

USMLE session #5

Psychoactive drug intoxication and withdrawal *SRY* gene

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1. Psychoactive drug intoxication and withdrawal

What kind of psychoactive drugs are there?

1. Depressants (e.g., alcohol)
 1. intoxication: mood elevation, ↓ anxiety, sedation
 2. withdrawal: anxiety, tremor, seizures
2. Stimulants (e.g., cocaine)
 1. intoxication: mood elevation, insomnia, tachycardia
 2. withdrawal: depression, lethargy, weight gain
3. Hallucinogens (eg. LSD)

1. Depressants

	intoxication	withdrawal
Alcohol ¹	slurred speech, ataxia, coma	severe: autonomic hyperactivity and delirium tremens
Opioids (e.g., morphine, heroin, methadone)	euphoria, respiratory and CNS depression, gag reflex, pinpoint pupils, seizures (overdose) <i>Treatment:</i> naloxone, naltrexone	dilated pupils, piloerection („cold turkey“), rhinorrhea, yawning, diarrhea <i>Treatment:</i> methadone, buprenorphine
Barbiturates	respiratory depression	Delirium, life-threatening cardiovascular collapse, psychotic symptoms (e.g., the belief that someone's going to kill him)
Benzodiazepines	Ataxia, minor respiratory depression <i>Treatment:</i> flumezenil	Rebound anxiety, tachycardia

¹ GGT – sensitive indicator of alcohol use. AST value is twice ALT value.

Delirium tremens

- life threatening alcohol withdrawal sy that peaks 2-4 days after last drink (typically after surgery in hospital)
- clinical findings:
 - autonomic hyperactivity (e.g., tachycardia, tremor, anxiety, seizures)
- treatment:
 - benzodiazepins

2. Stimulants

	intoxication	withdrawal
amphetamines	Euphoria, pupillary dilatation, prolonged wakefulness and attention	Anhedonia, ↑ appetite, hypersomnolence
cocaine	Hallucinations (including tactile – „cocaine bugs“), angina, sudden cardiac death <i>Treatment: α-blockers, benzodiazepines</i>	Hypersomnolence, malaise, severe psychological craving
Caffeine	Restlessness, ↑ diuresis, muscle twitching	Lack of concentration, headache
Nicotine	Restlessness	Irritability, anxiety, craving <i>Treatment: nicotine patch, bupropion/varenicline</i>

3. Hallucinogens

	Intoxication	Withdrawal (generally few)
PCP (phencyclidine, „angel dust“)	Aggressivity , vertical and horizontal nystagmus	
LSD	Perceptual distortion (visual, auditory), depersonalization, possible flashbacks	
Marijuana (cannabinoid)	Euphoria, perception of slowed time, ↑ appetite, conjunctival injection, amotivational syndrome in chronic users	

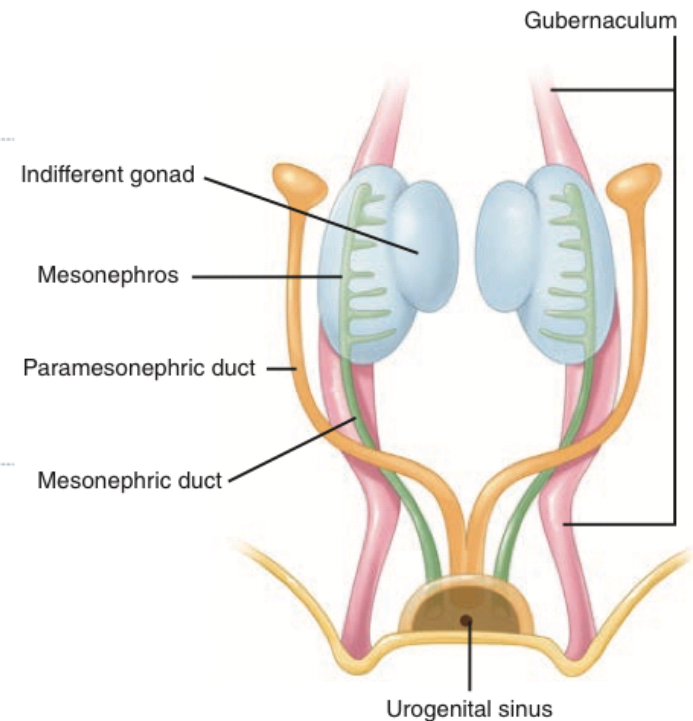
Source

- Tao Le, Vikas Bhushan: *First Aid for the USMLE Step 1 2014, McGraw Hill Professional, 2014, ISBN 0071831436.*

