



# Pharmacology Considerations Across the Life-span

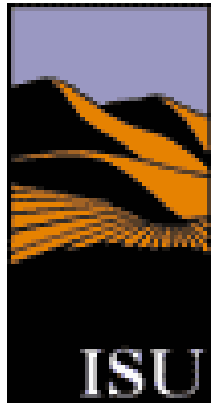
Roger Hefflinger, Pharm.D.

Associate Professor

Idaho State University

College of Pharmacy

Family Medicine Residency of Idaho



# Disclosure

- I have no fiscal connections to disclose with any of the manufactures of medications discussed during this presentation

# Objectives:

- Upon completion of this presentation the audience member shall be expected to:
  - Identify classes of medications that are more likely to have adverse events across the life-span
  - Organize therapy plans for appropriate management of various disease states across the life span
  - Modify existing therapy plans for more effective and potentially safer disease state management

# The “Life-Span”

- Fetal Development
  - First Trimester
  - Second Trimester
  - Third Trimester
- Gestational Issues
- Perinatal Issues
- Infant
- Toddler
- Adolescent
- Puberty
- Adult
  - Organ System Failure
    - Renal
    - Liver
- Geriatrics
- End of Life
  - Hospice Care

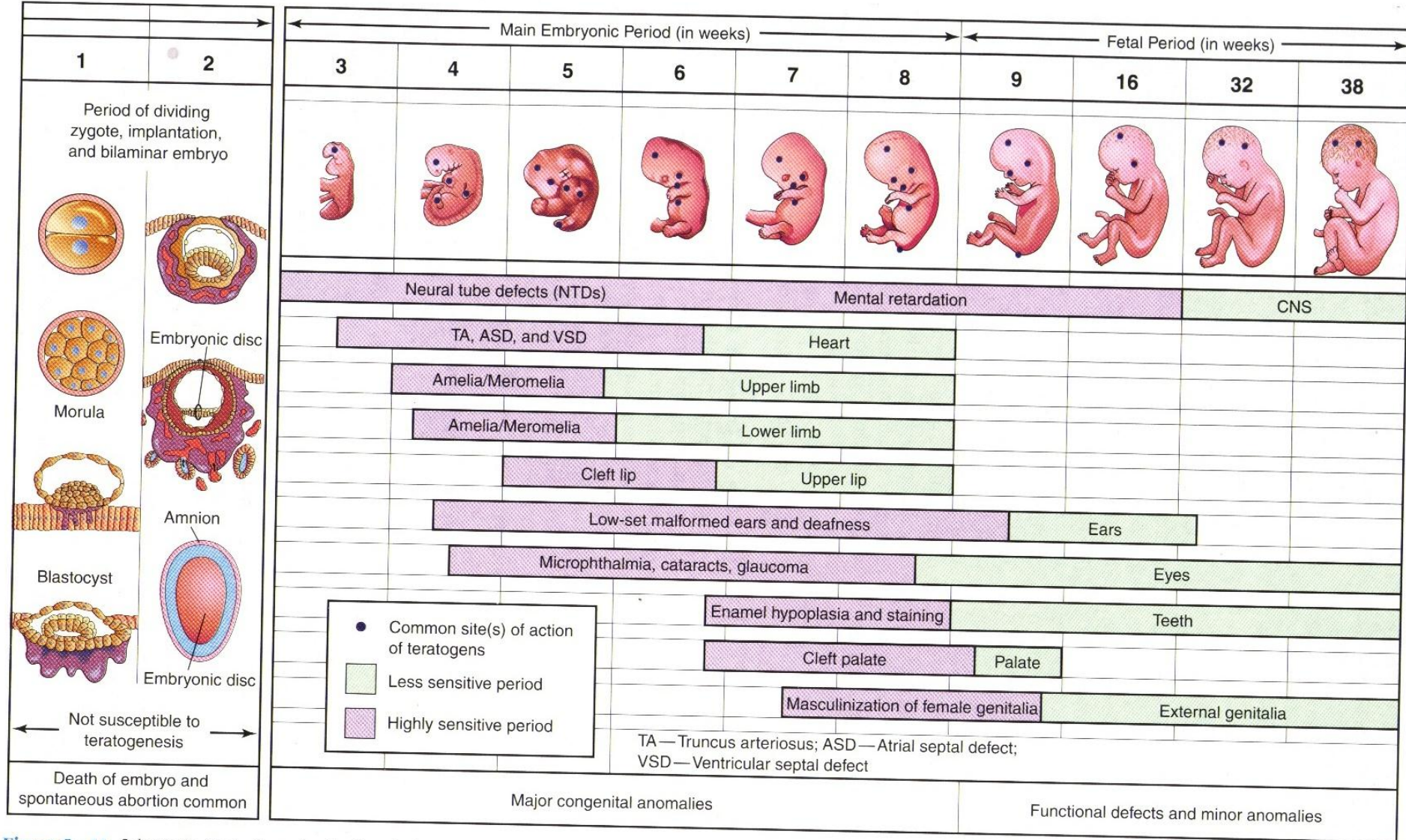
# What Factors Most Affected

- Pharmacokinetics of Medications:
- Dissolution
  - Stomach acid, motility, affect product delivery
- Absorption
  - Stomach acid inc/dec effect, concurrent medications
- First Pass Metabolism
  - Genetic inc/dec, enzyme inducers, enzyme inhibitors
- Distribution
  - Protein binding, albumin stores, fat stores
- Elimination
  - Gut, liver, renal function

# Teratogens:

- Any medication or toxin that may alter and cause abnormal or altered cell growth in the developing fetus resulting in physical defects in the fetus.

