

Withdrawal Syndromes

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Objectives



Substances

- Alcohol/Benzos
- Opioids
- Stimulants
- Cannabis



Withdrawal

- Symptoms
- Timeline
- Monitoring
- Treatment

Alcohol

Benzodiazepines

Alcohol Withdrawal

- Begins ~8h after last drink, peaks within 24-7h
- Symptoms:
 - Tremor, anxiety, nausea, headache
 - Increased heart rate/blood pressure, confusion, hallucinations, seizures
 - DTs
- ~5% will suffer delirium tremens (DTs)
 - Seizures, fever, severe confusion/delirium, agitation → can be fatal without medical intervention

Alcohol Withdrawal Symptoms

Minor Withdrawal (6-36 hrs)

- Tremors, anxiety, headache, sweating, palpitations, low appetite, GI upset, cravings
- normal mental status

Seizures (6-48 hrs)

- generalized tonic-clonic seizures, short postictal period

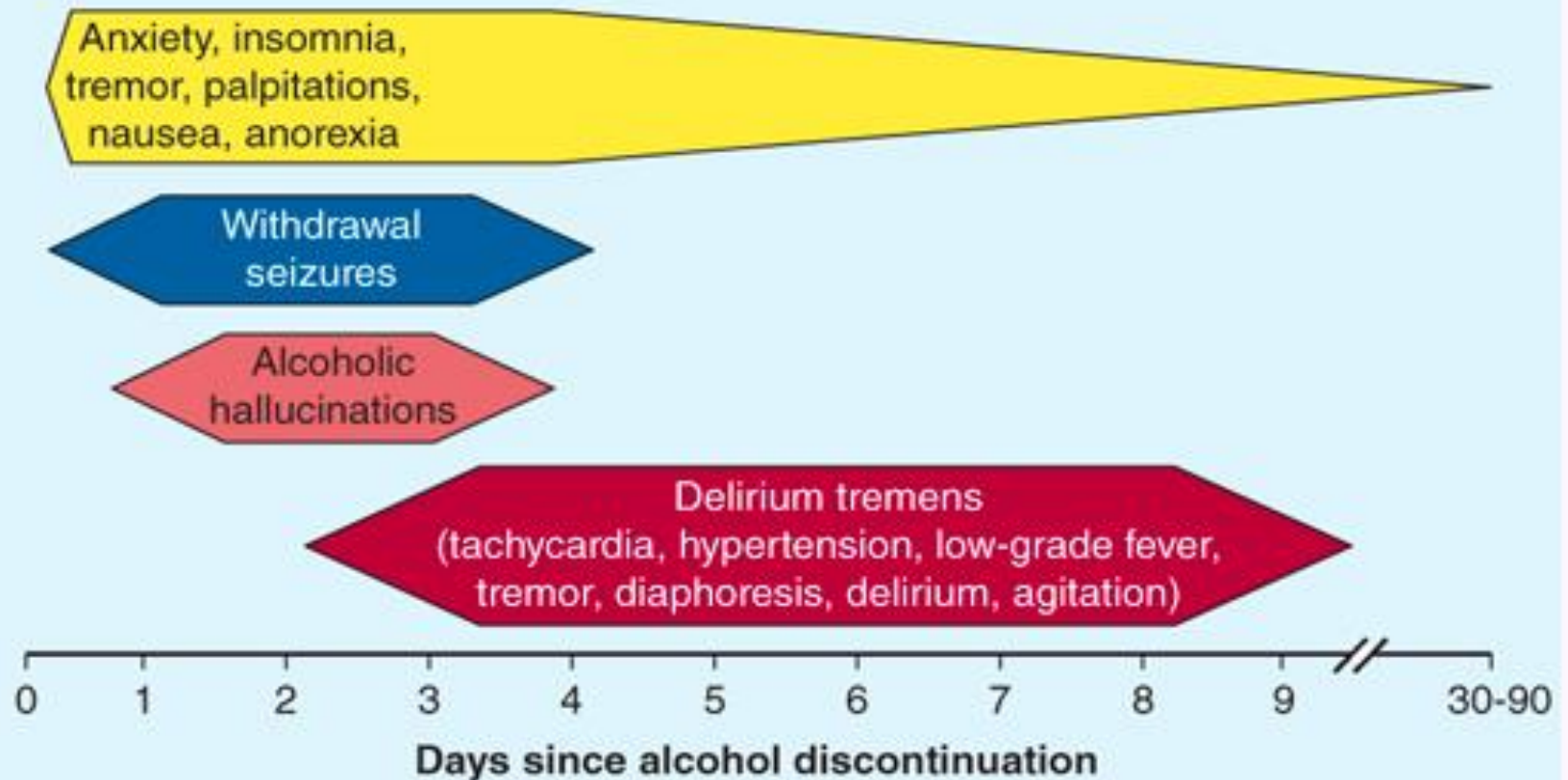
Alcoholic Hallucinosis (12-48 hrs)

