Did You Hear of the Opium Wars?

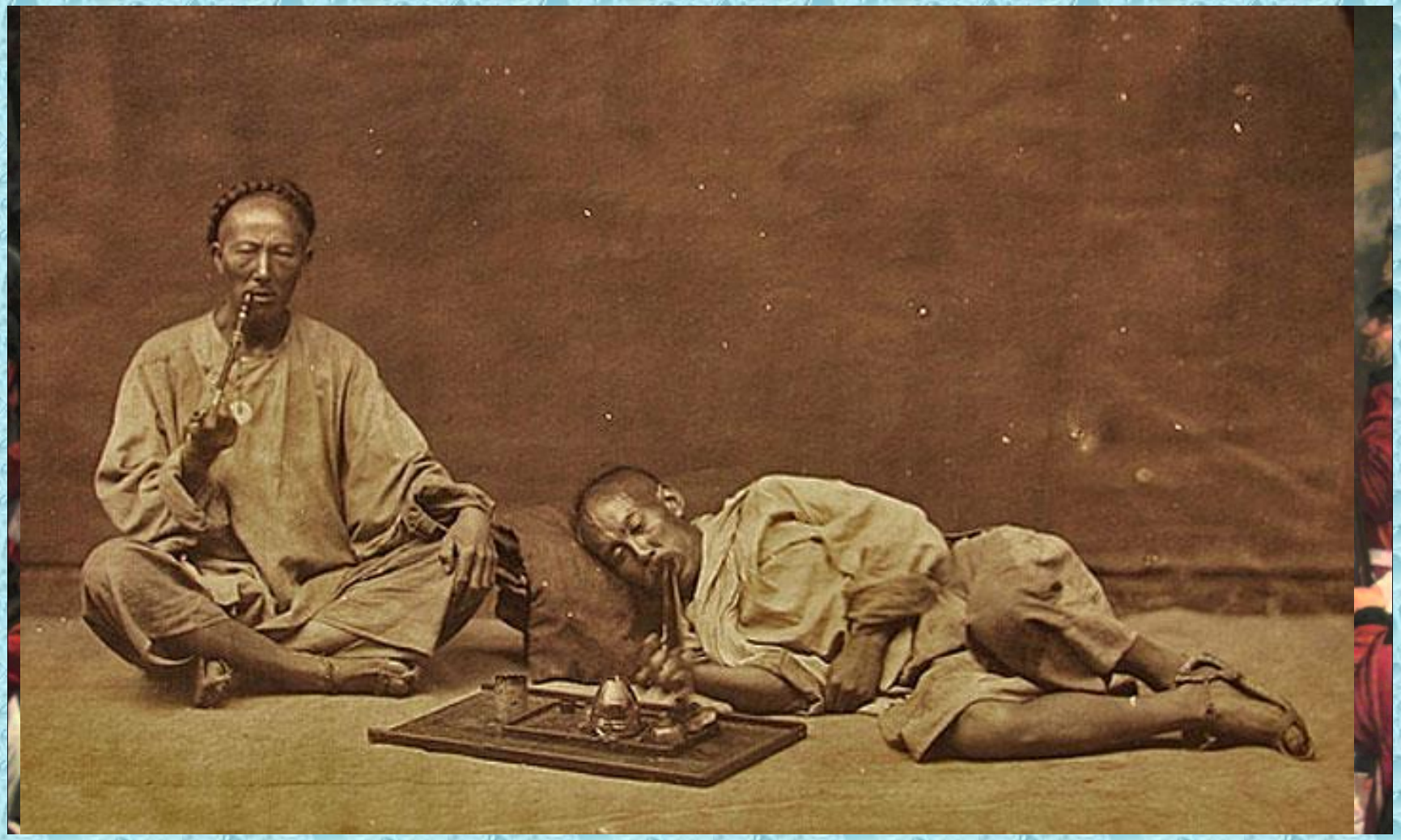
1839-1842, 1856-1860

China was self- satisfied, traded on tea, silver & silk

The balance of trade was in favor of China

Britain smuggled opium from India into the territory of China

By 1835 as many as 12 million Chinese were addicted to smoking opium



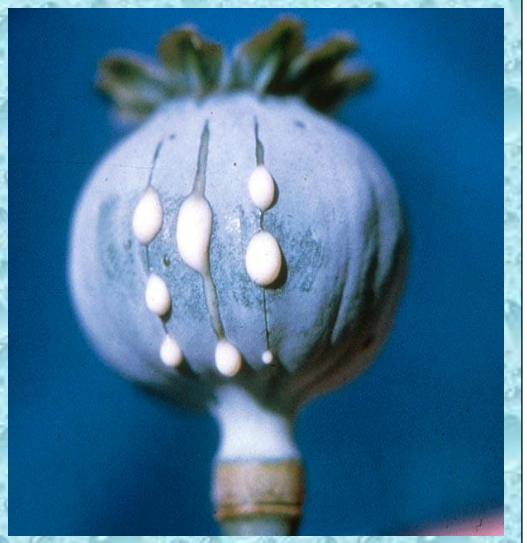
DRUGS USED IN MANAGEMENT OF PAIN

ILOS

Categorize the different classes of drugs used to relieve pain

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

Hints on the properties and 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 rea
medical advice

Impairs the patient functiona
psychological well being

Pain increases sympathetic ou
-Increases myocardial oxygen
-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

