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Pharmacy Continuing Education for Non-Pharmacists
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PharmCon is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

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Why Do People Misuse Drugs?

• Do not follow directions
• Do not read ingredients...take multiple products with the same ingredient
• Take drugs not prescribed for them
• OTC's are perceived safe even in large doses
• Dependence
• Abuse

Therapeutic Errors

• 10.2% of calls to U.S. poison centers (255,732 cases) (NPDS 2007)
• Examples:
  ➢ Inadvertent double-dose
  ➢ Wrong medication taken/given
  ➢ Doses taken too close together
  ➢ Confused units of measure
  ➢ > 1 product with same ingredient

OTC Drug Misuse

• 1/3 of those surveyed reported having misused OTC medications
  ➢ Higher dose – 22%
  ➢ Longer course – 17%
  ➢ Different purpose – 11%
• 35% of those misusing OTC’s reported at least 1 adverse effect
• Only 68% report reading instructions and warnings all of the time

Generation Rx:
Pharming

• Misuse/abuse of Rx and OTC’s is equal to or greater than the abuse of illegal drugs
• 20% of the U.S. population has taken Rx drugs for nonmedical reasons (NIDA 2005)
• 61% of teens surveyed believe that Rx pain relievers are easier to get than illegal drugs, and 41% believe they are safer than illegal drugs (Partnership for a Drug Free America 2008)

Lifetime Trial 2008 Teens

% of Teens Who Have Ever Tried:

Marijuana

Inhalants

Rx Drugs

Cough Medicine

Crack/Cocaine

Ecstasy

LSD

Meth

Heroin

GHB

2008 Partnership Attitude Tracking Study
Where People Obtain Pain Relievers

- Bought/Took from Friend/Relative: 14.8%
- Drug Dealer/Stranger: 3.9%
- Bought on Internet: 0.1%
- Other: 4.9%
- More than One Doctor: 1.6%
- One Doctor: 19.1%
- Bought/Took from Friend/Relative: 14.8%

2006 National Survey on Drug Use and Health

Complications from Rx and OTC Drug Misuse and Abuse

- Physical dependence
- Tolerance to therapeutic effect
- Inappropriate treatment of medical problems
- 741,425 ED visits for non-medical use of Rx or OTC pharmaceuticals
  - CNS agents (50%)
  - 247,669 opioids

Unintentional Drug Overdose Deaths

- Unintentional drug poisoning mortality rates increased 68.3% from 1999-2004
- 19,838 deaths in 2004
- 2nd only to motor vehicle accidents
- Rx opioids – deaths increased by 160% from 1999-2004

Rx Opioid OD

- 24% increase in U.S. ED visits due to nonmedical use of opioids (2004-2005, DAWN)
- 16 year old male and a friend are found unconscious by his parents on his bedroom floor. Another friend witnessed each crushing and snorting a tablet a few hours before.
- 16 yo: Unresponsive to pain, RR 6, P 76, BP 100/56, pulse ox 90%, lungs clear, skin cool, pale and dry, pupils 2 mm & minimally responsive, ECG: NSR
- EMS gave 0.4 mg naloxone x 2; respirations increased to 12, responded to pain and verbal stimuli.
- Upon awakening, he admitted to buying Oxycontin® from a neighbor who takes it for cancer pain. He crushed and snorted 1 tablet.
- Friend could not be resuscitated.

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Oxycodone
- Drug Abuse Warning Network (DAWN): the number of ER visits involving oxycodone misuse increased about 10-fold between 1996 and 2004.

OxyContin
- Controlled release form of oxycodone
- Wide range of strengths (10 mg-80 mg)
- Overdoses with as little as 1 tablet

Hydrocodone
- Most common opioid in ED visits
- In combination with acetaminophen or ibuprofen (Vicodin, Lortab, Vicoprofen...)

