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## Today's Scope

- Toxicity from plant cannabis and synthetic cannabinoids
- New suicidal trend (Charcoal-burning suicide)

# Management of Toxicity from Cannabis (plant marijuana) and Synthetic Cannabinoids



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## Scope

- The Differences between Cannabis and Synthetic Cannabinoids
- The Management of Toxicity from Cannabis (Plant Marijuana)
- The Management of Toxicity from Synthetic Cannabinoids

## The differences between CANNABIS vs SYNTHETIC CANNABINOIDS

#### Cannabis

Synthetic Cannabinoids (SCs)







#### **Example:**

- 1. <u>Cannabis sativa</u> L.
- 2. Cannabis indica Lam.
- 3. Cannabis ruderalis Janisch

Common name: Hemp



- SCs are sold under common names like <u>K2, Spice</u>, and synthetic marijuana
- SCs are the <u>designer drugs</u> that are sprayed onto plant matter
- Sold as herbal smoking blend, herbal incense
- Often labeled "not for human consumption"

## The differences between CANNABIS vs SYNTHETIC CANNABINOIDS

#### Cannabis

- Found 4000+ years ago
- Medical use in china 2000+ years ago
- Agonist of the cannabinoid-1 (CB1) receptors (psychoactive effect: high)
- The most potent substance to CB1 receptor in cannabis: THC

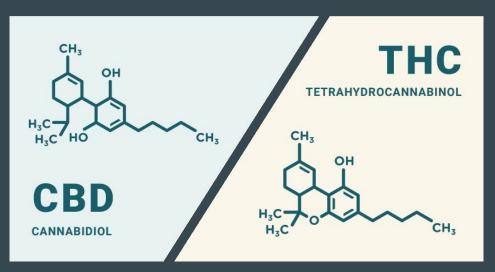
Hallucinogen

#### Synthetic cannabinoids (SCs)

- Saled on early 2000s
- First laboratory analysed since 2008
- Greater agonist and affinity of the CB1 receptor (CNS stimulants)
- Drug designs: similar structure to THC
- Several synthetic cannabinoid families
- Classified by base structures

  - New waves of the CNS stimulant 3x mortalities in 2014-2015!!

# Chemical structures of substances in Cannabis vs SCs





Cannabinoids

Endocannabinoid:

### Health hazards

#### Cannabis

- Death from trauma that caused by overdose (indirect)
- Chronic problem: Addiction, brain development, behavior, psychiatric disorders
- Cannabinoid Hyperemesis Syndrome (CHS)
  - Cyclical vomiting, abdominal pain
  - Refractory to conventional antiemetic drugs
  - Symptoms are better by hot shower or bathtub, topical capsaicin
  - Unnecessary endoscopy and surgery

#### Synthetic Cannabinoids (SCs)

- Death from the toxicity of substances
- Fake marijuana (sold as a real marijuana; market share)
- Increased violences, criminals in society and hospital from toxic psychosis/agitated delirium
- More addictive than marijuana

## Now situation (Cannabis oil in Srinagarind hospital)

**Case 1:** CA breast stage  $2 \rightarrow$  Delirium from marijuana oil (exclude other precipitating causes)

**Case 2-3:** Activate stroke fast track from ataxia and dysarthria

Case 4-5: dry mouth, restlessness, palpitation, tachycardia, severe dizziness, skin: not wet/not dry (need to rule out sympathomimetic or anticholinergic toxidrome), urine marijuana test: positive, amphetamine negative

**Case 6:** Illness (palpitation and unsteadiness) after eating friend's cookies and almost did car accident because symptoms started during car driving back (30 minutes post-ingestion)

#### All cases

- came to emergency room and initially covered history of ingestion.
- sublingually used marijuana oil that bought from online shop or received from friend/relatives.
- related on high socioeconomic status (high price per bottle)

## Route of exposure

- 1. Inhalation
- 2. Ingestion

## Purposes of exposure

- 1. Unintentional
- 2. Intentional
  - a. Recreational use/abuse
  - b. Medical/therapeutic
  - c. Self harm (rare)