- Visual, auditory, &/or tactile hallucinations
- intact orientation and normal VS

Delirium Tremens (48-96 hrs)

- **Delirium, confusion**, agitation, sweating
- ↑HR, ↑BP, fever

Alcohol Withdrawal Timeline



Source: Bertram G. Katzung, Anthony J. Trevor: Basic & Clinical Pharmacology, 13th Ed.
www.accesspharmacy.com

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Alcoholic Hallucinosis

- Starts 12-24h after the last drink and lasts about 24-48h
- Hallucinations are usually *visual*
 - commonly involves seeing insects or animals in the room
- **NOT** associated with altered cognition
 - No confusion/disorientation
 - Vital signs are usually normal
- Patients are aware that they are hallucinating and often very distressed

Delirium Tremens

- Rapid-onset, *confusion*, sometimes with hallucinations
- Agitation and signs of extreme autonomic hyperactivity: fever, ↑HR, ↑BP, and drenching sweats
- Mortality rates as high as 20%
 - With appropriate medical management, the mortality rate is 1-4%

DT Risk Factors

- Prior withdrawal delirium
- Specific signs of chronic alcohol intake
 - cirrhosis and/or malnutrition, low platelets/potassium/magnesium levels
- Development of alcohol withdrawal with a +BAL
- CIWA >15
- Increasing age
- Recent misuse of other CNS depressants (benzos)
- Comorbid illness: respiratory, cardiac

DSM 5

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.

B. **Two (or more)** of the following, developing within several hours to a few days after the cessation of (or reduction in) alcohol use described in criterion A:

1. Autonomic hyperactivity
2. Increased hand tremor
3. Insomnia
4. Nausea or vomiting
5. Transient visual, tactile, or auditory hallucinations
6. Psychomotor agitation
7. Anxiety
8. Generalized tonic-clonic seizures

Alcohol Withdrawal - Treatment

- **Benzodiazepines**
 - Diazepam (Valium)
 - Lorazepam (Ativan)
 - Chlordiazepoxide (Librium)
- **Symptom triggered vs. Scheduled taper**
- **Gabapentin** – mild-moderate symptoms, outpatient

WMS

- **Fixed-Schedule Dosing (WMS)**
 - Diazepam 10mg
 - 1 tab 4 times daily for 1 day, then
 - 1 tab 3 times daily for 1 day, then
 - 1 tab twice daily for 1 day, then
 - 1 tab once daily for 1 day
 - Lorazepam, Chlordiazepoxide
- **Symptom Triggered**
 - CIWA

Lorazepam (Ativan)

- **“At Risk” Clients – Lorazepam 1-2mg**
 - Patients with liver issues
 - Ex/cirrhosis or hepatitis
 - Medical comorbidities
 - Ex/COPD, seizures, cardiac issues
 - Risk for over-sedation
 - Ex/elderly, on opioids (methadone)
- Shorter half-life may prevent prolonged effects if over-sedation occurs
- Metabolized outside the liver

Adjunct Medications

- **Thiamine 100mg for 5 days**
 - Prevent Wernicke's Encephalopathy (acute brain disorder from thiamine deficiency – triad of confusion, ataxia, abnormal eye movements)
- **Gabapentin 100mg-300mg TID**
 - anxiety, cravings, insomnia, restless legs
- **Naltrexone 25mg-50mg daily**
 - cravings

Symptom Triggered Treatment - CIWA

- **CIWA-Ar** = Clinical Institutes Withdrawal Assessment Scale for Alcohol (revised)
- 10 item scale, each item scored independently
- Total score correlates to the **severity** of alcohol withdrawal and guides management
- NOT a diagnostic test – used to assess severity once the diagnosis has been made

CIWA-Ar

- The CIWA-Ar encompasses 10 areas
 1. Nausea and vomiting
 2. Tremor
 3. Sweating
 4. Anxiety
 5. Agitation
 6. Tactile disturbances
 7. Auditory disturbances
 8. Visual disturbances
 9. Headache
 10. Orientation

