



Toxicology in Pregnancy: Current Challenge & Clinical Management

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What is Poison ?



Substance with property that can be
Danger to Health and well-being



ติดตามข่าวได้ที่



ค้นหาข่าว

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ค้นหา



หน้าแรก

ข่าวในพระราชสำนัก

การเมือง

สังคม/อาชญากรรม

เศรษฐกิจ

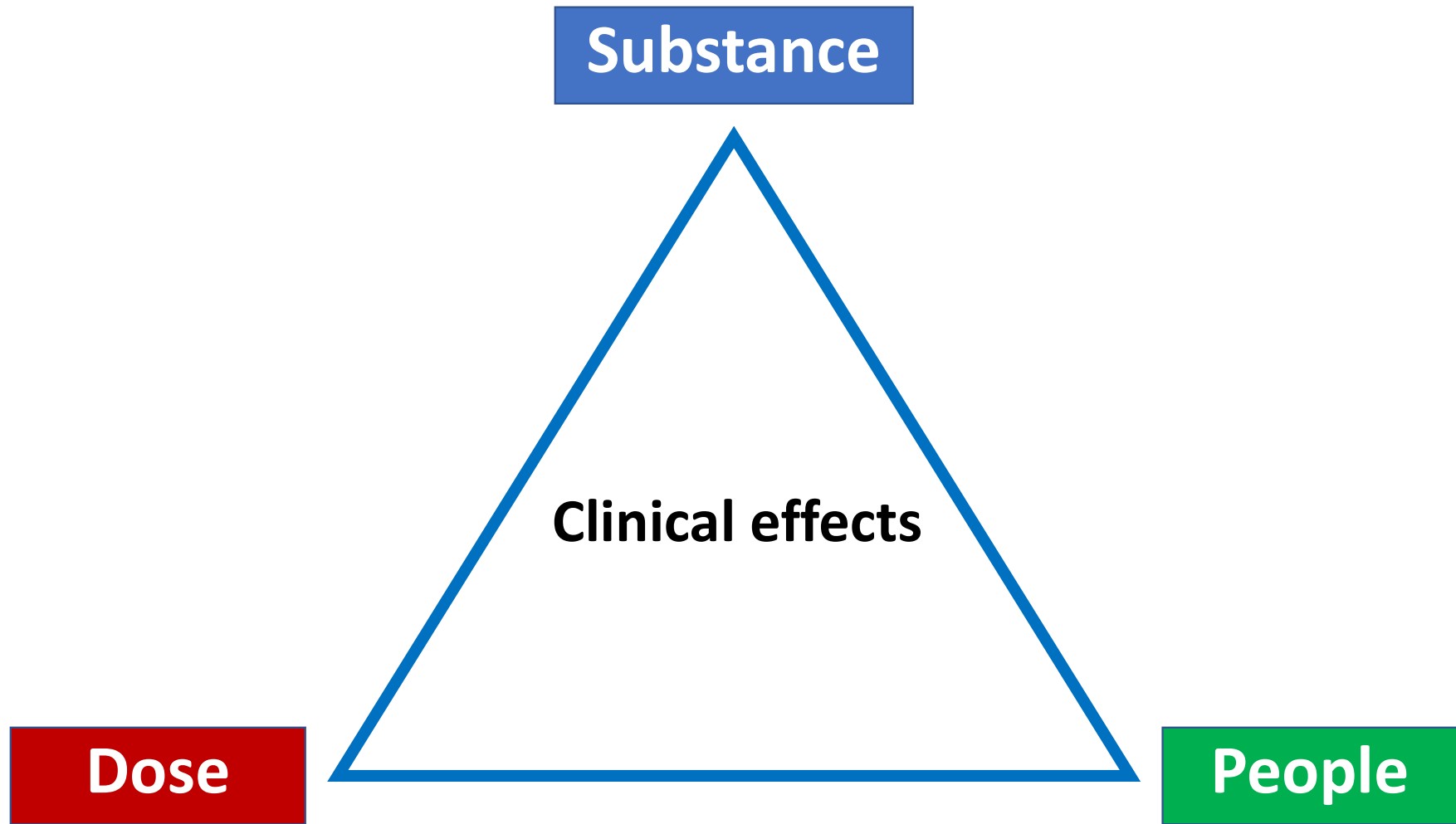
บันเทิง

สลด!! เด็กฝาแฝด น้ำท่วมปอดดับ!! หลังถูกบังคับดื่มน้ำ20ล.อ้างขับไล่ผี

08-10-2013 13:24

คอลัมน์ : ภูมิภาค / อาชญากรรม

tag : เด็กฝาแฝด น้ำท่วมปอดเสียชีวิต หลังถูกบังคับดื่มน้ำ20ล.



