AL-Mustaqbal university
College of Nursing

Pharmacology II

Dr. Ghada Ali
ghada.ali@uomus.edu.iq

lec1

Central Nervous System Drugs practice

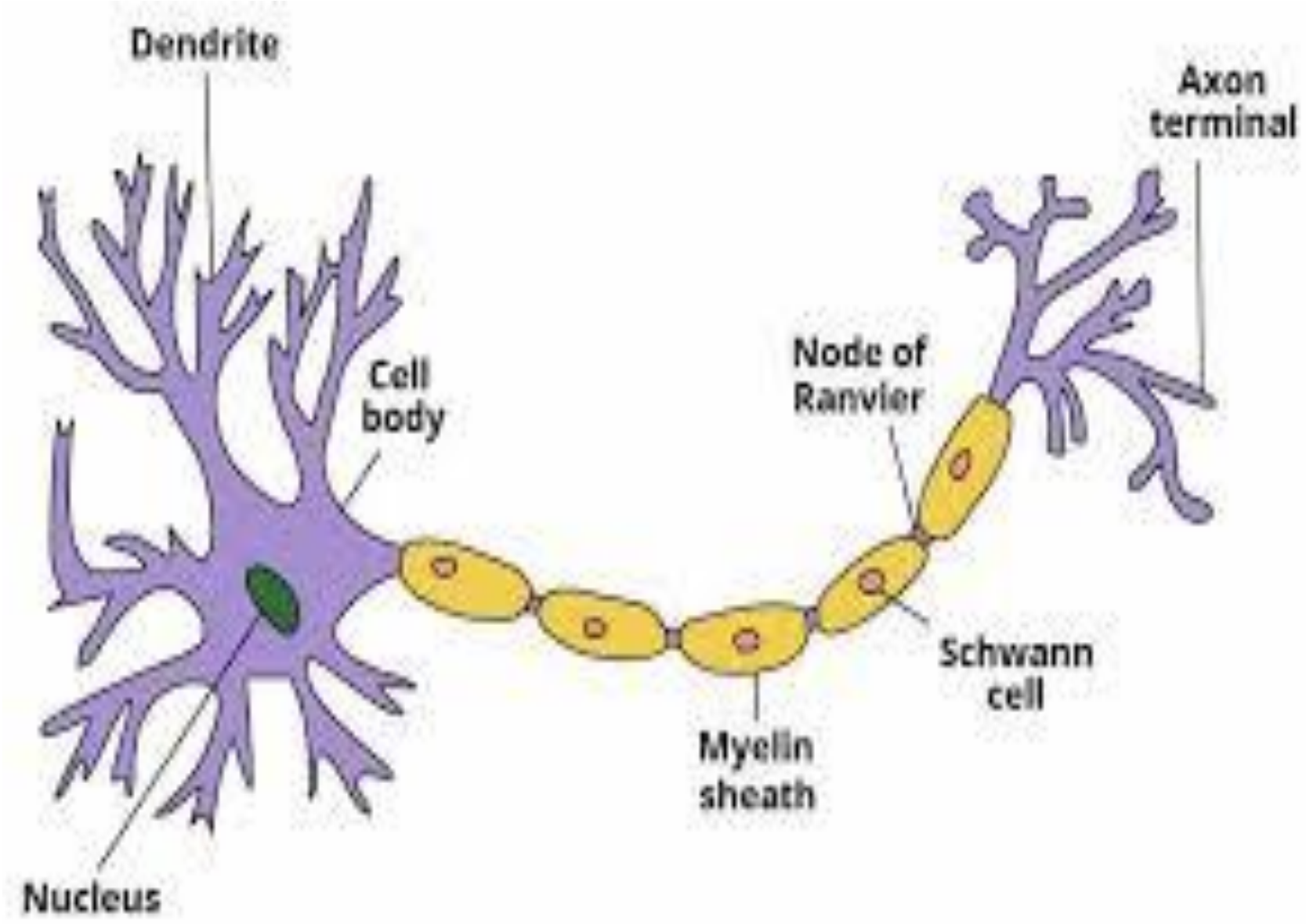
Introduction to CNS pharmacology

Neuron.. Structure and Function

- Neurons are **electrically excitable** cells composed, in general, of one or more dendrites ,a single soma, a single axon and one or more axon terminal

- **Dendrites** are designed to capture the **neurotransmitters** released by the presynaptic neuron and have a high concentration of **ligand-gated ion channels**.

