENANTHRENES	BENZOMORPHANS	PHENYLPIPERIDINES	DIPHENYLHEPTANES	PHENYLPROPYL AMINES
				
MORPHINE	PENTAZOCINE	FENTANYL	METHADONE	TRAMADOL
Buprenorphine* Butorphanol* Codeine Dextromethorphan* Dihydrocodeine Heroin (diacetyl-morphine) Hydrocodone* Hydromorphone* Levorphanol* Methylnaltrexone** Morphine (Opium, conc) Nalbuphine* Naloxone* Naloxegol* Naltrexone** Oxycodone* Oxymorphone*	Diphenoxylate Loperamide Pentazocine	Alfentanil Fentanyl Meperidine Remifentanil Sufentanil **Illicit Fentanyl** Furanyl fentanyl Acetyl fentanyl Fluoro-fentanyl Carfentanil	Methadone Propoxyphene	Tapentadol Tramadol
CROSS-SENSITIVITY RISK				
PROBABLE	POSSIBLE	LOW RISK	LOW RISK	LOW RISK

*Agents lacking the 6-OH group of morphine, possibly decreases cross-tolerability within the phenanthrene group
**6-position is substituted with a ketone group and tolerability is similar to hydroxylation

Jeffrey Fudin, BSPharm, PharmD, DAIPM, FCCP, FASHP, FFSMB

http://paindr.com/wp-content/uploads/2018/02/Opioid-Structural-Classes-Figure_-updated-2018-02.pdf

Mitragynine (Kratom)

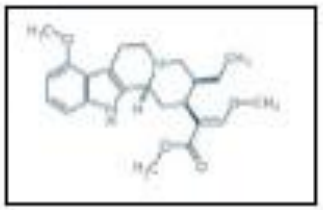


Table 1. NSAID Selectivity

More COX-1 Selective	Nonselective	5-50–fold COX-2 selective[a]	>50-fold COX-2 selective[a]
Ketorolac (Sprix, others)	Ibuprofen	Sulindac	Valdecoxib[b]
Flurbiprofen	Fenoprofen[c]	Diclofenac	Etoricoxib[d]
Ketoprofen	Sodium salicylate	Celecoxib (Celebrex)	Rofecoxib[b]
Indomethacin (Indocin, others)	Diflunisal	Meloxicam (Mobic, others)[e]	Lumiracoxib[d]
Aspirin		Etodolac	
Naproxen (Aleve, Naprosyn, others)			
Tolmetin			
Piroxicam (Feldene, others)			
Meclofenamate			

COX, cyclo-oxygenase; **FDA**, Food and Drug Administration; **NSAID**, non-steroidal anti-inflammatory drug

[a]Listed in order of increasing COX-2 selectivity

[b]Withdrawn from US market

[c]Equipotent for COX-1 and COX-2 selectivity

[d]At higher doses, COX-2 selectivity decreases and COX-1 inhibition is stronger than COX-2

[e]Not approved by the FDA

Case #2

JT is a 56 yom with a history of DM, HTN, and HLD.
He presents with MSSA bacteremia secondary to a diabetic foot infection. He has a history of penicillin allergy.