## Inhalation



Marijuana cigarette



Marijuana cigarette



Marijuana vaping

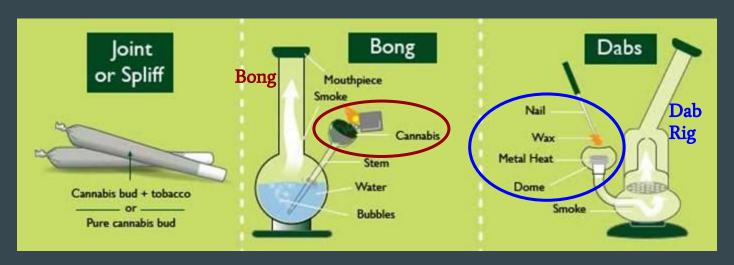


Marijuana dabbing



Marijuana bong

## The differences between BONG vs DABs



Dry weed
Bowel
Lighter need
Humidified by water
Bong

Wax Nail Metal heat No need water, Filter before inhalation Dab rig



## **Effects of Using Cannabis**

#### **INHALATION**

(smoking/vaping/dabbing)

**INGESTION** 

(eating/drinking)

Felt in seconds to minutes

Lasts up to 6 hours +

Felt in 30 minutes to 2 hours

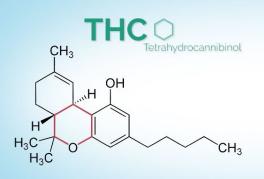
Last up to 12 hours +

## Break

Cannabis is toxic plant to animal.

Keep it away from your pet!!





## The Management of Cannabis (Plant marijuana) toxicity

#### Toxicology

- THC stimulates CB receptors throughout the body
  - CB receptors in pain pathway (Brain & spinal cord)
  - Central CB receptors: Antiemetic properties
  - Peripheral CB receptors: modulate immune function via cytokine release

Self reports ranking the need of the local ED visit after drug abuse

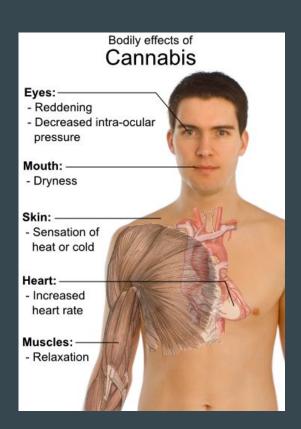
- 1. Mushrooms: 0.2%
- 2. Cannabis: 0.6%
- 3. LSD: 1.0%
- 4. Cocaine: 1.0%
- 5. Amphetamine: 1.1%
- 6. MDMA: 1.2%
- 7. Alcohol: 1.3%
- 8. Synthetic cannabinoids: 3.2%
- 9. Methamphetamine: 4.8%

**2017 Global Drug Survey** 

## Acute toxicity of Cannabis (Plant marijuana)

#### Mild to moderate toxicity

- somnolence, euphoria, alterations of senses and time perception, depersonalization, loss of social inhibition, giddiness, and mood alterations.
- Higher levels of intoxication result in decreased motor coordination, lethargy, muscle jerking, and ataxia.
- *Inhalational exposure* may result in pulmonary irritation, including sore throat, rhinitis, coughing and bronchitis



## Acute toxicity of Cannabis (Plant marijuana)

#### Severe toxicity

• In children, there are reports of significant altered mental status, mydriasis, hypotonia and even coma.



Marijuana butt



Marijuana hashish; the resin of the female cannabis plant



Marijuana food products

## **Acute toxicity of Cannabis** (Plant marijuana)

#### Severe toxicity

- In young man
  - died from trauma due to erratic behavior after ingesting edible marijuana cookie 3.5 hours post-ingestion
  - **Dabbing:** This method can produce a rapidly absorbed highly concentrated form of THC that is usually smoked. It is sometimes also known as "wax", "budder", "dabs" and "oil"
    - Teenager; agitation, seizure-like activity, hypertension, and hyperthermia after dabbing



investigate the scene of a multi-car crash



#### Chronic use

#### CANNABINOID HYPEREMESIS SYNDROME (CHS):

• Paradoxical, cyclic vomiting syndrome has been reported in individuals (more frequently observed in men) that chronically use marijuana.

