DRUGS USED IN MANAGEMENT OF PAIN

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MEDICAL PHARMACOLOGY
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A CASE OF OVERDOSE

ENT OF PAIN

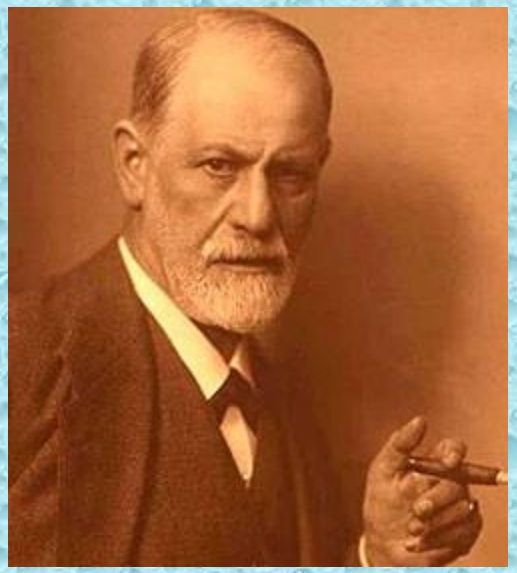
His cancer of the jaw was causing him

ny

Sigmund Freud, the father of psychoanalysis

EUTHENASIA

CAUSED THE DEATH OF SIGMUND FREUD?



His doctor administered increasing doses of **MORPHINE** that resulted in Freud's death on 23 September 1939

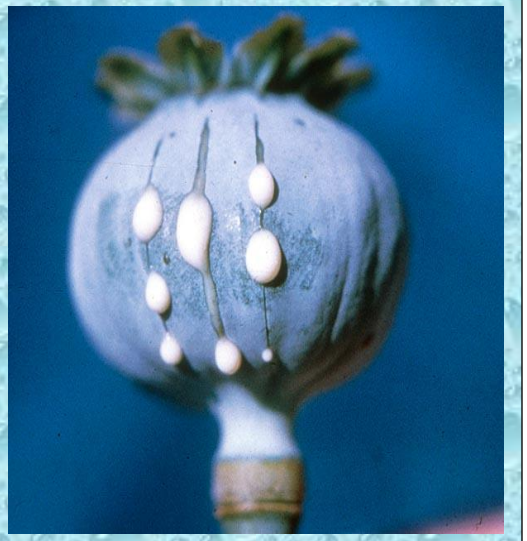
DRUGS USED IN MANAGEMENT OF PAIN

ILOS

Categorize the different classes of drugs used to relieve pain

Detail on the mechanism of action, pharmacokinetics & pharmacodynamic effects of morphine & its synthetic derivatives

Hints on the properties & clinical uses of morphine antagonists.



DRUGS USED IN MANAGEMENT OF PAIN

WHY SHOULD WE TREAT PAIN?

Pain is a miserable experience

Pain is the most common reaso
medical advice

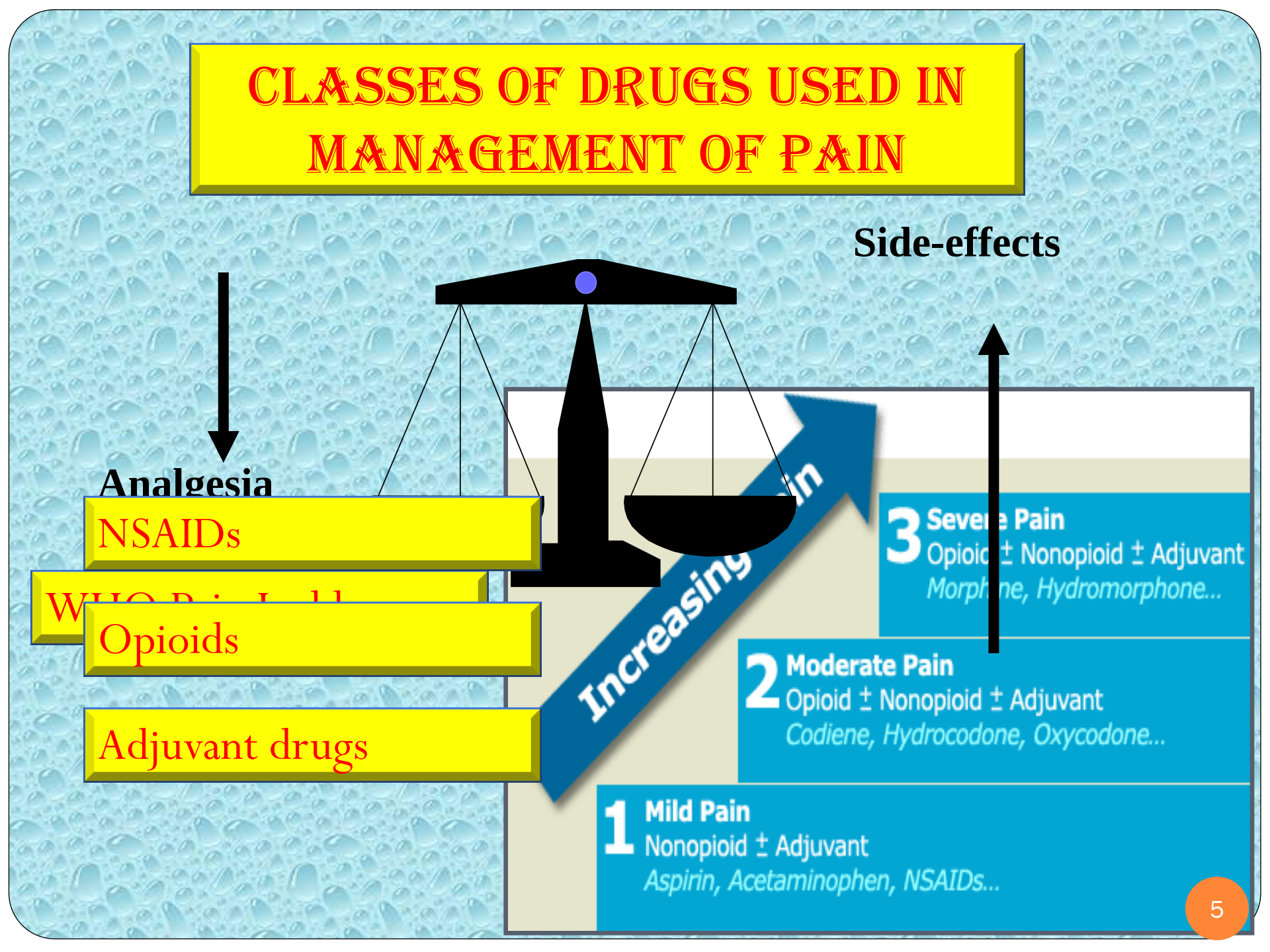
Impairs the patient functional a
psychological well being