CIWA - Ar

Clinical Institute Withdrawal Assessment for Alcohol, revised (CIWA-Ar)

Nausea and vomiting	Headache
0: No nausea or vomiting	0: Not present
1	1: Very mild
2	2: Mild
3	3: Moderate
4: Intermittent nausea with dry heaves	4: Moderately severe
5	5: Severe
6	6: Very severe
7: Constant nausea, frequent dry heaves and vomiting	7: Extremely severe
Paroxysmal sweats	Auditory disturbances
0: No sweats visible	0: Not present
1: Barely perceptible sweating, palms moist	1: Very mild harshness or ability to frighten
2	2: Mild harshness or ability to frighten
3	3: Moderate harshness or ability to frighten
4: Beads of sweat obvious on forehead	4: Moderately severe hallucinations
5	5: Severe hallucinations
6	6: Extremely severe hallucinations
7: Drenching sweats	7: Continuous hallucinations

Anxiety
0: No anxiety, at ease
1
2
3
4: Moderately anxious, guarded
5
6
7: Acute panic state, consistent with severe delirium or acute schizophrenia
Agitation
0: Normal activity
1: Somewhat more than normal activity
2
3
4: Moderately fidgety and restless
5
6
7: Paces back and forth during most of the interview or constantly thrashes about
Tremor
0: No tremor
1: Not visible, but can be felt at fingertips
2
3
4: Moderate when patient's hands extended
5
6
7: Severe, even with arms not extended

Visual disturbances
0: Not present
1: Very mild photosensitivity
2: Mild photosensitivity
3: Moderate photosensitivity
4: Moderately severe visual hallucinations
5: Severe visual hallucinations
6: Extremely severe visual hallucinations
7: Continuous visual hallucinations
Tactile disturbances
0: None
1: Very mild paresthesias
2: Mild paresthesias
3: Moderate paresthesias
4: Moderately severe hallucinations
5: Severe hallucinations
6: Extremely severe hallucinations
7: Continuous hallucinations
Orientation and clouding of sensorium
0: Oriented and can do serial additions
1: Cannot do serial additions
2: Disoriented for date by no more than 2 calendar days
3: Disoriented for date by more than 2 calendar days
4: Disoriented for place and/or patient
Total score is a simple sum of each item score (maximum score is 67)
Score:
<10: Very mild withdrawal
10 to 15: Mild withdrawal
16 to 20: Modest withdrawal
>20: Severe withdrawal

Anxiety
0: No anxiety, at ease
1
2
3
4: Moderately anxious, guarded
5
6
7: Acute panic state, consistent with severe delirium or acute schizophrenia

Visual disturbances
0: Not present
1: Very mild photosensitivity
2: Mild photosensitivity
3: Moderate photosensitivity
4: Moderately severe visual hallucinations
5: Severe visual hallucinations
6: Extremely severe visual hallucinations
7: Continuous visual hallucinations
Tactile disturbances

**Total score is a simple sum of each item score
(maximum score is 67)**

Score:

<10: Very mild withdrawal

10 to 15: Mild withdrawal

16 to 20: Modest withdrawal

>20: Severe withdrawal

5
6
7: Severe, even with arms not extended

(maximum score is 67)
Score:
<10: Very mild withdrawal
10 to 15: Mild withdrawal
16 to 20: Modest withdrawal
>20: Severe withdrawal

CIWA-Ar Pros

- Can be administered in under 5 minutes
- Provides an efficient and objective means of assessing alcohol withdrawal
- Symptom-triggered dosing
 - decreases treatment duration and total use of benzodiazepines
 - decrease over-sedation or under-treatment

CIWA Cons

- Staff's inexperience with CIWA scoring can complicate treatment decisions
- Many subjective elements
- Patient-reported symptoms can be related to something else
- Patients with CIWA >20 are so confused and agitated that they can't describe their symptoms
- By a CIWA of 8 the horse may be out of the barn