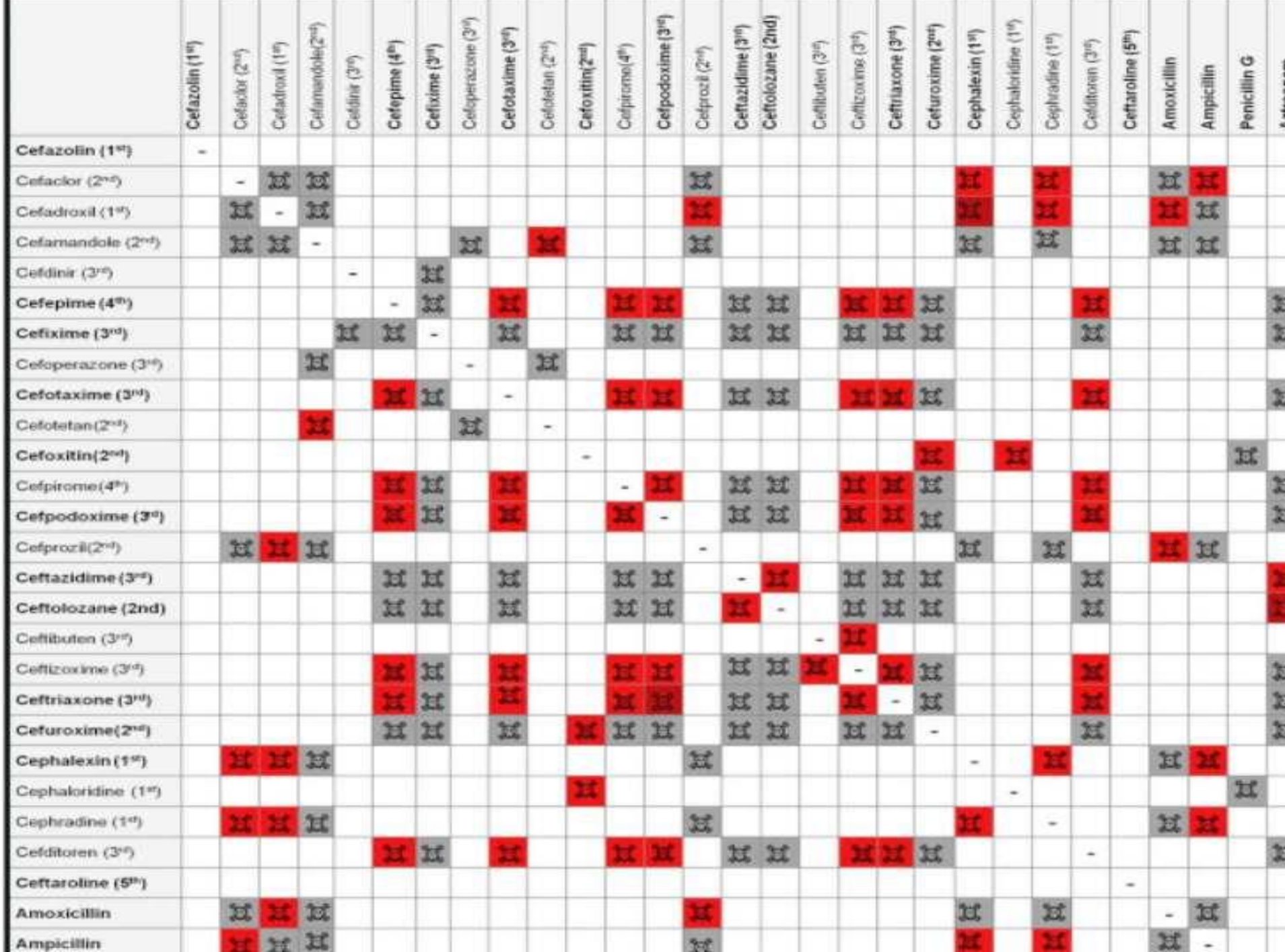
How would you manage his infection?

Cephalosporins

- Cross-reactivity with penicillin allergy is up to 10%
  - Higher incidence with 1st generation cephalosporins
  - Patients with negative skin test are at no higher risk than general population
- Management
  - Positive skin test – avoidance or desensitization
  - Mild reaction to penicillin – proceed with caution

Table 1: Penicillins and cephalosporins with similar side chains[7]

Similar C-7 Side Chain Cross reactions between agents within one group is possible		
Group 1	**Group 2**	**Group 3**
Penicillin	Amoxicillin	Cefepime
Cephalothin	Ampicillin	Ceftizoxime
Cephalodrine	Cefaclor	Cefpirome
Cefoxitin	Cephadrine	Cefotaxime
	Cephalexin	Cefpodoxime
	Cefadroxil	Ceftriaxone
	Cefatrizine	Cefetamet
		Cefeteram