DRUGS USED IN MANAGEMENT OF PAIN

CLASSES OF DRUGS USED IN MANAGEMENT OF PAIN

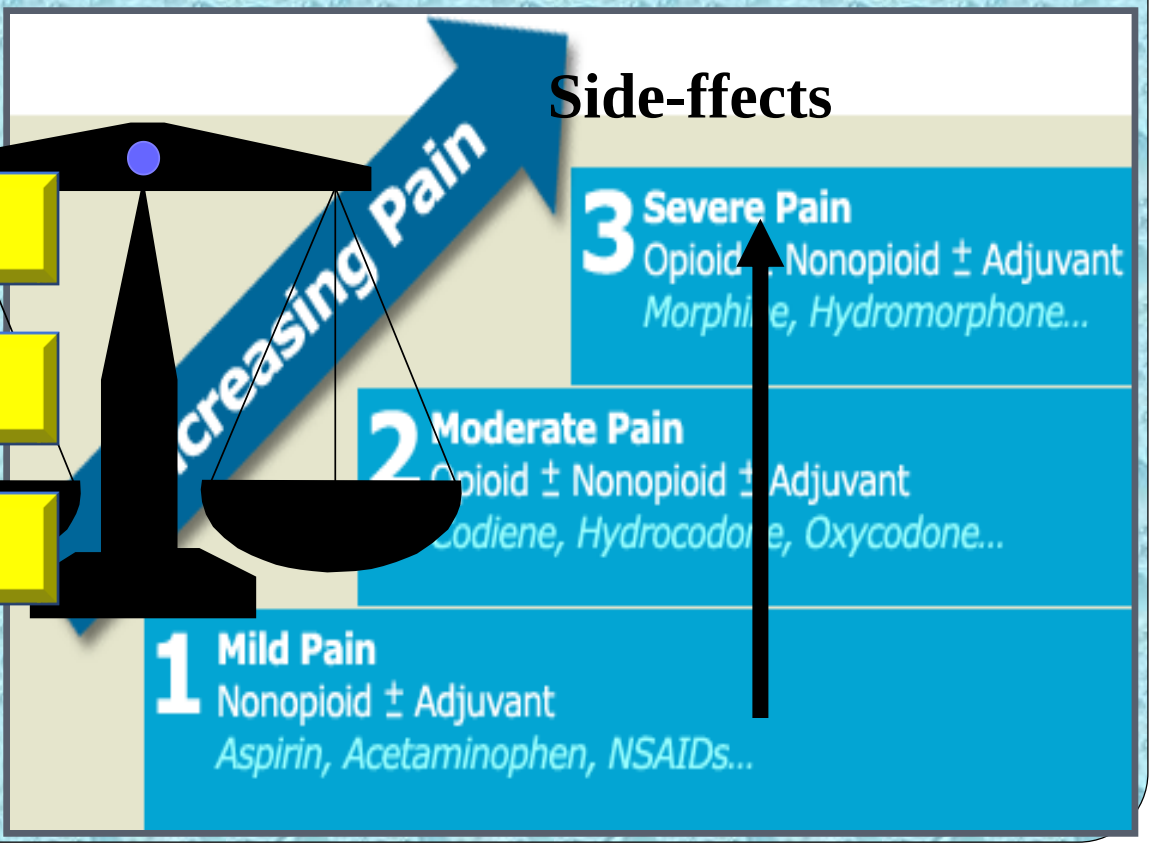
NSAIDs

WHO Pain Ladder

Opioids

Analgesia

Adjuvant drugs



NSAIDS

Generally the first 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 ceilling effect to analgesia