Real case (Bangkok): A young man presented with significant weight loss and intermittent intractable severe vomiting that not response to IV antiemetic drugs and physician took 7 years to diagnose CHS after many times work-up with GI medicine and surgeon (CT whole abdomen, Endoscopies was negative) about cyclical vomiting. The urine marijuana is positive.

## Pathophysiology of CHS

transient receptor potential valilloid 1 (TRPV1) agonist

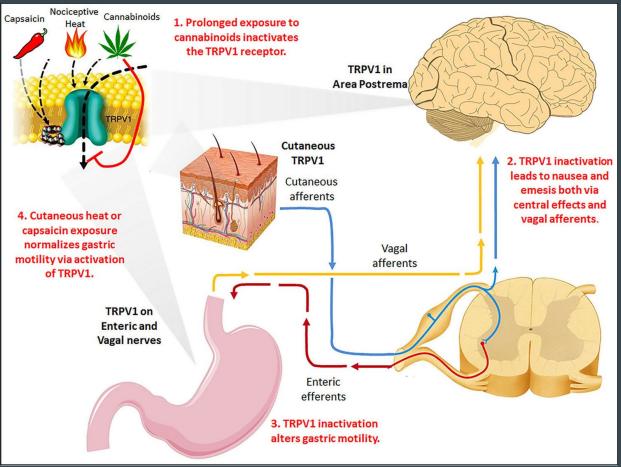


Figure 1: proposed mechanism of CHS; TRPV1 is expressed in area postrema of the medulla, along gastric enteric and vagal nerves, and on cutaneous receptors in the dermis and epidermis. Prolonged exposure to cannabinoids inactivates TRPV1, potentially resulting in central nausea, altered gastric motility, and abdominal pain. Exposure to nociceptive heat, such as with compulsive hot-water bathing, may transiently augment cutaneous TRPV1 firing and restore gastric motility, temporarily mitigating symptoms. Use of another TRPV1 agonist, capsaicin, may also provide relief. Cessation of marijuana use gradually leads to normalization of TRPV1 function and fully ameliorates symptoms.

ACG Case Rep J. 2018 Jan 3;5:e3. doi: 10.14309/crj.2018.3. eCollection 2018.

Successful Treatment of Cannabinoid Hyperemesis Syndrome with Topical Capsaicin.

## Treatment of CHS

- Quit cannabis
- IV antiemetic and adequate IV rehydration
- Case report of topical capsaicin to treat CHS
- CHS Symptoms persist last up hours to months
- Take hot shower or bathtub

Recovery phase
Last from days to months

Cannabinoid hyperemesis syndrome

Prodromal phase Nausea and abdominal discomfort, worse in the morning

Hyperemesis phase

Severe vomiting, diffuse abdominal pain, volume depletion, electrolyte imbalances, and rarely AKI, compulsive bathing







## Carcinogenicity

Marijuana smoking may increase the risk of cancers of the mouth, neck, and lungs, although it is difficult to experimentally study the carcinogenic potential of marijuana in humans. Obtaining a study sample of persons who consistently use marijuana over a long period of time who are not exposed to other carcinogens (eg, tobacco smoke) and can be evaluated over many years is problematic.



## **Monitoring**

- A) **No specific laboratory studies** are needed in most patients. Confirmatory testing at most facilities involves the use of a urine enzyme immunoassay, which may detect metabolites for up to several days after an acute exposure to weeks after chronic marijuana use. However, urine concentrations do not correlate with toxicity.
- B) **Prescription use of dronabinol (THC) can be distinguished from plant material** use by testing for *THCV (delta-9-tetrahydrocannabivarin)*, which only exists in the marijuana plant, but this is not done routinely.
- C) Specific THC concentrations are not readily available or useful.
- D) Other adjunctive tests may be necessary depending on the patient's symptoms. Obtain a serum glucose and electrolyte concentrations for altered mental status. Obtain a baseline ECG and continuous cardiac monitoring for tachycardia or altered cardiac rhythm.

