Opioids & opioids antagonists

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What are analgesics?

Drugs which relieve pain .They are classified into:

Narcotic

-Relieve all types of pain except itching and colic

-It is accompanied with Changes in mood

-Addiction liability

Non narcotic

-Relieve pain of moderate to low intensity

- No

-No

Simple	**Non steroidal antiinflammatory**	**Slowly acting antiinflammatory**
Analgesic	Analgesic	No
Antipyretic	Antipyretic	No
No	Antiinflammtory	Antiinflammatory
Example: Acetaminophin	Example:Salicylates	Example:: gold salts

Analgesics

Analgesics are the drugs (natural or synthetic origin)

which relieve pain by acting on CNS or peripheral pain mechanism

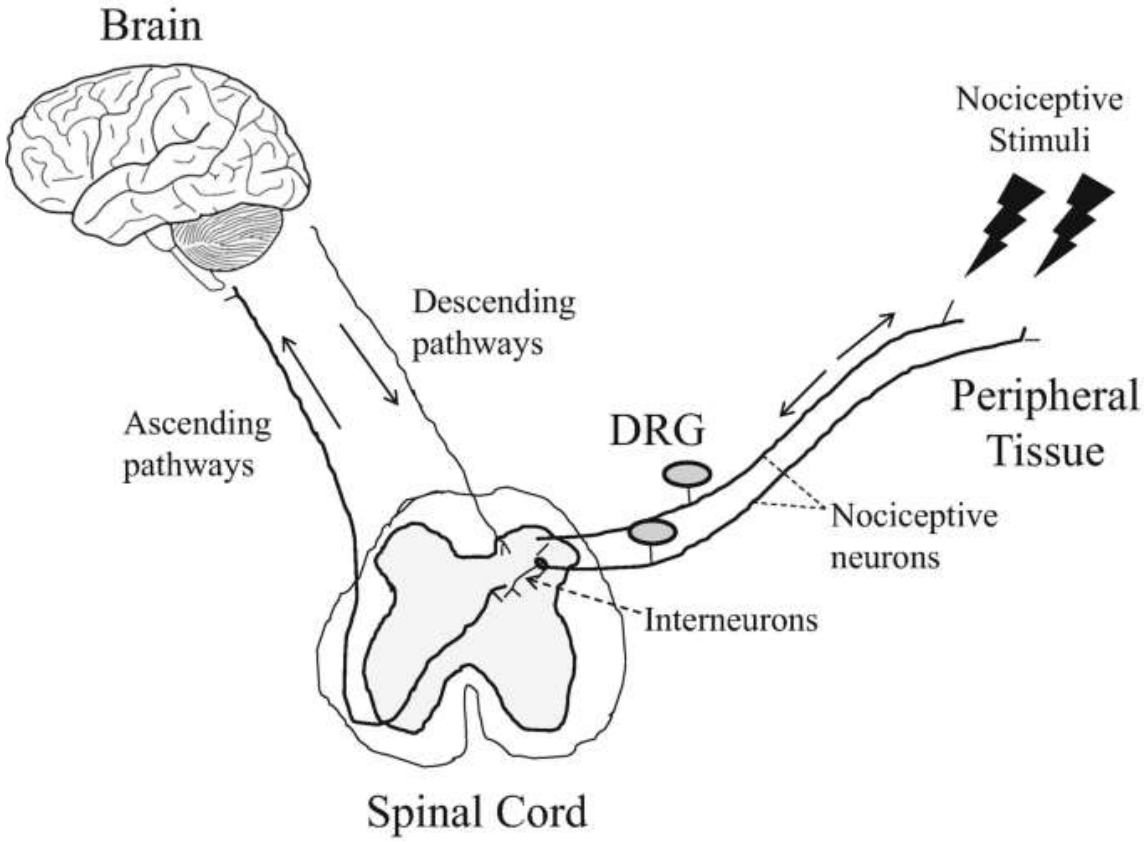
without causing loss of consciousness

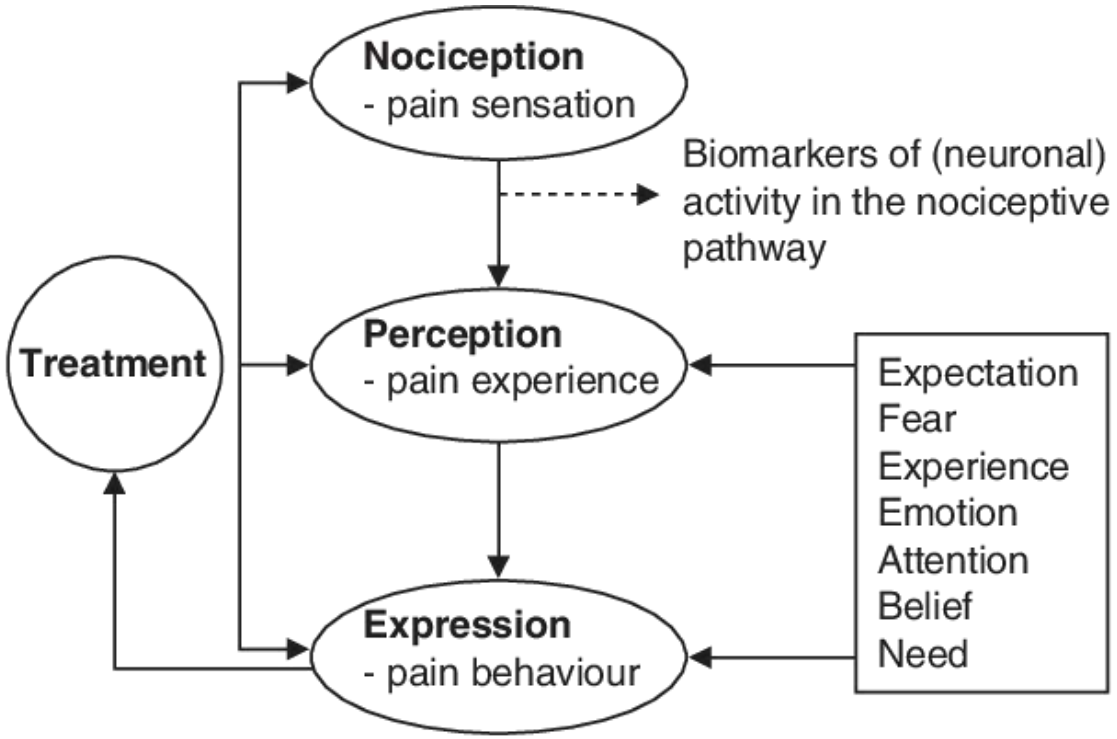
Analgesics can be divided into two main groups:

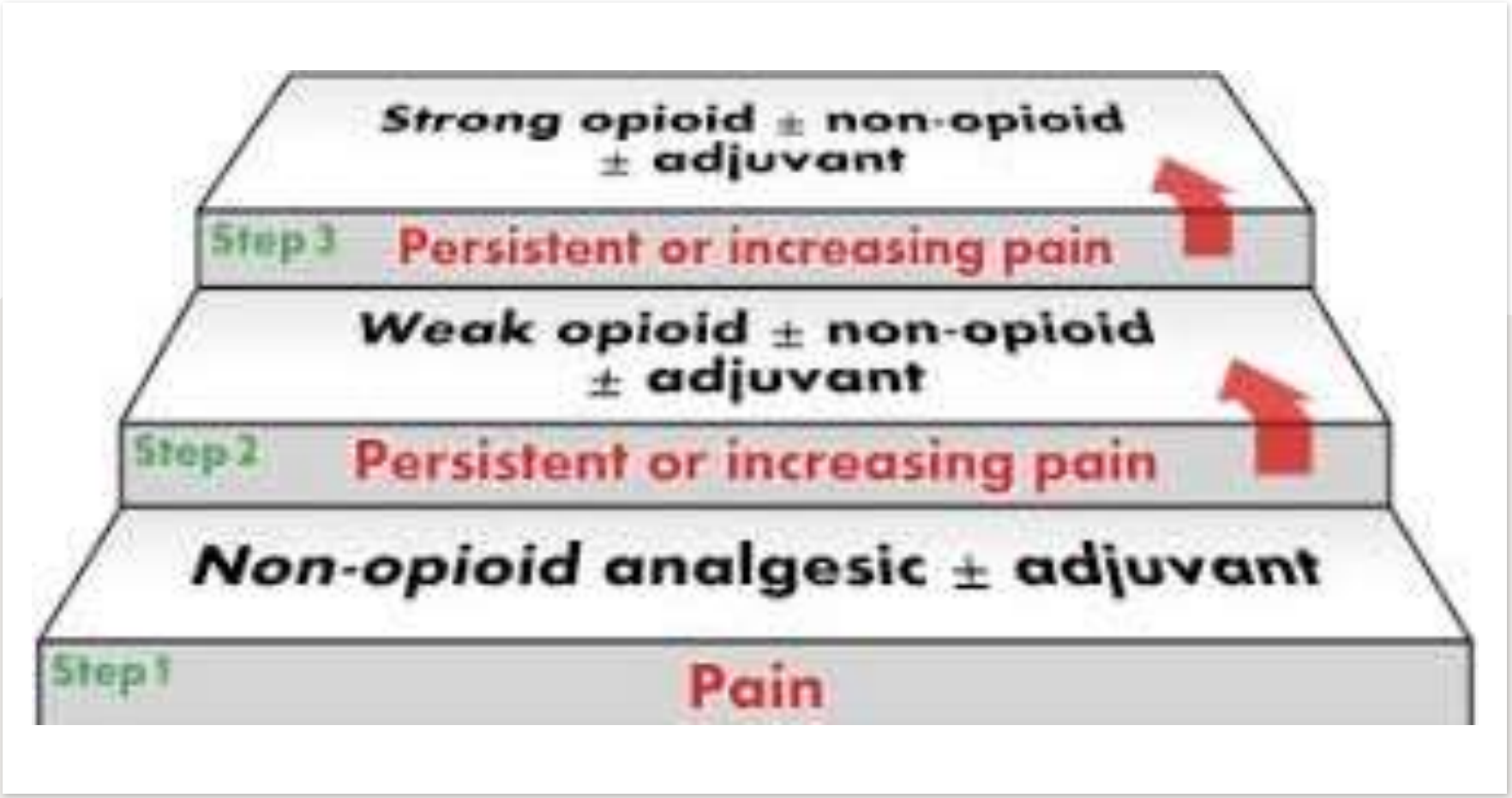
Opioid/narcotic/morphine-like analgesics.