ADJUVANT DRUGS

Drugs primarily indicated for clinical conditions other than pain

e.g. Anxiolytics, Neuroleptics, Antidepressants, Antiepileptics

May modify the perception of pain

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

Useful in neuropathic pain

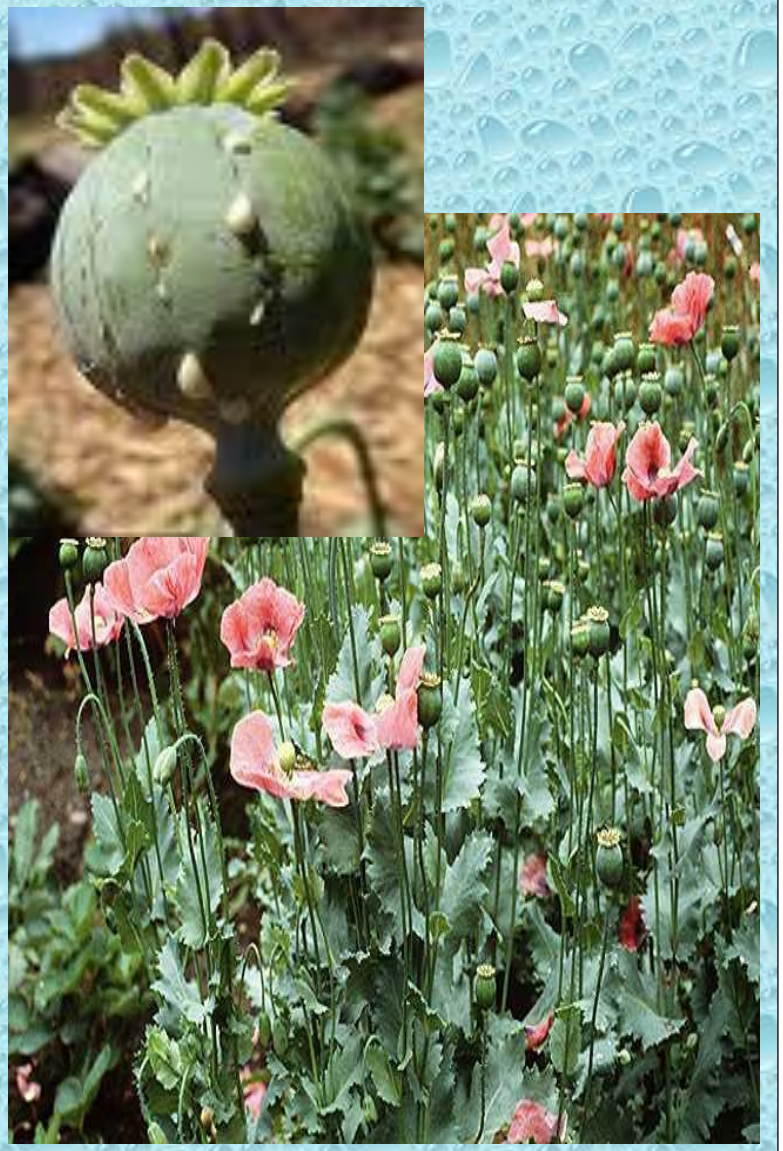
OPIOIDS

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

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

Opiates are drugs derived from opium and semisynthetic and synthetic derivatives

Opioids refer to opiates and endogenous opioid peptides, e.g. **β–** endorphin



OPIOID RECEPTORS

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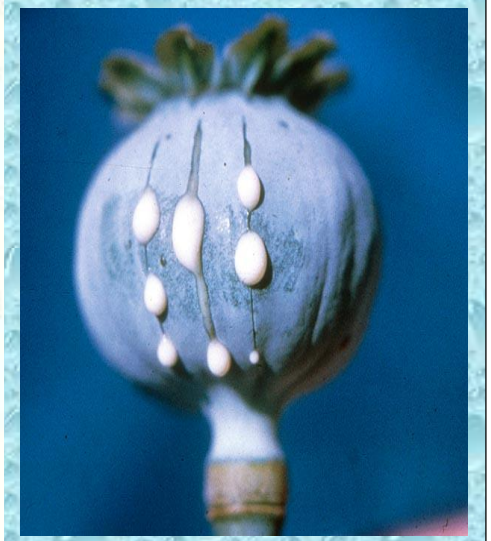
OPIOID RECEPTORS	
Opioid Receptor Class	Effects
Mu_1	Euphoria, supraspinal analgesia, confusion, dizziness, nausea, low addiction potential
Mu_2	Respiratory depression, cardiovascular and gastrointestinal effects, miosis, urinary retention
Delta	Spinal analgesia, cardiovascular depression, decreased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