Everything can be Poisonous
depending on
Substance
Dose
People

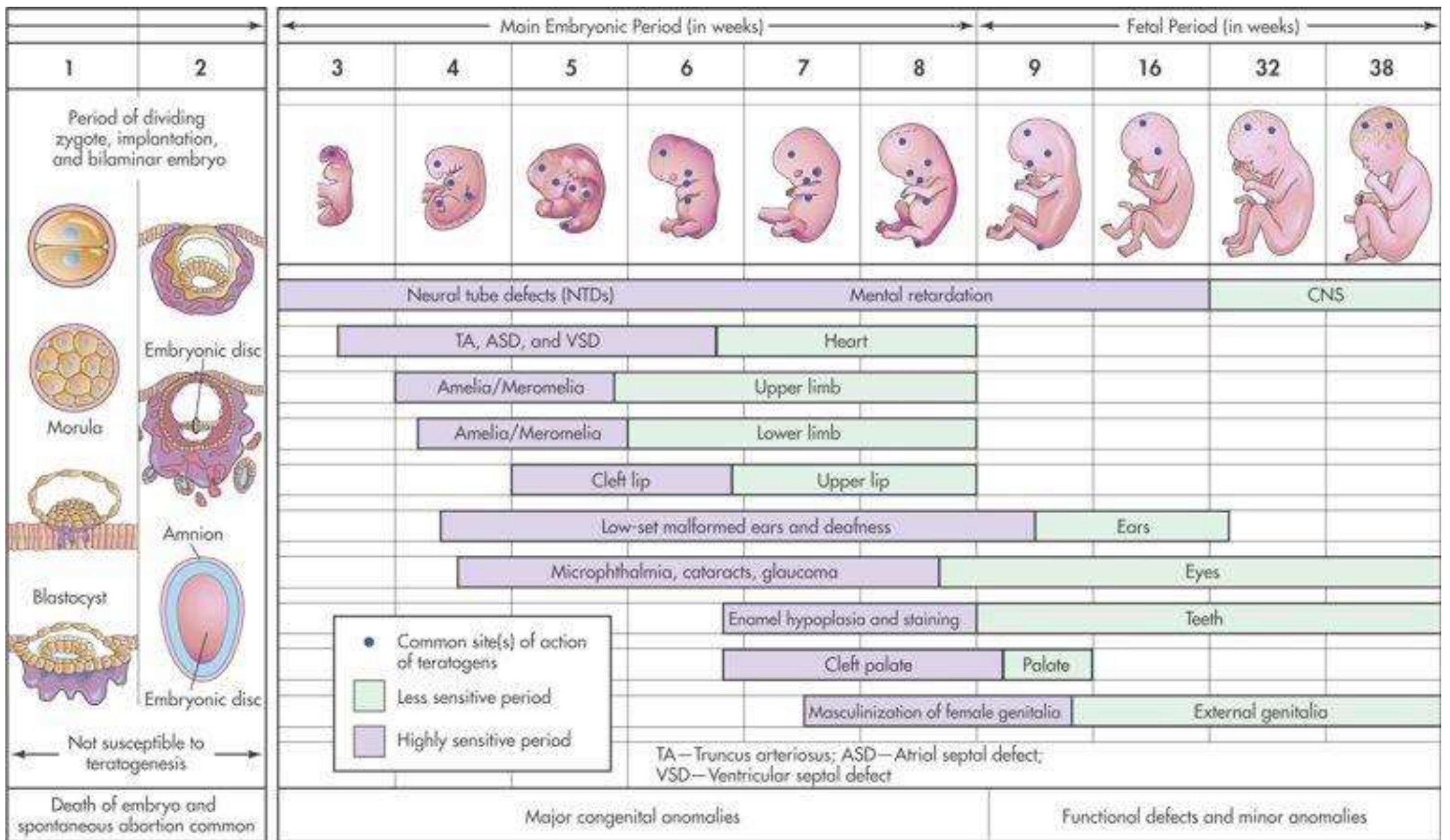
Pregnant Ladies



Baby(ies) & Mom

Physiological changes

Stages of pregnancy





**THE BEST WAY
TO KEEP YOUR BABY HEALTHY
IS TO KEEP YOURSELF
HEALTHY**

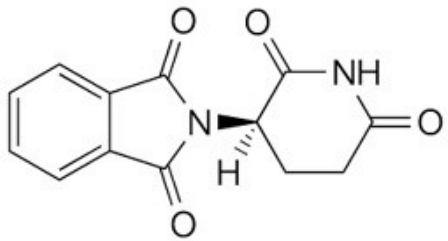
- 1 exercise daily
- 2 drink lots of H₂O
- 3 meditate
- 4 eat your veggies
- 5 sleep enough

brought to you by

Healthyher

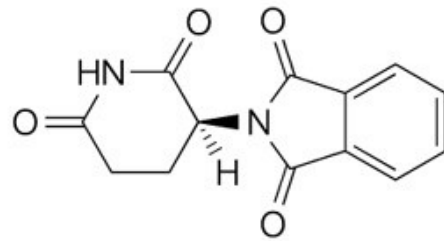
LIVING.COM

Some substances harm only the baby



R-(+)-Thalidomide

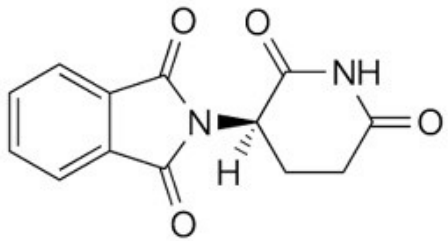
Sedative



S-(-)-Thalidomide

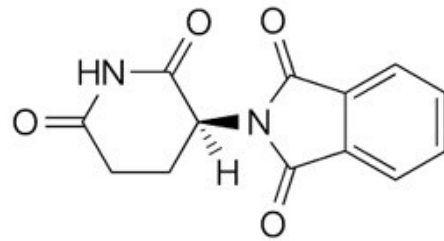
Teratogen in human

Some substances harm only the baby



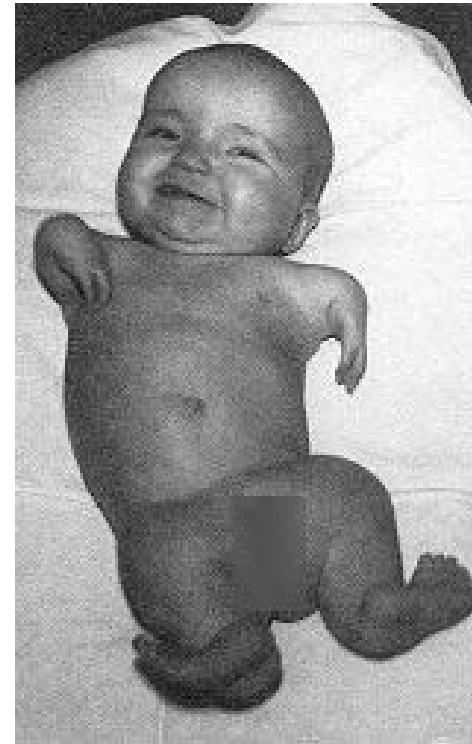
R-(+)-Thalidomide

Sedative



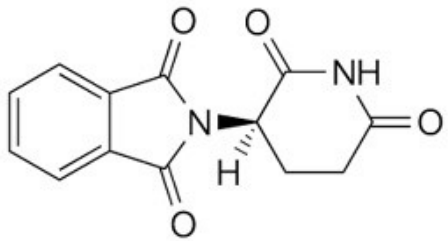
S-(-)-Thalidomide

Teratogen in human



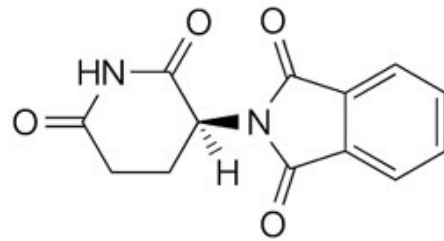
Phocomelia

Some substances harm only the baby



R-(+)-Thalidomide

Sedative

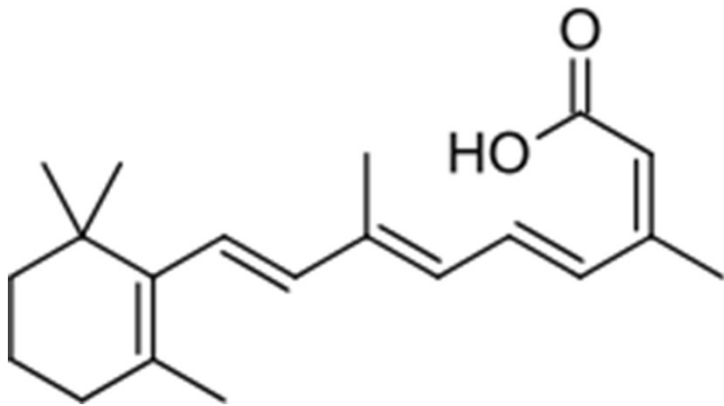


S-(-)-Thalidomide

Teratogen in human



Some substances harm only the baby



Isotretinoin
Acne medication
Teratogen in human;
CNS, craniofacial, heart defect

> Use The 2 Effective Forms Of Birth Control Together

- You must use both forms together all the time for at least 1 month before you start taking isotretinoin.
 - There is a 30-day mandatory waiting period during which you must be using both chosen forms of birth control before you are eligible to begin treatment with isotretinoin
- You must use both forms together while you are taking isotretinoin
- You must use both forms together for 1 month after isotretinoin treatment.

> Get Blood Or Urine Tests For Pregnancy

You must have a negative pregnancy test:

- To enter the iPLEDGE Program
- Before you start isotretinoin
- Performed in an approved lab each month before you can obtain your prescription
- Right after you finish your last isotretinoin dose
- 1 month after you finish your last isotretinoin dose

Always check pregnancy category before using the medication

Pregnancy Category	Description
A	No risk in controlled human studies: 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	No risk in other studies: 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.
C	Risk not ruled out: 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.
D	Positive evidence of risk: 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.
X	Contraindicated in pregnancy: 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.
N	FDA has not yet classified the drug into a specified pregnancy category.