Nonopioid/non-narcotic/aspirin-like analgesics.

Why do we feel pain?

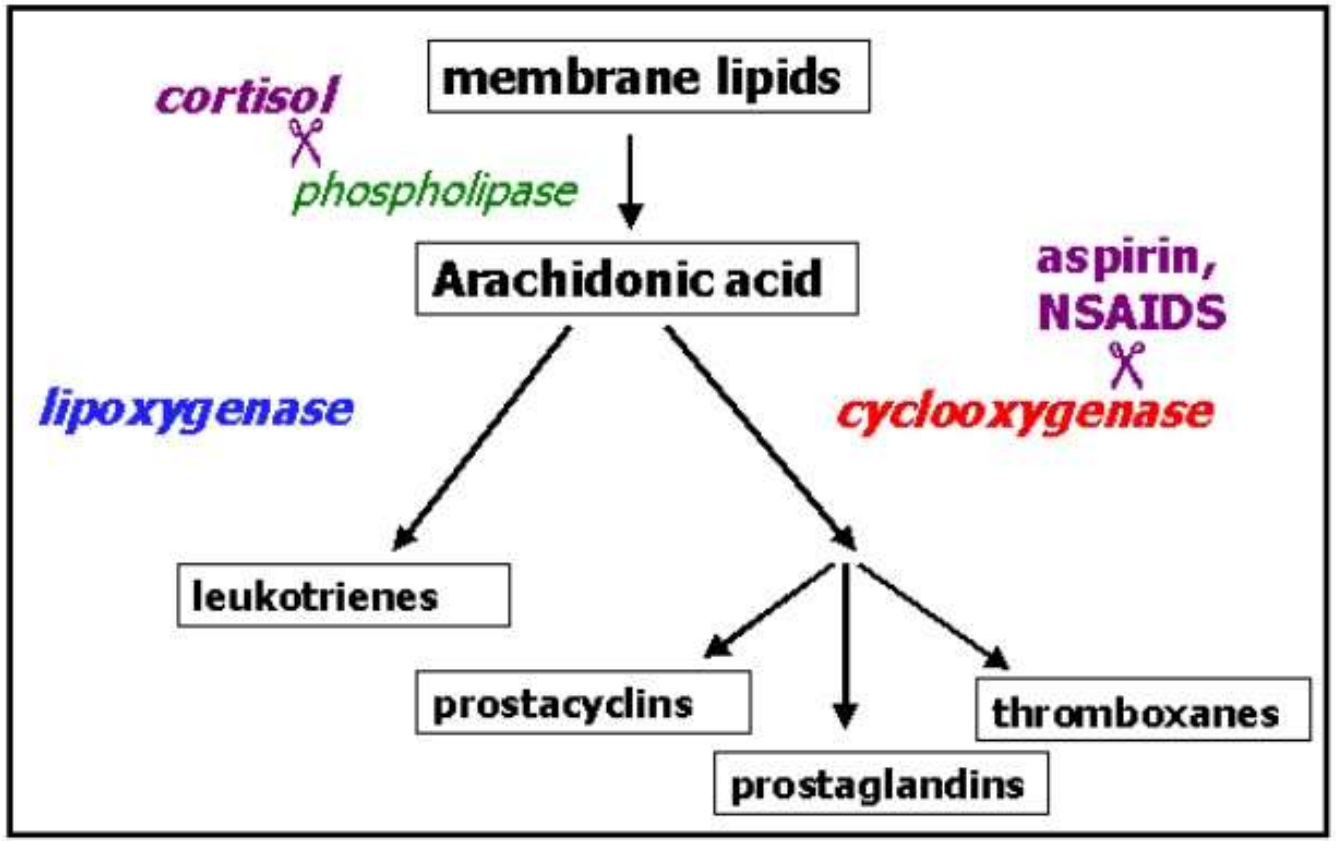





Strong opioid ± non-opioid
± adjuvant
Step 3
Persistent or increasing pain
Weak opioid ± non-opioid
± adjuvant
Step 2
Persistent or increasing pain
Non-opioid analgesic ± adjuvant
Step 1
Pain

Pain ladder

MECHANISM OF PAIN CAUSATION :



Opioid analgesics

The term *opioid* applies to any substance,

whether natural or synthetic,

that produces morphine-like effects that are blocked by antagonists such as naloxone

Classification of narcotic analgesics

1-Natural alkaloids

Morphine

Codeine

2- Semisynthetic compounds

Pholcodeine

Diacetyl morphine??

- **3- Synthetic compounds**
- Pethidine (meperidine in USA)
- Fentanyl
- Methadone
- Tramadol
- Sufentanil
- Alfentanil

opium poppy

This is mature opium poppy. The opium has just been cut and what is dripping from the seam is a milky latex sap containing a “naturally occurring narcotic alkaloid” including morphine and codeine. This morphine can then turn into semisynthetic narcotics

Narcotic (Opioid) analgesics

They are natural or synthetic opium alkaloid derivatives e.g., Morphine (natural) & Meperidine (synthetic)

They mimic the action of endogenous opioid peptides produced naturally by the body e.g., endorphins, enkephalins & dynorphins

They act on specific receptors in CNS known as opioid receptors

They are abused due to their ability to produce euphoria

Opoipeptides (endogenous opioids)

They include:

β-endorphin, met-enkephalin, leu-enkephalin & dynorphin.