United States FDA Pharmaceutical Pregnancy Categories	
<b>Pregnancy Category A</b>	Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
<b>Pregnancy Category B</b>	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.
<b>Pregnancy Category C</b>	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
<b>Pregnancy Category D</b>	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
<b>Pregnancy Category X</b>	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.



**Figure 9 - 11.** Schematic illustration of critical periods in human prenatal development. During the first 2 weeks of development, the embryo is usually not susceptible to teratogens; at this point, a teratogen either damages all or most of the cells, resulting in death of the embryo, or damages only a few cells, allowing the conceptus to recover and the embryo to develop without birth defects. The mauve areas denote highly sensitive periods when major defects may be produced (e.g., amelia, absence of limbs). The green sections indicate stages that are less sensitive to teratogens when minor defects may be induced (e.g., hypoplastic thumbs).

# Alcohol:

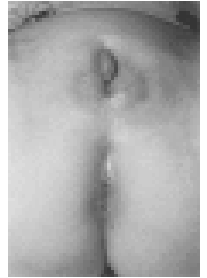
- Fetal Alcohol Syndrome



*From Jones KL, Smith DW: Recognition of the fetal alcohol syndrome in early infancy, Lancet 2:999–1001, 1973.)*

# First Trimester

## Egg Fertilization to week 12



- Category X:
  - Androgens
    - Secondary alterations of female sex organs when fetus inadvertently exposed during first 9-12 weeks after conception Danazol in 23 of 57 female infants exposed
  - 5 Alpha-reductase inhibitors
    - Finasteride Propecia<sup>®</sup>, Proscar<sup>®</sup>, Dutasteride Avodart<sup>®</sup>
      - Inhibit testosterone effects on developing male fetus resulting in sexual organ birth defects
  - Selective Estrogen Receptor Antagonists
    - Tamoxifen Nolvadex<sup>®</sup>, Raloxefene Evista<sup>®</sup>
      - Animal studies documented cardiac, uterine, fetal demise, reduced fertility

# First Trimester Cat X (cont)

- Retinoids:
- Isotretinoids
  - Accutane<sup>®</sup>,



 **iPLEDGE**<sup>™</sup>  
Committed to Pregnancy Prevention

Welcome  
Have Questions? Call our toll-free number **1-866-495-0654**  
Monday to Saturday, 9 AM - 12 AM (Midnight) ET

**THE ONLY WAY** 

This is a comprehensive program to help you get prepared, plan your treatments, and ensure you don't get pregnant during the course of isotretinoin therapy.

**SAFETY NOTICE**

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE. Under this program, prescribers must be registered and

**Login** for registered users  
Username:   
Password:   
[Forgot Password?](#)  

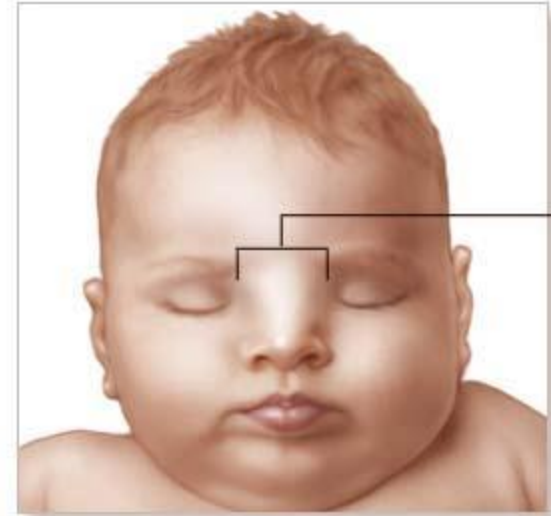
**Register**  
Enter here to register in the iPLEDGE Program for the first time or to change data on your registration form.

**How to Report**  
Call our toll free number **1-866-495-0654** to report any of the following:

**HOME**  
**PATIENT INFORMATION**  
**ABOUT ISOTRETINOIN**  
**ABOUT iPLEDGE**  
**PRESCRIBER INFORMATION**  
[Find a Participating Pharmacy](#)  
[FAQs](#)

# Anti Seizure Medications

- Seizures Themselves:
  - Preterm abortion
  - Hypoxic Brain injury
  - Impaired neuro/psyc function
- Valproic Acid
- Carbamazepine
- Phenytoin
- Others



Broad nasal  
bridge

ADAM.

Fetal Hydantoin  
Syndrome



# First Trimester Cat X

- Warfarin:
  - Spontaneous abortion, still birth, neonatal death, preterm abortion
  - Teratogen: First Trimester
    - Fetal Warfarin Syndrome 5-25%
  - Teratogen: Second Third Trimester
    - Optic atrophy blindness
    - Mental retardation
    - Stippling of the bones
    - Scoliosis
    - Shortened limbs



# Second Trimester

- Category X
- HMG Co-enzyme A reductase inhibitors “Statins”
  - Lovastatin Mevacor®
  - Fluvastatin Lescol®
  - Simvastatin Zocor®
  - Pravastatin Pravachol®
  - Pitivastatin Livalo®
  - Atorvastatin Lipitor®
  - Rosuvastatin Crestor®

Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

# Second Trimester

- Angiotensin-converting enzyme (ACE) inhibitors can cause fetal renal tubular dysplasia in the second and third trimesters, leading to oligohydramnios, fetal limb contractures, craniofacial deformities, and hypoplastic lung development. Fetal skull ossification defects have also been described. Fetal exposure in the first trimester is associated with an increased risk of birth defects.