Pain increases sympathetic outp
-Increases myocardial oxygen d
-Increases BP, HR

Pain limits mobility
-Increases risk for DVT/PE

- "The fifth vital sign" – American Pain Society 2003
- Identifying pain as the fifth vital sign suggests that the assessment of pain should be as automatic as taking a client's BP and pulse

CLASSES OF DRUGS USED IN MANAGEMENT OF PAIN



NSAIDS

Generally the 1st class of drugs used for controlling pain

Work at site of tissue injury to prevent the formation of the nociceptive mediators

Can decrease opioid use by ~30% therefore decreasing opioid-related side effects

They neither cause tolerance or dependence

Has a ceiling effect to analgesia.

ADJUVANT DRUGS

e.g. Anxiolytics,
Neuroleptics,
Antidepressants
Antiepileptics

May modify the perception of pain & remove the concomitants of pain such as anxiety, fear, depression

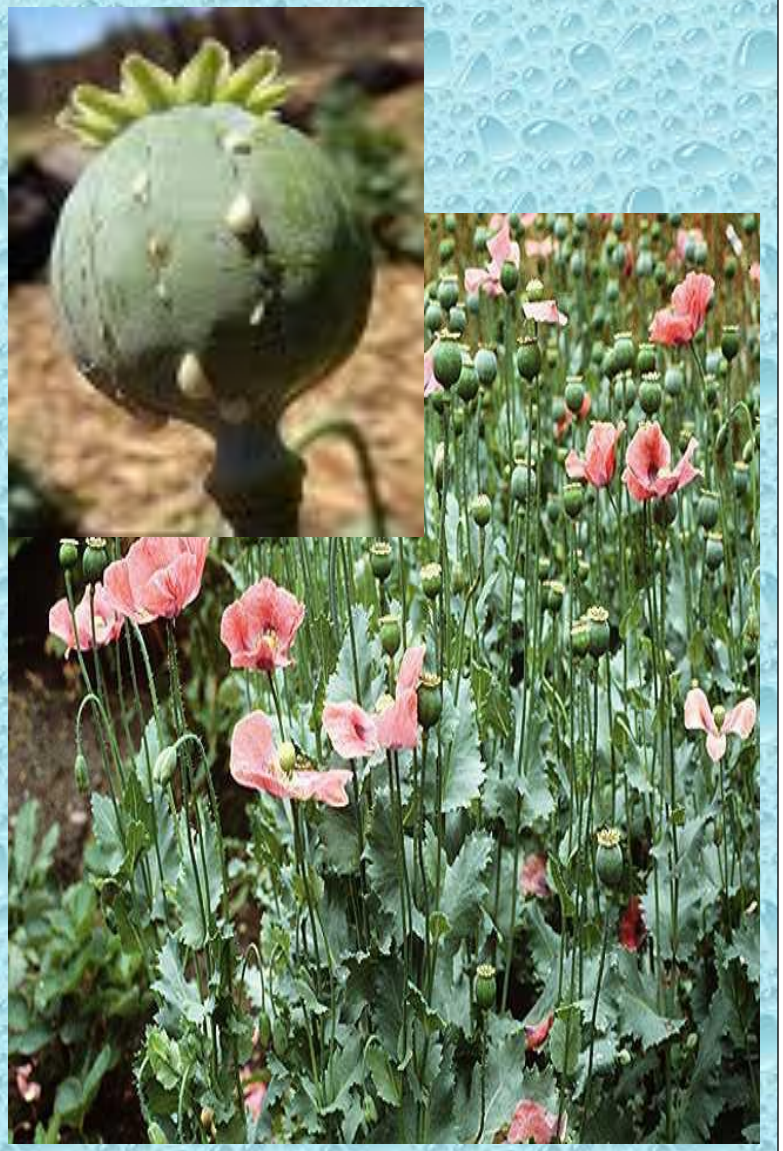
OPIOIDS

Opium is derived from the juice of the opium poppy, *Papaver somniferum*

The **natural** products include *morphine, codeine, papaverine* & *thebaine*

Opiates are drugs derived from opium & semisynthetic & synthetic derivatives

Endogenous opioid peptides, e.g. Endorphins, enkephalins & dynorphins.