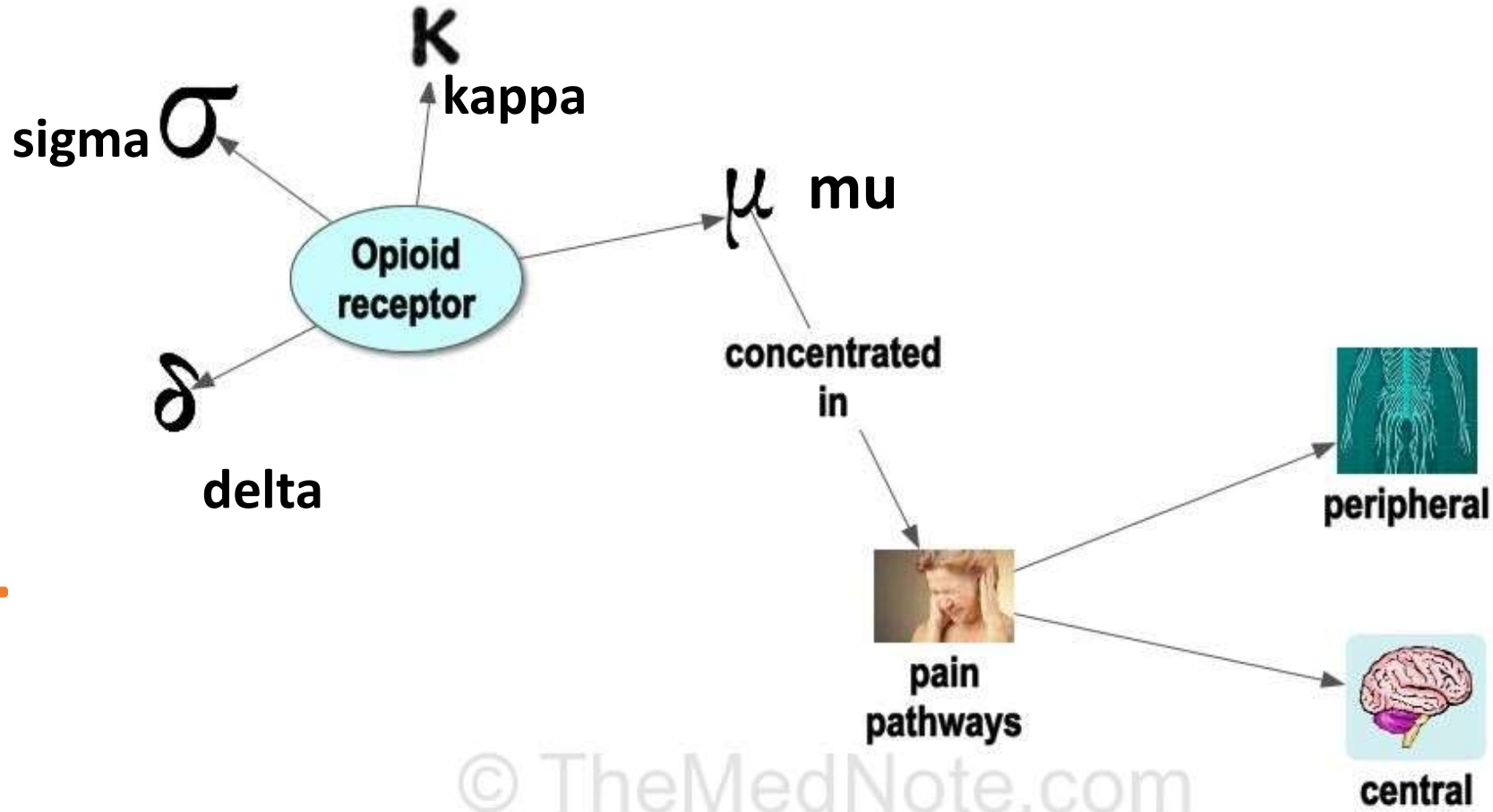
They are synthetized in the CNS.