Part 1: Iron toxicity

Iron element

- Ferrous fumarate (200mg, 75mg/mL)
33% Fe element → 66 mg, 25 mg/mL
- Ferrous sulfate (300mg)
20% Fe element → 60 mg
- Ferrous gluconate (500)
12% Fe element → 60 mg

Iron element & Toxicity

- Individuals demonstrate signs of GI toxicity after ingestion of “elemental iron” more than 20 mg/kg.
- Moderate intoxication occurs when ingestion of “elemental iron” exceeds 40 mg/kg.
- Ingestions exceeding 60 mg/kg can cause severe toxicity and may be lethal.

Iron toxicity

- GI irritant
- Impair oxidative phosphorylation and mitochondrial dysfunction
- Metabolic acidosis
- Organ dysfunction: liver, heart, kidney, coagulation

5 stages of iron toxicity

- Stage 1 (0-6 h)- Gastrointestinal (GI)
- Stage 2 (6-24 h)- Latent
- Stage 3 (6-48 h)- Metabolic/cardiovascular
- Stage 4 (2-5 d)- Hepatic & multiorgan failure
- Stage 5 (2-5 wk)- Delayed GI obstruction

Investigation

- Electrolyte & ABG → metabolic acidosis (either from lactate or Fe itself)
- Liver function test
- Prothrombin time, INR
- Abdominal X-ray: ในคนท้องควรจะ shield หรือหากชัดเจนมากกว่ากินมาเยอะ ไม่จำเป็นต้อง x-rays

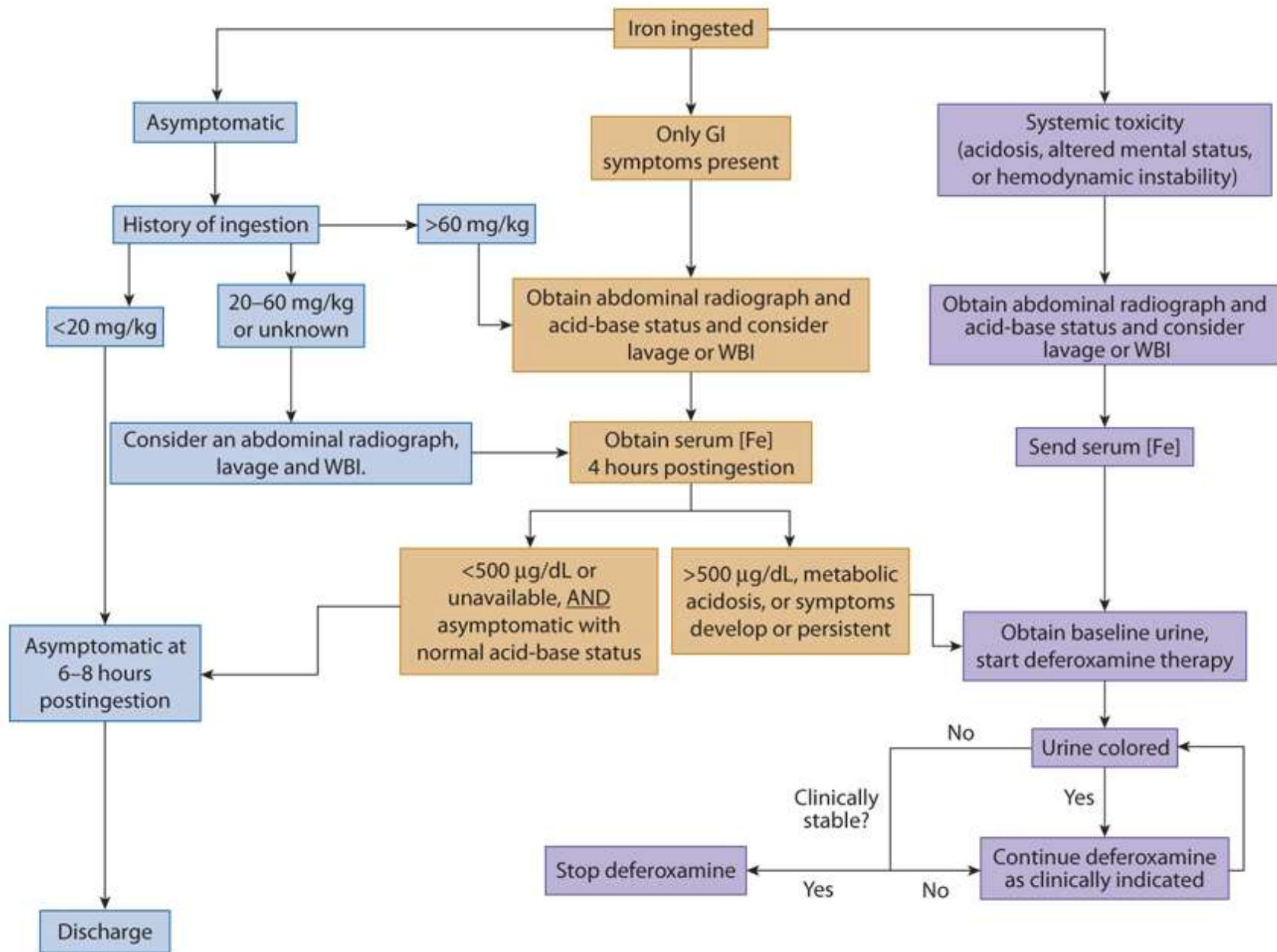


Investigation

- Serum iron concentration
 - **peak levels occur 4-6 hours**
 - > 350 mcg/dL is considered predictive of moderate symptoms (equivalent to > 40mg/kg)
 - > 500 mcg/dL is considered predictive of systemic toxicity (equivalent to > 60mg/kg)
- **> 6 hours iron levels fall** due to intracellular shift
levels **do not clearly correlate** with clinical toxicity
ประเมินที่ effect ที่เกิดเช่น **wide gap metabolic acidosis** หรือ organ injury (LFT)

Treatment

- Primary survey & resuscitation
- Symptomatic and supportive care
- NOT bind to activated charcoal
- Whole bowel irrigation
- Antidote: **Deferoxamine**



Iron: GI decontamination

3. Whole bowel irrigation

- Polyethylene glycol 3350 with electrolyte solution (PEG-ELS: Colyte, Macrogal, Forlax)
- Non-absorbable solution: osmotic diarrhea
- Use in case ingests
 - **Sustained release substance**
 - **Foreign body**
 - **Substance can not effectively remove by other way**
- ห้ามทำในกรณีกินกรด-ด่าง หรือสารที่เสี่ยงทางเดินอาหารทะลุร่วม

Iron: GI decontamination

3. Whole bowel irrigation

- Drink or NG drip: 1.5-2L/hr in adult;
(25ml/kg/hr in children)
- Give until clear watery stool
- Side effect: aspiration, abdominal cramping
- If administration too slow, Na can be absorbed which may lead to CHF

Part 2: Substance Abuse

สารเสพติด

- **Substance abuse**

สารที่มีฤทธิ์ต่อจิตประสาท นำไปสู่การติดสาร และเป็นอันตรายต่อสุขภาพ

- **Illicit Drugs**

ยาที่ถูกผลิต ขนย้าย และใช้เสพอย่างผิดกฎหมาย (ดูตามกฎหมายระหว่างประเทศ)

http://www.who.int/topics/substance_abuse/en/
<http://www.unodc.org/unodc/en/illicit-drugs/definitions/>

DSM V Diagnostic Criteria: Substance Use Disorder

SEVERITY: 2-3: mild 4-5: moderate 6 or more: severe

1. Taking the substance in larger amounts or for longer than you meant to.

2. Wanting to cut down or stop using the substance but not managing to do so.

3. Spending a lot of time getting, using, or recovering from use of the substance

4. Cravings and urges to use the substance

5. Not managing to do what you should at home, work, or school because of substance use

6. Continuing to use, even when it causes problems in relationships

7. Giving up important social, occupational, or recreational activities because of substance use

8. Using substances again and again, even when it puts you in danger

9. Continuing to use, even if you have a physical or psychological problem that could have been caused or made worse by the substance