Captopril  
Capoten®  
Enalapril  
Vasotec®  
Lisinopril  
Prinivil®  
Zestril®  
Benazapril  
Lotensin®  
Quinapril  
Accupril®  
Ramapril  
Altace®  
Perendopril  
Aceon®  
Trandolopril  
Mavik®  
Moexipril  
Univasc®  
Fosinopril  
Monopril®  
Also all the ARBS

# Category D

- Lithium: Eskalith<sup>®</sup>, Lithobid<sup>®</sup>
  - Cardiovascular and other teratogenic or toxic effects have been reported in infants born to lithium-treated mothers (Linden & Rich, 1983; Tunnessen & Hertz, 1972).
  - However, more recent epidemiological data have revealed that outcomes of most pregnancies with in utero exposure to lithium have resulted in normal infants, and that use of lithium during pregnancy may possess a lower fetal risk than previously believed (Cohen et al, 1994; Jacobson et al, 1992)

# Antidepressants:

- Fluoxetine: Prozac<sup>®</sup>: Category C
- Citalopram: Celexa<sup>®</sup>: Category C
- Escitalopram: Lexapro<sup>®</sup>: Category C
- Sertraline: Zoloft<sup>®</sup>: Category C
  
- Paroxetine: Paxil<sup>®</sup>: Category D
  
- Venlafaxine: Effexor and XR: Category C, B (aus)
- Bupropion: Wellbutrin, SR, XL: Category C

# Third Trimester

- Nonsteroid Anti-Inflammatory Medications

- May cause premature closure of the patent ductus arteriosus

- Infant renal failure

- Premature birth

And Celecoxib Celebrex

- **Propionic Acid**
  - Ibuprofen
    - Motrin et al
  - Fenpropfen
    - Nalfon
  - Ketoprofen
    - Orudis
    - Oruvail
  - Naproxen HCL
    - Naprosyn
    - EC Naprosyn
  - Naproxen Sodium
    - Anaprox RR
    - Naprelen SR
  - Flurbiprofen
    - Ansaid
  - Oxaprozin Daypro
- **Indene acetic acid**
  - Sulindac
    - Clinoril
- **Indole acetic acid**
  - Indomethacin
    - Indocin
- **Pyrole acetic acid**
  - Tolmentin
    - Tolectin
- **Phenylacetic acids**
  - Diclofenac Sodium
    - Voltaren, Arthrotec
  - Diclofenac Potassium
    - Cataflam
- **Miscellaneous**
  - Ketorolac Toradol
- **Fenamates:**
  - Mefanamic Acid
    - Ponstel
  - Meclofenamate
    - Meclomen
- **Oxicams:**
  - Piroxicam
    - Feldane
  - Meloxicam Mobic
- **Pyranocarboxylics**
  - Etodolac
    - Lodine
    - Etodolac XR
- **Naphthylakanones:**
  - Nabumetone
    - Relafen



## **Diflucan (fluconazole): Drug Safety Communication – Long-term, High-dose Use During Pregnancy May Be Associated With Birth Defects**

**08/03/2011**

**AUDIENCE:** OBGYN, Pharmacy, Infectious Disease

**ISSUE:** FDA is informing the public that treatment with chronic, high doses (400-800mg/day) of Diflucan (fluconazole) during the first trimester of pregnancy may be associated with a rare and distinct set of birth defects in infants. This risk does not appear to be associated with a single, low dose of fluconazole 150mg to treat vaginal yeast infection (candidiasis). Based on this information, the pregnancy category for fluconazole indications (other than vaginal candidiasis) has been changed from category C to category D. The pregnancy category for a single, low dose of fluconazole has not changed and remains category C.

## **Valproate Products: Drug Safety Communication - Risk of Impaired Cognitive Development in Children Exposed In Utero (During Pregnancy)**

**Including valproate sodium (Depacon), divalproex sodium (Depakote, Depakote CP, and Depakote ER), valproic acid (Depakene and Stavzor), and their generics**

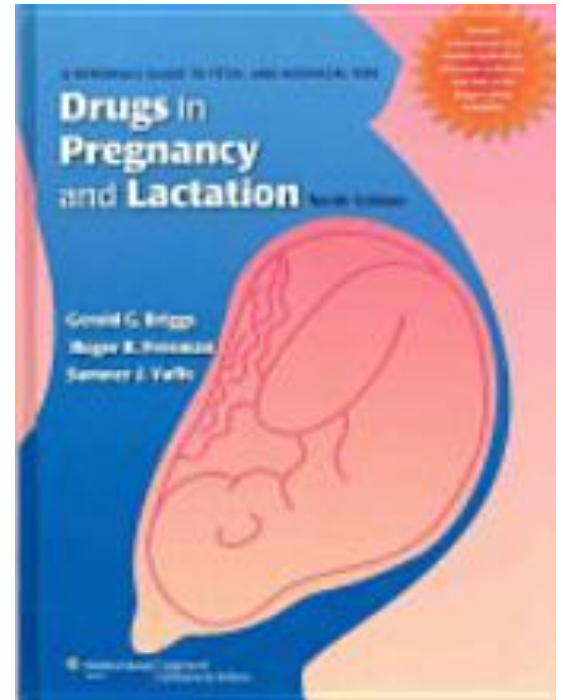
**06/30/2011**

**AUDIENCE:** OBGYN, Neurology, Psychiatry

**ISSUE:** FDA notified healthcare professionals that children born to mothers who take the anti-seizure medication valproate sodium or related products (valproic acid and divalproex sodium) during pregnancy have an increased risk of lower cognitive test scores than children exposed to other anti-seizure medications during pregnancy. This conclusion is based on the results of epidemiologic studies that show that children born to mothers who took valproate sodium or related products throughout their pregnancy tend to score lower on cognitive tests (IQ and other tests) than children born to mothers who took other anti-seizure medications during pregnancy. See the Drug Safety Communication for a data summary and additional information.