Example of Symptom-Triggered Regimen by CIWA score

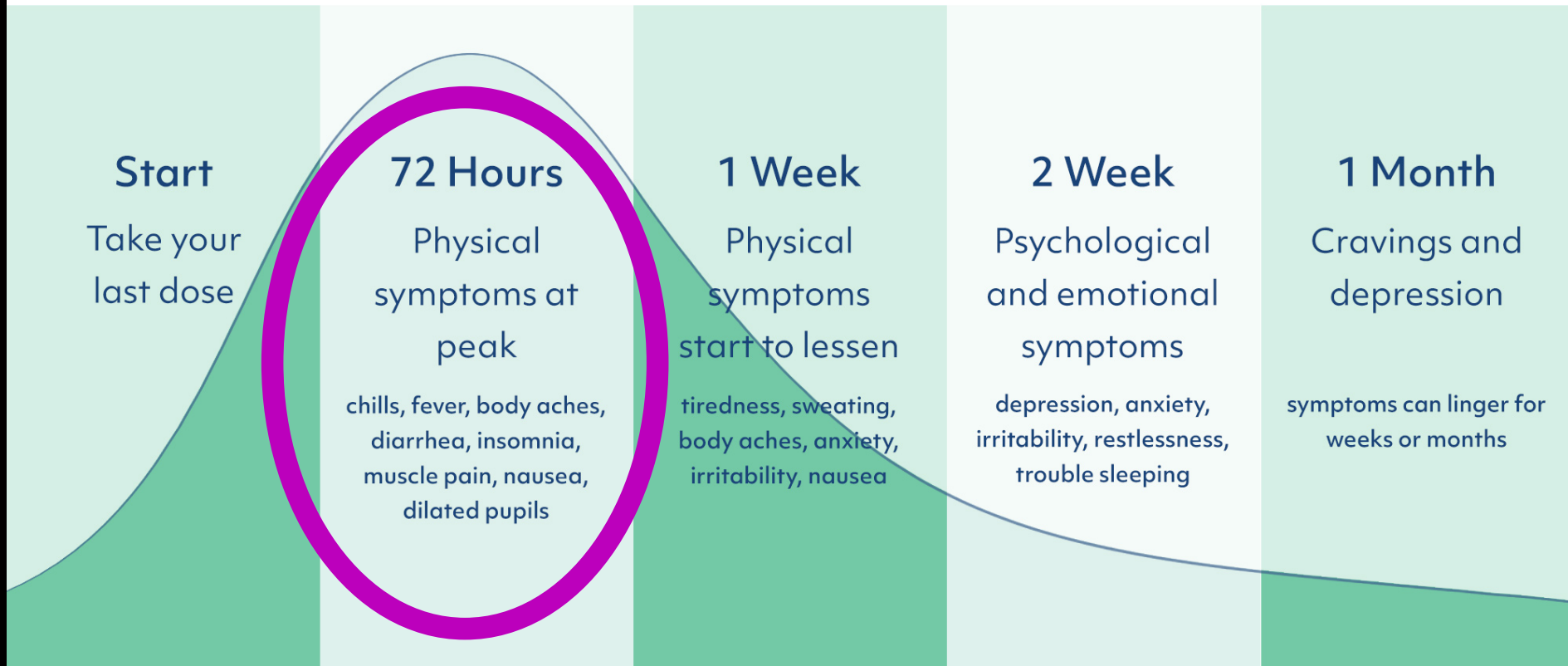
- CIWA score < 8
 - no medication necessary
 - reassess CIWA and VS q2h, and offer medication if CIWA score increases to ≥ 8
 - if score ≤ 8 for 48 hours, discontinue monitoring
- CIWA score 8-10
 - lorazepam 1-2 mg orally or IV
 - reassess CIWA and VS q2h, then re-dose
- CIWA score 11-15
 - lorazepam 2-3 mg orally or IV
 - reassess CIWA and VS q2h, then re-dose
- CIWA score 16-19
 - lorazepam 3-4 mg orally or IV
 - reassess CIWA and VS q2h, then re-dose
- CIWA score > 20 - evaluate for transfer to ICU

Benzodiazepine Withdrawal

- Same symptoms as alcohol withdrawal
- In some cases, protracted withdrawal can last months or even years without treatment
- Treatment = same as Alcohol Detox
- Shorter acting benzos are changed to long acting ones, then tapered

Opioids

Opiate Withdrawal Timeline



Sweating
Yawning
Runny nose
Watery eyes
Goosebumps

Symptoms can be severe but are usually not life-threatening.