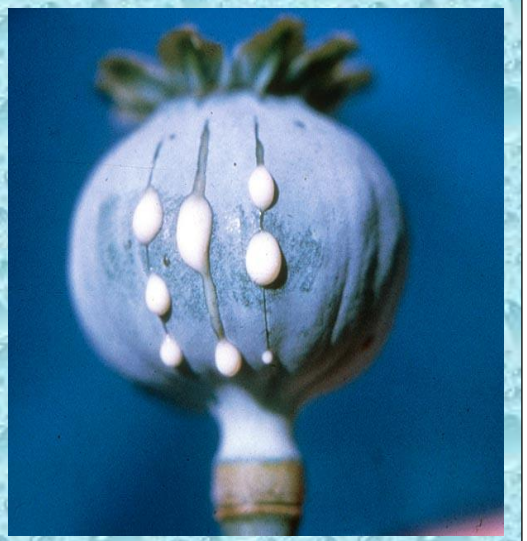
ORL-1 **Nociceptin receptor**

Antagonizes dopamine transport

All of them are typical G-protein coupled receptors

CLASSIFICATION OF OPOIDS

According to their source



According to ag gonistic actions

Morphine

Heroin

According to their specificity of action on recepto

Pethidine, Methadone

Morphine,codeine, heroin→μ -receptor agonists

Pure antagonist; Nalaxone, Naltraxone,

Pentazocine agonist at k - receptors

MECHANISM OF ACTION

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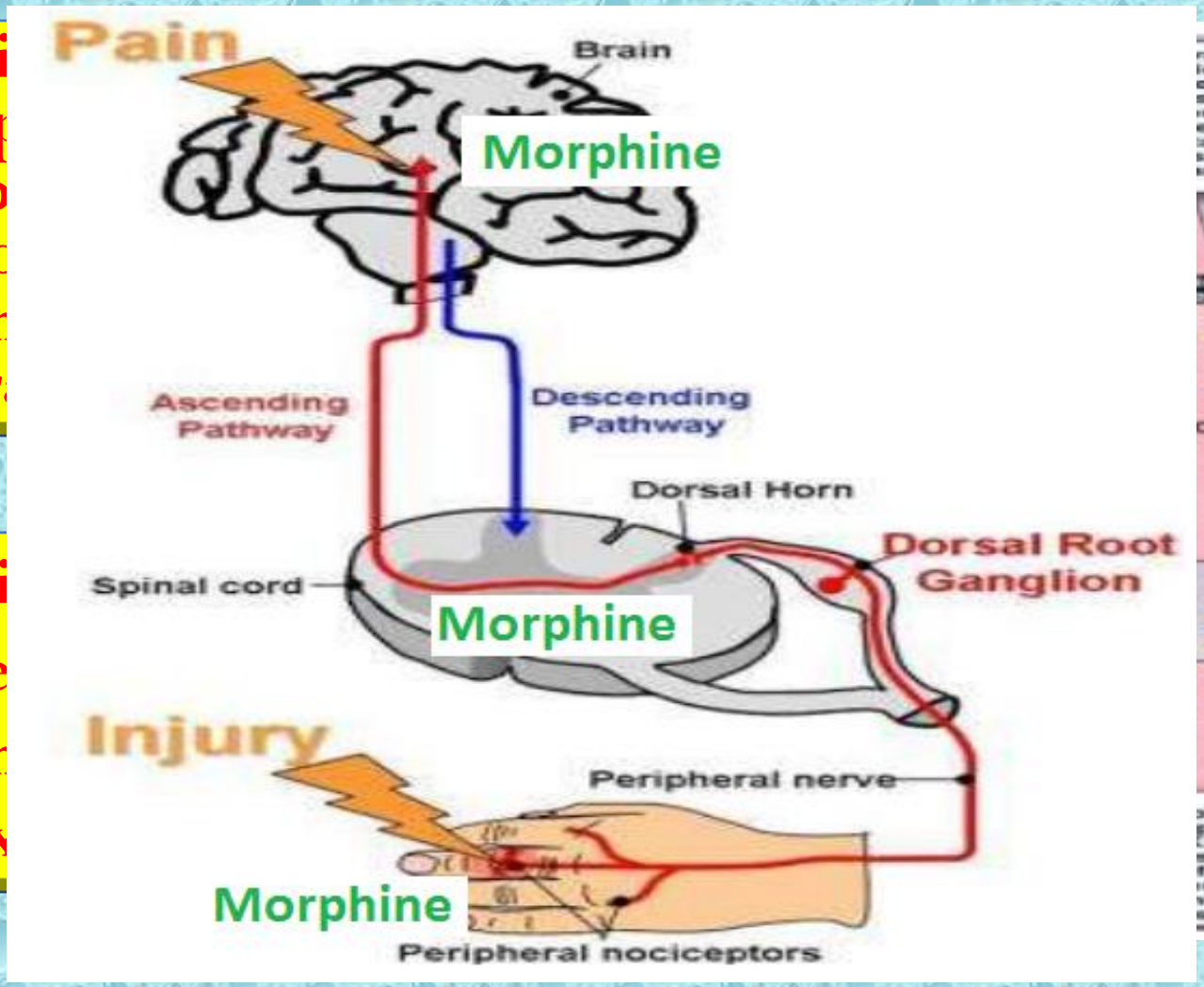
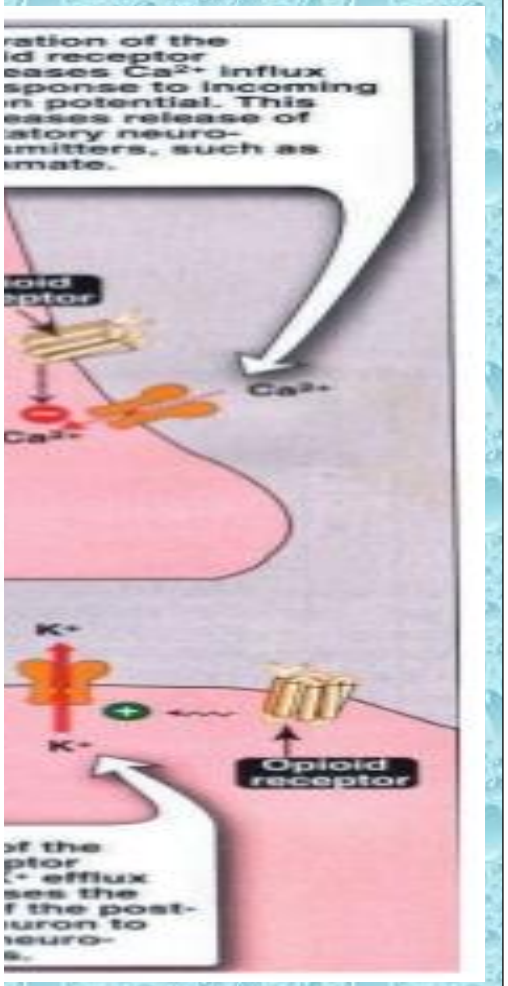
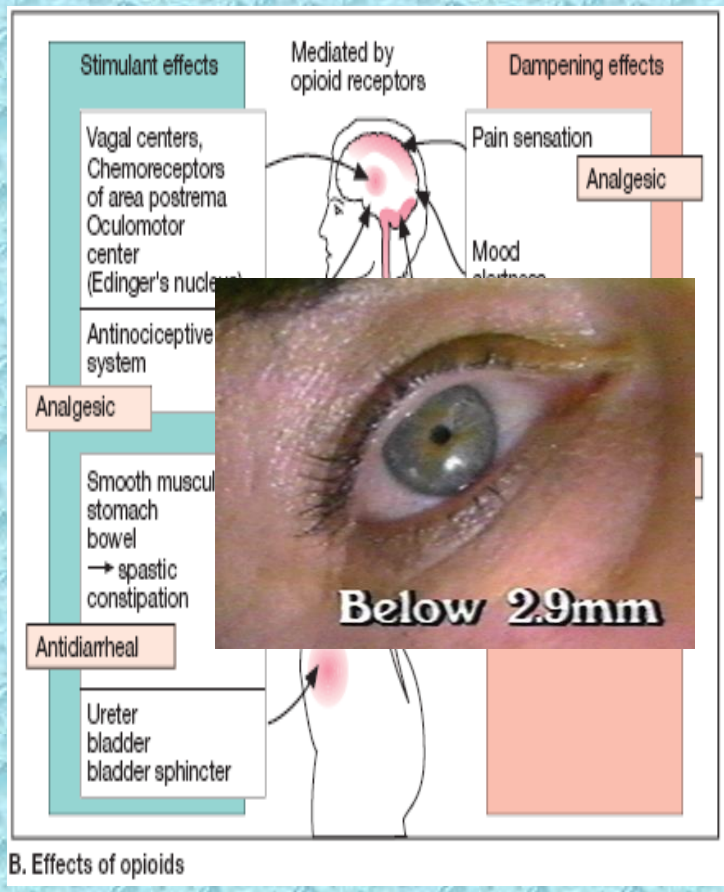




PHARMACODYNAMIC ACTIONS

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



B. Effects of opioids

Effects on GIT:- ↑in tone ↓motility →severe constipation.
Contraction of gall bladder +constriction of biliary sphincter →↑pressure in the biliary tract

TOLERANCE & DEPENDENCE

TOLERANCE

DEPENDENCE dly with opioids (with morphine 12–24 hours)

Physical dependence

Tolerance develops to respiratory depression, analgesia, euphoria and sedation

Lasting for a few days(8-10 days) in form of ↑ body ache, insomnia, diarrhea, goose flesh, lacrimation