*10. Needing more of the substance to get the effect you want (tolerance)

*11. Development of withdrawal symptoms, which can be relieved by taking more of the substance

*Criteria not met if taking prescribed drugs under supervision

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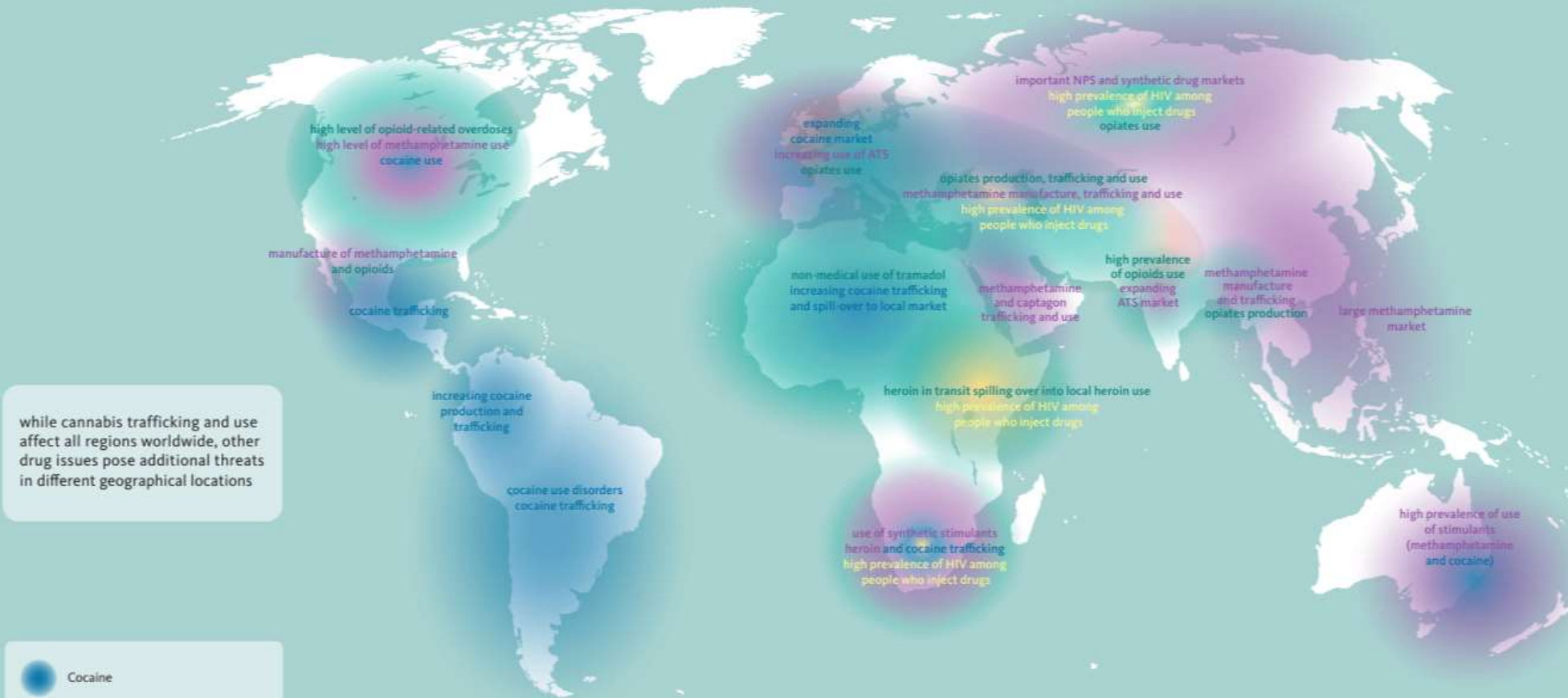
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THE WORLD DRUG PROBLEM COMMON CHALLENGE, LOCAL DYNAMIC



while cannabis trafficking and use affect all regions worldwide, other drug issues pose additional threats in different geographical locations

- Cocaine
- Opioids/Opiates
- Amphetamine-type stimulants (ATS)
- HIV among people who inject drugs

<https://www.unodc.org/unodc/en/data-and-analysis/world-drug-report-2024.html>

ทำไมคนถึงใช้สารเสพติด

การรับมือกับความทุกข์ และแรงกดดัน

ต้องการการผ่อนคลาย
ต้องการความพึงพอใจที่ชีวิตปกติไม่ตอบโต้

การเจ็บป่วย

การเจ็บป่วยทางกาย การปวดเรื้อรัง
โรคทางจิตประสาท

ต้องการเพิ่มสมรรถภาพ ร่างกายหรือการทำงาน

ความอยากรู้อยากลอง

อยากรู้ว่าได้ผลเป็นอย่างไร
ได้ข้อมูลความเชื่อผิดๆ

สังคม

การเข้าถึงยาเสพติด
การยอมรับในสังคมและครอบครัว

กรรมพันธุ์ และการเลี้ยงดู

การศึกษาศาสตร์เป็นการเจ็บป่วยของ
ร่างกาย จิตใจ ครอบครัวและสังคม

Illicit drug users: pregnancy

- How drug effects on pregnancy
- How drug effects on fetus
- How pregnancy effect drug uses

Illicit drug users: pregnancy

- How drug effects on pregnancy
- How drug effects on fetus
- How pregnancy effect drug uses
 - Pain
 - Stress
 - Nausea
 - Other reasons

Illicit drug users: general consideration

- Infection risk: HIV, TB, osteomyelitis
- Arteriosclerosis or vasculitis
 - Vascular access
 - Coronary a. disease
- Malnutrition, hypovolemia, and electrolyte imbalance
- Control symptoms of intoxication
- Aware of withdrawal symptoms
- Adequate analgesia

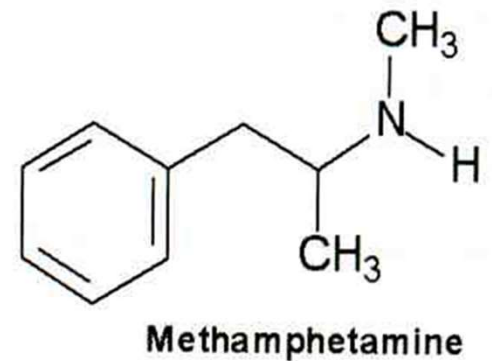
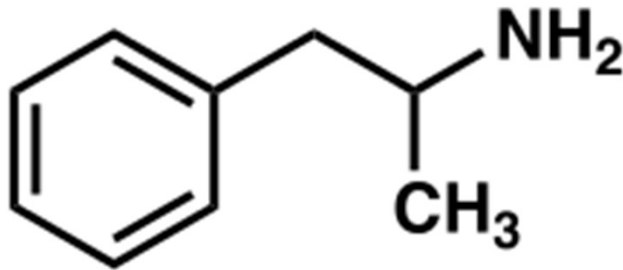
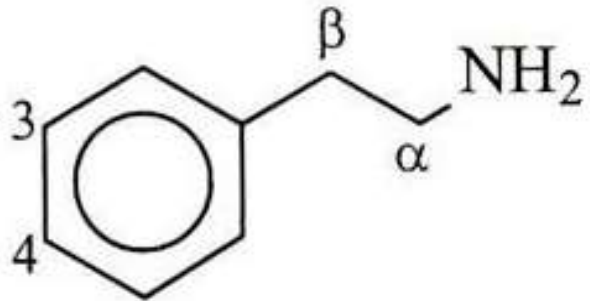
Test positive for illicit drugs or alcohol