DSM 5

A. Presence of either of the following:

1. Cessation of (or reduction in) opioid use that has been heavy and prolonged
2. Administration of an opioid antagonist after a period of opioid use

B. **Three (or more)** of the following developing within minutes to several days after Criterion A:

- Dysphoric mood
- Nausea or vomiting
- Muscle aches
- Lacrimation or rhinorrhea
- Pupillary dilation, piloerection, or sweating
- Diarrhea
- Yawning
- Fever
- Insomnia

Opioid Withdrawal - Treatment

- Opioid Agonists - one opioid is replaced with another and then slowly withdrawn
 - **Methadone**
 - longer acting than street drugs
 - can relieve the symptoms of withdrawal and cravings without the high
 - **Suboxone**
 - partial agonist at opioid receptor
 - Buprenorphine + Naloxone
- Can be used for detox, but most known for its use in long-term maintenance.

Suboxone

- Suboxone

- Combination of buprenorphine and naloxone (4:1)
 - Buprenorphine = partial opioid agonist
 - Naloxone = opioid blocker
- Can cause withdrawal if it is injected
- It is a very safe drug, with minimal risk of overdose

WMS

Suboxone

- Mod-Severe Withdrawal symptoms: COW>12
- **Induction: First dose Day 1:**
 - 2mg test dose, reassess within 1-2hrs)
 - Symptoms resolved and no precipitated withdrawal - no further doses
 - Partially Improved, no sedation or precipitated w/d - give additional 2-4mg q 1-3hr until withdrawal resolves to **Max of 12mg** on Day 1.
- **Day 2:**
 - If w/d symptoms resolved, give total Day 1 dose and maintain in single daily dose
 - If ongoing w/d symptoms:
 - Give additional 2-4mg q 1-3hr up to **Max dose 16mg** (reassess 1hr after each additional dose)
- **Day 3:** Adjust dose by 2-4mg daily to effect, to **Max dose of 24mg**
- Refer to RAAM clinic on Discharge

Goal (maintenance dose): withdrawal symptoms and cravings are controlled without feeling intoxicated or over-sedated (usually 12-24mg daily)

Opioid Withdrawal - Treatment

- Non-opioid Agonists – symptomatic relief
 - **Clonidine** - help reduce anxiety, agitation, muscle aches, sweating, runny nose, and cramping.
 - It does not help reduce cravings.
 - Meds for symptoms management: diarrhea, nausea, body aches, insomnia

Adjunctive Treatments for Opioid Withdrawal Symptoms

- Anxiety, irritability, restlessness
 - Benzodiazepines, Atarax
- Diarrhea
 - Loperamide
- Nausea/vomiting
 - Dimenhydrinate (Gravol)
- Insomnia
 - Trazodone, Mirtazapine, Seroquel
- Muscle aches, joint pain, headache
 - Ibuprofen, Acetaminophen, NSAIDs

WMS

- **Lorazepam 1mg tablet**
 - 1 tablet, PO, BID today (00/0)
 - 1 tablet, PO, TID x 2 days
 - 1 tablet, PO, BID x 1 day
 - 1 tablet, PO, OD x 1 day
- **Clonidine 0.1mg tablet**
 - 1 tablet, PO, BID today (00/0)
 - 1 tablet, PO, TID x 2 days
 - 1 tablet, PO, BID x 1 day
 - 1 tablet, PO, OD x 1 day

WMS

Symptom Management

- Ibuprofen 600mg or Naproxen 500mg (aches)
- Dimenhydrinate 50mg (nausea/vomiting)
- Loperamide 4mg (Diarrhea)
- Trazodone 50mg or Seroquel 25mg (insomnia)
- Atarax 25mg-50mg PO, TID prn (anxiety, restlessness)

COWS

- Clinical Opioid Withdrawal Scale (COWS)
- 11 signs/symptoms of opioid withdrawal rated 0 to 5
- Determines the stage of severity of withdrawal
- Allows for monitoring symptoms over time
- Used in Suboxone induction

COWS

Clinical Opioid Withdrawal Scale (COWS)

Patient's name: _____	Date and time: ___/___/___:_____
Reason for this assessment: _____	
Resting pulse rate: _____ beats/minute Measured after patient is sitting or lying for one minute	GI upset: Over last half-hour
0 pulse rate 80 or below 1 pulse rate 81 to 100 2 pulse rate 101 to 120 4 pulse rate greater than 120	0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: Over past half-hour not accounted for by room temperature or patient activity	Tremor: Observation of outstretched hands
0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness: Observation during assessment	Yawning: Observation during assessment
0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute

<p>Pupil size</p> <p>0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible</p>	<p>Anxiety or irritability</p> <p>0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult</p>
<p>Bone or joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored</p>	<p>Gooseflesh skin</p>
<p>0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</p>	<p>0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection</p>
<p>Runny nose or tearing: Not accounted for by cold symptoms or allergies</p>	<p>Total score: _____ The total score is the sum of all 11 items</p>
<p>0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks</p>	<p>Initials of person completing assessment: _____</p>

Score: 5 to 12 = mild; 13 to 24 = moderate; 25 to 36 = moderately severe; more than 36 = severe withdrawal.