Psychological dependence lasting for months / years → craving

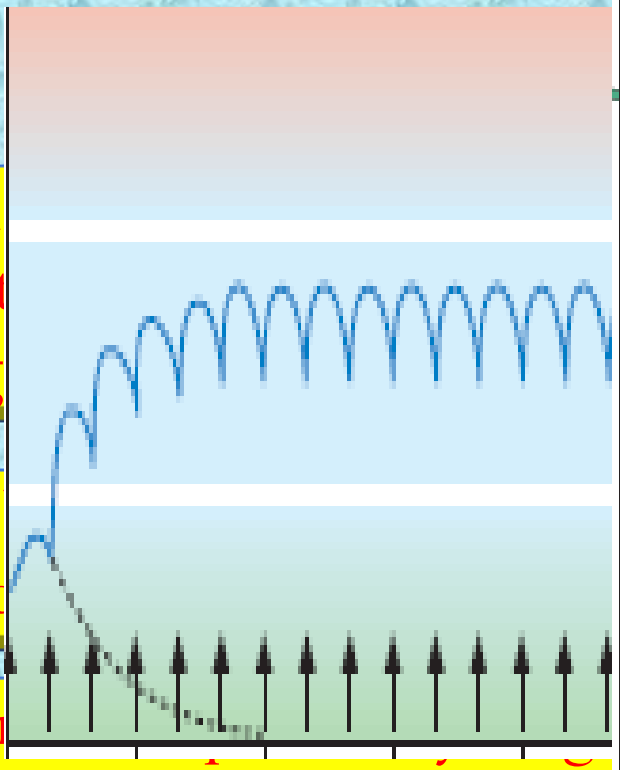
PHARMACOKINETICS

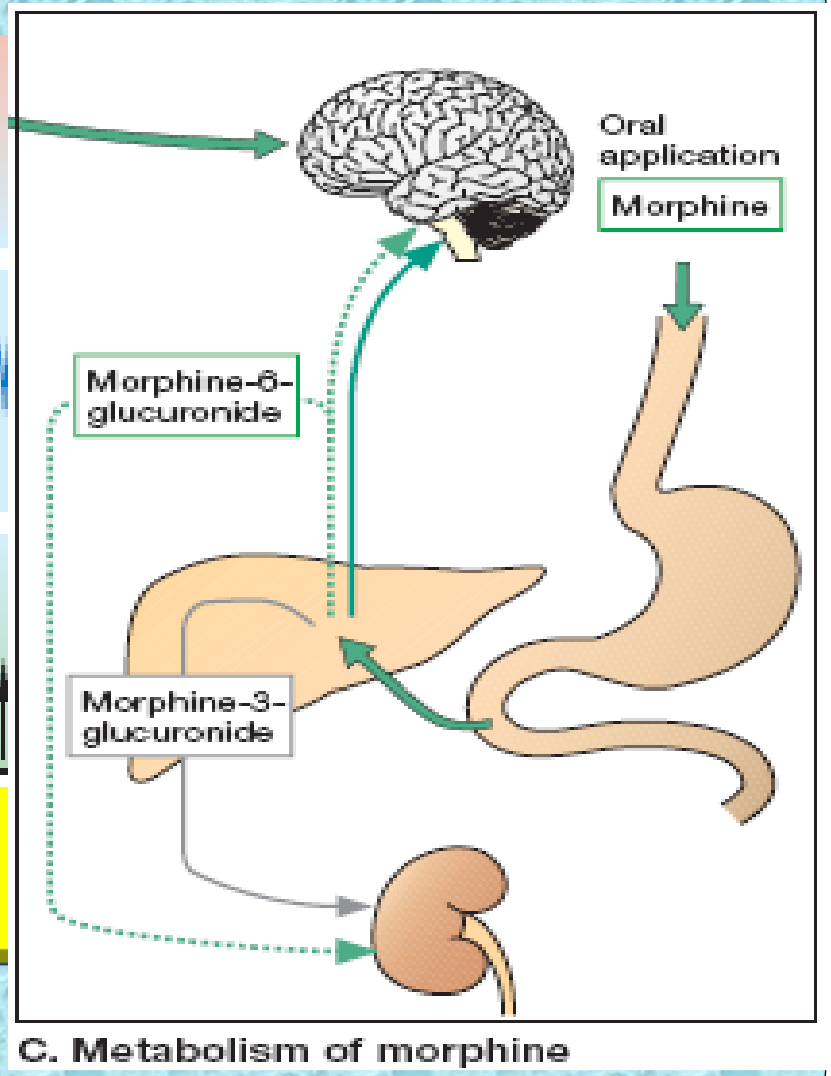
t ½ is 2-3h

It is slowly &
(bioavailabilit
-Medically g

Metabolized
glucuronic ac

Undergoes e
-crosses BBB
-crosses placenta.





C. Metabolism of morphine

CLINICAL INDICATIONS

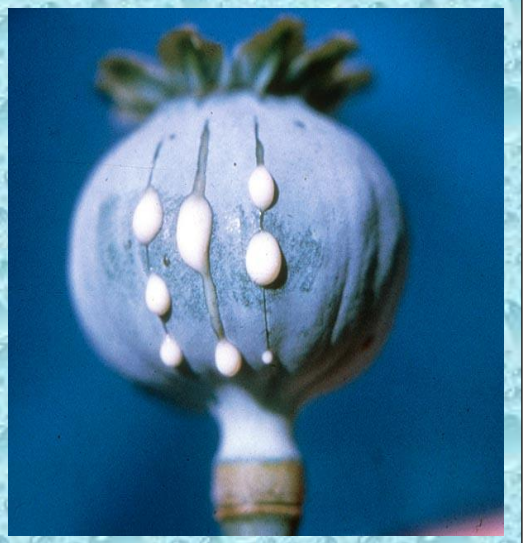
CONTROL PAIN; cancer pain, severe burns, trauma
Severe visceral pain (not renal/biliary colic, acute pancreatitis)