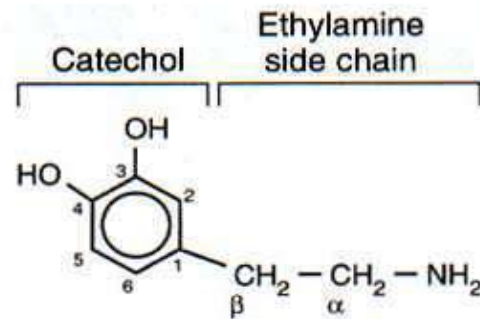
- 53% of patients with gunshot wounds
- 32.9% of victims of motor-vehicle accidents
- 32.9% of patients with falls
- 28.6% of pedestrians

2.1) Amphetamine & Derivatives

Amphetamine: introduction

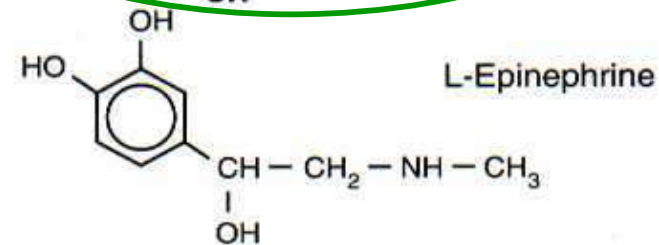
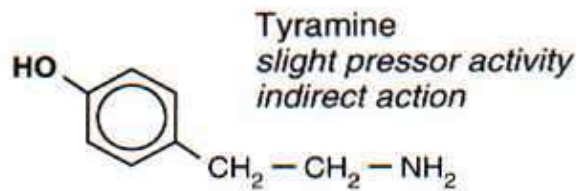
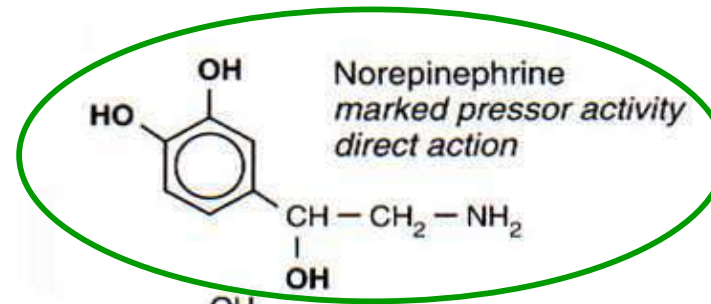
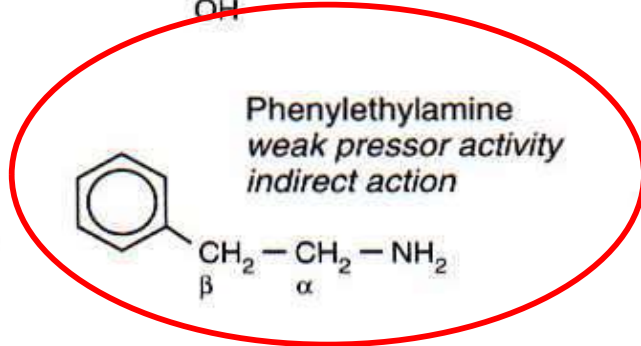
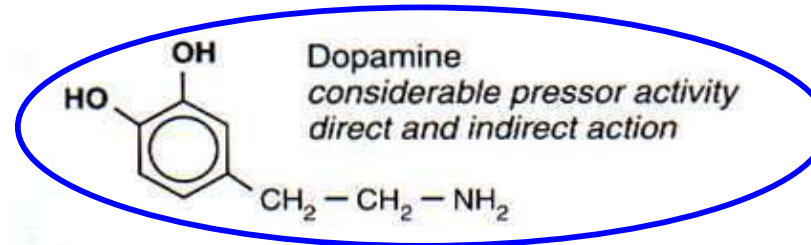
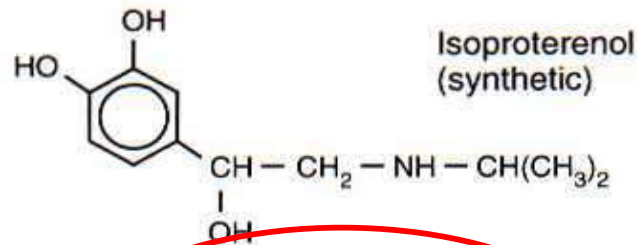
- Phenyl ethylamine stimulants
- Structure similar to dopamine and norepinephrine





(Side-chain carbons
α and β starting
from nitrogen)