OPIOID RECEPTORS

Anatomical distribution in brain, spinal cord, & the periphery

OPIOID RECEPTORS		
Opioid Receptor Class		Effects
Mu_1	μ	Euphoria, supraspinal analgesia, confusion, dizziness, nausea, low addiction potential
Mu_2	μ	Respiratory depression, cardiovascular and gastrointestinal effects, miosis, urinary retention
Delta	δ	Spinal analgesia, cardiovascular depression, decreased brain and myocardial oxygen demand
Kappa	k	Spinal analgesia, dysphoria, psychomimetic effects, feedback inhibition of endorphin system

ORL-1 **receptor**

Nociceptin ligand

All of them are typical G-protein coupled receptors

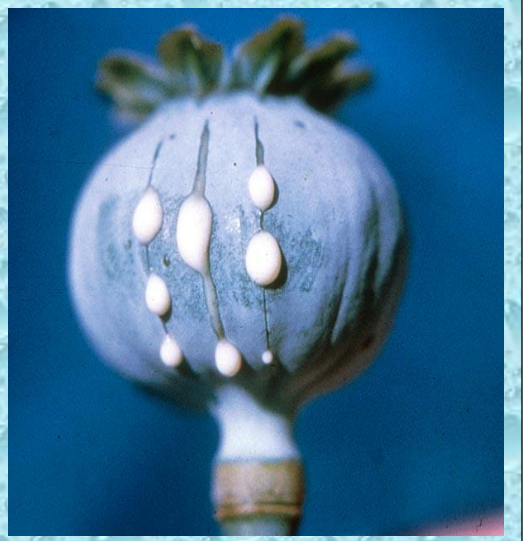
CLASSIFICATION OF OPOIDS

According to their source

According to ago Morphine, Codeine **c actions**

Semisynthetic Heroin

According to their specificity of action on recept Pethidine, Methadone

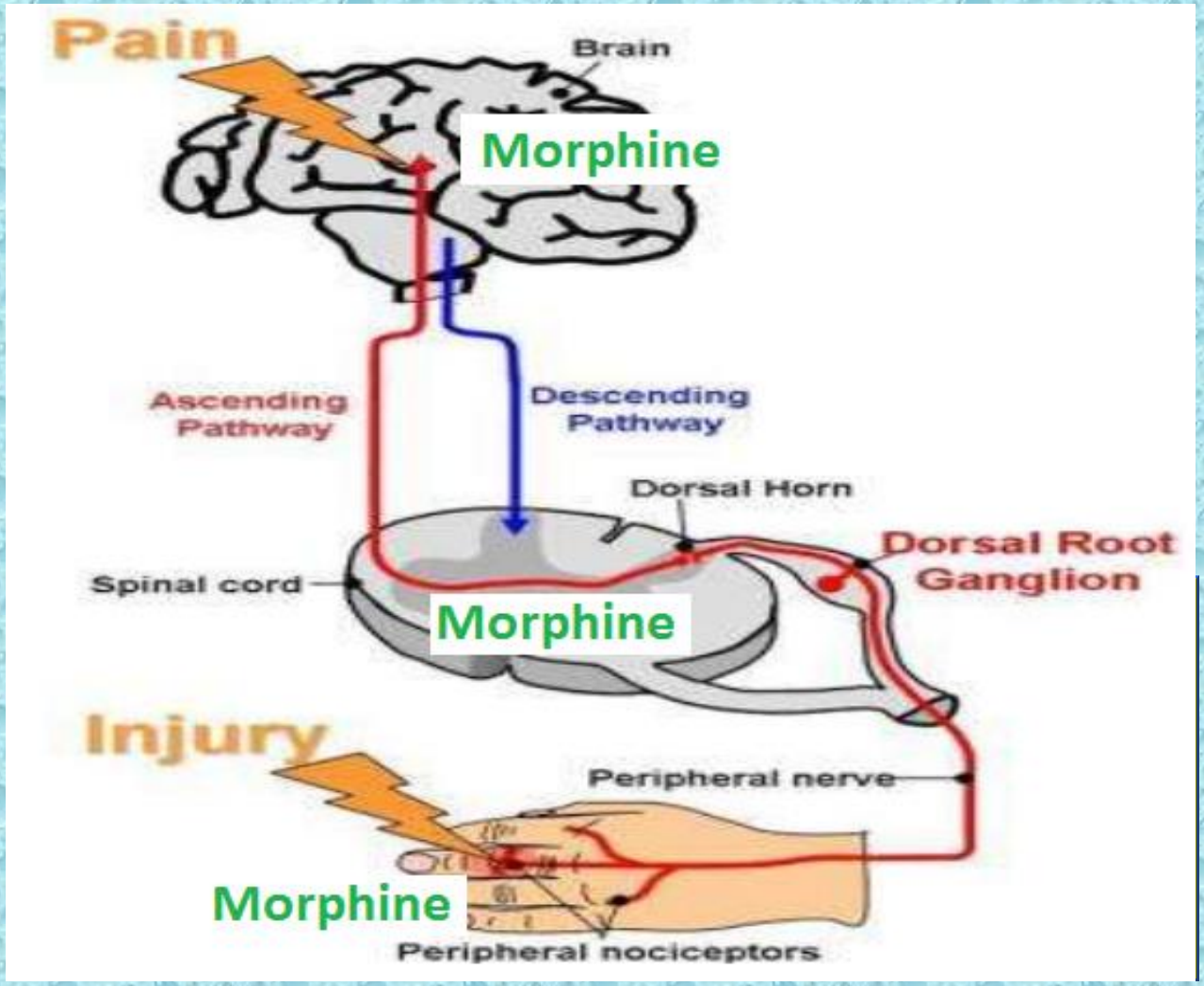


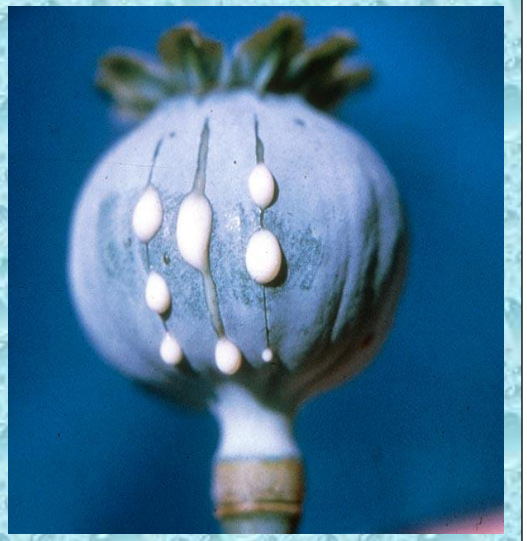
Morphine, codeine, heroin → μ-receptor agonists

Pure antagonist; Nalaxone, Naltraxone