Acute pulmonary edema

Myocardial infarction

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

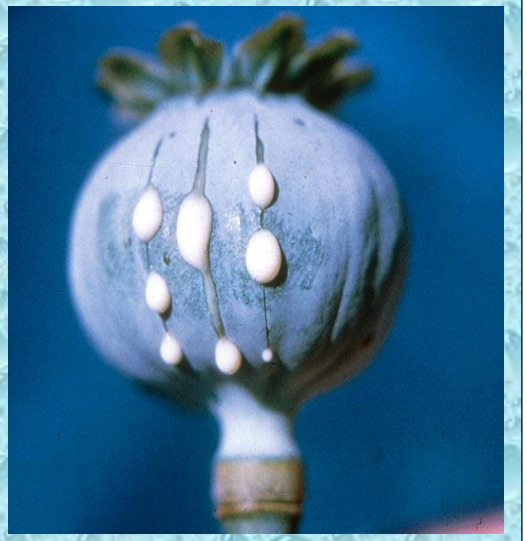
Preanesthetic medication



ADRS

- CONSTIPATION
- RESPIRATORY DEPRESSION
- ITCHING
- NAUSIA,VOMITING
- CONSTRICTED PUPIL
- SEDATION

Crincs

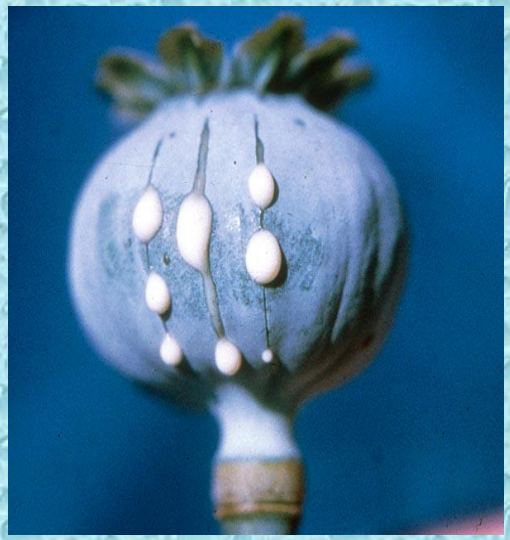


CONTRINDICATIONS

HEAD INJURY

BRONCHIAL ASTHMA or impaired pulmonary function

Biliary colic



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

With MAOIs

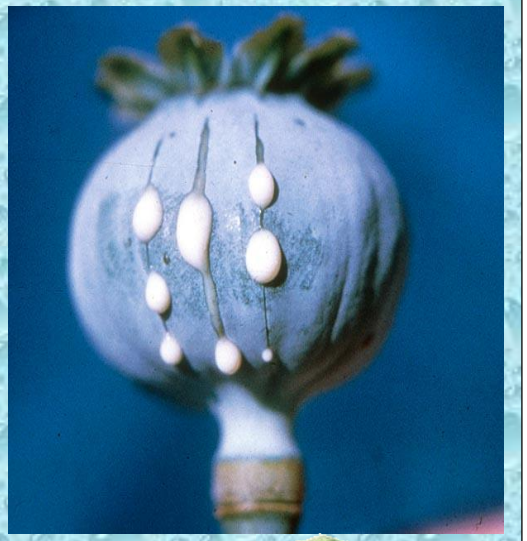
Not given infants, neonates or during child birth→ ↓conjugating capacity → accumulate → ↓ respiratory

CODEINE

μ Agonist

Dependence < morphine

Used in mild & moderate pain, cough, diarrhea



TRAMADOL

Synthetic, μ agonist , less potent than morphine

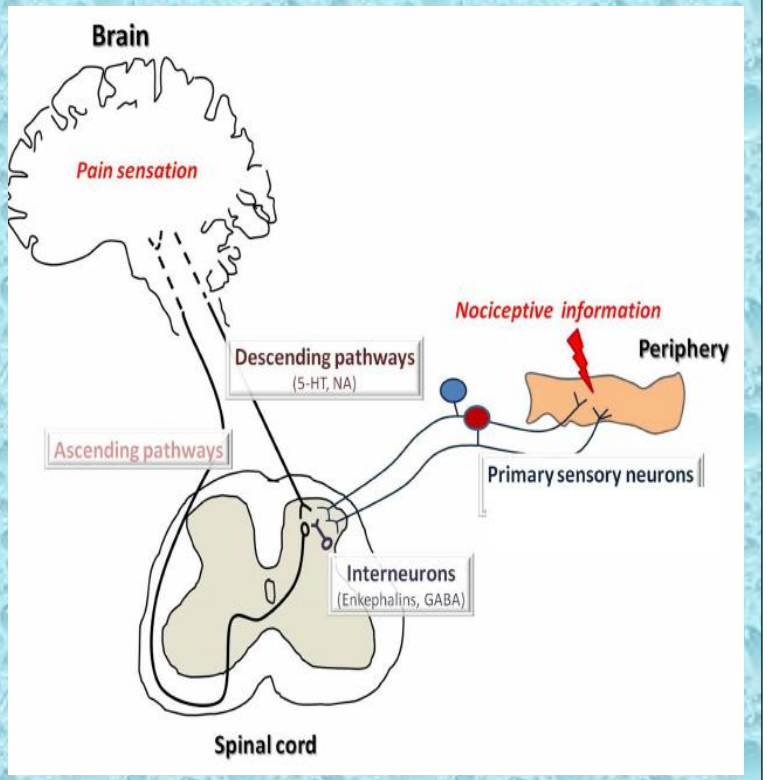
NE & 5HT reuptake

ADRS

-Mild - moderate acute & chronic visceral pain

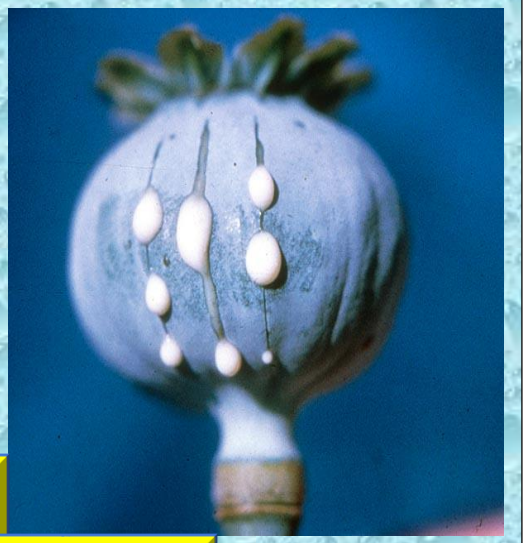
-During labor

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



PETHIDINE [MEPERIDINE]

Synthetic more effective κ agonist



ACTIONS

INDICATIONS

stipating , depressant

than morphine

ADRS

diarrhea

suppressant effect

Preanaesthetic medication (better)

Blurred vision, Dry mouth, Urine retention

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

FENTANYL

CLINICAL USES

ore potent

ine

ADRS

supplement during anesthesia, (IV or intrathecal)

Respiratory depression (most serious)

CV effects are less.