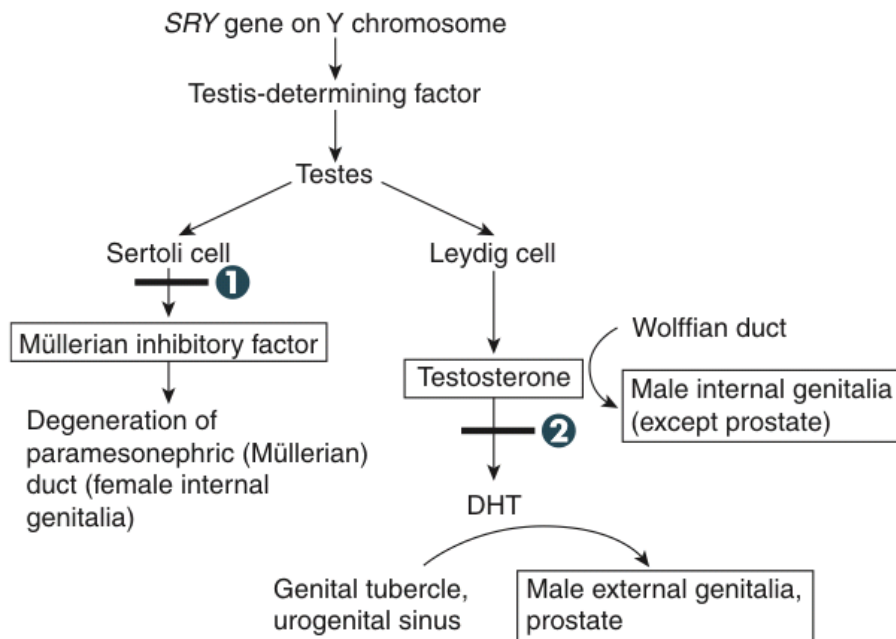
2. *SRY* gene

Genital embryology

Female	Default development. Mesonephric duct degenerates and paramesonephric duct develops.
Male	<p>SRY gene on Y chromosome—produces testis-determining factor (testes development). Sertoli cells secrete Müllerian inhibitory factor (MIF) that suppresses development of paramesonephric ducts.</p> <p>Leydig cells secrete androgens that stimulate the development of mesonephric ducts.</p>
Paramesonephric (Müllerian) duct	Develops into female internal structures—fallopian tubes, uterus, and upper portion of vagina (lower portion from urogenital sinus). Müllerian duct abnormalities result in anatomical defects that may present as 1° amenorrhea in females with fully developed 2° sexual characteristics (indicator of functional ovaries).
Mesonephric (Wolffian) duct	Develops into male internal structures (except prostate)— S eminal vesicles, E pididymis, E jaculatory duct, and D uctus deferens (SEED).



SRY gene



- 1 No Sertoli cells or lack of Müllerian inhibitory factor: develop both male and female internal genitalia and male external genitalia
- 2 5α -reductase deficiency: inability to convert testosterone into DHT; male internal genitalia, ambiguous external genitalia until puberty (when \uparrow testosterone levels cause masculinization)

3. Questions

Q1 A 60-year-old man is brought to the hospital after a fall outside of a neighborhood bar. Radiologic studies indicate that the patient has a fractured hip and surgery is performed immediately. Two days later, the patient begins to show an intense hand tremor and tachycardia. He tells the doctor that he has been “shaky” ever since his admission and that the shakiness is getting worse. The patient states that while he feels frightened, he is comforted by the fact that the nurse is an old friend (he has never met the nurse before). He also reports that he has started to see spiders crawling on the walls and can feel them crawling on his arms. The doctor notes that the patient’s speech seems to be drifting from one subject to another. Of the following, what is the most likely cause of this picture?

- (A)** Alcohol use
- (B)** Alcohol withdrawal
- (C)** Heroin use
- (D)** Heroin withdrawal
- (E)** Amphetamine withdrawal

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The answer is B. The most likely cause of tremor, tachycardia, illusions (e.g., believing the nurse is an old friend), and visual and tactile hallucinations (e.g., formication—the feeling of insects crawling on the skin) in this patient is alcohol withdrawal, since use of alcohol during the past few days of hospitalization is unlikely. His fractured hip may have been sustained in the fall while he was intoxicated. Heroin use and heroin and amphetamine withdrawal generally are not associated with psychotic symptoms.

Q2 A 43-year-old man with a 5-year history of HIV tells his physician that he has been smoking marijuana a few times a day to treat his symptoms of nausea and lack of appetite. To obtain the marijuana, the patient notes that he grows it in his backyard. The doctor's best response to this patient's revelation is

- (A)** I am sorry but growing or using marijuana is illegal and I must notify the police
- (B)** I have read about other patients growing marijuana
- (C)** Are you aware that marijuana can cause respiratory problems?
- (D)** There are a number of medications that I can prescribe to help alleviate your nausea and lack of appetite in place of marijuana
- (E)** Do you think that using marijuana has negative long-term effects?

The answer is D. The best response to this patient's revelation about growing and using marijuana is to recommend effective but safer substitutes, e.g., prescription medications to treat his nausea and lack of appetite. It is neither appropriate nor necessary for a physician to report the patient's actions to the police. Also, this HIV-positive patient is likely to be more concerned about feeling ill in the short term than long-term consequences of marijuana use such as respiratory problems.