Pentazocine agonist at k –receptors & antagonist at μ-receptors.

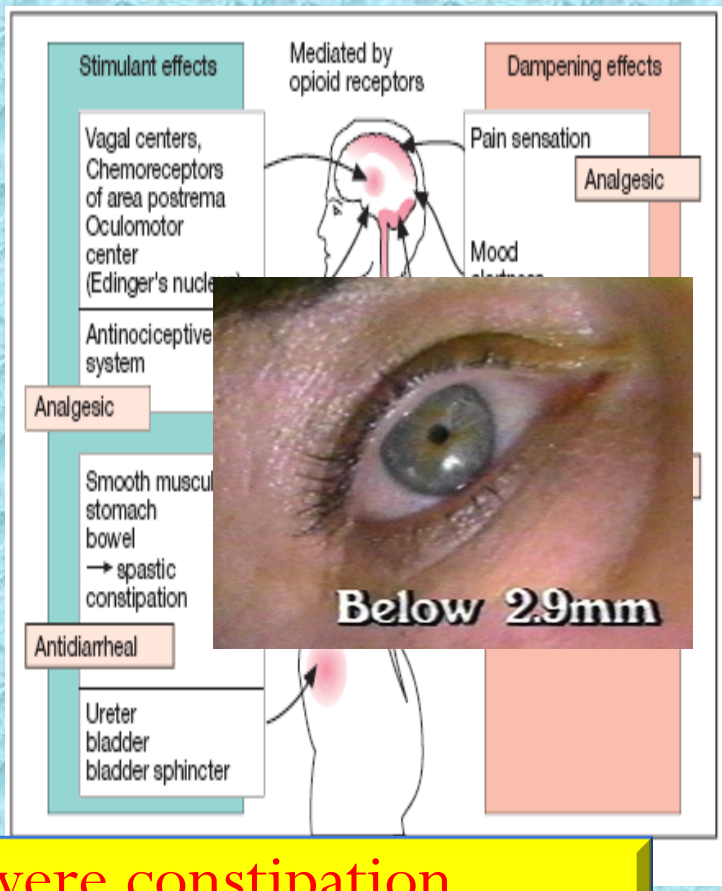
MECHANISM OF ACTION





PHARMACODYNAMIC ACTIONS OF MORPHINE

- Analgesia [in acute & chronic pain]
- Euphoria & sedation
- Respiratory depression
- Depression of cough reflexes
- Nausea & vomiting → ↑CRTZ
- Pin point pupil (miosis)
- Releases histamine from mast cells



Effects on GIT:- ↑in tone ↓ motility → severe constipation.
Constriction of biliary sphincter → ↑pressure in the biliary tract & biliary colic.
Depress renal function & contract gall bladder .

MORPHINE

TOLERANCE & DEPENDENCE

TOLERANCE

DEPENDENCE

T pidly with opioids (with morphine 12–24 hours)

Physical dependence (abstinence)

Withdrawal manifestations develops

Tolerance develops to respiratory depression, analgesia, euphoria & sedation

form of ↑ body ache, insomnia, diarrhea, gooseflesh, lacrimation

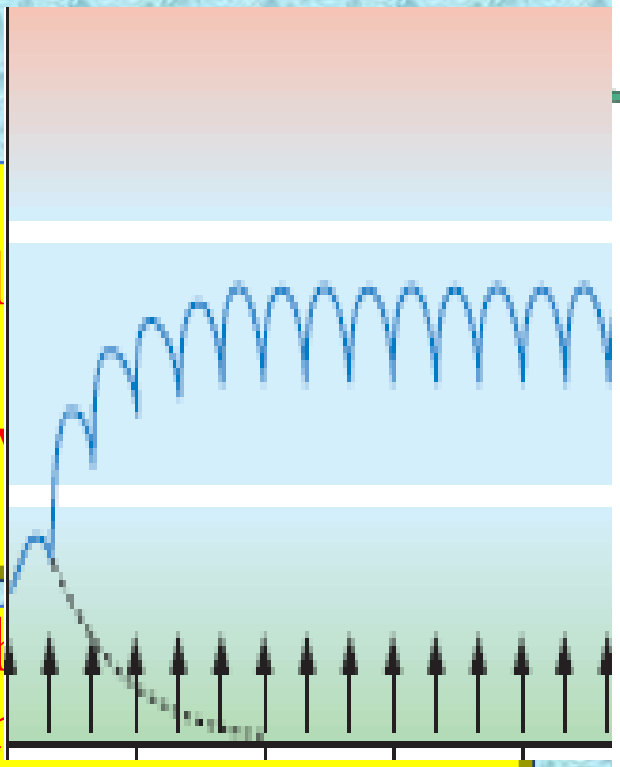
Psychological dependence lasting for months / years → craving