Cefazolin (1st)
Cefaclor (2nd)
Cefadroxil (1st)
Cefamandole(2nd)
Cefdinir (3rd)
Cefepime (4th)
Cefixime (3rd)
Cefoperazone (3rd)
Cefotaxime (3rd)
Cefotetan (2nd)
Cefoxitin(2nd)
Cefpirome(4th)
Cefpodoxime (3rd)
Cefprozil (2nd)
Ceftazidime (3rd)
Ceftolozane (2nd)
Ceftibuten (3rd)
Ceftizoxime (3rd)
Ceftriaxone (3rd)
Cefuroxime (2nd)
Cephalexin (1st)
Cephaloridine (1st)
Cephradine (1st)
Cefditoren (3rd)
Ceftaroline (5th)
Amoxicillin
Ampicillin
Penicillin G

Similar side chains	Penicillin	Amoxicillin	Ampicillin	Cephalexin	Cefuroxime	Cefoxitin	Ceftriaxone	Cefotaxime	Cefepime	Ceftazidime
Penicillin						X				
Amoxicillin			X	X						
Ampicillin		X		X						
Cephalexin		X	X							
Cefuroxime						X	X	X		
Cefoxitin	X				X					
Ceftriaxone					X			X	X	X
Cefotaxime					X		X			X
Cefepime							X			
Ceftazidime							X	X		

Carbapenems

- Incidence of hypersensitivity 0.3-2.3%
- Cross-reactivity
  - Proven, suspected, or possible IgE mediated reaction to β lactams: 1.6 to 5.9%
  - Proven IgE mediated reaction to β lactams: 0.5%
  - Positive PCN skin test: 0.06 to 1.9%
  - Negative PCN skin test: no reaction
- Management
  - In patients with proven IgE mediated reactions to β-lactams, consider graded challenge in ICU

Ann Pharmacother 2009;43:304-15.
Clin Infect Dis 2014;59:1113-22.

Monobactams (Aztreonam)

- No clinical cross-reactivity between β-lactam antibiotics and aztreonam
- Exceptions:
  - Cystic fibrosis patients can develop sensitization reactions
  - Ceftazidime shares similar structure, use in caution with ceftazidime allergy

Ann Pharmacother 2009,43:304-15.

SULFONAMIDES

Sulfonamide-Associated Reactions

- Anaphylaxis
- Angioedema
- Erythema multiforme
- Flushing
- Photosensitivity
- Pustular eruption
- Urticaria
- Bullous eruption
- Erythroderma
- Fixed drug eruption
- Lupus erythematosus
- Psoriasis
- Vasculitis
- Exanthema
- Aphthous stomatitis
- Erythema nodosum
- Exfoliative dermatitis
- Sweet's syndrome
- Pruritus
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Serum sickness
- Hepatitis
- Hemolytic anemia

Allergy 1999;54 (Suppl 58):28-32.