Bradycardia may still occur

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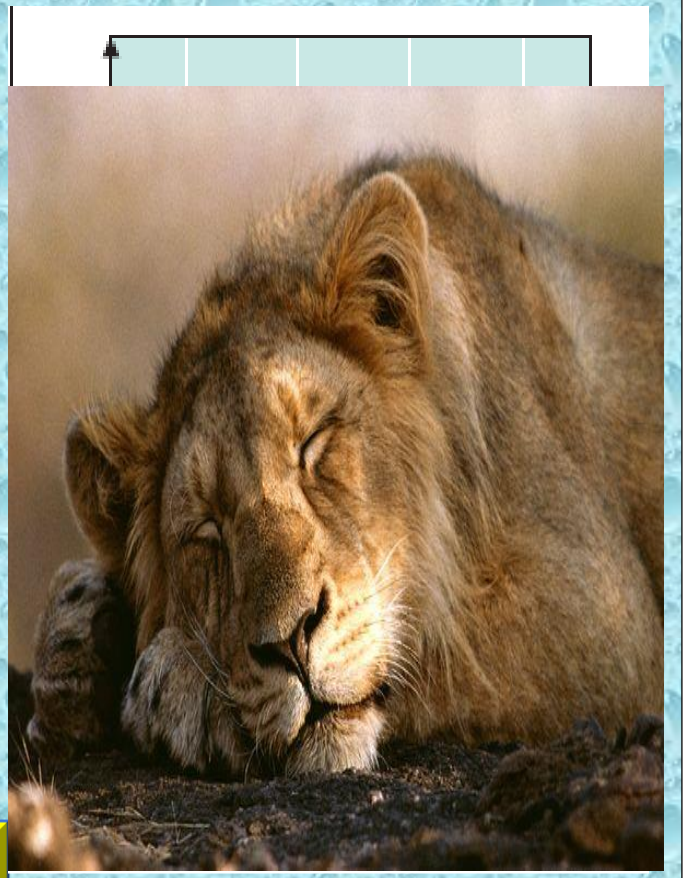
NEUROLEPTANALGESIA