Catecholamine structure

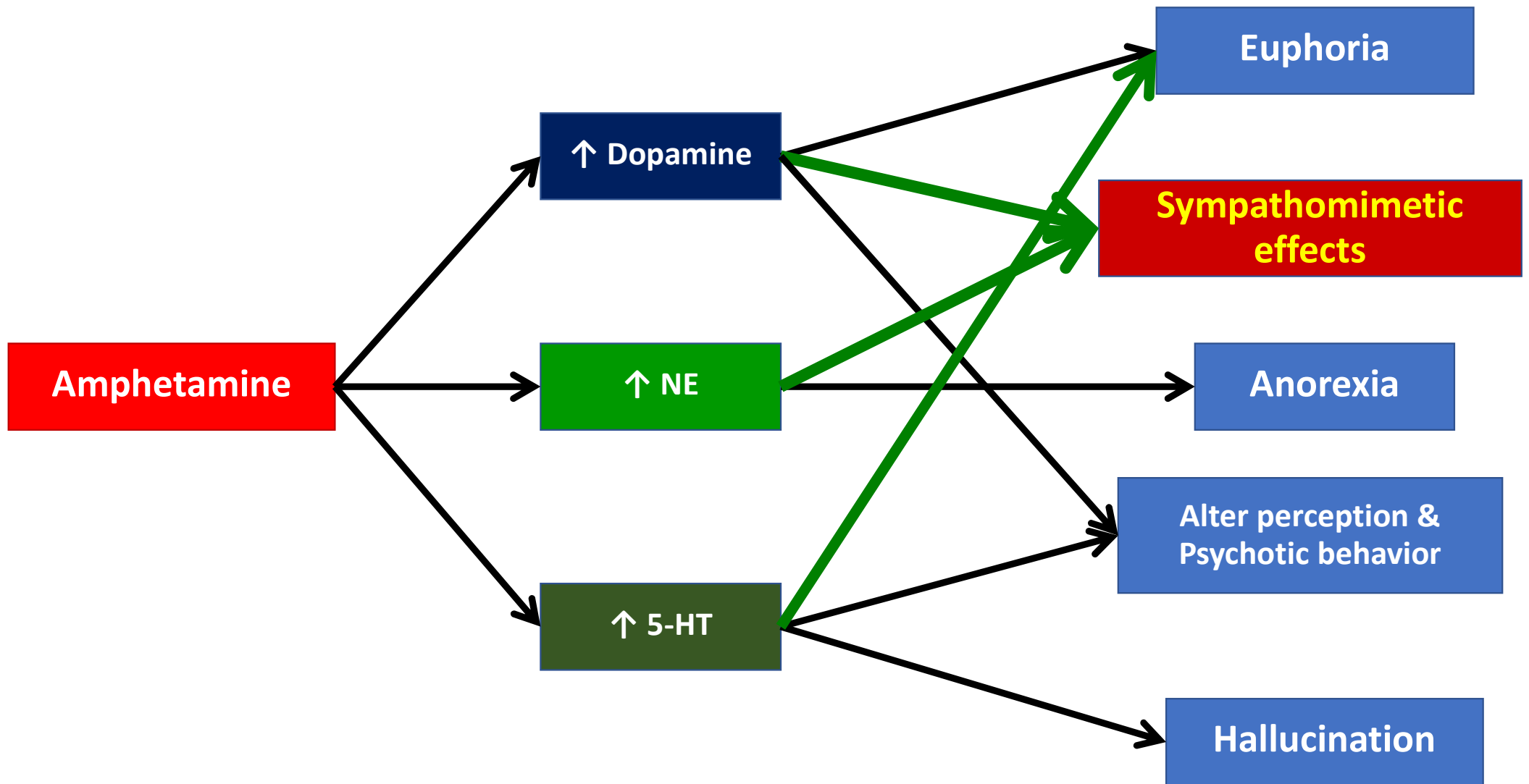


Amphetamine: uses

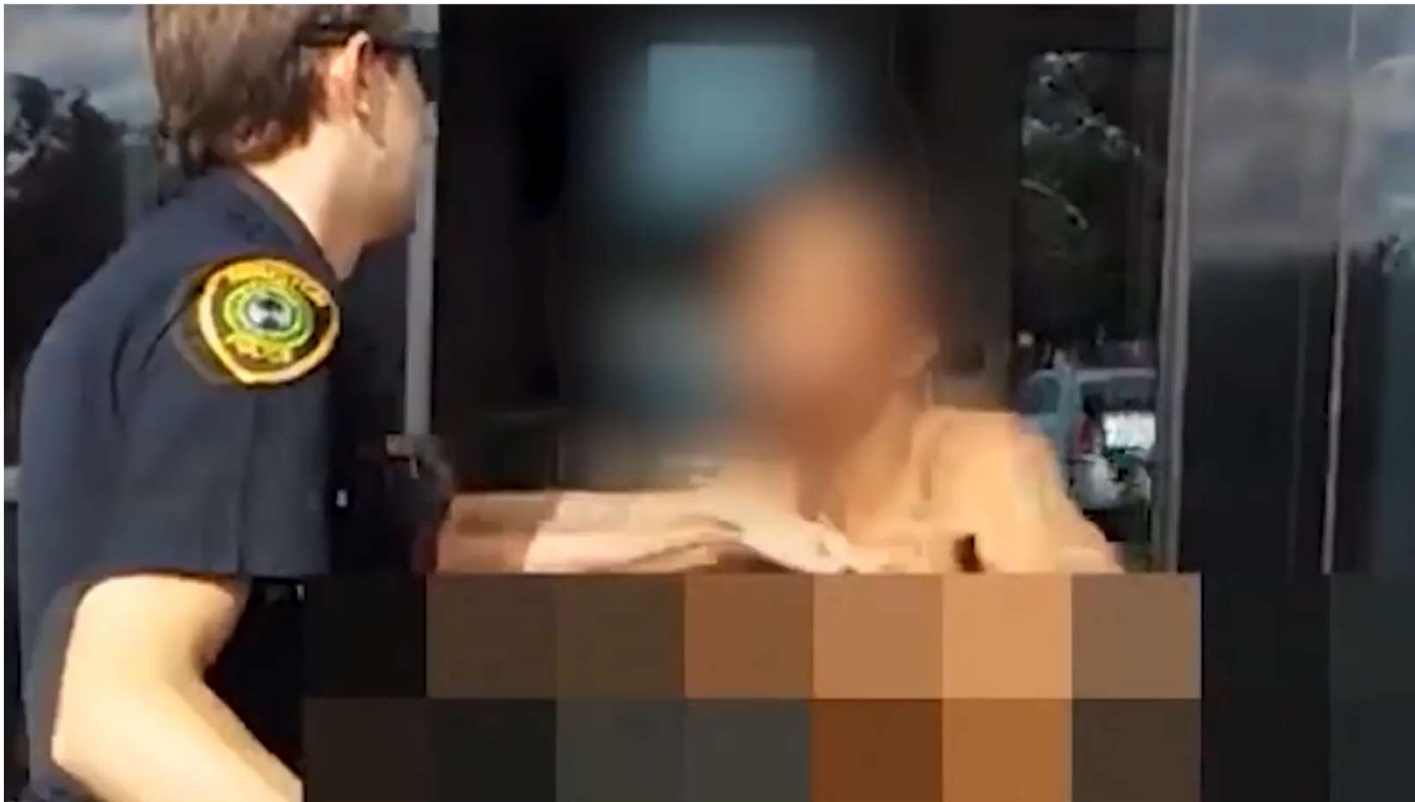


Amphetamine: pathophysiology

- Stimulate release & block reuptake of norepinephrine (NE) and dopamine (DA)
- At higher dose, stimulate release & block reuptake of serotonin (5HT)
- ↑ extracellular but ↓ vesicular storage of NE, DA, and 5HT



Synthetic stimulants



Fox 11 LA

<https://www.youtube.com/watch?v=bMfk4EfVgU>

Amphetamine: complications

- Acute

- Myocardial ischemia
- Aortic dissection
- Stress induced cardiomyopathy
- Intracerebral hemorrhage
- Rhabdomyolysis
- Disseminated intravascular coagulation
- Renal failure
- Electrolyte imbalance

- Chronic

- ↑risk of MI and stroke
- Cardiomyopathy
- Aortic or mitral regurgitation
- Pulmonary hypertension
- Psychosis & hallucination
- Vasculitis

Amphetamine: stimulant withdrawal symptoms

- Craving
- Depression and anxiety
- Sleepiness
- Exhaustion
- Increased appetite (extreme hunger)

Amphetamine: investigation

- Positive urine test results generally indicate use within 1-4 days
- But could be up to a week following heavy chronic use
- Screening (rapid chemical test kit and immunoassay) can be falsely positive, need confirmation (GC-MS, LC-MS-MS)

Amphetamine: acute poisoning treatment

- 1. Control agitation:** benzodiazepines, phenobarbital, propofol, droperidol
2. Control hypertension:
Control agitation
Vasodilators: nicardipine, nitroprusside, phentolamine, hydralazine
3. Control tachycardia:
Control agitation
Antiarrhythmics: diltiazem, verapamil
4. Control temperature: evaporation, tepid sponge, IV fluid
5. Treat complications

Amphetamine Abuse & Pregnancy

Amphetamine & high-risk pregnancy

- ↑ NE and 5-HT in intervillous space
- Placental vasocontraction
- ↓ placental blood flow

- General risk for illicit drug users:
infection and malnutrition

Amphetamine & high-risk pregnancy

- Abortion
- IUGR
- Pre-eclampsia
- Placenta previa
- Placental abruption
- Premature rupture of membrane, PROM
- Preterm labor
- Gestational hypertension

J Perinatol. 2012; 32:737-47.

Psychosomatics. 2016; 57:115-30.

Obstet Gynecol. 2008; 111:341-7.

› [Am J Obstet Gynecol](#). 2014 Oct;211(4):429.e1-7. doi: 10.1016/j.ajog.2014.06.005. Epub 2014 Jun 4.