Sulfonamides and Loop Diuretics

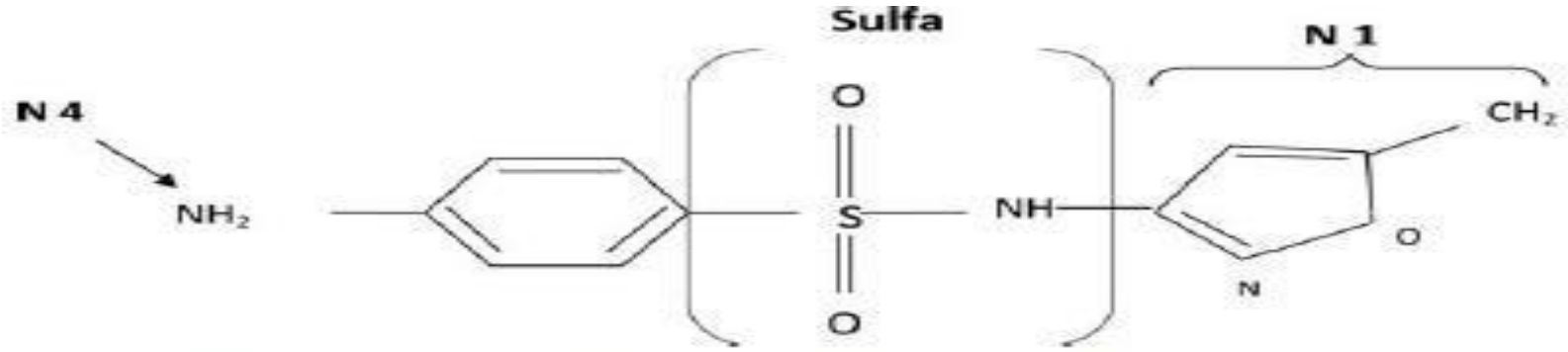


FIGURE 4. Sulfamethoxazole (SMX) molecule structure.

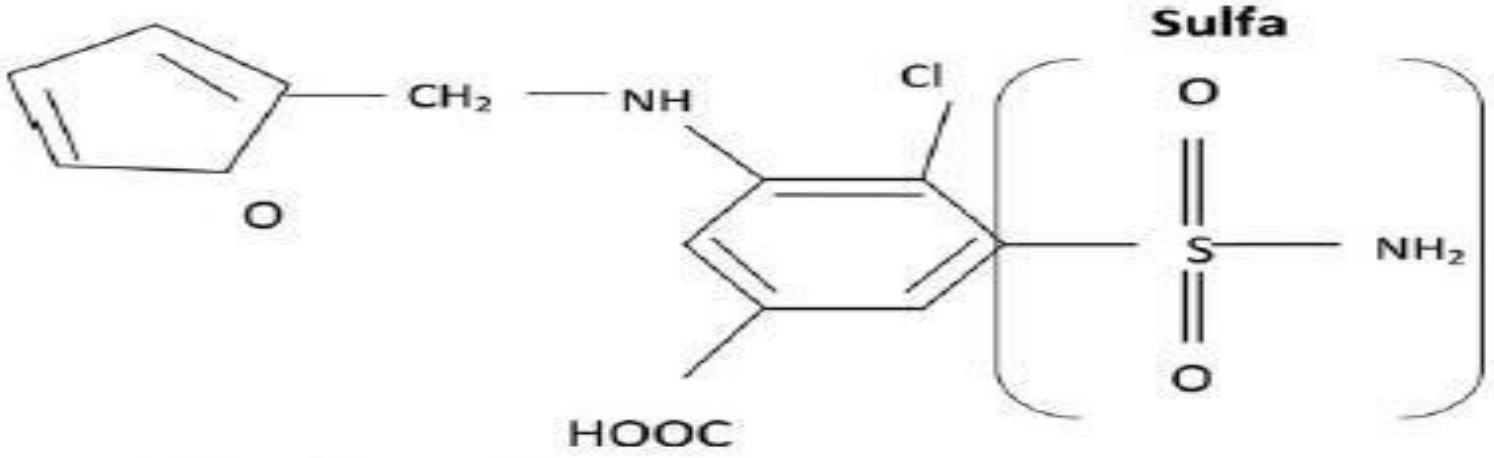


FIGURE 5. Furosemide molecule structure.

Journal of Hospital Medicine 2011;6(5):E1-E5.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Absence of Cross-Reactivity between Sulfonamide Antibiotics and Sulfonamide Nonantibiotics

Brian L. Strom, M.D., M.P.H., Rita Schinnar, M.P.A., Andrea J. Apter, M.D., David J. Margolis, M.D., Ph.D., Ebbing Lautenbach, M.D., M.P.H., M.S.C.E., Sean Hennessy, Pharm.D., Ph.D., Warren B. Bilker, Ph.D., and Dan Pettitt, D.V.M.