## Laboratory tests/monitoring

- Urine enzyme immunoassay
  - Positive test imply prior usage or sidestream smoke
  - Positive test
    - single marijuana cigarette smoking possible detection for several days
    - Casual use of marijuana were positive for <u>2-4 wks post-exposure</u>

## Xenobiotics or Conditions Reported to Produce Inaccurate Screening Test Results for Tetrahydrocannabinol (THC)

#### Urine screening for marijuana (immunoassay)

False Negative <sup>a</sup>		False Positive
Bleach (NaOCI)	Niacin	Dronabinol
Citric acid	Potassium nitrite (KNO2)	Efavirenz
Detergent additives	Table salt (NaCl)	Ethacrynic acid
Dettol	Tetrahydrozoline	Hemp seed oil
Dilution	Vinegar (acetic acid)	Nonsteroidal antiinflammatory drugs
Glutaraldehyde	Water	Promethazine
Lemon juice		Riboflavin

<sup>&</sup>lt;sup>a</sup>Xenobiotics "possibly" producing false-negative urine test results are usually added to a urine sample, not ingested.

## Treatment "ABCDE DDEAD"

- Support respiratory and cardiovascular function
- Airway (A)
  - ETI if comatose
- Breathing (B)
  - In inhalational exposure: Observe RR,
     SpO<sub>2</sub>, B2 agonist inhales if bronchospasm
- Circulation (C)
  - Hypotensive episode; use trendelenburg position for postural hypotension, rarely need IV loading
  - Cardiac arrhythmias: Atrial fibrillation
- Disability (D)
  - Agitation, coma; ETI
  - $\circ$  Seizures  $\rightarrow$  BZPs,
- Extracauses of life threatening conditions (E)
  - $\circ$  Severe delirium  $\rightarrow$  BZP

- Diagnosis (D)
  - History + Physical Exam + Investigation urine screening for marijuana: positive
- Decontamination (D)
  - Not need GI decontamination (lavage, SDAC, and WBI)
  - Rarely be benefit in cannabis (rarely found serious complication)
- Enhanced elimination (E)
  - No role of blood removal, MDAC, and urine alkalinization
- Antidote and specific treatment (A)
  - There is no antidote
- Disposition (D)
  - Next page

## Patient disposition

#### Oral exposure

#### Admission criteria

- Prolonged symptoms/ concerns for social situation (e.g. young child) should be admitted to the hospital
- o Rarely necessitate an ICU admission
- Criteria for discharge; clear improvement and adequate safeguards in the home environment for young children

#### • Home criteria

- Most adult with minimal to moderate symptoms can be managed at home
- Children with inadvertent marijuana exposure (plant material, medical marijuana edibles containing marijuana) should be evaluated in a healthcare facility

#### Consult criteria

• Child abuse team should be involved in children cases, toxicologist can be contacted for any questions or concerns

#### Observation criteria

- Any patients with self-harm attempt using marijuana or any exposed child should be sent to the healthcare facility for evaluation.
- Patients should be observed until they are clearly improving or asymptomatic which normally should not be more than a few hours.

## Break



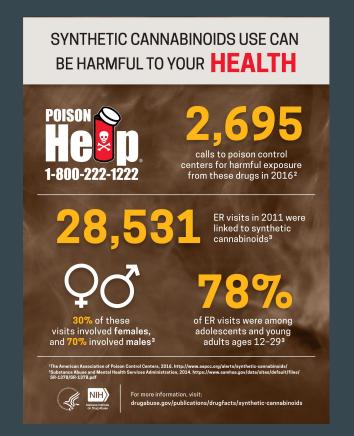




## The Management of Synthetic Cannabinoids (SCs) toxicity

#### Toxicology

- SCs (THC homologs) → stimulate CB1 and CB2 receptor
- Cannabis like effects
- 28 x greater potency than THC



## **Acute toxicity**

#### MILD TO MODERATE TOXICITY

- alterations in mood and perception, xerostomia, reddened conjunctiva, and an increase in pulse rate, similar to marijuana (THC).
- Hyperemesis, similar to marijuana, has been observed in a patient following excessive use.
- Other effects reported that may not follow the current pattern of exposure to THC compounds have included hypertension, agitation, tremors, paranoia, hallucinations and, rarely, hypokalemia.
- The onset of effects after inhalation is rapid and gradually resolves.