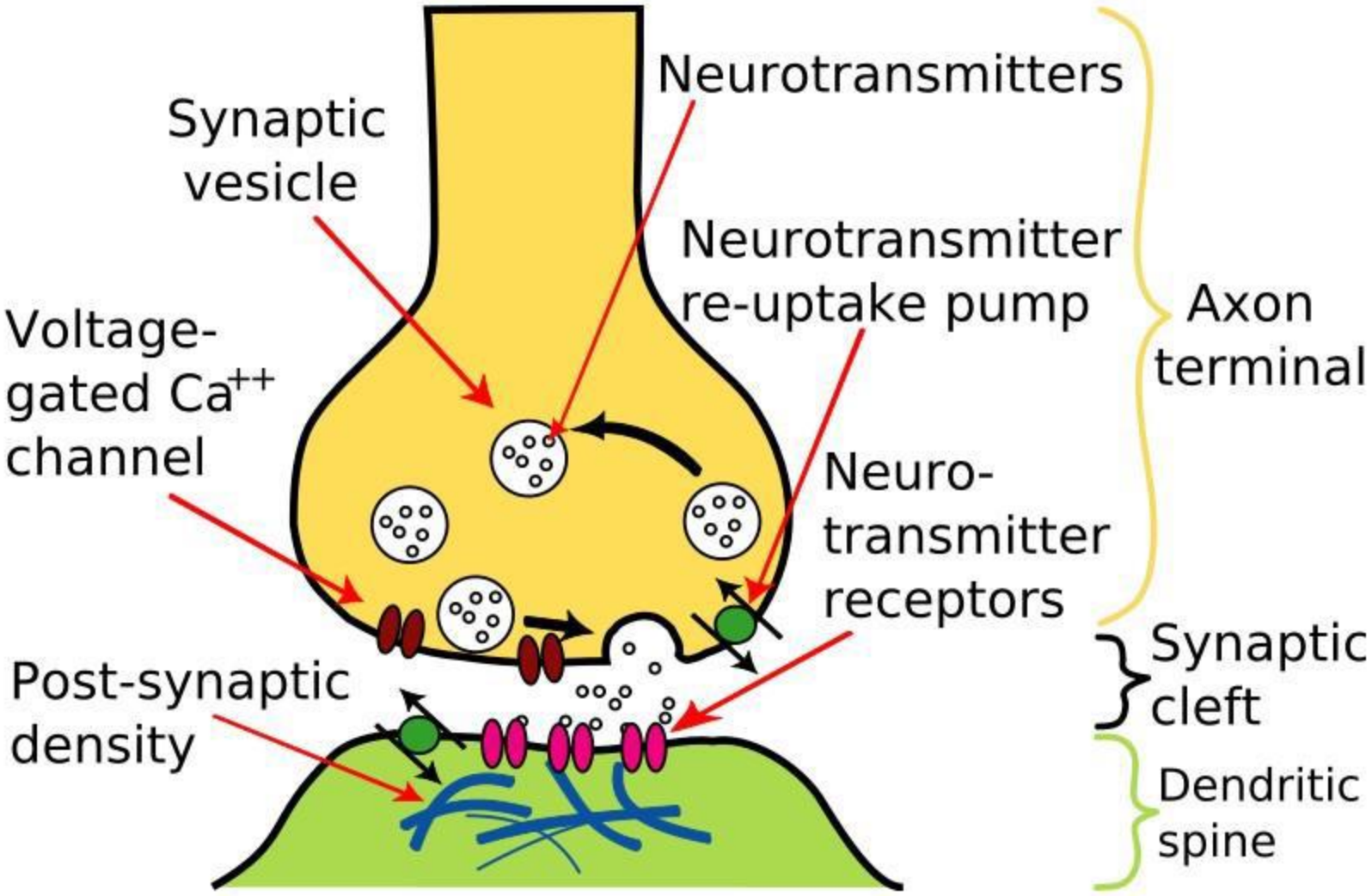
- **The axon** hillock is characterized by having a very high concentration of **voltage-activated sodium channels**