# Most Comprehensive Resource

- Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk [Book] by Gerald **Briggs**, Roger K. Freeman, Sumner J. Yaffe in Books
- Newest edition 2011
  - \$118-124
- Online resources:
  - Micromedex \$\$\$\$
  - <http://www.reprotox.org>



# Gestational Changes

## Mother altered kinetics?

- Much larger volume of distribution-
  - Decrease distribution free drug to target site
  - Do we need the drug?- Adjust the dose
- Pregnancy induced insulin resistance:
- Gestational Diabetes
  - Avoid Orals
    - Sulfonylureas, Metformin, Insulin Sensitizers, DPP-4 Inh
  - Use Insulin
    - Basal (Lantus) plus prandial (log or reg)
    - May need NO insulin immediately after delivery!

# Gestational Concerns

- Mother to Infant Drug Transfer-
- Drugs in breastfeeding
  - Sedatives, Opioids- infant respiratory depression

Hypertension	Fetal—perinatal death, IUGR, PTD Maternal—progression of target end-organ damage, superimposed preeclampsia, abruption	Fetal cyanide poisoning might develop after several hours of sodium nitroprusside—avoid prolonged infusions. The most commonly used agents include methyldopa, labetalol, and hydralazine. Avoid beta-blockers in the first trimester (teratogenic). Avoid ACEIs and ARBs.
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## – Oral Contraception:

- Estrogen/Progestin containing decrease milk production
- Progestin only BC acceptable

# Peri-Natal Issues

## Prevention of maternal to infant

- Herpes Simplex
  - Acyclovir Zovirax
  - Valacyclovir Valtrex
  - Famcyclovir Famvir
- Controversial yet safe
  - Acyclovir 400 mg TID-QID
  - Start weeks 32-35
- HIV: Prevent transmission
- Mother not on therapy:
  - Zidovudine alone or
  - 3 drug based regimen containing zidovudine
- Mother on therapy
  - Don't use Efavirenz
- Continue Zidovudine in infant for 6 weeks



# Peri-Natal Issues

## Prevention of maternal to infant

- Group B Streptococcus Positive Mothers:
  - Checked weeks 35-37
- These infections can occur as the baby moves through the birth canal of a woman who is colonized with GBS.
- Early-onset infections—
  - Early-onset infections occur during the first week of life, generally within the first 24–48 hours after birth.
  - Lung infections, blood infections, meningitis
- Late-onset infections—
  - These infections occur after the first 6 days of life.
- Prevent:
  - Antibiotics around delivery

# Premature Infants

- Pharmacologic considerations:
  - Altered metabolism-
  - VOLUME

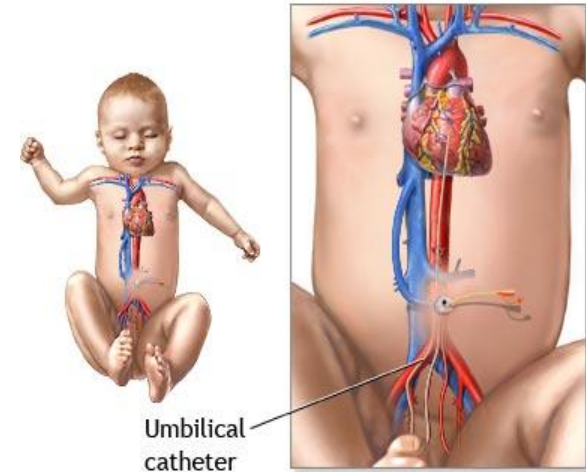
## Step 2: Fluids:

*Adequate parenteral nutrition is most often restricted by the amount of fluids that can be administered.*

*100cc for each first 10 kg =  
50 cc for each second 10 kg =  
20 cc for each additional kg =*

*Total CC fluid =  
Divided by 24 = RATE/hour*

- To Keep Open “TKO” umbilical artery catheter
  - Volumes:
  - Antibiotics, Theophylline, Nutritional support



# Infants, Children

PHYSIOLOGIC ALTERATION	NEONATE	INFANTS	CHILDREN
Gastric pH	> 5	4 to 2	Normal (2-3)
Gastric emptying time	Irregular	Increased	Slightly increased
Intestinal motility	Reduced	Increased	Slightly increased
Intestinal surface area	Reduced	Near adult	Adult pattern
Microbial colonization	Reduced	Near adult	Adult pattern
Biliary function	Immature	Near adult	Adult pattern

PHYSIOLOGIC ALTERATION	NEONATE	INFANTS	CHILDREN
Plasma albumin	Reduced	Near adult	Near adult
Fetal albumin	Present	Absent	Absent
Total proteins	Reduced	Decreased	Near adult
Total globulins	Reduced	Decreased	Near adult
Serum bilirubin	Increased	Normal	Adult pattern
Serum free fatty acids	Increased	Normal	Adult pattern

PHYSIOLOGIC ALTERATION	NEONATE	INFANTS	CHILDREN
Oral absorption	Erratic	Increased	Near adult
Intramuscular absorption	Variable	Increased	Near adult
Percutaneous absorption	Increased	Increased	Near adult
Rectal absorption	Very efficient	Efficient	Near adult