GI: gastrointestinal.

Reproduced from: Wesson DR, Ling W. *The Clinical Opiate Withdrawal Scale (COWS)*. *J Psychoactive Drugs* 2003; 35:253.

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<p>Runny nose</p> <p>symp</p>	
<p>0 1 2 4 do</p>	

Score:
5 to 12 points: Mild withdrawal
13 to 24 points: Moderate withdrawal
25 to 36 points: Moderately severe withdrawal
37 to 48 points: Severe withdrawal

Score: 5 to 12 = mild; 13 to 24 = moderate; 25 to 36 = moderately severe; more than 36 = severe withdrawal.

GI: gastrointestinal.

Reproduced from: Wesson DR, Ling W. *The Clinical Opiate Withdrawal Scale (COWS)*. *J Psychoactive Drugs* 2003; 35:253.

Supportive Treatment

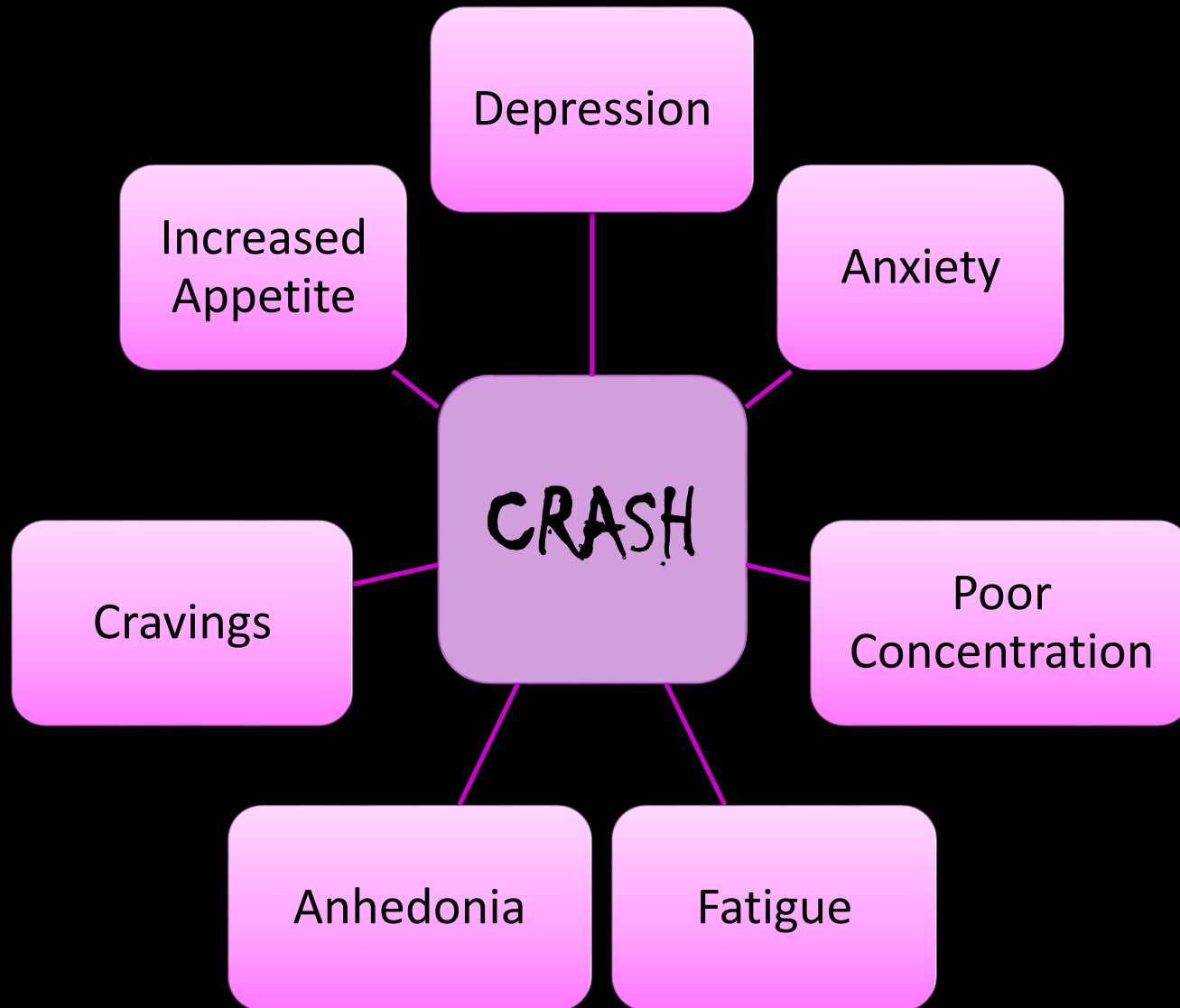
- A calm, quiet environment with supportive and reassuring staff can help patients overcome most symptoms of acute opioid withdrawal and decreases the need for pharmacologic interventions.
- Patients who have diarrhea, vomiting, or sweating should be monitored for dehydration and fluid levels maintained