MORPHINE

PHARMACOKINETICS

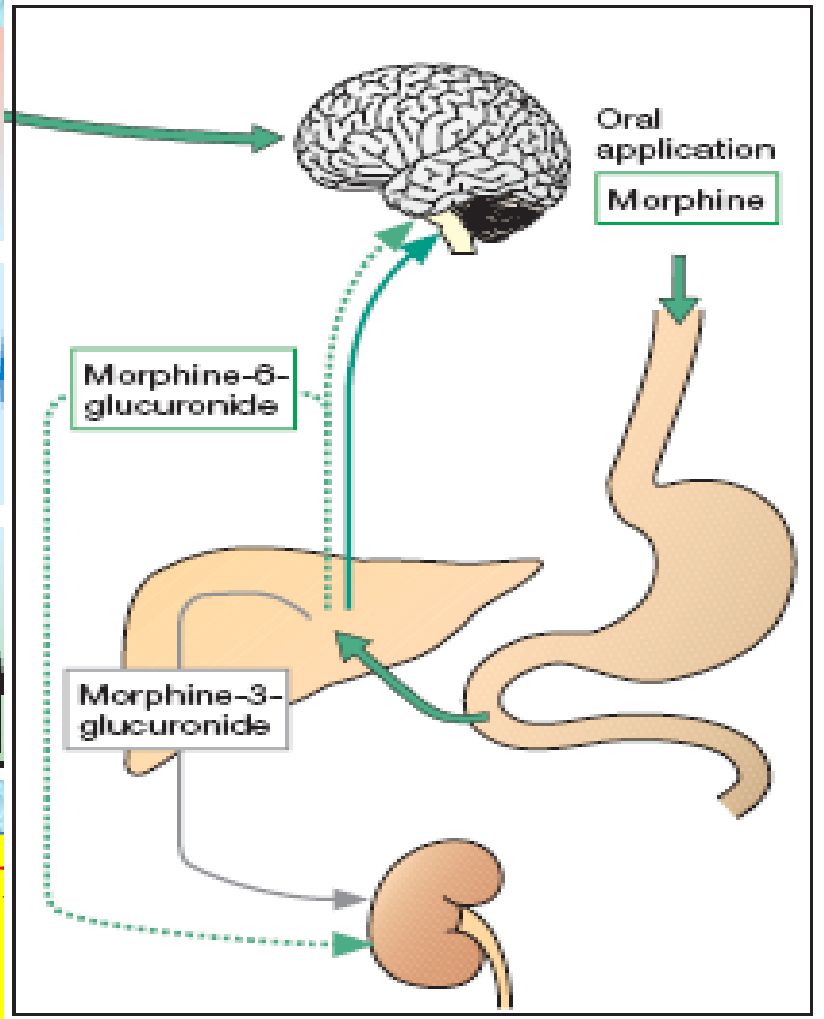
t ½ is 2-3h

It is slowly &
absorbed oral
20-40%).
-Medically gi
IV injection.



Metabolized l
with glucuror

Undergoes enterohepatic recyclin
-crosses BBB
-crosses placenta.



C. Metabolism of morphine

MORPHINE

CLINICAL INDICATIONS

CONTROL PAIN; cancer pain, severe burns, trauma, Severe visceral pain (not renal/biliary colics, acute pancreatitis)

Acute pulmonary edema

Myocardial ischemia

Non painful conditions e.g. heart failure (to relieve distress)

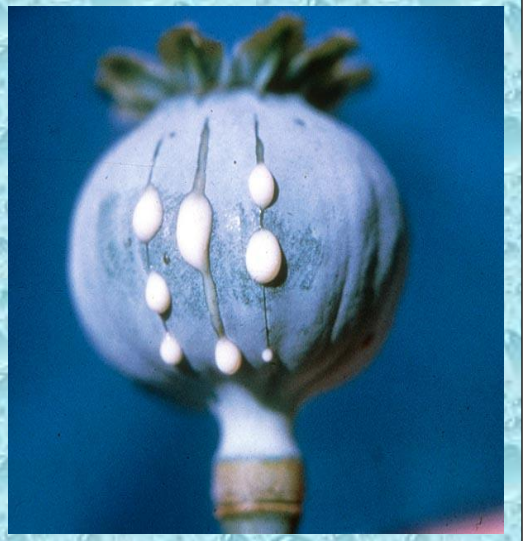
Pre-anesthetic medication.

MORPHINE

ADRS

- CONSTIPATION
- RESPIRATORY DEPRESSION
- ITCHING
- NAUSEIA, VOMITING
- CONSTRICTED PUPIL
- SEDATION.