Methadone
- Analgesic, opioid addiction treatment
- Long duration of action: 24-36 hours
- Old drug but overdoses and fatalities increasing dramatically in some areas

Fentanyl
- 80-100 times more potent than morphine
- OD’s after chewing fentanyl patches
- OD’s from not removing old patches before applying new patches
- 2006: illicit fentanyl OD’s and deaths
- Negative opiate screen

Buprenorphine
- Subutex (2mg, 8mg) and Suboxone (with naloxone, 2mg/0.5mg, 8mg/2mg) SL tablets
- Approved for office-based opioid dependence
- High affinity for opioid receptor but has a “ceiling effect”
- Is diverted and abused by those who are addicted to low doses of opiates
  - To get high or to self-treat withdrawal

Buprenorphine
- If used after withdrawal begins lessens withdrawal symptoms
- If used soon after or before opioid use withdrawal
- If on Suboxone and then use heroin no effect from heroin
- If crushed and used IV withdrawal
- Less toxic than other opioids in OD’s
**Opioid Toxidrome**

- Lethargy, coma
- Respiratory depression
- Constricted pupils
- Hypotension, bradycardia, hypothermia

**Naloxone**

Used diagnostically; reverses CNS and respiratory depression 0.4-2.0 mg IV, IM, intranasal

Might require higher doses

Short duration: 1.5 hours

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**Stimulants**

- Amphetamines
  - Adderall
- Methylphenidate (Ritalin)
- Pseudoephedrine, phenylephrine
- Caffeine
- Herbal stimulants

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**Stimulant Abuse/Misuse**

- 33% increase in US ED visits due to nonmedical use of stimulants (2004-2005, DAWN)

- Prescription stimulants are referred to as the “new caffeine”

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**Adderall – The Drug of Choice**

- 5.9% students reported using Rx stimulants not prescribed for them
- Adderall was perceived by 90% of students to be easy to obtain
  - Only behind alcohol (100%) and marijuana (95%)
  - Ritalin - 70% of students
- Used instead of coffee or energy drinks because they are “more effective, last longer, safe, and have less calories”.

(DEWS Investigates, October 2006)

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**Stimulant Abuse/Misuse**

- ~ 8% of college students report using prescription stimulants that were not prescribed for them (U of Mich 2005)

- Reasons:
  - “Helps me concentrate” – 58%
  - “Helps increase my alertness” – 43%
  - “Gives me a high” – 43%
  - “Counteracts the effects of other drugs” – 8%
  - Other reasons – 14%

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But is Adderall use associated with other drug use?

Yes, according to the 2009 National Survey on Drug Use and Health
**Unintentional Pediatric Stimulant Overdoses**

- Parents giving excessive amounts to children to calm them, toddlers with access to meds
- PCC in Detroit reported 251 cases of pediatric methylphenidate overdoses in 2 years; 6-11 year olds - many therapeutic errors (Arch Ped Adol Med 2000, 154:1199)

**Stimulants - Mechanism**

- Sympathomimetics
- Stimulate alpha and beta adrenergic receptors
- Central nervous system stimulation
- Stimulate the release of and/or block the reuptake of neurotransmitters (norepinephrine, serotonin, dopamine)

**Stimulant Toxidrome**

- Agitation, hallucinations, paranoia
- Tremor, seizures
- Tachycardia, hypertension, chest pain, MI
- Hyperthermia
- Warm skin, diaphoresis
- Dilated pupils
- CV collapse
- Hemorrhagic stroke

**Acetaminophen**

- Found in more than 600 OTC & Rx products
- Take > 1 product with acetaminophen
- Take too much, too often

**Chronic Acetaminophen Case**

- A 62 year old man with chronic alcohol abuse and arthritis is admitted to the hospital with a history of a recent increase in alcohol consumption and chronic ingestion of 6-8 g per day of acetaminophen for about a week.

- Initial laboratory values: bilirubin 3.6 mg/dL (nl 0.2-1), AST 2870 IU/L (nl 1-30), ALT 2300 IU/L (nl 1-30) and INR 3.0
- The plasma acetaminophen level on admission was 73 mcg/mL
- AST/ALT increased to >7000
- Recovered in 7 days with antidotal treatment and supportive care
**Acetaminophen Metabolism**

- Acetaminophen → CYP450
  - 5-15% → Unchanged APAP
  - 40-67% → APAP glucuronide
  - 20-46% → APAP sulfate
- NAPQI → Glutatione
- NAPQI → Cysteine, mercaptate conjugates

**Acetaminophen**

- **Acute toxic dose**
  - children: > 200 mg/kg
  - adults: > 10 g
- **Toxicity with chronic use**
  - > 100-200 mg/kg/day in children
  - > 4-10 g/day in adults
  - Risk factors: chronic alcoholism, enzyme-inducing drugs, malnutrition, liver disease

**Acetaminophen Liver Failure Cases On The Rise**

- 662 acute liver failure patients at 22 transplant centers from 1998-2003
- 275 (42%) from APAP
  - 1998: 28% due to APAP
  - 2003: 51% due to APAP
- 44% of APAP cases were suicide attempts
- 48% were unintentional OD’s