Dendrite
Axon terminal
Cell body
Node of Ranvier
Schwann cell
Myelin sheath
Nucleus

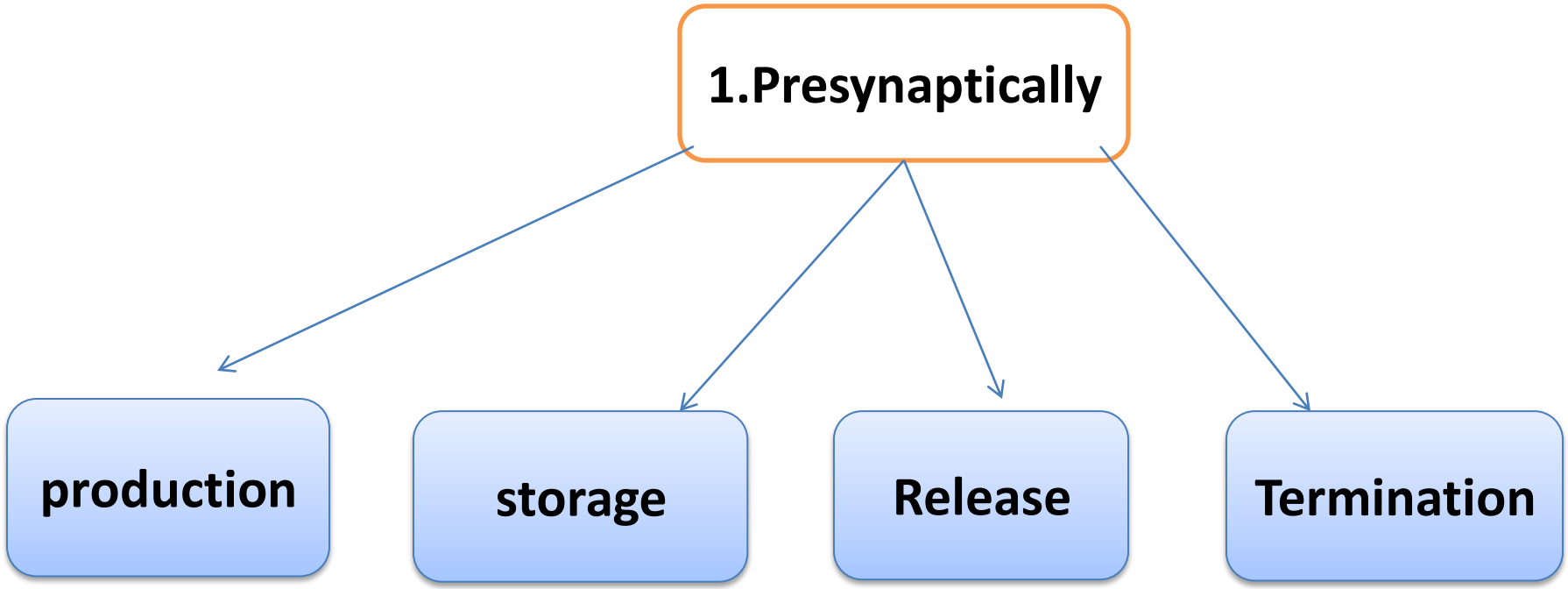
Synapse

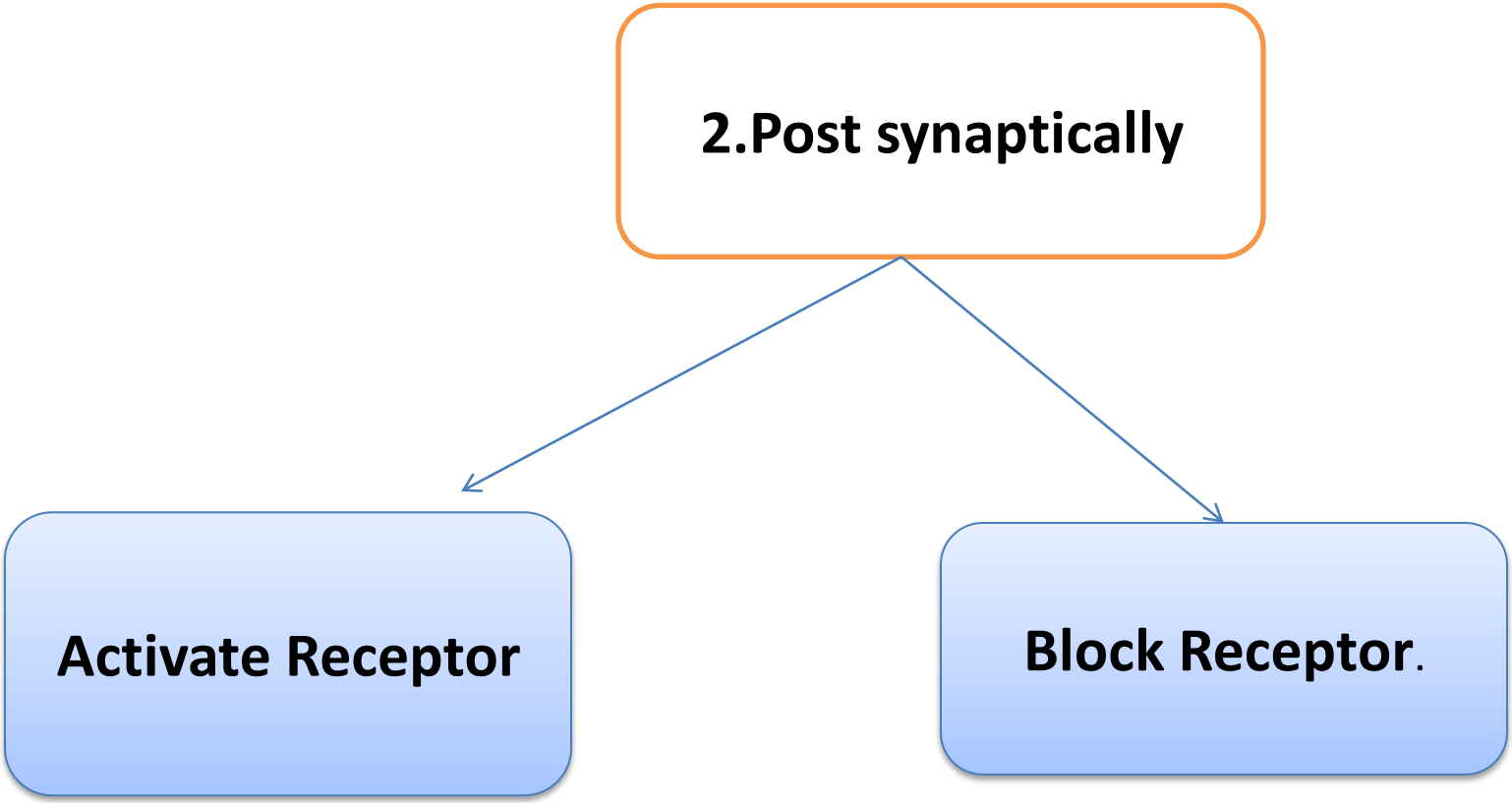
The site of transmission of electric nerve impulses between two nerve cells (neurons) or between a neuron and a gland or muscle cell (effector)
When an action potential arrives at the end of the pre-synaptic axon(top),it causes the release of **neurotransmitter** molecules that open ion channels in the post-synaptic neuron (bottom)

The combined excitatory and inhibitory post synaptic potentials of such inputs can begin a**new action potential** in the post-synaptic neuron


Synaptic vesicle
Neurotransmitters
Neurotransmitter re-uptake pump
Voltage-gated Ca++ channel
Neuro-transmitter receptors
Post-synaptic density
Axon terminal
Synaptic cleft
Dendritic spine