CRINCS



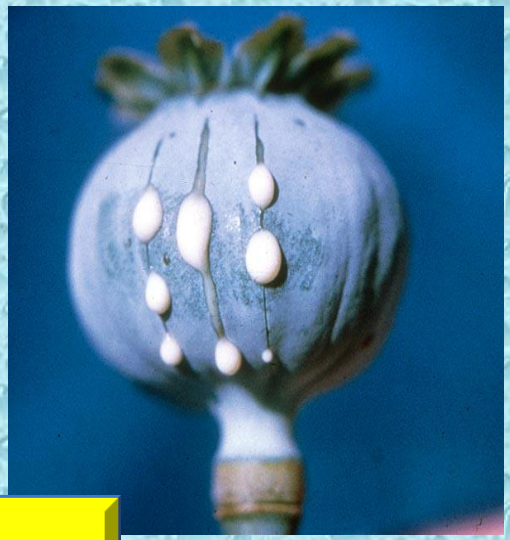
MORPHINE

CONTRAINDICATIONS

HEAD INJURY

BRONCHIAL ASTHMA or impaired pulmonary function

Biliary colic & pancreatic pain



Elderly are more sensitive; ↓metabolism, lean body mass & renal function

With MAOIs

Not given infants, neonates or during child birth → ↓conjugating capacity → accumulate → ↓ respiratory

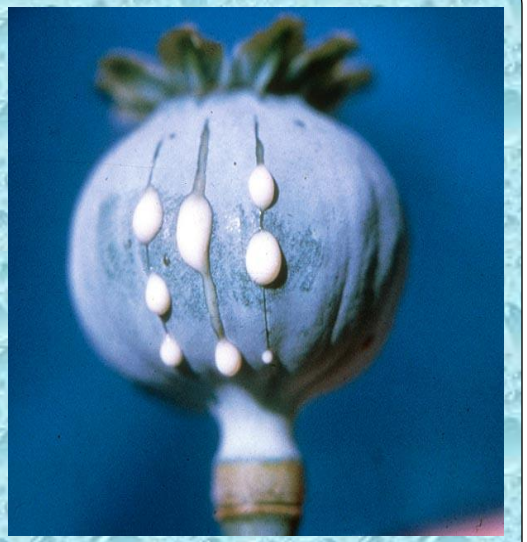
CODEINE

Natural opioid, **μ agonist**

Dependence < morphine

Used in mild & moderate pain, cough, diarrhea.

TRAMADOL



Synthetic, μ agonist , less potent than morphine

NE & 5HT reuptake

ADRS

-Mild - moderate acute & chronic visceral pain

-During labor

mouth, Dizziness, Sedation

-Less adverse effects on respiratory & C.V.S.

PETHIDINE (MEPRIDINE)

Synthetic, more effective κ agonist

ACTIONS

LESS analgesic, constipating, depressant on faetal

INDICATIONS

rphine

As in morphine b gh & diarrhea

ADRS

No cough suppre

Tremors, Convulsions, Hyperthermia, Hypotension

Preanaesthetic medication (better)

Blurred vision, Dry mouth, Urine retention

Used in obstetric analgesia (No ↓ resp.)

Used in severe visceral pain; renal & biliary colics (sm. relaxant)

FENTANYL

CLINICAL USES

ore potent

ine

ADRS

supplement during

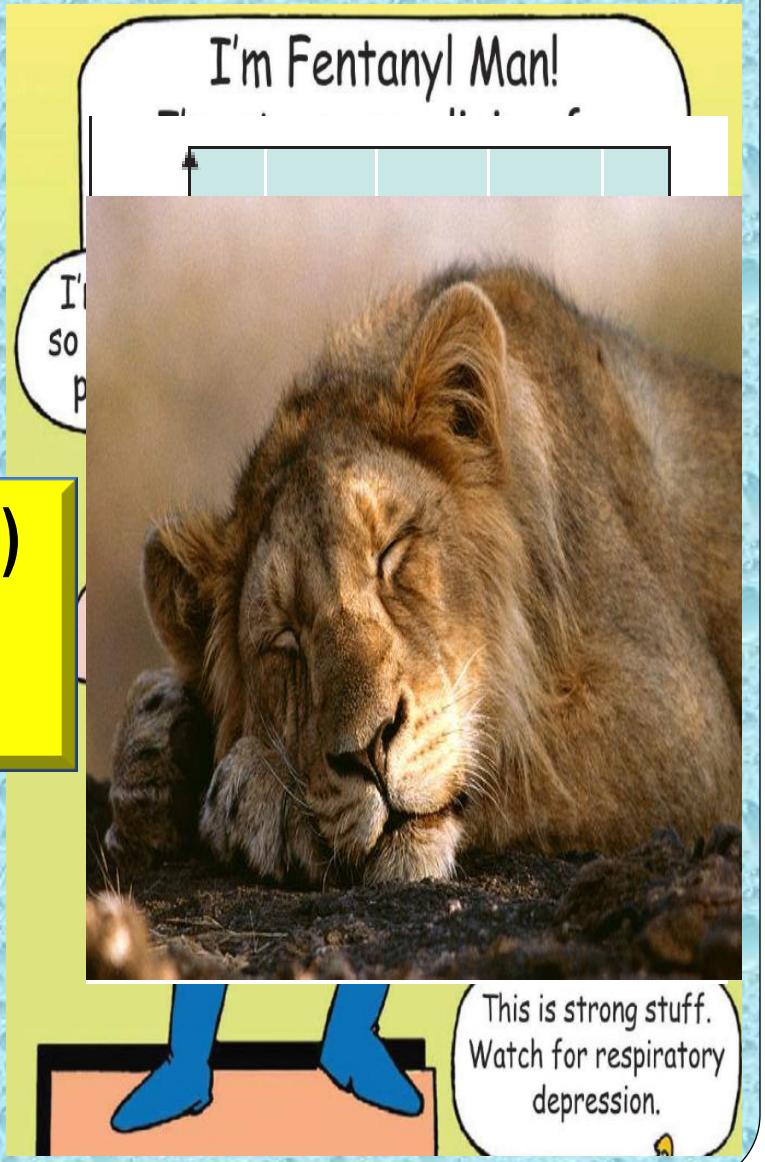
Respiratory depression (most serious)