Actions: morphine-like

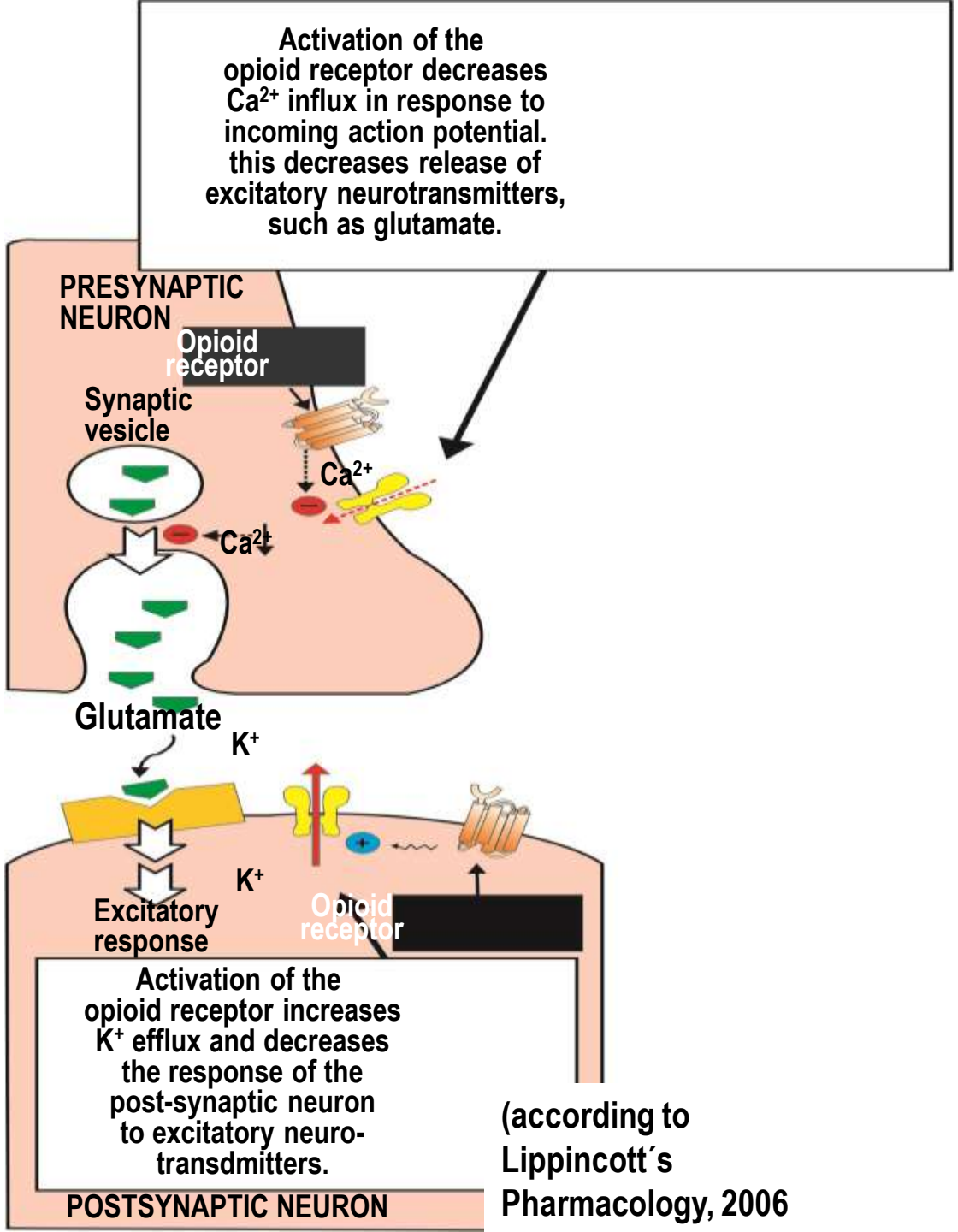
They can not be used clinically: because they do not pass BBB.

N.B. Recently, there are evidences that morphine & codeine may present in mammalian tissues.

Opoid receptors



Mechanism of action of opioid receptor agonists in the spinal cord.



(according to Lippincott´s Pharmacology, 2006

Opioid receptors

They are present in CNS & GIT

They are members of the G-protein-coupled receptor family and inhibit adenylyl cyclase

They are also associated with ion channels, increasing postsynaptic K^+ efflux (hyperpolarization) or reducing presynaptic Ca^{++} influx

They are classified into 4 types

Opioid receptors

1- Mu (μ) receptors:

- **Analgesia, euphoria, sedation, miosis, dependence, respiratory depression & constipation**

2- Kappa (κ) receptors:

Analgesia, sedation & miosis

3- Delta (δ) receptors:

Spinal analgesia & constipation

4- Sigma (σ) receptors:

Hallucination & dysphoria

Morphine

Natural alkaloid found in opium plant

Mechanism of action

Morphine stimulates opioid receptors in CNS & spinal cord. This leads to:

1- ↓ Adenylyl cyclase → ↓cAMP

2- ↑ K^+ efflux → hyperpolarization

3- ↓ Ca^{++} influx → ↓release of pain mediators e.g., substance P & excitaory NTs e.g., glutamate