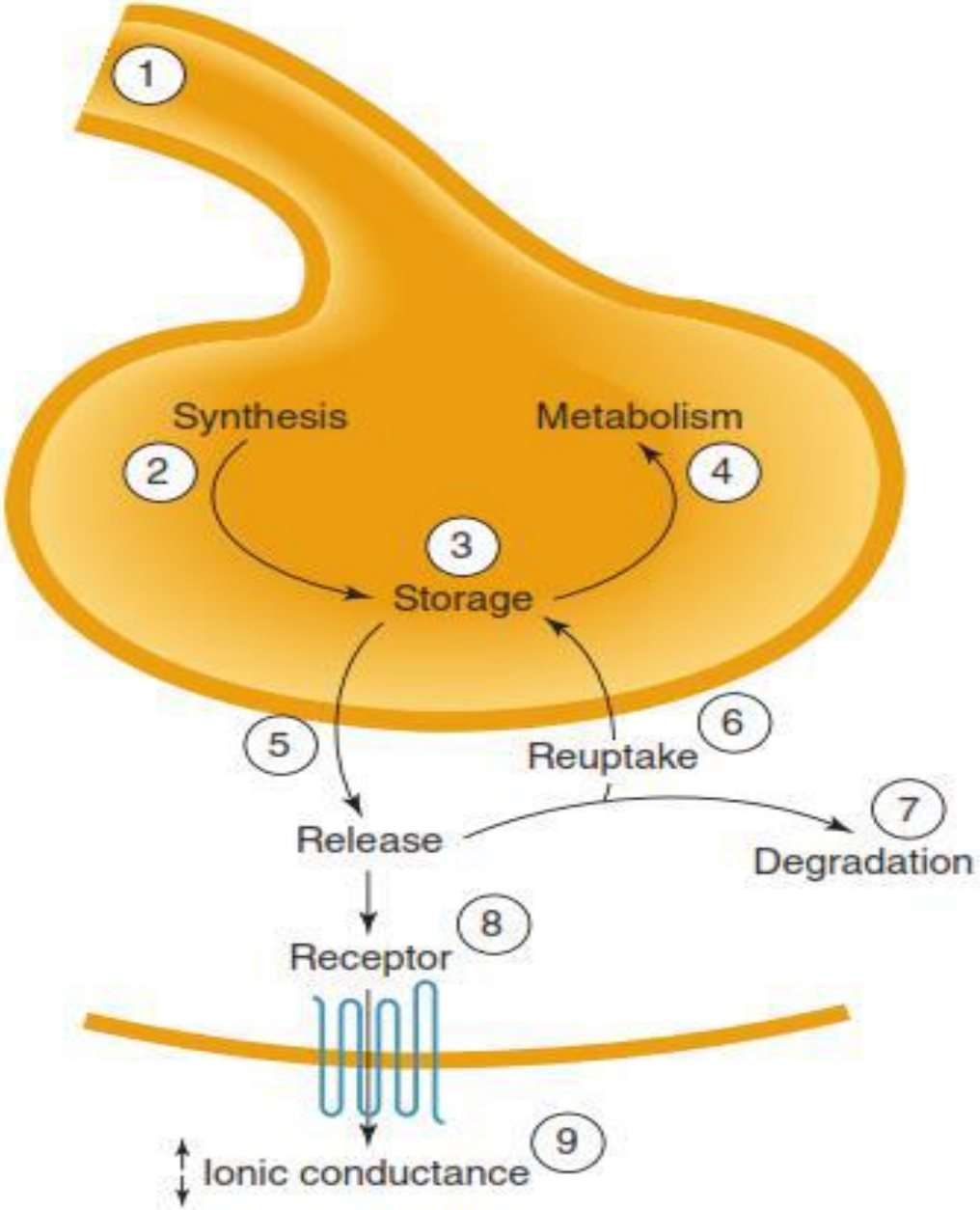
Drugs affecting the CNS may act by:




2.Post synaptically
Activate Receptor
Block Receptor.