#### **SEVERE TOXICITY:**

- Severe agitation, hyperthermia, recurrent seizures, SVT, rhabdomyolysis (infrequent) and psychosis have been reported.
- STEMI has been reported in several adolescents, and can occur in patients with normal coronary arteries.
- Acute renal injury has been reported among teenagers after smoking a new synthetic cannabinoid referred to as XLR-11. Acute renal failure and significant rhabdomyolysis occurred in a young adult following an episode of persistent hyperemesis after using a synthetic cannabinoid product.
- The type and amount of THC homologs, contained within herbal products, can vary considerably.
- There is a possibility of severe overdose due to batch-to-batch variability within the same product. In addition, there is very little known regarding the herbal mixtures used as the delivery vehicle; the herbs themselves may also have additive psychoactive properties.

## Case reports of ADULTERATED SYNTHETIC CANNABINOID PRODUCTS:

- Spring 2018: US poison center reported they found many cases presented with coagulopathy and bleeding after smoking synthetic cannabinoids.
- Blood products were required in some cases with FFP being the most likely product.
- No specific synthetic cannabinoid was identified during this outbreak.
- Confirmatory testing identified 3 different anticoagulants (ie, brodifacoum, difenacoum and bromadialone); brodifacoum was the most common.



## **Laboratory/Monitoring**

- A) No specific laboratory studies are needed in most patients. Obtain specific laboratory studies based on symptoms observed in the patient, since the constituents of many of these products may contain multiple chemicals unrelated to the reported synthetic cannabinoid consumed.
- B) THC homologs are not structurally related to delta-9 tetrahydrocannabinol, the active ingredient in marijuana and are, therefore, undetectable via routine toxicologic screening methods (ie, urine).
- C) Monitor fluid and electrolyte status in symptomatic patients. Mild hypokalemia and severe vomiting have been rarely reported following inhalational exposure to these compounds.
- D) Obtain a baseline ECG and institute continuous cardiac monitoring for tachycardia or altered cardiac rhythm.

## Treatment "ABCDE DDEAD"

- Support respiratory and cardiovascular function
- Airway (A)
  - ETI if comatose
- Breathing (B)
  - In inhalational exposure: Observe RR, SpO<sub>2</sub>, B2
     agonist inhales if bronchospasm
- Circulation (C)
  - Hypotensive episode use trendelenburg position for postural hypotension, rarely need IV loading
  - Cardiac arrhythmias: Atrial fibrillation
- Disability (D)
  - Violence, agitation, seizures, coma; ETI
  - Repeated seizures → BZPs, phenobarbital, propofol, avoid phenytoin
- Extracauses of life threatening conditions (E)
  - Hyperthermia; external cooling by mist and fan
  - Rhabdomyolysis and AKI
  - Coagulopathy (rodenticide contaminate); FFP

#### • Diagnosis (D)

 History + Physical Exam + investigation urine screening for marijuana : Negative

#### • Decontamination (D)

- Not need GI decontamination (lavage, SDAC, and WBI)
- Rarely benefit in cannabis (rarely found serious complication)

#### • Enhanced elimination (E)

- No role of blood removal, MDAC, urine alkalinization
- Role of hemodialysis in Uremia, refractory acidosis & hyperkalemia
- Role of urine alkalinization in severe rhabdomyolysis

#### • Antidote and specific treatment (A)

- There is no antidote
- Disposition (D)
  - Next page

## Patient disposition

#### 1) HOME CRITERIA:

• Most adult cases with minimal to moderate symptoms can be managed at home if a responsible adult is present. The vast majority of exposures are recreational in nature and do not require any medical intervention, however referral for substance abuse treatment may be indicated.

#### 2) OBSERVATION CRITERIA:

• Any patient with a self-harm attempt or any exposed child (as exposures may be considered a form of child neglect or abuse) should be sent to a healthcare facility for evaluation. Patients should be observed until they are clearly improving or asymptomatic, which normally should not be more than a few hours.

#### 3) ADMISSION CRITERIA:

Any patients with prolonged symptoms or concerns for a patient's social situation (eg, young child) should be
admitted to the hospital, and depending on the severity of their symptoms, may rarely necessitate an ICU
admission. However, most patients exposed do not exhibit severe toxicity. Criteria for discharge includes clear
improvement or resolution of symptoms and adequate safeguards in the home environment for young children.