PHYSIOLOGIC ALTERATION	NEONATE	INFANTS	CHILDREN
Cytochrome P450 activity	Reduced	Increased	Slightly increased
Phase II enzyme activity	Reduced	Increased	Near adult
Blood esterase activity	Reduced	Normal (by 1 yr)	Adult pattern
Presystemic enzyme activity	Reduced	Increased	Near adult

PHYSIOLOGIC ALTERATION	NEONATE	INFANTS	CHILDREN
Glomerular filtration	Reduced	Normal (by 1 yr)	Adult pattern
Active tubular secretion	Reduced	Near normal	Adult pattern
Active tubular reabsorption	Reduced	Near normal	Adult pattern
Active drug excretion	Reduced	Near normal	Adult pattern
Passive drug excretion	Reduced	Increased	Adult pattern
Excretion of basic drugs	Increased	Increased	Near normal

*Adapted from Morselli PL: Development of physiological variables important for drug kinetics. In Morselli PL, Pippenger CE, Penry JK, editors: Antiepileptic drug therapy in pediatrics, New York, 1983, Raven Press, pp 1–12.*

# Infants, Children

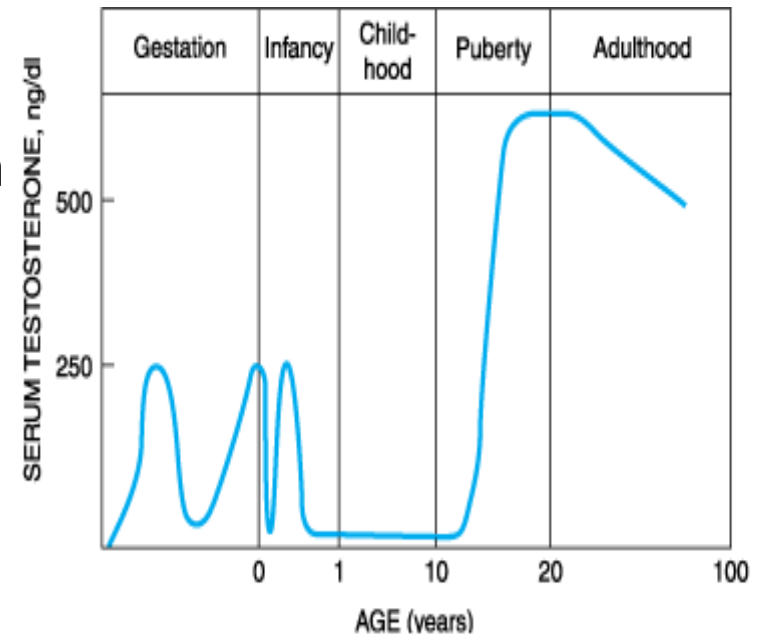
- Biliary function abnormalities:
  - Ceftriaxone Rocephin<sup>®</sup> IV for meningitis
  - More likely to get biliary sludging and hyperbillirubenemia
- Increased Liver p-450 system activity in infants and children: Theophylline Dosing:
  - Oral: “Slow clinical titration preferred”
    - 1-9 years old                      LD 5mg/kg, MD 4 mg/kg q 6
    - 9-16 or smokers                LD 5mg/kg, MD 3 mg/kg q 6
    - Non-smokers                      LD 5 mg/kg, MD 3 mg/kg q 8
    - Older, cor pulmonale        LD 5 mg/kg, MD 2 mg/kg q 8
    - CHF                                LD 5 mg/kg, MD 1-2 mg/kg q 12

# Puberty: Females

- Excessive surge in estrogens, progestins
  - Onset of menses
- Menstrual Symptoms
  - Cramps:
    - NSAIDS- All will work may get individual patient preference
  - Bloating:
    - PRN Diuretics-
      - HCTZ- weak, Furosemide- Strong
      - OTC stuff- most have NSAIDS and “Natraceutical” diuretics

# Puberty Males

- Normal surge of testosterone
- Male Sex Organ Development:
  - Epididymis, Vas deferens, Seminal Vesicles, Prostate, Scrotum and penis
- Skeletal muscles:
  - Anabolic effect- mass and strength
- Larynx:
  - Deepening of the voice
  - Epiphysial cartlagious plates
- Hair:
  - Beard, Mustache, Chest, Abdomen
- Skin:
  - Acne



Source: Brunton LL, Lazo JS, Parker KL: *Goodman & Gilman's The Pharmacologic Basis of Therapeutics*, 11th Edition: <http://www.accessmedicine.com>

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# What happens when this occurs?

- Mood swings
- Depression?
- Anxiety?
- Bipolar disorder?
- Medication potentially altering adolescent neurons?
- Higher risk of suicidality?
- Social isolation?
  - Deviant behavior
- Sex?-
- Yes/no-
- Birth Control!!!
  - Monophasic
  - Biphasic
  - Triphasic
  - Quatraphasic
  - Progestin only
  - Patch
  - IUD
  - Vaginal Ring

**Adherence?  
Must take as  
instructed or  
they do not  
work**

# Adult Medicine

- Finally to the area in which I actually work!
- All medications are formulated for effective dosing in the “Normal” adult population
- Very general rule- Lower tablet strengths availability is/are generally acceptable starting dose for desired action
  - Citalopram: 10,20, 40 mg- 10 mg HS good start
  - HCTZ: 12.5, 25, 50 mg- 12.5 mg q d good start

# Adult Medicine

- Drugs with a “Narrow Therapeutic Window” deserve to be monitored.