CNS Drugs may alter:

(1) The action potential in the presynaptic fiber;
(2) synthesis of transmitter;
(3) storage;
(4) metabolism;
(5) release;
(6) reuptake;
(7) degradation;
(8) receptor for the transmitter; or
(9) receptor-induced decrease or increase in ionic conduction


1
Synthesis
2
Metabolism
4
3
Storage
5
Reuptake
6
7
Release
Degradation
8
Receptor
9
Ionic conductance

Drugs that act in the CNS

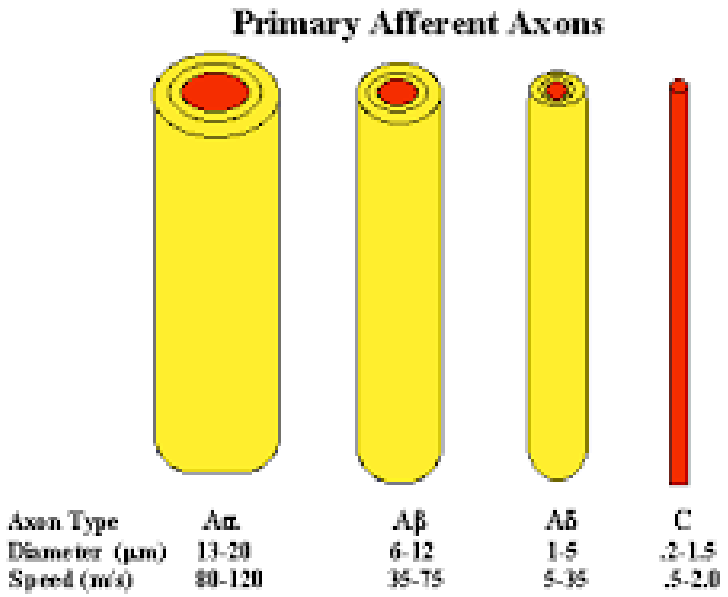
- Centrally acting analgesics (Narcotic analgesics).
- CNS depressants, sedatives and hypnotics.
- General and Local anesthetics.
- Anti-depressant drugs, Anti-psychotic drugs.
- Anti-Parkinson drugs and anti-epileptic drugs.
- CNS stimulants and drug abuse.

Centrally acting analgesics (Narcotic analgesics).

- **Pain** is an unpleasant, sensory, emotional sensation associated with actual or potential tissue injury. It requires a person to remove the cause of the damage or seek relief from the pain.
- Pain is the most common symptom prompting people to seek health care. When not managed effectively, pain may greatly impair quality of life and ability to perform activities of daily living. Opioid analgesics are drugs that provide pain relief by affecting people's perception and tolerance of moderate to severe pain.
- The causes of pain include **nerve damage**, **actual tissue injury**, **cancer**, or **surgery**.
- Pain may be classified according to its origin in body structures (e.g., somatic, visceral, neuropathic), duration (e.g., acute, chronic), or cause (e.g., cancer).

Acute pain may result from injury, trauma, spasm, disease processes, and treatment or diagnostic procedures that damage body tissues. The intensity of the pain is usually proportional to the amount of tissue damage.

Acute pain is called **fast pain** because it is felt quickly after a pain stimulus is applied. It is produced by mechanical and thermal stimuli and conducted to the spinal cord by **A-delta fibers** in the peripheral nerves. **Glutamate** is the neurotransmitter secreted in the spinal cord at the A-delta nerve fiber endings



Chronic (noncancer) pain (i.e., lasting 3 months or longer) demands attention less urgently, may not be characterized by visible signs, and is often accompanied by emotional stress, increased irritability, depression, social withdrawal, financial distress, loss of libido, disturbed sleep patterns, diminished appetite, weight loss, and decreased ability to perform usual activities of daily living
Chronic (noncancer) pain may also be called **slow pain**. It can be caused by mechanical, thermal, and chemical stimuli and is described as burning, aching, or throbbing. Slow, **chronic pain** is transmitted by C nerve fibers to the spinal cord and brain. **Substance P** is the neurotransmitter at **C nerve fiber** endings; it is released slowly and accumulates over seconds or minutes.