**Phase I: up to 24 hours (if acute)**

- Nausea
- Vomiting
- Malaise
- Lethargy

**Phase II: up to 4 days**

- GI symptoms subside
- RUQ pain
- Elevated liver function tests
- Prolonged INR

**Phase III: 3-5 days**

- Markedly elevated liver enzymes (>10,000 U/L), bilirubin and INR
- Jaundice
- Hypoglycemia
- Coagulation defects
- Metabolic acidosis
- Encephalopathy
- Renal failure
- Death

**Phase IV: 4 days - 2 weeks**

- Resolution of hepatic and renal dysfunction
- No permanent sequelae

**Assessment & Treatment**

- Plasma levels, history
- Activated Charcoal for recent acute OD’s
- Acetylcysteine
- Liver Transplant
Acetylcysteine

- **EARLY**
  - Glutathione precursor and substitute
  - Increases sulfate conjugation
- **LATE**
  - Improves microcirculatory blood flow
  - Scavenges oxygen free radicals
  - Oral or intravenous administration
  - Delay decreases effectiveness
  - Most effective if initiated within 10 hours of overdose

Oral N-Acetylcysteine

- 140 mg/kg po load; 70 mg/kg po q4h X 17 doses (72 hours total)
- Some patients may be treated with a shorter course (36 hours)
- Adverse effects: nausea, vomiting

Intravenous Acetylcysteine (Acetadote®)

- 300 mg/kg, divided in 3 doses, over 21 hours total
- Longer infusion sometimes required, especially for chronic OD’s or late presenters
- Adverse effects: flushing, urticaria, angioedema, respiratory distress, hypotension

Antihistamines

- H1 receptor antagonists
  - Chlorpheniramine, brompheniramine, diphenhydramine, doxylamine, loratadine...
  - Older antihistamines bind to peripheral and central H1 receptors, and cholinergic, α and β-adrenergic receptor sites
  - 2nd generation are peripherally selective

Diphenhydramine Misuse

- A 45 year old is questioned by the pharmacist when he was noticed buying Unisom SleepGels® weekly.
- He revealed a 6 month history of using Unisom SleepGels® to relieve aggressive feelings... up to 60 capsules (3000 mg) daily.
- He reported a pleasant feeling in his head & abdomen, a calming effect, staring into space more often, blurred vision and dry mouth.

Anticholinergic Toxidrome

“Mad as a hatter, hot as a hare, dry as a bone, red as a beet, blind as a bat”

- Confusion, hallucinations, coma
- Hyperthermia
- Dry, flushed, warm skin
- Dilated pupils
- Hypertension, tachycardia
- Urinary retention
**Diphenhydramine**
- Used in excessive amounts for sleep or as a sedative
- Abused dose (hallucinations): 150-700 mg
- Acute toxic dose: >7.5 mg/kg (or ≥ 300 mg)
- Sodium channel blockade
  - QRS, QT prolongation

**Cough Medicine Abuse**
- A 16 year old girl was found sleeping on the lawn outside of her home when her parents came home from work. When awakened, she was confused and hallucinating. She admitted to ingesting 20 “Triple C” tablets after school to get high.
- HR 150, BP 170/100, RR 18, pupils are 5 mm & reactive with horizontal nystagmus.

**Dextromethorphan**
- Semi-synthetic opioid
- Abuse or misuse by teens increased >300% from 2000 to 2003 (U.S. poison centers)
- DXM, dex, C-C-C, Robo, Red Devils, Triple C
- > 80% cases are with Coricidin products
- Abused dose = ≥ 200-400 mg (range of 100-1200 mg)
- Effects are similar to phencyclidine (PCP)
- Produces hallucinations, CNS depression, seizures
- Hypertension, tachycardia, agitation, ataxia often seen
- Treatment – Naloxone??

**What Pharmacists Can Do...**
- Provide clear advice on how to take medications...
  - Do not take multiple products with the same ingredient
  - Do not take more than is prescribed; always read labels
  - OTC’s are generally not meant to be taken chronically
- Counsel patients on how to safeguard their medicines at home.
- Educate patients on how to dispose of their meds.
- Watch for escalating use of OTC or Rx drugs.
- Look for fake or altered prescriptions, prescriptions from multiple doctors (doctor shopping), an increase in sales of cough and cold meds.
- Be wary of reports of missing drugs.
- Control access to some OTC’s.