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



METHADONE

Weaker synthetic μ- agonist val

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

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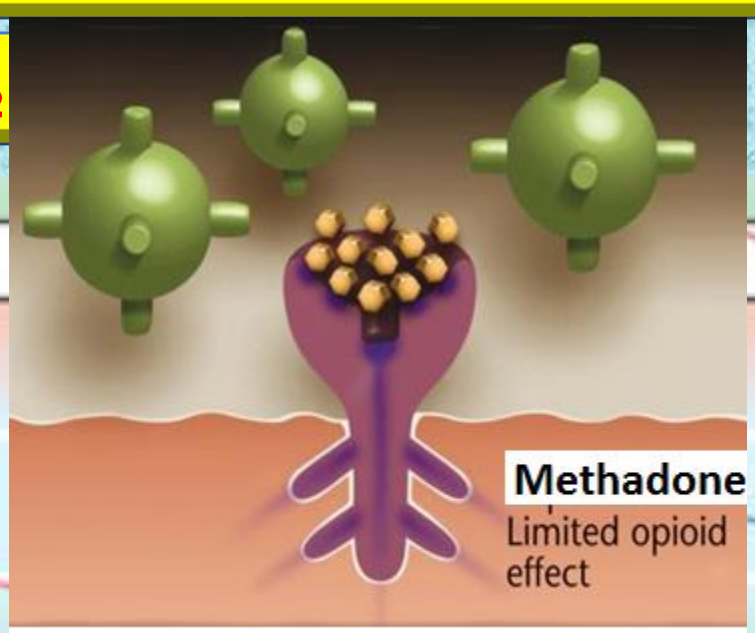
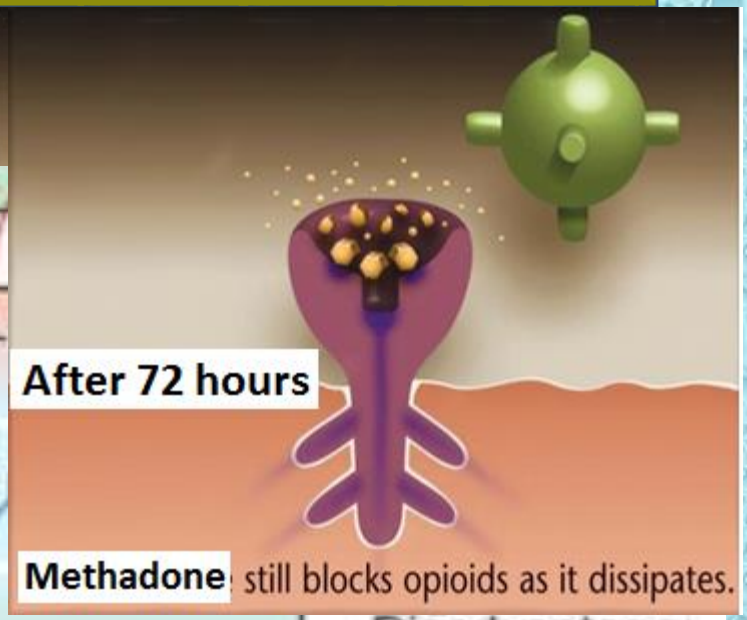
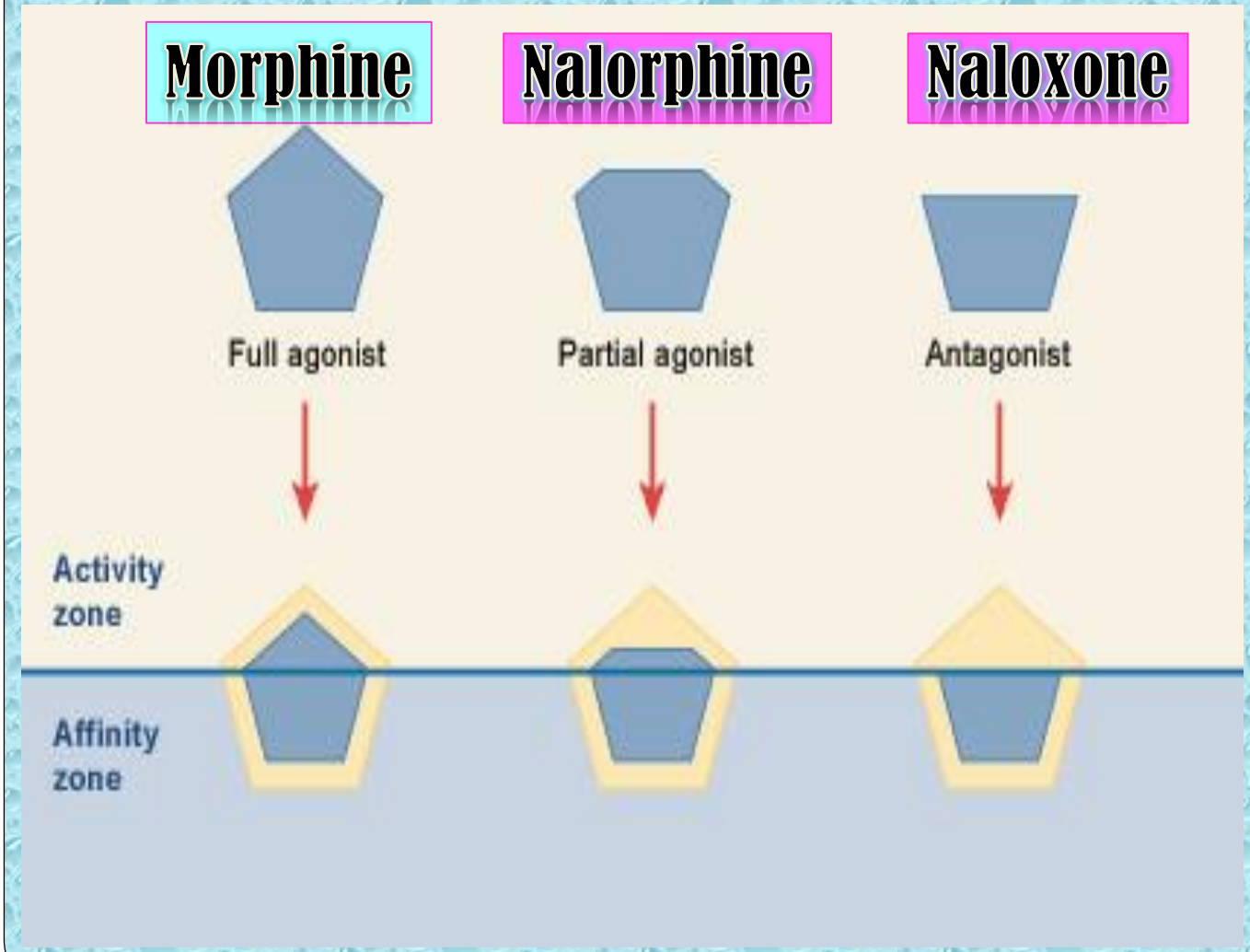
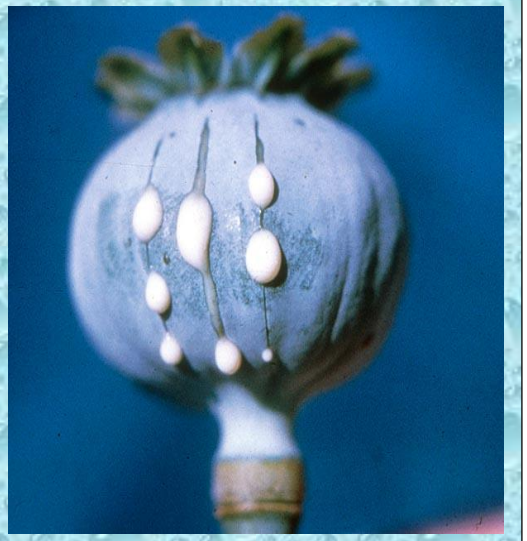




Disadvantage: dose difficult to titrate

OPIOID ANTAGONISTS

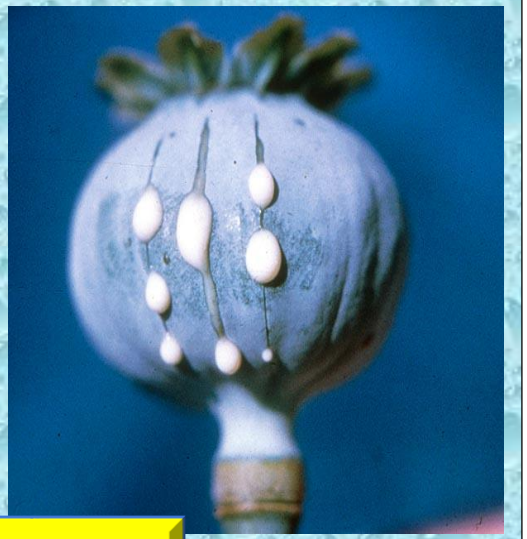




NALOXONE

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**]