Opioid agonists

Morphine sulfate the prototype, is an opium alkaloid used mainly to relieve moderate to severe pain administration is most often oral or parenteral. Patient response depends on route of administration and dosage

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	**Children**
Morphine (Duramorph, Infumorph, Kadian, MS Contin, Mitigo; M.O.S.-S.R, MS Contin SRT, Statex, Teva-Morphine SR)	C	PO immediate release, 5–30 mg every 4 h PRN PO controlled release, 30 mg or more every 8–12 h IM, subcutaneously 5–20 mg/70 kg every 4 h PRN IV injection, 2–10 mg/70 kg, diluted in 5 mL water for injection and injected slowly, over 5 min IV continuous infusion, 0.1–1 mg/mL in 5% dextrose in water solution, by controlled infusion pump Epidurally, 2–5 mg/24 h; intrathecally, 0.2–1 mg/24 h Rectal, 10–20 mg every 4 h PCA dosing based on institutional protocols; standard parameters: 2-mg bolus, 1-mg dose, lockout interval 10 min, 4-h maximum limit 30 mg, basal rate not recommended for starting PCA Older adult, PCA dosing per institutional protocols typically 25% of adult dose and requires more intense monitoring and dose individualization	IM, subcutaneous 0.05–0.2 mg/kg (up to 15 mg) every 4 h

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	Children
Codeine (✱ Codeine Contin, PMS-Codeine, Ratio-Codeine)	C	Pain: PO, subcutaneous, IM 15–60 mg every 4–6 h PRN; usual dose 30 mg; max, 360 mg/24 h Cough: PO 10–20 mg every 4 h PRN; max, 120 mg/24 h	1 y or older, pain: PO, subcutaneous, IM 0.5 mg/kg every 4–6 h PRN 2–6 y, cough: PO 2.5–5 mg every 4–6 h; max, 30 mg/24 h 6–12 y, cough: PO 5–10 mg every 4–6 h; max, 60 mg/24 h
Fentanyl (Actiq, Duragesic, Subsys, Lazanda; ✱ Abstral, Fentora, Matrix Patch, PMS-Fentanyl MTX)*	C	Preanesthetic sedation: IM 0.05–0.1 mg 30–60 min before surgery Analgesic adjunct to general anesthesia: IV total dose of 0.002–0.05 mg/kg, depending on surgical procedure Adjunct to regional anesthesia: IM or slow IV (over 1–2 min) 0.05–0.1 mg PRN Postoperative analgesia: IM 0.05–0.1 mg, repeat in 1–2 h if needed General anesthesia: IV 0.05–0.1 mg/kg with oxygen and a muscle relaxant (max dose 0.15 mg/kg with open heart surgery, other major surgeries, and complicated neurologic or orthopedic procedures) Chronic pain (Duragesic transdermal system): 2.5–10 mg every 72 h	Children weighing at least 10 kg: conscious sedation or preanesthetic sedation, 5–15 mcg/kg of body weight (100–400 mcg), depending on weight, type of procedure, and other factors; max dose, 400 mcg, regardless of age and weight. 2–12 y: general anesthesia induction and maintenance, IV 2–3 mcg/kg
Hydrocodone (Hysingla ER, Zohydro ER) Hydrocodone (with acetaminophen: Paracetamol, Lortab, Vicodin HP) (with ibuprofen: Ibudone, Reprexain, Vicoprofen, Xylon; ✱ Vicoprofen)	C With acetaminophen: C With ibuprofen: C	Hysingla ER: 20 mg once daily and then increase 10–20 mg every 3–5 d PRN Zohydro ER: 10 mg every 12 h and then increase 10 mg every 12 h every 3–7 d PRN With acetaminophen: 1–2 tablets every 4–6 h as needed for pain, not to exceed 4 g of acetaminophen daily With ibuprofen: 1 tablet (hydrocodone 2.5–0 mg/ibuprofen 200 mg) every 4–6 h as needed for pain, not to exceed five tablets daily; consider reducing dosing in elderly	2–13 y or <50 kg: hydrocodone 0.1–0.2 mg/kg/dose, not to exceed 6 doses a day or the max recommended dose of acetaminophen. ≥16 y: refer to adult dosing for hydrocodone with ibuprofen. Extended-release products containing hydrocodone should not be given to children younger than 6 y of age and should be used with caution in children 6–12 y of age
Hydromorphone (Dilaudid; ✱ Hydromorph Contin, Jurnista)	C	PO 2–4 mg every 4–6 h PRN IM, subcutaneous, IV 1–2 mg every 4–6 h PRN (may be increased to 4 mg for severe pain) Rectal suppository 3 mg every 6–8 h	Dosage not established
Meperidine (Demerol; ✱ Demerol)	C	PO, IM, IV, subcutaneous, PO 50–150 mg every 3–4 h Obstetric analgesia: IM, subcutaneous 50–100 mg when pain becomes regular; may repeat at 1- to 3-h intervals	PO, IM, subcutaneous 1.1–1.8 mg/kg/dose, up to adult dose, every 3–4 h as needed
Methadone (Dolophine; ✱ Metadol, Metadol-D)	C	PO (opioid naive) initial 2.5 mg every 8–12 h IV, IM, subcutaneous, initial 2.5–10 mg every 8- to 12-h titrate slowly to effect	Neonatal abstinence syndrome PO, IV 0.05–0.2 mg/kg/d divided every 8 h
Oxycodone (OxyContin, Xtampza ER; ✱ Oxy IR, OxyNEO, PMS-Oxycodone CR, Supeudol)	B/C (based on manufacturer)	PO, immediate release, 5 mg every 6 h PRN; 10–30 mg every 4 h PRN for other formulations PO, controlled release, 10 mg every 12 h, increased if necessary	Not recommended for children younger than 12 y of age