Pharmacological actions of morphine

1- CNS

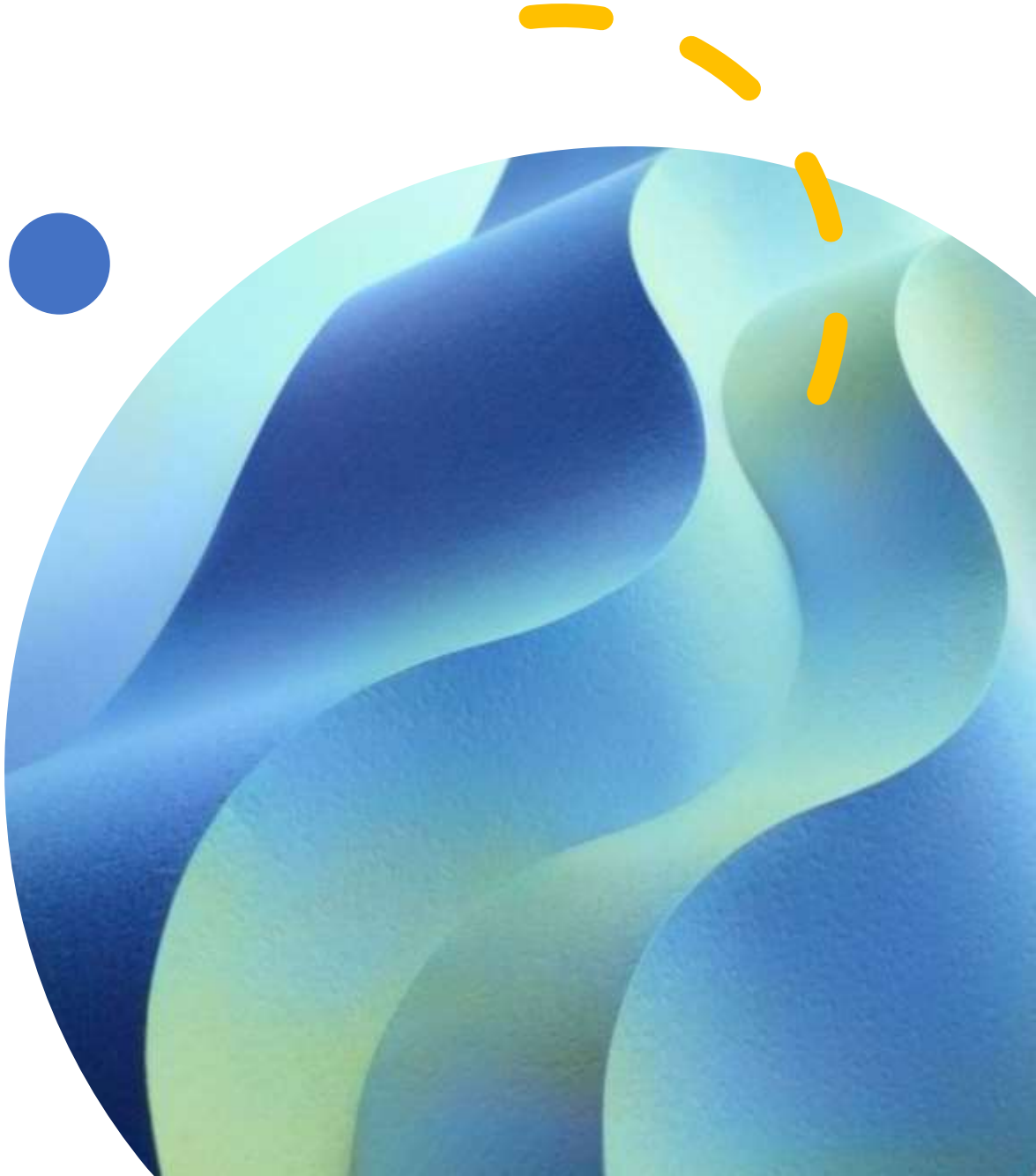
- Analgesia (reduce pain) & euphoria
- Cough suppression (Inhibits cough center)
- Vomiting (Stimulates CTZ)
- Hypoxia (Inhibits respiratory center)

Pharmacological actions of morphine

2- CVS

Bradycardia (Stimulates vagal center)

Hypotension (Inhibits vasomotor center)



Pharmacological actions of morphine

3- Eye

- Pin-Point Pupil (PPP) due to stimulation of oculomotor nerve

4- GIT

- Constipation (Inhibits intestinal motility)

Pharmacological actions of morphine

5- Endocrine effects

- Increases release of antidiuretic hormone (ADH)
- Decreases release of lutenizing hormone (LH), follicle stimulating hormone (FSH) & adrenocorticotropic hormone (ACTH)

Therapeutic uses of morphine

1- Severe pain (Post-operative, trauma, cancer & myocardial infarction)

2- Pre-anesthetic medication

3- Cough suppressant

Therapeutic uses of morphine

4- Pulmonary oedema: As it can:

- Decrease pulmonary pressure
- Decrease patient anxiety
- Suppress cough
- Slow respiration

Adverse effects of morphine

- Respiratory depression
- Vomiting
- Hypotension
- Bradycardia
- Urine retention
- Constipation
- Addiction