#### 4) CONSULT CRITERIA:

• Social work or child abuse teams should be involved in cases involving children. Toxicologists and poison centers can be contacted for any questions or concerns.

### **Abstinence syndrome**

- Abrupt discontinuation of chronic use can cause profuse sweating, tremors, palpitations, insomnia, headache, depression, diarrhea, nausea, and vomiting.
- Treat with benzodiazepines

### Take home points

- $\star$  Cannabis toxicity is not serious, except in children, or dabbing.
- ★ Cannabis use can be caused fatal trauma due to the delayed onset of action, involving with motor coordination, unsteadiness, and level of consciousness.
- ★ Common symptoms in cannabis toxicity are palpitation, dry mouth, ataxia, behavior changes. The supportive treatment is mainstay.
- ★ Synthetic cannabinoids toxicity is very serious and are classified as CNS stimulants, not hallucinogens.
- ★ The violence control are the first priority, seizures and hyperthermia need to detect and promptly treat, the supportive treatment is key.

### CANNABIS

กัญชา ฐรกิจ การเมือง 🙂 ารแพทย์

Charcoal-burning suicide

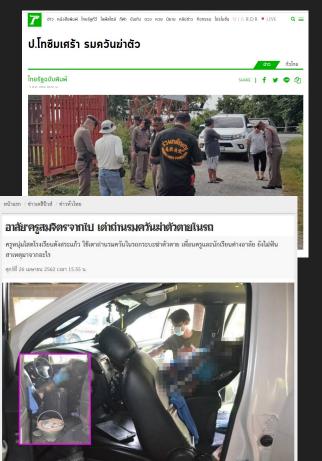
### Charcoal-burning suicide



น่าเศร้า หนุ่มแว่นเปิดเพลงรักเพลงเดียววนซ้ำๆ ก่อน จุดเตาถ่านรมควันฆ่าตัวตายคาเก๋ง



REGIONAL



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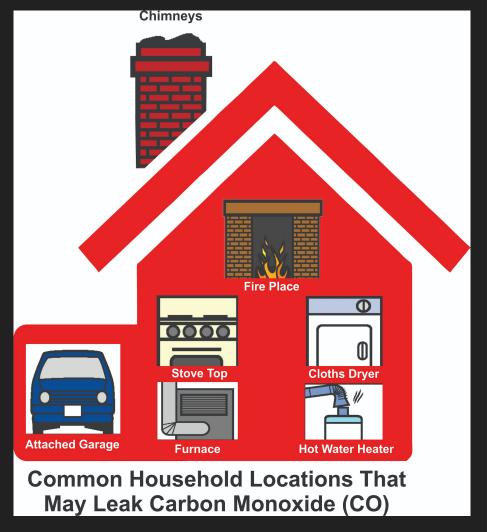
### These situations that you should think about *CO poisoning!!*











# Family members develop headache in the same house simultaneously

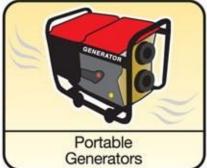
In winter season, very low ambient temperature

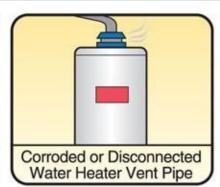
- Many people develops CO poisoning due to leakage of CO from many sources.
- Need CO detector device establishing in the house.

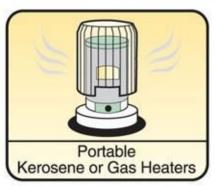


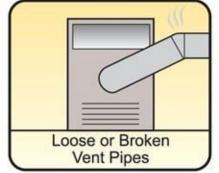
### **Potential Sources of Carbon Monoxide**