Drug	Pregnancy Category	Routes and Dosage Ranges	
		Adults	**Children**
Oxymorphone	C	PO (opioid naive), 5–10 mg every 4–6 h; conversion from stable parenteral dose 10 times the total parenteral requirement in divided doses every 4–6 h PO, extended release (opioid naive), 5 mg every 12 h, increased by 5–10 mg every 12 h every 3–7 d until pain relieved; conversion from stable parenteral dose 10 times the total parenteral requirement in two divided doses IM, subcutaneous 1–1.5 mg every 4–6 h PRN IV 0.5 mg every 4–6 h PRN Labor analgesia: IM 0.5–1 mg	Dosage not established
Tramadol (Ultram, ConZip; Durela, Tridural, Ultram, Zytram XL)	C	PO 50–100 mg every 4–6 h PRN (max, 400 mg/d) Renal impairment (CrCl < 30 mL/min): PO 50–100 mg every 12 h (max dose, 200 mg/d) Hepatic impairment (cirrhosis): PO 50 mg every 12 h Older adults (65–75 y): same as adults, unless they also have renal or hepatic impairment Older adults (>75 y): <300 mg daily, in divided doses	Dosage not established

Opioid agonists/antagonists

Opioid agonists/antagonists act on the same pain receptors in the CNS as morphine and other opiates, resulting in interference with pain transmission and/or pain sensation. These agents have agonist activity at some receptors and antagonist activity at others. Because of their agonist activity, they are potent analgesics with a lower abuse potential than pure agonists. However, they are considered **second-line drugs** for treatment of moderate to severe pain. Because of their antagonist activity, they should not be given to people who have been receiving analgesics, and they may produce withdrawal symptoms in people with dependence. **Pentazocine** was the original prototype, but its use is low

Butorphanol will serve as the prototype which is a synthetic, agonist similar to morphine in analgesic effects and ability to cause respiratory depression. Prescribers order it for moderate to severe pain. Administration may be parenteral; after IM or IV use, analgesia peaks in 30 to 60 minutes. Alternatively, administration may be topical to nasal mucosa by a metered spray; after nasal application, analgesia peaks within 1 to 2 hours.

Opioid antagonists

An antagonist (antidote) reverses analgesia and the CNS and respiratory depression caused by agonists. However, an opioid antagonist does not relieve the depressant effects of other drugs, such as sedative–hypnotic, antianxiety, and antipsychotic agents. The chief clinical use of an antagonist is to relieve opioid induced CNS and respiratory depression.

The prototype of this class is **naloxone** .It is essential that this drug be readily available in all health care settings in which opioids are given. In addition, inhaled naloxone is now available either

(1) with a prescription in all states or

(2) without a prescription to patients and their caregivers using narcotics for pain in many states. Some states have approved peace officers (first responders) to carry naloxone when on duty.

Naltrexone is an opiate antagonist that acts in the brain to prevent opiate effects (e.g., pain relief, feelings of well-being), making it effective in decreasing the desire to take opiates and in treating alcohol dependence.


شكرا لكم
thank you