Stimulants

Stimulant Withdrawal

- Cocaine, Crystal Meth, Prescription stimulants (Adderall, Ritalin)
- Psychological features, but rarely medically serious

Stimulant Withdrawal Symptoms



Stimulant Withdrawal Timeline

CRASH

Day 1-4

Severe Fatigue

↑Appetite

Anxiety

Agitation

WITHDRAWAL

Week 1-4

Cravings

Insomnia

Anxiety

Depression

EXTINCTION

Week 5+

Cravings

Mood Swings

Depression

Anhedonia

DSM 5

A) Dysphoric mood

B) **Two or more** of the following symptoms developing within hours to days of stimulant cessation:

- Fatigue
- Vivid or unpleasant dreams
- Sleep problems (insomnia or hypersomnia)
- Increased appetite
- Psychomotor retardation or agitation

Stimulant Withdrawal - Treatment

- No medications show significant effects in reducing symptoms of acute stimulant withdrawal
- Physical signs are usually minor and rarely require treatment
- **Benzodiazepines** may lessen symptoms
- **Antidepressants** may help (ex/ Mirtazapine)
- **Bupropion** - thought to potentially alleviate stimulant withdrawal symptoms by facilitating dopamine neurotransmission
- Studied: Baclofen, Hydroxyzine, Desipramine

WMS

- Symptom management and supportive care
- Psychosis
 - Diazepam 5mg or Lorazepam 0.5mg prn
 - Olanzapine 5mg (if Diazepam not effective)
- Cravings/Abstinence:
 - Olanzapine 5mg twice daily
 - Mirtazapine 30mg at night

Cannabis

Cannabis Withdrawal

- Symptoms appear within 24-72 hours
 - peak in 1st week
 - largely resolve after 1-2 weeks

Cannabis Withdrawal

Irritability, Anxiety, Depression, Restlessness

Sleep difficulty

Poor focus/concentration

Cravings

Decreased appetite or weight loss

Abdominal pain

Shakiness or tremors

Sweating, fever, chills

Headache

DSM 5

- A. Cessation of cannabis use that has been heavy and
- B. **Three or more** of the following signs and symptoms develop within approximately one week after cessation of heavy, prolonged use:
 1. Irritability, anger, or aggression.
 2. Nervousness or anxiety.
 3. Sleep difficulty (ie, insomnia, disturbing dreams).
 4. Decreased appetite or weight loss.
 5. Restlessness.
 6. Depressed mood.
 7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

Cannabis Withdrawal - Treatment

- No medication is approved for the treatment of cannabis withdrawal
- Some evidence:
 - Dronabinol - synthetic form of THC
 - Nabiximols - cannabis plant extract of THC, combined in a 1:1 ratio with CBD
 - **Gabapentin** - found to reduce cannabis withdrawal symptoms

Summary

- **Alcohol Withdrawal** – potentially life-threatening
 - Benzodiazepines
 - Scheduled vs symptoms triggered (CIWA)
- **Opioid Withdrawal** – flu-like symptoms can be severe but not life-threatening
 - COWS
 - Opioids (Suboxone, Methadone) vs Non-Opioids (clonidine)
- **Stimulant and Cannabis Withdrawal** – Physical signs are usually minor and self-limiting
 - No approved medications
 - Symptom management

References

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Thank you!

