SPU الجامعة السورية الخاصة
SYRIAN PRIVATE UNIVERSITY

السنة الرابعة

علم السموم التطبيقي والشرعي

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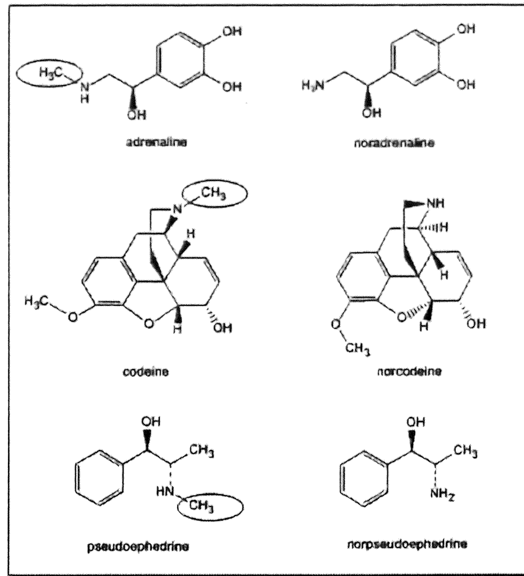
- 1- Naloxone (Narcan®) is a pure opioid antagonist available as an injectable only.

- dramatically reverses the CNS and respiratory depression
- - (in this capacity, naloxone is also indicated in the diagnosis of suspected acute opioid overdose).
- Depending on the extent of narcotic overdose, a continuous infusion of naloxone may be required, especially in the presence of opioids with longer half lives, such as propoxyphene or methadone.

- As respiration improves, naloxone, which has a half-life of 60 to 90 min, may be discontinued and resumed as necessary.
- If there is no response after 10 mg of naloxone, concomitant ingestion with other depressants is likely.
- 2- Naltrexone (Revia®) is also a pure opioid antagonist available as oral tablet dosage form only.



- **A 50-mg dose of naltrexone blocks the pharmacological effects of opioids by competitive binding at opioid receptors.**
- **It is also indicated in the treatment of alcohol dependence.**
- **Naltrexone has been noted to induce hepatocellular injury when given in excess.**

- **3- Nalmefene (Revex®),**
- **is indicated for the complete or partial reversal of natural or synthetic opioid effects.**
- **It is a 6-methylene analog of naltrexone.**

- **Several drugs have agonist activity at some receptors (k) and antagonist activity at other (μ) receptors.**

- **4- Nalbuphine (Nubain®) is a potent analgesic with narcotic agonist and antagonist actions.**

- **Other mixed agonist-antagonist compounds are designated as partial agonists, such as:**
- **butorphanol (Stadol®), buprenorphine**
- **(Buprenex®), and pentazocine (Talwin®and various tablet combinations).**
- **These compounds are potent analgesics and weakly antagonize the effects of opioids at the μ-receptor, while maintaining some agonist properties at the**
- **-k and δ-receptors.**
- **Drug enforcement personnel and customs officials respond to different conditions of opioid overdose, especially those involving *body packers* and *body stuffers.***

- The drug carriers, who differ only in the apparent manner of sealing and concealing illicit drug packets, run into problems when the packets leak or burst.
- The overall clinical response to the situation requires rapid detection with body cavity searches and abdominal radiographs.
- *1 Decontamination with activated charcoal, *2gastric lavage,*3 high-dose continuous infusion with naloxone, and attention to the*4 ABCs of emergency management of toxicity in anticipation of a developing opioid syndrome are also warranted.

TOLERANCE AND WITHDRAWAL

- *The Department of Mental Health and Substance Dependence at the World Health Organization (WHO), in collaboration with the U.S. National Institute on Drug Abuse (NIDA), defines several terms important in understanding drug abuse and the phenomena of tolerance and withdrawal.*
- Addiction involves compulsive psycho-active drug use with an overwhelming involvement in the securing and using of such drugs.

- **As described below, the withdrawal syndrome occurs as a result of sudden or abrupt discontinuation of the substance.**
- **Compulsive drug use involves the psychological need , often referred to as "craving."**
- **In this case, the uncontrollable drive to obtain the drugs is necessary to maintain an optimum state of well-being.**

- **Habituation refers to psychological dependence.**
- **Physical physiological dependence involves the need for repeated administration in order to prevent withdrawal (abstinence) syndrome.**
- **In fact, with repeated chronic dosing, seizure threshold for opiate narcotics is elevated, threatening the precipitation of seizure upon withdrawal (rebound effect).**

- The more complex phenomenon of tolerance requires the satisfaction of several criteria.
- With repeated administration, addicted individuals necessitate greater amounts of drug in order to achieve the desired effect.

- While a diminished euphoric effect continues with progressive tolerance, the increasing doses threaten induction of respiratory depression.
- Increased metabolism, adjustment to the sedative, analgesic, and euphoric effects, are proposed as possible mechanisms for the development of tolerance
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- **Depending on the drug, the withdrawal syndrome is precipitated hours after the last narcotic dose with peak intensity occurring at about 72 h .**

- **The intensity of the syndrome is greatest with heroin, followed by morphine, and methadone.**

- **Heroin withdrawal is characterized by acute, sudden symptoms of greater vigor while methadone withdrawal is distributed over 7 to 10 days and of lower intensity.**

- **Although the syndrome is rarely fatal, administration of an opioid at any time during withdrawal alleviates the condition.**

Characterization of the Opioid Withdrawal Syndrome

Stage	Time after Last Dose	Signs and Symptoms
Anticipatory	3–4 h	Withdrawal, fear, craving, compulsive drug seeking behavior
Early withdrawal	8–12 h	Lacrimation, sweating, listless behavior, anxiety, restlessness, stomach cramps
	12–16 h	Restless sleep, nausea, vomiting, mydriasis, anorexia, tremors, cold clammy skin, fever, chills, compulsive drug seeking behavior

Stage	Time after Last Dose	Signs and Symptoms
	48–72 h	Peak intensity; tachycardia, hypertension, hypothermia, piloerection (goose-flesh appearance of skin, "cold turkey"), muscle spasms, continued nausea, vomiting, dehydration, compulsive drug seeking behavior, risk of cardiovascular collapse

- Protracted abstinence 6 months

Stimulus-driven cravings, anorexia, fatigue bradycardia, hypotension