Cross-Reactivity of Sulfonamide Antibiotics and Nonantibiotics

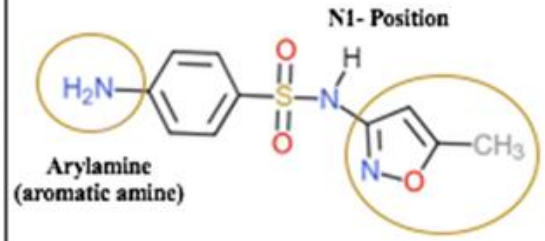
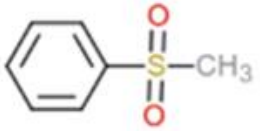
- Retrospective cohort study of 20,279 patients who received a sulfonamide antibiotic followed by a sulfonamide nonantibiotic within 60 days

Table 1. Sulfonamide Nonantibiotic Drugs.

Acetazolamide	Cyclopenthiazide	Glyburide	Probenecid
Acetohexamide	Dapsone	Glymidine	Quinethazone
Bendroflumethiazide	Diazoxide	Hydrochlorothiazide	Sulfasalazine
Benzthiazide	Dichlorphenamide	Hydroflumethiazide	Sulthiame
Bumetanide	Furosemide	Indapamide	Tolazamide
Chlorothiazide	Glibornuride	Mefruside	Tolbutamide
Chlorpropamide	Gliclazide	Methyclothiazide	Torsemide
Chlorthalidone	Glimepiride	Metolazone	Xipamide
Clopamide	Glipizide	Piretanide	
Clorexolone	Gliquidone	Polythiazide	

N Engl J Med 2003;349(17):1628-35.

History of "Sulfa Allergy"

Sulfonamide Nonantibiotic	Sulfonamide Antibiotic (Sulfonylarylamine)	Sulfate, Sulfite, Sulfur
		
Diamox® Neptazane™ Trusopt® Azopt® Cosopt® Furosemide	Sulfamethoxazole Sulfacetamide Sulfasalazine Sulfadiazine Blephamide® Bactrim® Septra®	Atropine Gentamycin Neomycin Timolol Polytrim® Amoxicillin
Low Risk of Cross-Reactivity **Eye doctors Can *Prescribe* With Caution**	High Risk of Cross-Reactivity **Do NOT Prescribe**	No Risk of Cross-Reactivity **No Concern With Prescribing**