Outcomes in pregnancies complicated by methamphetamine use

Margaret C Gorman ¹, Kaebah S Orme ², Nancy T Nguyen ², Edward J Kent 3rd ², Aaron B Caughey ²

Affiliations + expand

PMID: 24905417 DOI: [10.1016/j.ajog.2014.06.005](#)

- Retrospective cohort study of pregnancies during 2005-2008 in California
- 8,542 amphetamine users
- 2,031,328 controls

TABLE 3

Adjusted odds ratios for outcomes among methamphetamine users vs control subjects^a

Outcome of interest	Odds ratio	95% confidence interval
Preeclampsia	2.7	2.4–3.0
Severe preeclampsia	3.9	3.3–4.6
Eclampsia	4.4	2.6–7.3
Pregnancy-associated hypertension (gestational hypertension + preeclampsia)	2.3	2.2–2.5
Gestational hypertension	1.8	1.6–2.0
Gestational diabetes mellitus	0.4	0.4–0.5
Abruption	5.5	4.9–6.3
Intrauterine fetal death	5.1	3.7–7.2
Very preterm delivery (<32 wk)	4.5	4.0–5.1
Preterm delivery (<37 wk)	2.9	2.7–3.1

^a Controlled for maternal age (≥ 35 years or < 20 years), race/ethnicity, insurance status (private insurance vs public or no insurance), prenatal care, parity, education (≤ 12 years or > 12 years), prenatal care, chronic hypertension, diabetes mellitus, gestational diabetes mellitus, tobacco exposure, and alcohol exposure.

Gorman. Methamphetamine use in pregnancy. *Am J Obstet Gynecol* 2014.

TABLE 2

Unadjusted incidence of outcomes among methamphetamine users vs control subjects

Outcome of interest	Incidence among methamphetamine users,^a %	Incidence among control subjects,^b %	P value
Preeclampsia	6.8	2.9	< .001
Severe preeclampsia	2.5	0.8	< .001
Severe preeclampsia among those with pregnancy-associated hypertension	21.6	13.5	< .001
Eclampsia	0.3	0.1	< .001
Pregnancy-associated hypertension (gestational hypertension + preeclampsia)	11.6	5.8	< .001
Gestational hypertension	5.6	3.2	< .001
Gestational diabetes mellitus among those who delivered at term	2.7	6.1	< .001
Abruption	5.2	0.8	< .001
Intrauterine fetal death	1.4	0.3	< .001
Very preterm delivery (<32 wk)	5.3	1.2	< .001
Preterm delivery (<37 wk)	23.4	8.9	< .001

^a n = 8542; ^b n = 2,031,328.

Gorman. Methamphetamine use in pregnancy. *Am J Obstet Gynecol* 2014.

Amphetamine & fetal outcome

- Cleft lip, cleft plate
- Biliary atresia
- Birth asphyxia
- Low birth weight
- Small for gestational age
- Abnormal development: cardiac, limb, urinary system
- Withdrawal symptom: hypotonia, poor feeding, depression

J Perinatol. 2012; 32:737-47.

Curr Opin Obstet Gynecol. 2007; 19:578-85.

J Med Assoc Thai. 2005; 88:1506-13.

TABLE 3

Adjusted odds ratios for outcomes among methamphetamine users vs control subjects^a

Outcome of interest	Odds ratio	95% confidence interval
Birthweight		
<2500 g	3.5	3.3–3.8
>4000 g	0.5	0.4–0.6
Neonatal death	3.1	2.3–4.2
Neonatal death adjusted for gestational age	0.7	0.5–1.1
Jaundice adjusted for gestational age	1.1	1.0–1.1
Infant death	2.5	1.7–3.7
Infant death adjusted for gestational age	1.8	1.1–2.7

^a Controlled for maternal age (≥ 35 years or < 20 years), race/ethnicity, insurance status (private insurance vs public or no insurance), prenatal care, parity, education (≤ 12 years or > 12 years), prenatal care, chronic hypertension, diabetes mellitus, gestational diabetes mellitus, tobacco exposure, and alcohol exposure.

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Unadjusted incidence of outcomes among methamphetamine users vs control subjects

Outcome of interest	Incidence among methamphetamine users, ^a %	Incidence among control subjects, ^b %	P value
Birthweight			
<2500 g	17.2	5.0	< .001
>4000 g	4.5	8.8	< .001
Neonatal death			
Term neonates	0.5	0.1	< .001
Preterm neonates	2.1	1.6	.07
All neonates	0.8	0.2	< .001
Jaundice among those born preterm	25.7	27.0	.16
Infant death			
Term infants	0.4	0.1	< .001
Preterm infants	0.6	0.3	< .001
All neonates	0.4	0.1	< .001

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Gorman. Methamphetamine use in pregnancy. *Am J Obstet Gynecol* 2014.

Pregnancy care

Antenatal care

- Monitor: BP, proteinuria, EKG, body weight, nutritional status, infection, and fetal growth
- Screening for placental previa
- Discuss for detoxification
 - Underlying condition and precipitating factors for drug abuse
 - Med: bupropion (B), mirtazapine (C), naltrexone (C), SSRI (C); except paroxetine (D)

Perinatal care

- Method of anesthesia
 - Method of labor
- } according to obstetrics condition
- Beware of complications
 - Placental previa, abruptio placenta, PROM
 - Fetal distress
 - Intoxication: seizure, high BP, arrhythmia
 - Withdrawal

Postnatal care

- Manage of withdrawal symptom
- Lactation in cases with amphetamine abuse:
last abuse \geq 48 h
Urine amphetamine negative \geq 24 h
- With therapeutic use of d-amphetamine or methylphenidate
Can start nursing without treatment interruption

Br J Clin Pharmacol. 2009; 67: 455–9.

J Hum Lact. 2016; 32:333-9.

Drugs and Lactation Database (LactMed)

Amphetamine & Anesthetic Consideration

Amphetamine: anesthetic consideration

- Symptomatic: agitate delirium case may not cooperative
Need more sedation
- Chronicity: deplete catecholamine storage
Risk for hypotension
- Positive screening test is NOT mean symptomatic

Amphetamine: anesthetic consideration

In asymptomatic case with prescription use:

- No need to postpone the operation
- Continue the medication
- Caution with vasopressor
- Caution with atropine
- If hypotension develop use direct vasoconstrictor (epinephrine, phenylephrine)

Paediatr Anaesth. 2012;22(4):341-4.

Br J Anaesth. 2008;100(3):421-2.