CV effects are less

Bradycardia may still occur.

In combination with droperidol as NEUROLEPTANALGESIA

In cancer pain & severe postoperative pain; (transdermal patch changed every 72 hrs).



METHADONE

Weaker synthetic μ- agonist [illegible]al

In non addicts, it causes tolerance & dependence but not as severe as that of morphine

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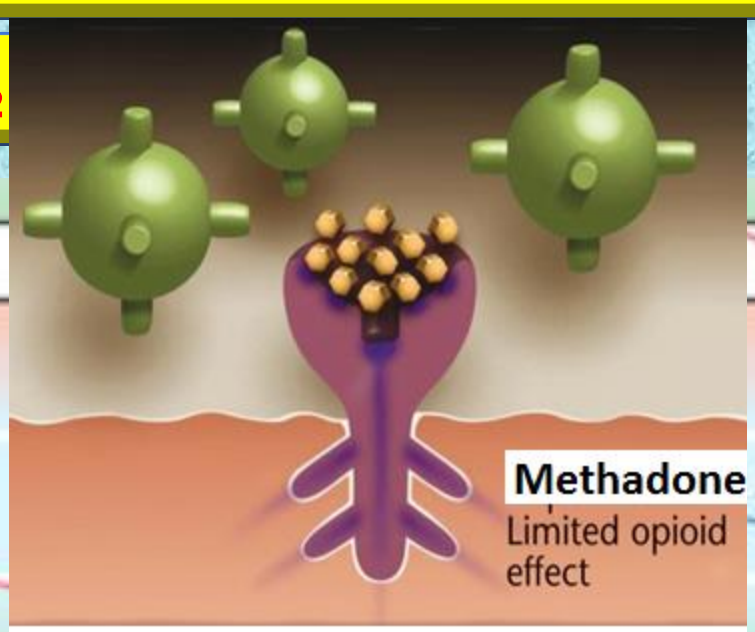
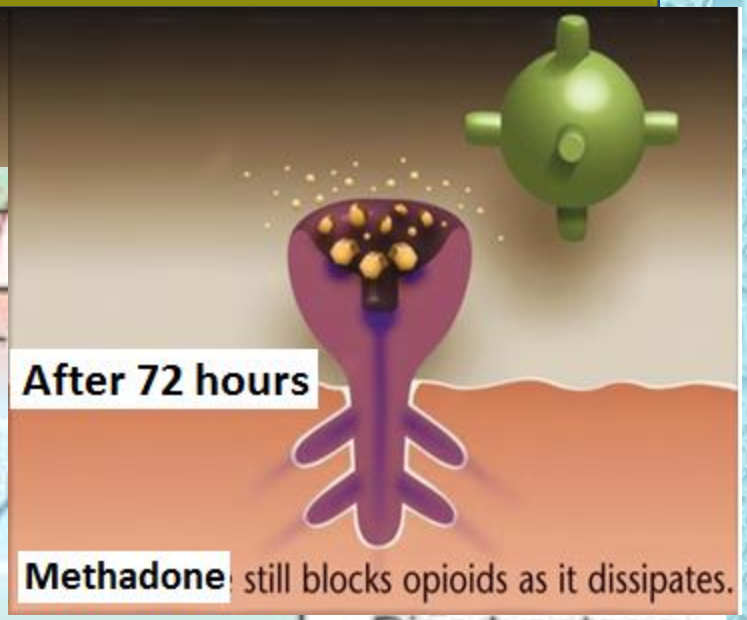