- Digoxin Lanoxin

- Levothyroxine Synthroid, Levoxyl

- Warfarin Coumadin

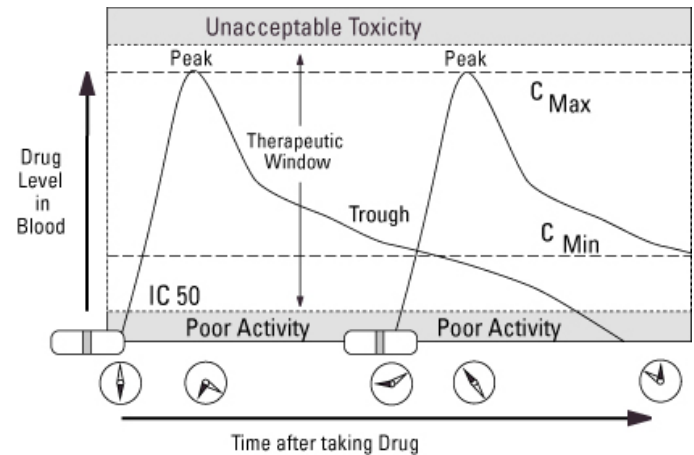
- Sodium channel blocker for seizure disorder

- Enzyme inducers and inhibitors- look for interactions!

- Birth Control lose of efficacy

- Monitor for established drug levels

- For Bipolar?, Migraine?, Depression?, Psychosis?



# Adult Medicine Drug Interactions

## Substrates- metabolized this route

SUBSTRATES							
1A2	2B6	2C8	2C9	2C19	2D6	2E1	3A4,5,7
amitriptyline caffeine clomipramine clozapine cyclobenzaprine estradiol fluvoxamine haloperidol imipramine N-DeMe mexillettine naproxen olanzapine ondansetron phenacetin_ acetaminophen→NAPQJ propranolol riluzole ropivacaine tacrine theophylline tizanidine verapamil (R)warfarin zileuton zolmitriptan	bupropion cyclophosphamide efavirenz ifosfamide methadone	paclitaxel torsemide amodiaquine cerivastatin repaglinide	NSAIDs: diclofenac ibuprofen lornoxicam meloxicam S-naproxen_Nor piroxicam suprofen  Oral Hypoglycemic Agents: tolbutamide glipizide  Angiotensin II Blockers: losartan irbesartan  Sulfonylureas: glyburide glibenclamide glipizide glimepiride tolbutamide  amitriptyline celecoxib fluoxetine fluvastatin glyburide nateglinide phenytoin-4-OH2 rosiglitazone tamoxifen torsemide S-warfarin	Proton Pump Inhibitors: lansoprazole omeprazole pantoprazole rabeprazole  Anti-epileptics: diazepam→Nor phenytoin(O) S-mephenytoin phenobarbital  amitriptyline carisoprodol citalopram chloramphenicol clomipramine cyclophosphamide hexobarbital imipramine N-DeMe indomethacin R-mephobarbital moclobemide nelfinavir nilutamide primidone progesterone proguanil propranolol teniposide R-warfarin→8-OH	Beta Blockers: carvedilol S-metoprolol propafenone timolol  Antidepressants: amitriptyline clomipramine desipramine imipramine paroxetine  Antipsychotics: haloperidol perphenazine risperidone→9OH thioridazine zuclopenthixol  alprenolol amphetamine aripiprazole atomoxetine bupropion chlorpheniramine chlorpromazine codeine (→O-desMe) debrisoquine dexfenfluramine dextromethorphan duloxetine encainide flecainide fluoxetine fluvoxamine lidocaine metoclopramide methoxyamphetamine mexillettine minaprine nebivolol nortriptyline ondansetron oxycodone perhexiline phenacetin phenformin promethazine propranolol	Anesthetics: enflurane halothane isoflurane methoxyflurane sevoflurane  acetaminophen→ NAPQJ aniline2 benzene chlorzoxazone ethanol N,N-dimethyl formamide theophylline→ 8-OH	Macrolide antibiotics: clarithromycin erythromycin (not 3A5) NOT azithromycin telithromycin  Anti-arrhythmics: quinidine→3OH (not 3A5)  Benzodiazepines: alprazolam diazepam→3OH midazolam triazolam  Immune Modulators: cyclosporine tacrolimus (FK506)  HIV Antivirals: indinavir nelfinavir ritonavir saquinavir  Prokinetic: cisapride  Antihistamines: astemizole chlorpheniramine terfenadine  Calcium Channel Blockers: amlodipine diltiazem felodipine lercanidipine nifedipine2 nisoldipine nitrendipine verapamil  HMG CoA Reductase Inhibitors: atorvastatin cerivastatin