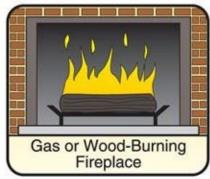










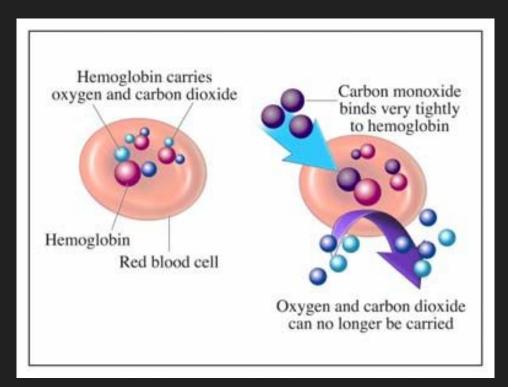


### Atypical exposure that make CO poisoning in human:

Ingestion a kind of solvent called "methylene chloride" or "dichloromethane (DCM)"



### Mechanism of Toxicity



CO generate from incomplete combustion

Carbon monoxide (CO) has stronger affinity to Hb than oxygen about 250 times.

All tissue hypoxia

**S&S:** hypoxic symptoms

### CARBON MONOXIDE POISONING WHAT ARE THE SYMPTOMS?



#### Typical Symptoms of Carbon Monoxide Poisoning Only a guide, people may experience symptoms differently Death (if not removed from CO exposure) 50 +...... Unconsciousness, Seizure Pounding Headache, Confusion, Shortness of Breath, ······ Blurred Vision, Loss of Coordination, Uncontrolled Loss of Consciouness, Vertigo, Chest Pain, Memory Loss INCREASING 30-40 ..... Bad Headache, Breathing Difficulty, Impaired Judgement, % of CO Vision Impairment, Drowsiness, Stomach Pain INTHE BLOOD 20-30 ...... Headache, Slight Drowsiness, Dizziness, Respiratory Rate Increases 10-20 ······ Slight Headache, Nausea LESS THAN ······ None 10

### Apply this scheme when you don't know COHb level.

- Loss of consciousness and Coordination → 40-50%
   COHb level
- Impairment of vision and judgement 30-40%COHb level
- Drowsiness, dyspnea →
   20-30% COHb level
- Mild headache, nausea →
   10-20% COHb

50%

ตาย

หมดสติ

ปวดหัว ซึม/หอบ ตา/ตัดสินใจ 10% 20% 30% 40%

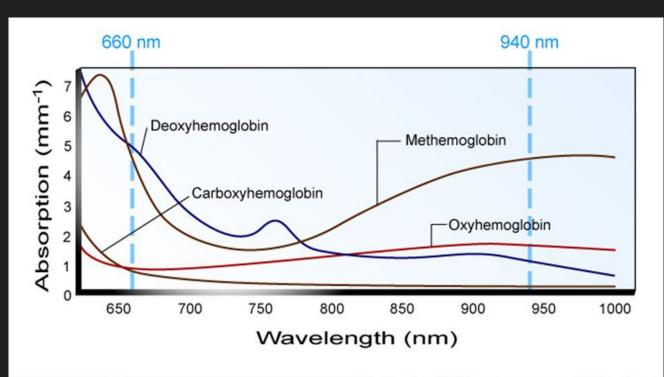
### How to cope with charcoal burning suicide

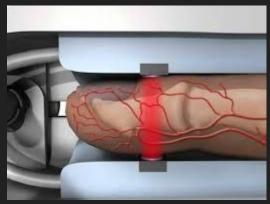
- Recognize CO poisoning
  - Prehospital: pulse CO-oximetry
  - Inhospital: CO-oximetry (blood gas machine)





### Pulse oximetry: cannot detect CO poisoning





### CO level

#### Human

- Non smoker <2.5 %</li>
- Smoker: <5%

The antidote for CO poisoning is OXYGEN

Treat until COHb level less than 5%

## Cherry red skin is a late sign!

## Cannot use for diagnosis

### Management of CO poisoning

- Remove the patient from exposure and give oxygen 100% by non-rebreather mask or ET tube as soon as possible
- Early intubation in case of inhalation injury
- Prehospital pulse CO-oximetry in case of suspected CO poisoning (e.g. fire accident, CO leakage in house, charcoal burning suicide)
- Prehospital CPAP may be required
- Consider hyperbaric oxygen treatment (HBOT) in severe cases