Contraindications

- **1-Respiratory diseases e.g., Asthma**
- **Inhibits RC**
- **Increases histamine release**
- **2- Adrenal insufficiency**
- Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.
- **3- Pregnancy**
- **<u>Neonatal Opioid Withdrawal Syndrome</u>**
- **Prolonged use of Morphine Sulfate Injection during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated**
- **Can pass placenta: Neonatal asphyxia**
- **4- known or suspected GIT obstruction including paralytic ileus, BILIARY COLIC?**
- **5-** *Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness*
- *6- Benign prostatic hyperplasia?*

Morphine drug interactions

- Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants, including alcohol, can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death.
- The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome*:*
- Selective serotonin reuptake inhibitors (SSRIs)
- tricyclic antidepressants (TCAs)
- monoamine oxidase (MAO) inhibitors

Classification of opioid drugs

1- Strong agonists

2- Partial agonists: Mixed agonist/antagonists

3- Miscellaneous

4- Opioid antagonists

1- Strong agonists

Examples: Morphine, Meperidine, Methadone, Heroin & Fentanyl

- **Act mainly on μ receptors**
- **Have some actions on κ & δ receptors**

2- Partial agonists: Mixed agonist/antagonists

Buprenorphine is a partial μ agonist

- **Less euphoric, longer duration**
- **Used in treatment of heroin addiction**

Examples: Pentazocine, butorphanol & Nalbuphine

- **Agonist at κ receptors (analgesia) but competitive antagonist at μ receptors**

3- Miscellaneous

A- Codeine (methyl morphine)

- It is a moderate agonist
- Less potent analgesic than morphine
- Lower abuse potential than morphine
- May be used in treatment of dry cough
- **Note:**
  - In most cough preparations codeine has been replaced by Dextromethorphan (Free of analgesic & addictive properties)

3- Miscellaneous

B- Tramadol *(Tramal, Tamol, Contramal)*

- It is a weak μ agonist
- Weakly inhibits reuptake of NE & 5-HT
- Used in treatment of moderate pain
- It has been lately abused

3- Miscellaneous

C- Diphenoxylate *(Lomotil)* & Loperamide *(Imodium):*

- **They are synthetic opioids**
- **They have some anticholinergic activity**
- **They are taken orally for treatment of diarrhea**

4- Opioid antagonists

A- Naloxone

- Used in morphine poisoning
- Short acting (1-2 hrs), given IV

B- Naltrexone

- Long acting (Up to 48 hrs), given orally

C- Nalmefene

- Similar to naloxone but longer half-life (8-10 hrs)

Narcotic antagonists

A narcotic antagonist reverses the actions of a narcotic

Specific antagonists have been developed to reverse the respiratory depression associated with the opiates

The narcotic antagonists in use today are :

Naloxone , Naltrexone , and Nalmefene

Narcotic antagonists

Naloxone can restore respiratory function within 1 to 2 minutes after administration.

Naltrexone is used primarily for the treatment of narcotic dependence to block the effects of the opiates, especially the euphoric effects experienced in opiate dependence

تعرف على متعاطى الترامادول من خلال الأعراض الأتية:

- الترنح اثناء المشى او السير بسحب القدم
- احمرار خفيف الى متوسط فى العينين وشبه مغلقتين
- الاكل الدائم والشرب الدائم والأكثر من المعتاد لأن الترامادول او المخدرات تشعر متعاطيها بالجوع و العطش
- التحدث بلسان ملتوى او ثقيل وتأتأة فى الكلام
- الكذب المستمر فيخفى مكان تواجده ولايخبر متى عودته فى حال خروجه
- حب العزلة و إغلاق الباب عليه وعدم الاهتمام بأحد من عائلته
- ترك الصلاة والصيام والطاعة

تعرف على متعاطى الترامادول من خلال الأعراض الأتية:

- لايهتم كثيرا بمظهره ونظافته الشخصية
- تردى وضعه المالى ويطلب المزيد من المال بشكل مستمر
- يقوم بحركات و تصرفات غير مناسبة كالضحك او البكاء فجأة
- التغير السريع والمفاجىء فى المزاج فتجده من عصبى الى هادىء او العكس
- تدنى مستوى التحصيل العلمى الدراسى وفقد التركيز والحفظ
- الشعور الدائم بالخوف و المراقبة ودائم الدفاع عن نفسه حتى لو لم يتم توجيه تهمة له


Thank you