# Adult Medicine Drug Interactions

## Inhibitors- Stop the metabolism

### INHIBITORS

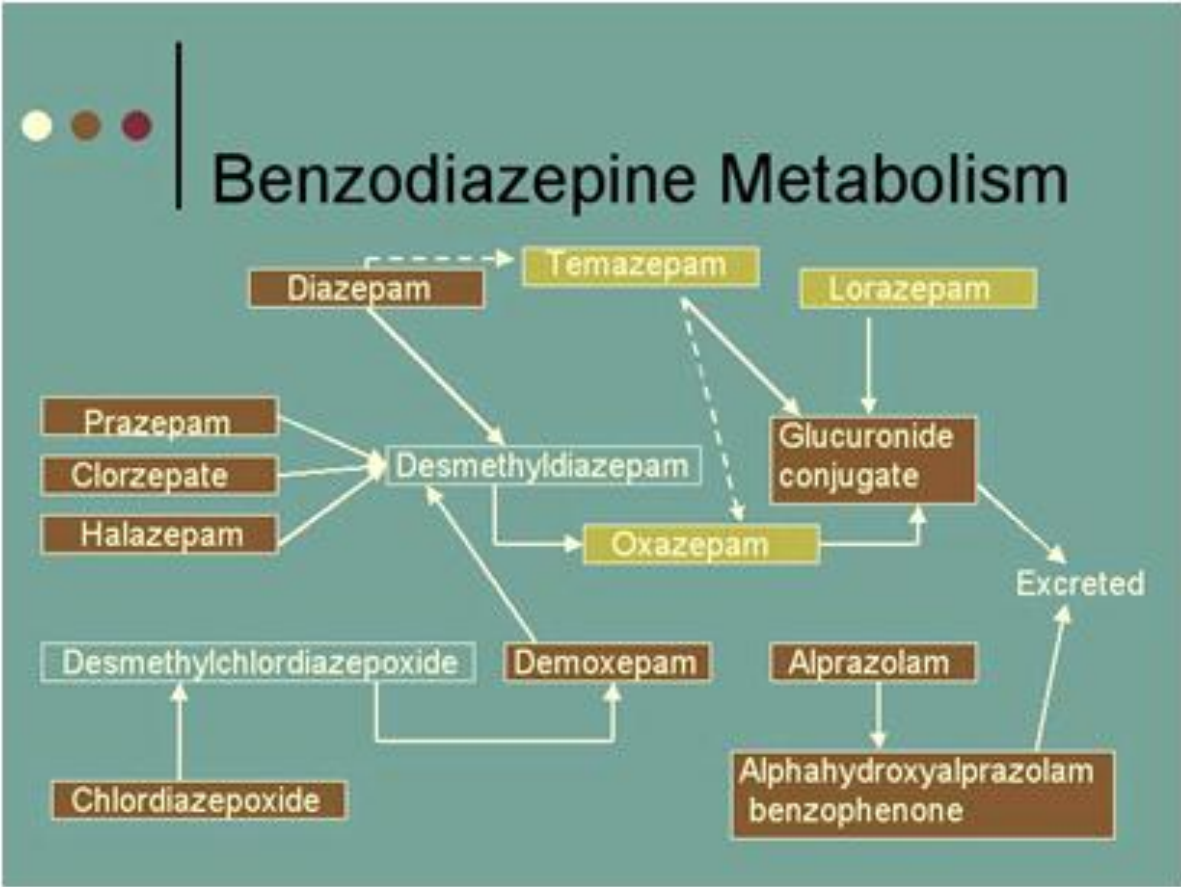
1A2	2B6	2C8	2C9	2C19	2D6	2E1	3A4,5,7
fluvoxamine ciprofloxacin cimetidine amiodarone fluoroquinolones furafylline interferon methoxsalen mibefradil	thiotepa ticlopidine	gemfibrozil trimethoprim glitazones montelukast quercetin	fluconazole amiodarone fenofibrate fluvastatin fluvoxamine isoniazid lovastatin phenylbutazone probenecid sertraline sulfamethoxazole sulfaphenazole teniposide voriconazole zafirlukast	PPIs: lansoprazole omeprazole pantoprazole rabeprazole chloramphenicol cimetidine felbamate fluoxetine fluvoxamine indomethacin ketoconazole modafinil oxcarbazepine probenecid ticlopidine topiramate	bupropion fluoxetine paroxetine quinidine duloxetine terbinafine amiodarone cimetidine sertraline celecoxib chlorpheniramine chlorpromazine citalopram clemastine clomipramine cocaine diphenhydramine doxepin doxorubicin escitalopram halofantrine histamine H1 receptor antagonists hydroxyzine levomepromazine methadone metoclopramide mibefradil midodrine moclobemide perphenazine ranitidine red-haloperidol ritonavir ticlopidine tripeleonnamine	diethyl- dithiocarbamate disulfiram	HIV Antivirals: indinavir nelfinavir ritonavir clarithromycin itraconazole ketoconazole nefazodone saquinavir telithromycin aprepitant erythromycin fluconazole grapefruit juice verapamil diltiazem cimetidine amiodarone NOT azithromycin chloramphenicol ciprofloxacin delaviridine diethyl- dithiocarbamate fluvoxamine gestodene imatinib mibefradil mifepristone norfloxacin norfluoxetine star fruit voriconazole

# Adult Medicine Hepatic Impairment

- You need to destroy 95% of your hepatocyte function before you start to lose medication clearing ability
- Transaminitis:
  - AST/ALT elevations- Most drugs with transiently elevate
- Liver Function-
  - INR- synthetic marker of clotting factor production
    - Auto anticoagulated- other drugs contribute bleed risk?
  - Albumin- synthetic
    - Alter distribution of protein bound medications

# Potentially Clinically Significant

- Benzodiazepines for etoh withdrawal



Short Acting:  
Lorazepam  
Ativan  
Oxazepam  
Serax  
Alprazolam  
Xanax

# Adult Medicine Renal Impairment

Cockcroft-Gault GFR =  $(140 - \text{age}) * (\text{Wt in kg}) * (0.85 \text{ if female}) / (72 * \text{Cr})$

- Cockcroft and Gault
- “Normal” GFR
  - 100-130
- “Obligated to look GFR”
  - 60
- “Most drugs need GFR dosing adjustment”
  - 30
- “Most All drugs need renal dosing”
  - 15