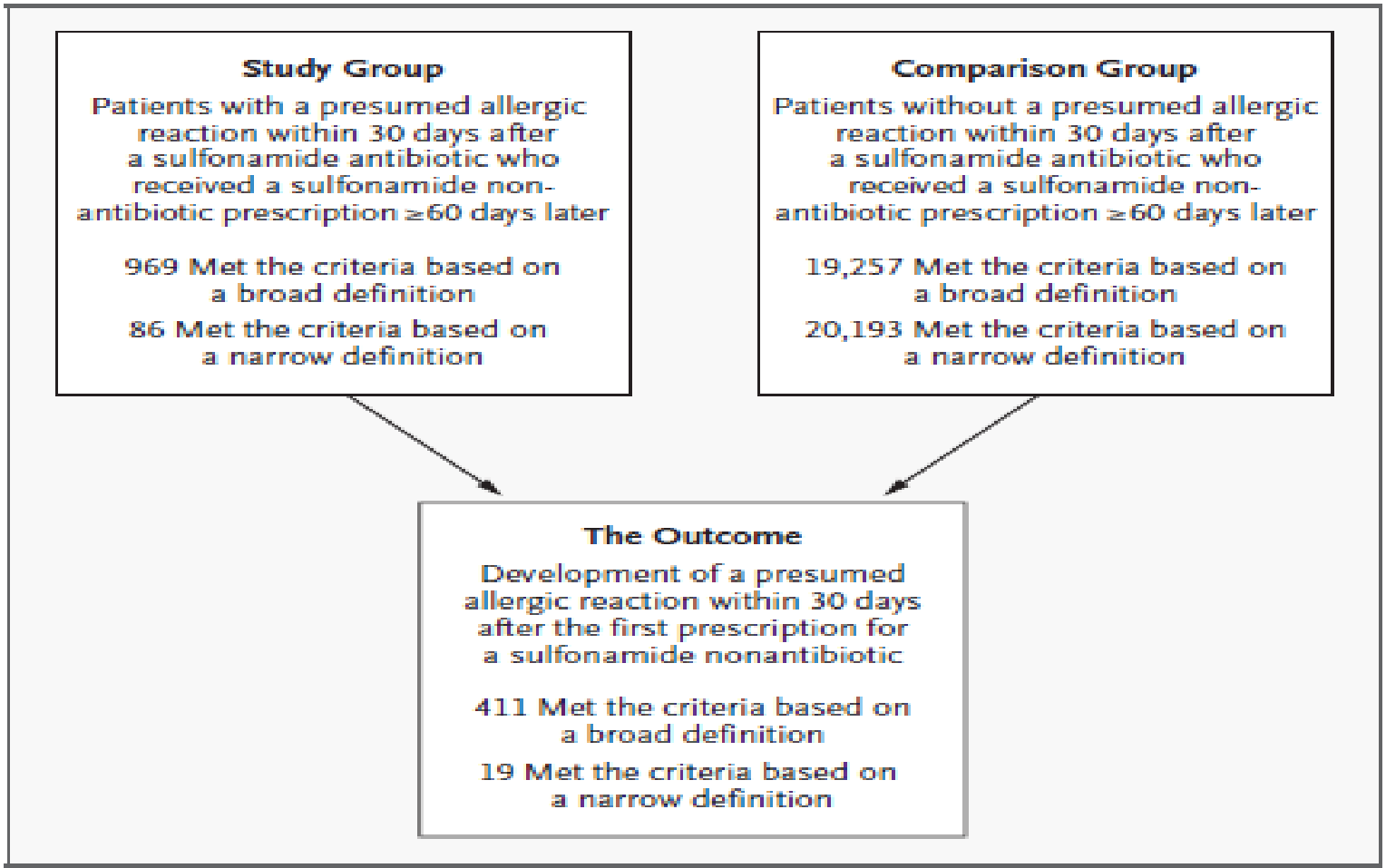


Figure 1. Primary Analysis of a Cohort of Patients Who Had Received a Sulfonamide Antibiotic and Who Subsequently Received a Sulfonamide Nonantibiotic.

A narrow outcome was defined by the occurrence of reactions such as urticaria, anaphylactic shock, erythema multiforme, and drug allergy. A broad definition also included asthma, eczema, and unspecified adverse effects of a drug. For a complete list, see Supplementary Appendix 1, available with the full text of this article at http://www.nejm.org.

Cross-Reactivity of Sulfonamide Antibiotics and Nonantibiotics

- Most common reactions observed
  - Asthma (70.1%)
  - Eczema (14.1%)
  - Adverse drug reaction (11.4%)
- 18 patients had symptoms consistent with type I hypersensitivity
- Previous reaction to a sulfonamide antibiotic was associated with a 2.8 times higher likelihood of having a reaction to the nonantibiotic
  - Similar risk was observed for patients with a sulfonamide allergy who received penicillin

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Ethacrynic Acid

- Non-sulfa loop diuretic
- Approx. $3000 per dose for IV
- 1:1 conversion from IV:PO
- Higher incidence of ototoxicity compared to other loop diuretics
- Reserve for patients with allergic reactions to loop diuretics