Q3 A 35-year-old man is brought to the emergency department confused and anxious. The man reports that someone is trying to kill him but he does not know who the person is. Initial physical examination reveals elevated heart and respiration rates. While in the emergency room the patient has a seizure and then develops life-threatening cardiovascular symptoms. The drug that this patient is most likely to be withdrawing from is

- (A)** phencyclidine (PCP)
- (B)** lysergic acid diethylamide (LSD)
- (C)** heroin
- (D)** secobarbital
- (E)** marijuana

The answer is D. This 35-year-old patient is most likely to be withdrawing from secobarbital, a barbiturate. Barbiturate withdrawal symptoms appear about 12–20 hours after the last dose and include anxiety, elevated heart and respiration rates, psychotic symptoms (e.g., the belief that someone is trying to kill him), confusion, and seizures, and can be associated with life-threatening cardiovascular symptoms. There are few physical withdrawal symptoms associated with marijuana, phencyclidine (PCP), or lysergic acid diethylamide (LSD), and those associated with heroin are uncomfortable but rarely physically dangerous.

Q4 A 56-year-old woman presents to her physician because of recent onset of chest pain and dyspnea. Six weeks earlier the patient suffered an MI. Her physical examination is remarkable for a friction rub over the fifth intercostal space in the midclavicular line together with an elevated jugular venous pressure. Which of the following myocardial complications is this individual most likely suffering from?

- (A) Cardiac arrhythmia
- (B) Dressler's syndrome
- (C) Left ventricular failure
- (D) Thromboembolism
- (E) Ventricular rupture

The correct answer is B. Dressler's syndrome is an autoimmune phenomenon that results in fibrinous pericarditis. This delayed pericarditis typically develops 2–10 weeks post-MI and presents clinically as chest pain and a pericardial friction rub. It is generally treated with nonsteroidal antiinflammatory agents or corticosteroids.


Answer A is incorrect. Cardiac arrhythmia is a common cause of post-MI death and typically occurs 2 days post-MI. It does not typically present with a friction rub.

Answer C is incorrect. Left ventricular failure occurs in 60% of people who suffer from MI and can present as CHF or cardiogenic shock.

Answer D is incorrect. Thromboemboli are typically systemic emboli that originate from mural thrombi and can lead to cerebrovascular accidents, transient ischemic attacks, and renal artery thrombosis.

Answer E is incorrect. Ventricular rupture is a cause of post-MI death that typically occurs 4–10 days post-MI. It often presents with persistent chest pain, syncope, and distended jugular veins.

MI complications

- cardiac arrhythmia (most commonly ventricular fibrillation), important cause of death, common in first few days
- LV failure and pulmonary edema
- cardiogenic shock
- ventricular free wall rupture -> cardiac tamponade; papillary muscle rupture -> severe mitral regurgitation; interventricular septum rupture -> VSD
 - greatest risk 6-14 days postinfarct
- ventricular pseudoaneurysm formation ->  CO, risk of arrhythmia, embolus from mural thrombus
 - greatest risk approximately 1 week post-MI
- postinfarction fibrinous pericarditis - friction rub (1-3 days post MI)
- Dressler syndrome

Q5 A newborn girl is diagnosed as dysmorphic by a pediatrician in the newborn nursery. On physical examination the girl has a broad neck, wide-spaced nipples, and a systolic ejection murmur. An echocardiogram is performed and demonstrates coarctation of the aorta. The echocardiography technologist also runs his transducer across the patient's abdomen and notices a renal abnormality associated with this patient's syndrome. The most likely observed renal abnormality increases this patient's risk for developing which disease?

- (A) Neuroblastoma
- (B) Ovarian cancer
- (C) Transitional cell carcinoma
- (D) Uterine cancer
- (E) Wilms' tumor

The correct answer is E. This patient has classic findings associated with Turner's syndrome, a genetic disorder resulting from a 45,XO complement of chromosomes. Approximately 25%–30% of patients will have associated renal anomalies, including horseshoe kidney, pelvic kidney, or duplicated collecting systems. Patients with horseshoe kidneys are approximately four times more likely to develop Wilms' tumor when compared to the general population.

Answer A is incorrect. Although it has been suggested that patients with Turner's syndrome are at increased risk of developing malignancy, they do not have a specific increased risk of developing neuroblastoma.

Answer B is incorrect. Although it has been suggested that patients with Turner's syndrome are at increased risk of developing malignancy, they do not have a specific increased risk of developing ovarian cancer. Familial BRCA gene mutations or no history of childbirth each increases the risk of ovarian cancer.

Answer C is incorrect. Although it has been suggested that patients with Turner's syndrome are at increased risk of developing malignancy, they do not have a specific increased risk of developing transitional cell carcinoma. Smoking greatly increases the risk of transitional cell carcinoma.

Answer D is incorrect. Although it has been suggested that patients with Turner's syndrome are at increased risk of developing malignancy, they do not have a specific increased risk of developing uterine cancer. Unopposed estrogen secretion (eg., hormone replacement therapy without progesterone) increases the risk of uterine cancer.