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Cannabis

In EMERGENCY:

Pot heads will not attend ED unless something is seriously wrong. Catastrophic problems include

Acutely Pleasant Intoxication: often co-existing with motor vehicle accident

- Tachycardia
- Euphoria
- Impairment of coordination and reaction time
- Postural hypotension
- Short term memory impairment

Acutely Unpleasant Intoxication and overdose…

RARE: but when it happens it presents with

- Palpitation, Tachycardia, arrhythmia
- Confusion, psychomotor slowing, extreme sedation
- Sedation may progress to respiratory depression with polysubstance abuse
- Nausea, vomiting, dizzyness

Cannabinoid Hyperemesis: "Bath, bucket and bong syndrome"

Extremely unhappy people, suffering **a Constant need to shower and persistent nausea with vomiting** having had ceased cannabis some time ago and only recently resumed. This horror does not continue for very long. Supportive care only.

Cannabinoid Psychosis: usually a first-time user…. Presents with florid psychotic symptoms following an episode of intoxication. Thus a pre-morbid schizophrenia is unveiled.

SALIENT FEATURES OF HISTORY:

PHYSICAL EXAMINATION:
As all the scars are internal, physical exam is usually uninformative. Look to signs of other drug use, alcoholism, and features suggestive of chronic bronchitis.

Related to biological consequences:

Chronic cough history
Previous psychiatric admissions
Questions about anxiety, depression, dysthymia

Related to social consequences:

Withdrawal, failure in work, education or relationships

Related to forensic history:

Extent of legal repercussions, eg. driving, possession etc…

Mental State Examination rarely yields surprises, but when it does…..

AREAS OF INTEREST:

- **Thought form and content** (delusional? Derailed?)
- **Perceptual disturbance** (hallucinating, are we?)
- **Cognitive impairment (attention + short term term memory)**

INVESTIGATIONS:

Fire the standard casualty department broadside:

FBC
EUC
LFT

Whatever the results, they will not be attributable to cannabis as such; instead it will be the hyperemesis, or the malnutrition, or the concomitant alcoholism.

FEATURES OF WITHDRAWAL:

- sleep disturbance
- irritability
- loss of appetite
- consequent weight loss
- nervousness
- anxiety
- sweating
- upset stomach.
- Sometimes chills, high temperature and tremors

The withdrawal syndrome usually lasts for less than a week, although the sleep disturbances may persist for a longer period. Onset typically occurs between Days 1-3, peak effects between Days 2-6, and most effects last 4-14 days.

INTERESTING:
Tobacco causes mainly alveolar and small-airway disease; cannabis smoke damage seems to favour the larger bronchi.

Other considerations in long-term users:

Psychosocial impairment (withdrawal, demotivation, dysthymia- esp. adolescent users)
Chronic Bronchitis
Impairment of immune function (rarely clinically ignificant)
Infertility in males (reduced sperm count and motility)
Low birth weight infants in females

MANAGEMENT

ACUTE: in the EMERGENCY setting: supportive care

ACUTE PSYCHOSIS? That may require some sedation (diaz, midaz)
Consider schedule II 21-D admission
Consider typical antipsychotic agents if severe

DETOXIFICATION:

Mild and comfortable, usually; amenable to hand-holding and aromatherapy
Still psychotic? –olanzapine or risperidone for 2-6 weeks
Ugly withdrawal? Cant sleep, cant eat, snapping at everyone?

- Mirtazapine30 to 60mg nocte (a sedating antidepressant)
- Alternatively an SSRI ..
- Mood stabilizers may be needed (eg. gabapentin)

MAINTENANCE:

Avansa (mirtazapine) appears to improve rates of relapse.
Support groups exist. Efficacy is uncertain.
Significant positive lifestyle changes are most predictive of good outcome

CANNABIS Vs. TOBACCO: pathology

- Both produce carbon monoxide, but weed burns at a higher temperature and thus produces more.
- Both contain carcinogenic benzopyrenes and benzoanthracenes but **weed has more of them.**
- **A joint: produces 5 x the Carboxyhemoglobin level, 3x the tar inhalation, 30% more tar retention** than a cigarette
- Most of this derives from the fact that joints are smoked differently: long drags, deep inhalations, longer retention of smoke, and no filter.

NEUROPHARMACOLOGY OF CANNABIS

Active ingredient: Delta- 9- Tetrahydrocannabinol

2 cannabinoid receptor types:

CB1:

found primarily but not exclusively in the brain. They are most prevalent in the hippocampus, cerebral cortex, basal ganglia, and cerebellum.

CB2:

CB2 receptors are also found in the brain but more so expressed by cells of the immune system, especially B cells.

The CB receptor is a G protein mediated receptor that affects primarily calcium and potassium channel activation. Functional changes are most notable in neuronal excitability and neurotransmitter release.

THERE ARE ENDOGENOUS LIGANDS:
Anandamide, 2-arachidonylglycerol….

INGESTED OR SMOKED

Smoking delivers 30 per cent or more of the total THC in a cannabis cigarette to the blood stream. The proportion of THC absorbed after taking cannabis by mouth is 2-3 times less, because after absorption in the gut the drug is largely degraded by metabolism in the liver before it reaches the general circulation.

CYP 450

Distributed to lipids, esp. white matter of the brain. Pharmacological effects persist for more than 4-6 hours after smoking or 6-8 after oral ingestion.

CB-1 receptors are **largely inhibitory;**
they are PRE-SYNAPTIC and don't appear on dendrites or neuronal soma.
Interestingly, there are no receptors in the brainstem: is this why its hard to die from a THC overdose?...

Deadwyler et al. (1995) suggested that the inhibitory effect of CB_1 receptor activation on adenylate cyclase activity causes a decreased phosphorylation of A-type K^+ channels by the cAMP-dependent enzyme protein kinase A. This, in turn, would activate the A-type K^+ channels and cause a shortening of the duration of presynaptic action potentials as they invade axon terminals.

Indirect Mu-Opioid effect:
Possible explanation for addictiveness; Opioids + THC = enhanced analgesic effect; naltrexone following THC = some signs of opiate withdrawal.

Indirect dopaminergic effect:
Possible explanation for addictiveness; NA reward system is activated, but is it the THC alone or is it operant conditioning from rewarding use of THC in social situations?

Indirect GABA-ergic effect:
Possible explanation for sedation

MANY OTHERS:
Melatonin level increase ~200-fold;
? circadian rhythm disruption? Possible explanation for sleep disturbance associated with withdrawal?
GABA-A-inhibitory effects in hippocampus:
Interneurons most affected; ? explanation for short term memory loss? This GABA effect coincides with an NMDA receptor inhibition, so there is less glutamate as well as GABA…
LEPTIN (the hunger-suppressing satiety hormone) is also affected (inhibited), hence the munchies?...

Long Term Effects:
Small but significant deficits in short term memory (eg. in word recall tasks) and in acquisition of new skills.
Potentially, a predisposition to psychosis with long-term heavy use.