### Carbon Monoxide and half-life elimination for blood

Method of O <sub>2</sub> therapy	Elimination half-life
Room air	240-360 minutes (4-6 hours)
Oxygen 100%	80 minutes (1.33 hours)
Hyperbaric oxygen	22 minutes

### In case of fire accident

- Burn
- Inhalation injury
- CO poisoning
- CN poisoning
- Methemoglobinemia

 Need many equipments and antidotes







### **Equipments and drugs**

- O<sub>2</sub> therapy: mask with bag
- Endotracheal intubation and mechanical ventilator
- Bronchodilator
- Pulse CO-oximetry or CO-oximetry
- Cardiac monitoring
- ABG machine
- 7.5%NaHCO<sub>3</sub> IV
- Crystalloid IV fluids
- Refer to hyperbaric therapy, if indicated for CO poisoning
- Antidote kit of Cyanide: 3%Sodium nitrite, 25%Sodium thiosulfate or Hydroxocobalamin
- Methylene blue for methemoglobinemia

### Hyperbaric therapy: CO poisoning

#### Potential indications

- 1. history of a loss of consciousness
- metabolic acidosis
- 3. age more than 36 years
- 4. pregnancy
- carboxyhemoglobin level greater than
   and
- cerebellar dysfunction



### **Sodium nitrite**

### Indication

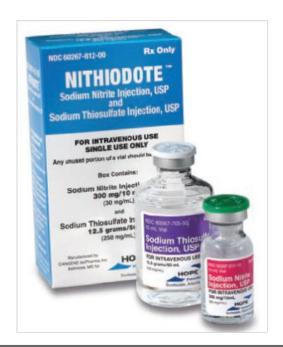
Symptomatic cyanide poisoning with high suspicious,

Not for all smoke inhalation victims

Hydrogen sulfide poisoning

#### Contraindications

- Preexisting with metHb level >40%
- Severe hypotension
- Concurrent CO poisoning



### Sodium thiosulfate

### **Indications**

- Acute cyanide poisoning or suspected
- Cisplatin overdose

Give alone or combination with nitrite or hydroxocobalamin

### Contraindication

None

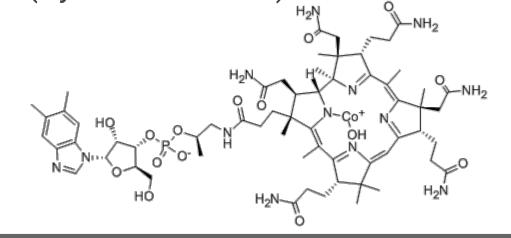


### In case of pregnancy with CO poisoning

Prefer hydroxocobalamin over nitrite hydroxocobalamin

Pregnancy category C

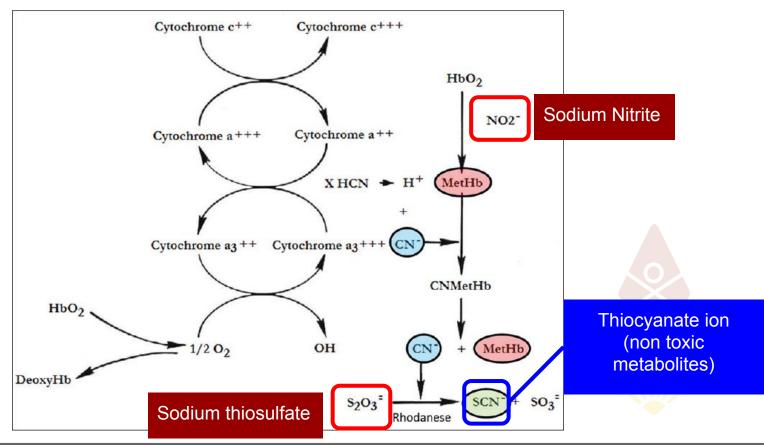
 Similar with vitamin B12 (Cyanocobalamin)





- One 250-mL glass vial containing 5 g of lyophilized hydroxocobalamin for injection
- 2. 1 Sterile transfer spike
- 3. 1 Sterile intravenous infusion set
- 4. 1 Quick-use reference guide
- 5. 1 Package insert

### Mechanism of cyanide antidote



Antidote app in mobile phone
Antidote request in Thai
Call to Thai poison control centers