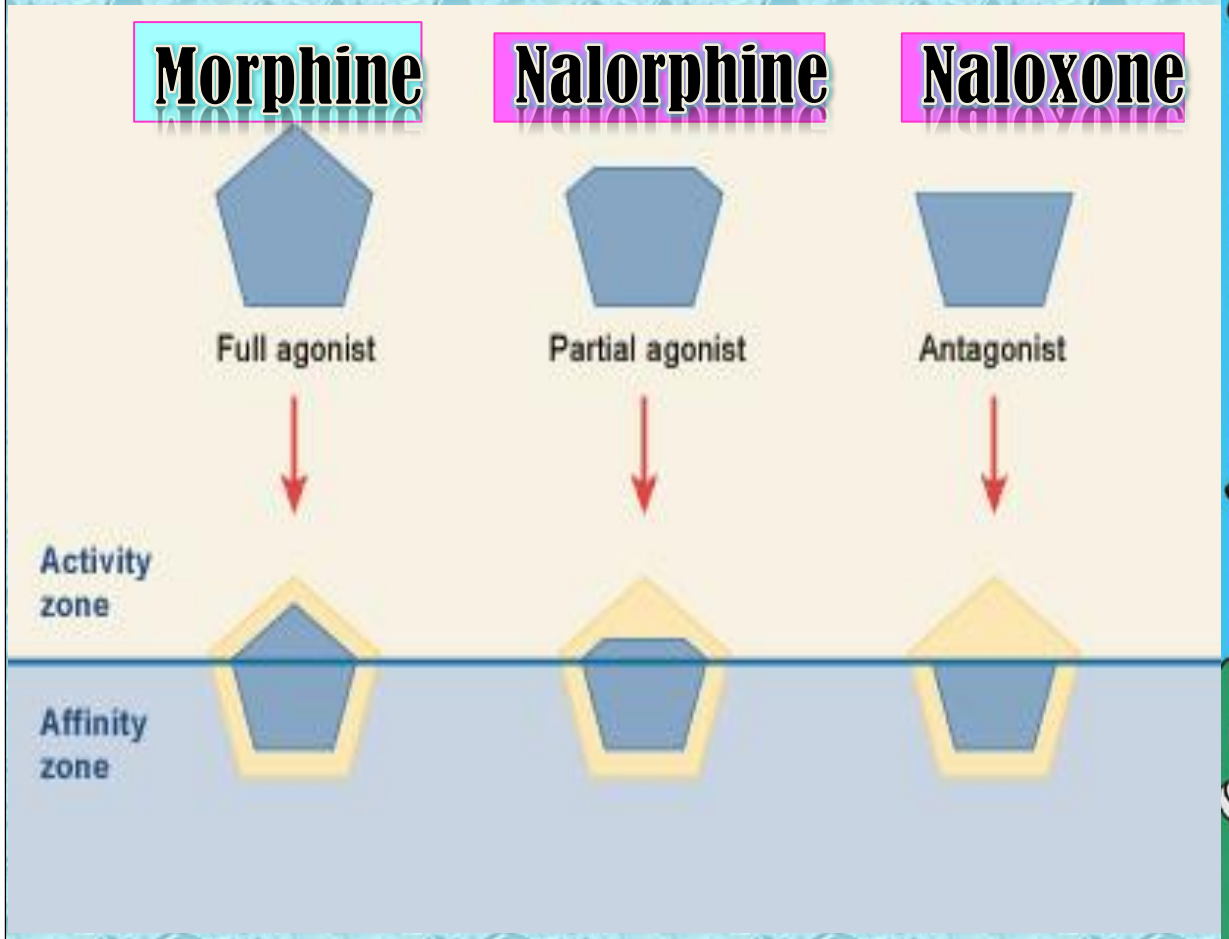
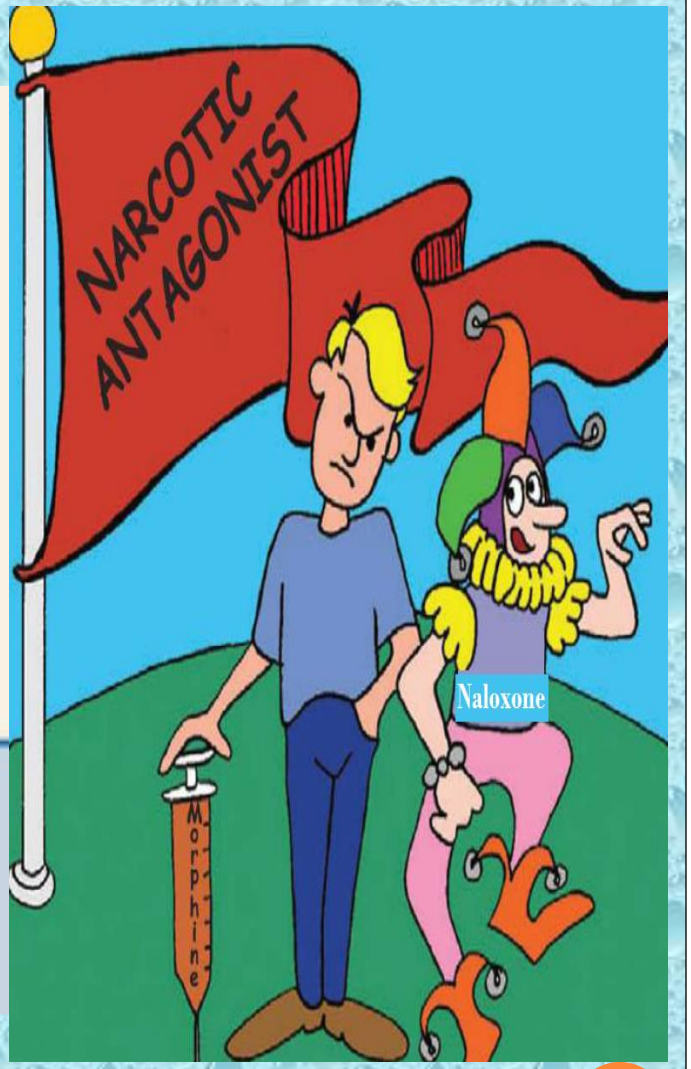




Disadvantage: dose difficult to titrate

OPIOID ANTAGONISTS





NALOXONE

Pure opioid antagonist

Used to treat respiratory depression caused by opioid overdose

To reverse the effect of analgesia on the respiration of the new born baby

Effect lasts only for 2-4 hours

Precipitates withdrawal syndrome in addicts

NALTREXONE

Very similar to naloxone but with longer duration of action [$t_{1/2}$=**10h**].