Morphine has been described as the gold standard of opioid therapy.

Agonist to all opioids receptors with high affinity to μ receptor. Duration 4–6H
Advantages:

1. Less expensive than fentanyl
2. As an analgesic in hospital settings to relieve pain, treatment of visceral pain as well as somatic pain
3. Morphine can cause profound vasodilatation
4. Sedation, another therapeutic effect of morphine, occurs at much higher plasma levels
5. Slow onset of action: 1 hour after injection = delayed respiratory depression (12 to 18 hours)

Why? Cause it is hydrophilic, and thus it has a slower onset with a longer clinical effect,” prolonged latency-to-peak effect” this is why morphine is less likely to cause acute respiratory depression compared to the more rapid acting drugs because the relationship between minute ventilation and the partial pressure of carbon dioxide changes more slowly unlike nonopioid analgesics.

5. Morphine has several metabolites, including morphine-6-glucuronide, which causes additional analgesia

so that multiple routes are available for drug

6. Miosis ‘kapa receptor’
7. Sedation, another therapeutic effect of morphine, occurs at much higher plasma levels
8. Cough centers are suppressed
9. Euphoria
10. Anxiolysis
Disadvantages

1– slow onset of time means that clinicians are more likely to inappropriately “stack” multiple morphine doses in a patient experiencing severe pain, thus creating the potential for a toxic

2– has high hepatic extraction ratio
Accumulation of M6G to potentially toxic levels in dialysis patients is another important implication of this active metabolite

3– Respiratory depression

4– confusion

5– Urinary retention

6– ileus

7– hypotension, bradycardia

8– constipation

9– nausea and vomiting

10– biliary colic
Synthetic Opioids:
- Pethidine (Mepiridine) and
- Fentanyl

**Pethidine** is a morphine–like opioid. It's synthetic
- Mu receptor and bind to kappa
- Discovered in research for atropine–like compounds
Advantages:

1- Rapid onset of action The sedative and analgesic effects of meperidine after intravenous dosing occur within 2 to 4 minutes, lasting 3 to 4 hours.
2- Safe in asmatic patient
3- As an analgesia in obstetric practice and did not appear to delay labour
Disadvantages:
1– Meperidine is 10-fold less active than morphine.
2– Not used in chronic pain because its active metabolite, (normeperidine) long half life 15h, it is excitatory and can cause seizures.
3– Meperidine > serotonin syndrome, Symptoms include high body temperature, agitation, increased reflexes, tremor, sweating and diarrhea.
5– Drug interactions.
6– Has atropine-like effects, including dry mouth and blurred vision (cycloplegia and sometimes mydriasis, vagolytic in smooth muscles – less miosis,
7– Respiratory depression
Fentanyl is a synthetic opioid.

- It is available for intravenous, transmucosal, and transdermal use.
- Strong agonist mu and also can bind to kappa.
- More potent, however, with a dose of 0.1 mg equianalgesic to 10 mg morphine and 75 mg meperidine.
Advantages:

1. Higher lipophilicity compared to morphine. This higher lipid solubility allows fentanyl to cross the blood–cerebrospinal fluid barrier more rapidly and produce analgesic effects more quickly than morphine.
2. Faster redistribution and an elimination half-life of 4 hours.
3. The analgesic effects of fentanyl are 80 to 100 times more potent than the morphine effects. ((100 mg oral morphine per day ~ 1 mg))
4. Fentanyl is metabolized in liver into norfentanyl, an inactive metabolite that is then renally excreted.
5. IV fentanyl onset occurs within 60 seconds with shorter duration of action (30 to 40 min) than morphine, making it ideal for scenarios like intubation that require rapid induction and recovery from sedation and analgesia.
6. Serum half-life of fentanyl is prolonged why? High lipid solubility of fentanyl that allows it to accumulate in adipose and other lipid-rich tissue.
7. Miosis,
8. Euphoria
Disadvantages:

1–Fentanyl also has reduced propensity to cause histamine release from mast cells, as well as decreased activity on the vasomotor center. These advantages of fentanyl make it theoretically less likely to cause significant hypotension compared to morphine.

- Cause hypotension indirectly by decreasing central sympathetic outflow.

- 2– prolong respiratory depression and delay the recovery from sedation.
- gastrointestinal adverse effects.
- 3–respiratory depression produced by fentanyl may be of longer duration than its analgesic action.

- 4– more rapid development of tolerance severe tachyphylaxis compared to morphine.
- 5–fentanyl–induced chest wall rigidity.
- 6–Coughing due to fentanyl it can sometimes be explosive,. Coughing occurs because fentanyl constricts the tracheal smooth muscle, stimulating the irritant receptors or ?
- 7–bradycardia, direct stimulation of the central vagal nucleus.
The correct use of analgesics to make the prescribed treatments effective

1. Analgesics should be given at regular intervals.
2. Analgesics should be prescribed according to pain intensity as evaluated by a scale of intensity of pain.
3. Dosing of pain medication should be adapted to the individual.
4. Analgesics should be prescribed with a constant concern for detail.
The 1986 version of the WHO analgesic ladder

- If the pain is not properly controlled, one should then introduce a weak opioid.
- If the use of this medication is insufficient to treat the pain, one can begin a more powerful opioid.
- One should never use 2 products belonging to the same category simultaneously.
- The analgesic ladder also includes the possibility of adding adjuvant treatments for neuropathic pain or for symptoms associated with cancer.
Step up, step down

- This version of the analgesic ladder can be used in a bidirectional fashion: the slower upward pathway for chronic pain and cancer pain, and the faster downward direction for intense acute pain, uncontrolled chronic pain,
Thank you.