2.2) Opioid and Opiates

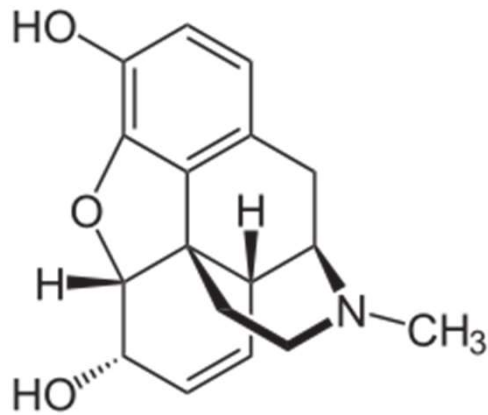
Opioid: introduction

- Opium poppy (*Papaver somniferum*)
Morphine

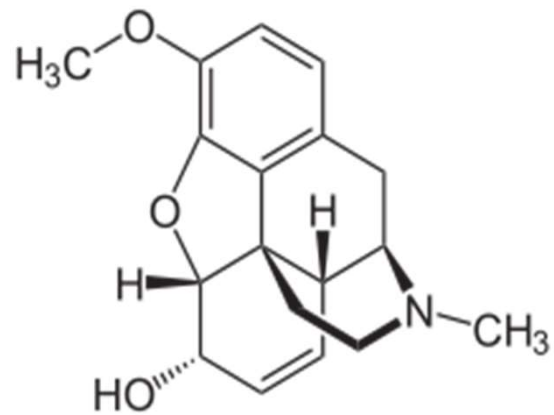


Opioid: introduction

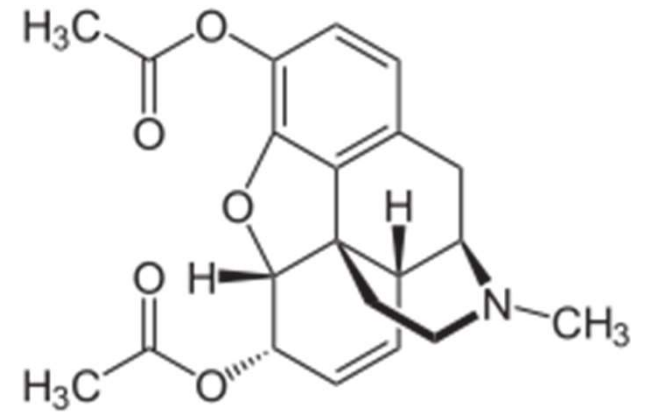
- Opiates: morphine, codeine
- Semisynthetic: heroine, oxycodone, hydrocodone
- Synthetic: meperidine, fentanyl, tramadol, buprenorphine, methadone



morphine



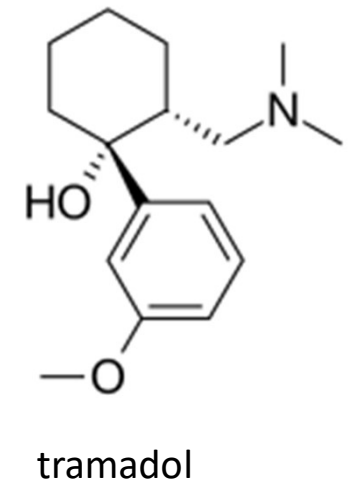
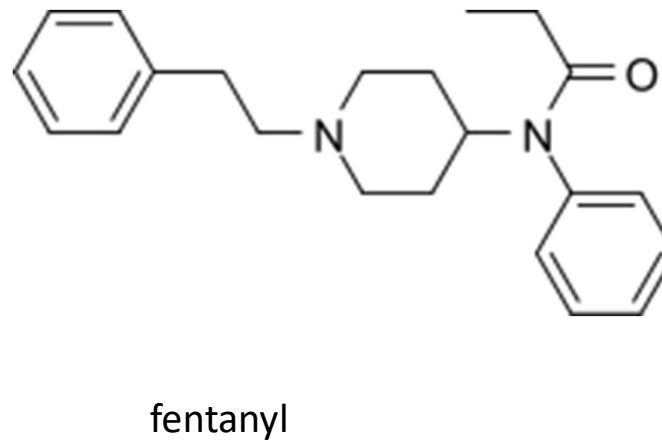
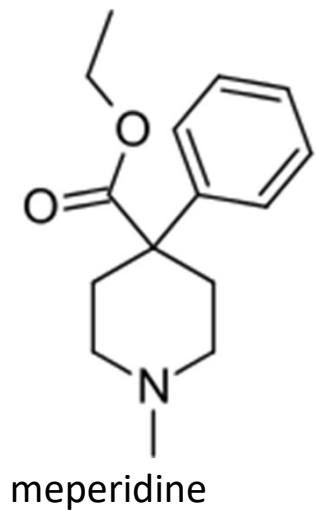
codeine



heroine

Opioid: introduction

- Opiates: morphine, codeine
- Semisynthetic: heroine, oxycodone, hydrocodone
- Synthetic: meperidine, fentanyl, tramadol, buprenorphine, methadone



Opioid: pathophysiology

- Mu-receptors:
analgesia, sedation, euphoria, respiratory depression, miosis, cough suppression, ↓ HR, ↓ GI motility, pruritus
- κ-receptors:
analgesia, sedation, miosis, dysphoria, and hallucinations
- δ-receptors:
some analgesia and antidepressant effect.
- Nociceptin/orphanin FQ receptors:
analgesic, anxiolytic

Opioid: clinical effects

- CNS depression: Lethargy, Coma
- Pin-pointed pupil
- ↓RR, HR, BP
- Non-cardiogenic pulmonary edema
- Seizure common in meperidine, tramadol, fentanyl
- QT prolongation: methadone
- Constipation

Opioid: investigation

- Urine screening (immunoassay) detect opiates (morphine, codeine) and heroin
- NOT detect oxycodone, hydrocodone, buprenorphine, meperidine, tramadol, fentanyl

Opioid: acute poisoning treatment

- Ventilator support
- Naloxone: mu-opioid receptor antagonist
Aim for adequate spontaneous respiration
NOT aim to regain full consciousness
Rebound effects: agitation, pain, hypertension, tachycardia, dyspnea

Opioid: acute poisoning treatment

- Naloxone: mu-opioid receptor antagonist
Onset: 2-3 minutes
Duration: 30-90 minutes

Dose 0.4 mg IV IM SC; may
start 0.01-0.04mg in chronic abuser/dependence
Intra-tracheal 2-2.5 times of IV dose
May need repeated dose or IV infusion
Still need to observe respiration

Opioid Abuse & Pregnancy

Opioid & high-risk pregnancy

- IUGR
- Preeclampsia
- Preterm labor
- PROM
- Fetal distress
- Postpartum hemorrhage

- General risk for illicit drug users:
infection and malnutrition

Curr Opin Obstet Gynecol. 2007; 19:578-85.
Obstet Gynecol 2017; 130:e81–94.

Opioid & fetal outcome

- Microcephaly
- Low birth weight
- Birth asphyxia
- Intoxication: lethargy and apnea
- Neonatal abstinence syndrome (withdrawal; onset 72h -2wk): agitated, poor feeding, ↑ muscle tone, seizure

Curr Opin Obstet Gynecol. 2007; 19:578-85.

Obstet Gynecol 2017; 130:e81–94.

Pregnancy care

Antenatal care

- Monitor: BP, proteinuria, body weight, nutritional status, infection, and fetal growth
- Discuss for detoxification
 - Underlying condition and precipitating factors for drug abuse
 - Opioid replacement therapy: methadone (C), buprenorphine (C)
Other med: naltrexone (B), clonidine (C), paracetamol (B)

Perinatal care

- Method of anesthesia
 - Method of labor
- } according to obstetrics condition
- May have tolerance with opioid
 - Stop naltrexone at least 2-3 days before labor (for opioid can have analgesic effect)
 - Notify PED for monitoring birth asphyxia and neonatal abstinence syndrome

Postnatal care

- Manage of withdrawal symptom (opioid replacement therapy)
- Avoid lactation in cases with opioid abuse; especially codeine, meperidine, tramadol
- Cases with therapeutic use of methadone, buprenorphine, intrathecal morphine, or intrathecal fentanyl can start nursing without treatment interruption

Opioid & Anesthetic Consideration

Opioid: anesthetic consideration

- Tolerance: need more analgesic dose
- Cases with long standing treatment: continue their med
- Regional anesthesia:
spinal/epidural morphine, or fentanyl +/- lidocaine
- Additional analgesics:
paracetamol, alpha 2 agonist

Summary

- **Iron Toxicity**
 - Serum iron peak at 4-6 h
 - Determine risk by element iron/body weight (mg/kg)
- **Common drugs of abuse** (amphetamine, opioid)
 - Pathophysiology
 - Clinical effects
 - Substance and pregnancy
 - Pregnancy care
 - Anesthetic considerations

Reference

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Thank you



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