## Metformin

### Contraindication:

SrCr > 1.5 men

SrCr > 1.4 Women

CrCl < 60

# Adult Medicine Significant Interactions

- Lithium
  - Very effective under used
  - Short yet significant list
- NSAIDs
- Diuretics
- ACEs, ARBs,
- Lithium toxicity may be fatal
- MAO-Inhibitors
- Parkinsons
  - Selegiline Eldepryl<sup>®</sup>
  - Transdermal Emsam<sup>®</sup>
  - Rasagiline Azilect<sup>®</sup>
- REFRACTORY Depression
  - Parnate<sup>®</sup>
  - Nardil<sup>®</sup>
  - Marplan<sup>®</sup>
- Anti- MRSA antibiotic
  - Linezolid Zyvox<sup>®</sup>

# Geriatric Medicine

- Lean mass declines
  - Sarcopenia, decrease strength, mass
  - Andropause?
    - Androgen replacement therapy males?
- Fat deposits increase
  - Alterations of fat deposited medications
    - Lipophilicity
    - Altered loading doses
- Gastrointestinal PH changes
  - B-12 deficiency
  - Folate deficiency
  - Iron deficiency
  - Drug induced?
    - PPI
- Albumin decreases
  - Less protein binding
  - More free drug = toxicity
- Less balance
  - Falls- drug induced dizzy

# Geriatric Medicine Beers List

- <http://www.fmda.org/beers.pdf>
- Comprehensive list of every medication that may cause ADR in elderly patients

<i>Cardiac Drugs</i>		
Amiodarone ( <i>Cordarone</i> , <i>Pacerone</i> ) (B)	QT prolongation, torsades de pointes, lack of efficacy in elderly <sup>5</sup>	Depends on type of arrhythmia; flecainide ( <i>Tambocor</i> ), sotalol ( <i>Betapace</i> ), beta-blocker, dofetilide ( <i>Tikosyn</i> ) <sup>27</sup>
Beta-blockers in patient with asthma, COPD, or Raynaud's disease (C) <sup>15</sup>	Worsening disease <sup>15</sup>	Alternate antihypertensive; nitrate or calcium channel blocker <sup>15</sup>
Calcium channel blocker in patient with systolic heart failure (C) or chronic constipation (B, C)	Worsening heart failure; constipation <sup>5,15</sup>	Diuretic, ACE inhibitor, appropriately titrated beta- blocker <sup>15</sup>
Digoxin ( <i>Lanoxin</i> ) doses >0.125 mg/d except for atrial arrhythmias (B)	Toxicity due to reduced renal clearance <sup>5</sup>	Dose reduction, with monitoring <sup>19</sup>
Disopyramide ( <i>Norpace</i> ) (B, C)	Negative inotrope; anticholinergic; sudden death <sup>5,15</sup>	Depends on type of arrhythmia; for atrial fibrillation, digoxin, quinidine, procainamide, sotalol, flecainide <sup>15,27</sup>

# “Collective Overconsumption” - rgh

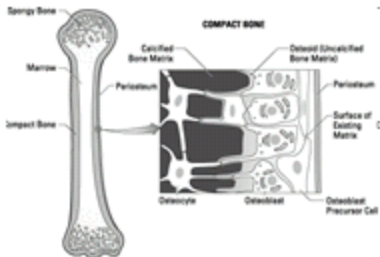
- 2 Distinct different phenomenon
- #1- “Tipping over the edge”
  - Poly-pharmacy and the latest dosage change of medication addition causes the patient adverse events
  - Make small dosing changes and only 1 drug change at a time
- #2- “Oh my goodness- Loved one is on TOO MANY medications”
  - When you break it down individually- they are not

# Geriatric Medicine

- Fixed income concerns:
- If you have a sample in your office- it is not inexpensive
  - Co-pay waivers
  - Actual costs health plan
- What disease can you not manage generically?
- Price matching education
  - Every chain will price match if the PATIENT asks
  - Does not work if they have insurance
    - Less than co-pay?

# Geriatric Medicine: Bone Health

- Bisphosphonates
  - Alendronate
    - Fosamax PO
  - Abandronate
    - Boniva PO
  - Risedronate
    - Actonel PO
  - Zoledronic Acid
    - Reclast IV
- Women are 4 times more likely to develop osteoporosis than men
  - 77% of women who are osteoporotic are undiagnosed
- 1 in 3 women will develop a fracture
- 1 in 8 men will develop a fracture



**Don't forget the Calcium 1500 mg a day  
And the Vitamin D- 400-800 units a day!**

# Hospice Concerns

- Die with dignity
- Treat pain appropriately
- Morphine High dose
  - Morphine 3 Glucuronide is INACTIVE
    - 95% of MSO4 metabolite
  - Morphine 6 Glucuronide is ACTIVE
  - M3G ANTAGONIZES M6G and MSO4
- May be worth you while to switch to another phenanthrene opioid

# Hospice Concerns

- “The death rattles”
  - Air hunger
  - Inhaled morphine effective
  - Injectable and oral opioids effective
- Constipation
  - Softeners at minimum, senna, stimulates, Mirilax<sup>®</sup>
- Hypersecretions:
  - Glycopyrralate Robinul<sup>®</sup>
    - 1-2 mg PO TID-QID, IM or IV 0.1 mg Q 3-4 hours

# Summary The “Life-Span”

- Fetal Development
  - First Trimester
  - Second Trimester
  - Third Trimester
- Gestational Issues
- Perinatal Issues
- Infant
- Toddler
- Adolescent
- Puberty
- Adult
  - Organ System Failure
    - Renal
    - Liver
- Geriatrics
- End of Life
  - Hospice Care

# Questions?



roger@otc.isu.edu

