Sedation and Pain Control

Why do we need to worry about pain control?

- Pemphigus Vulgaris
- Vulvodynia
- PG
- Ulcers
- Operative and Post-operative

Types of pain

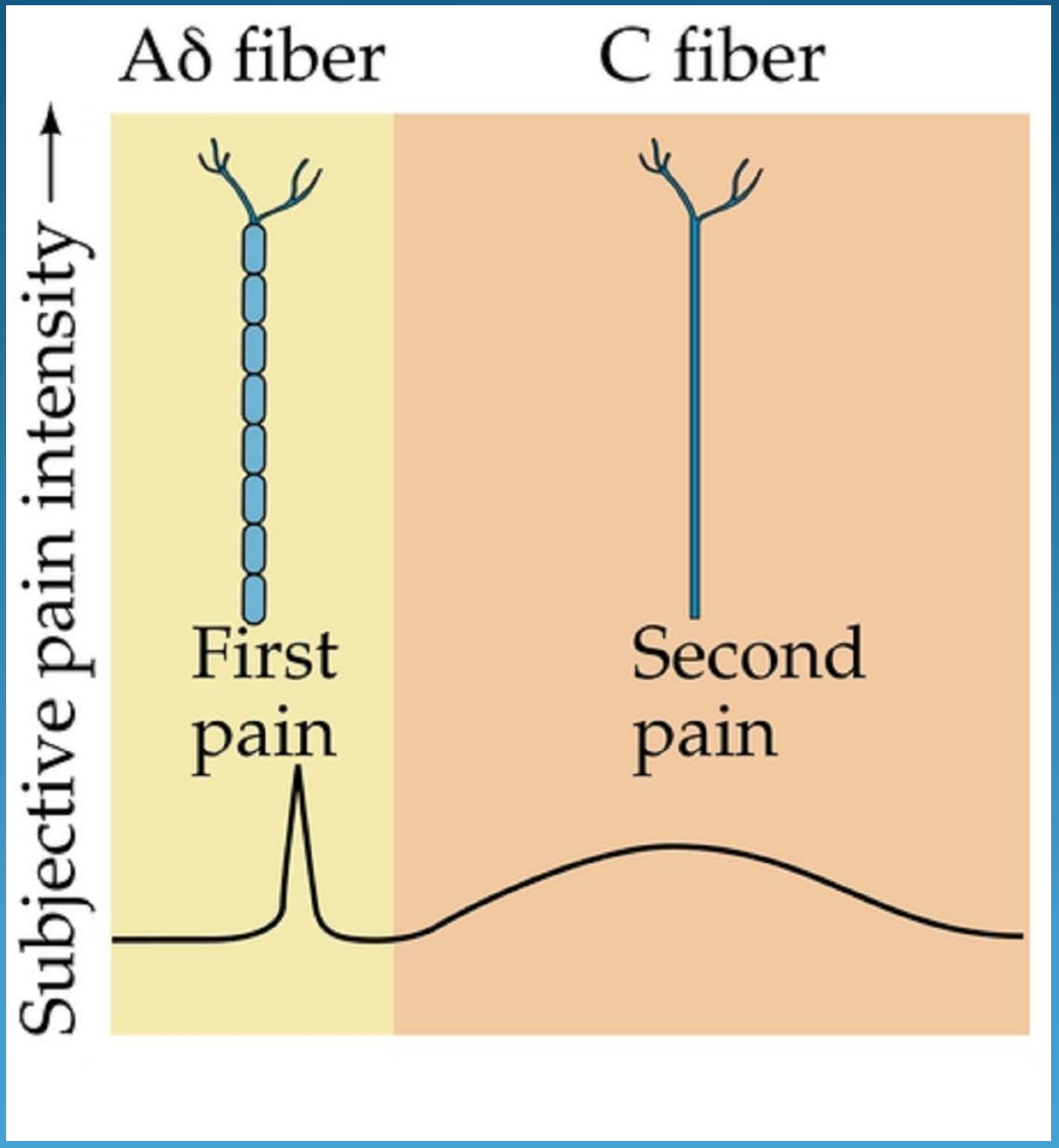
- Acute
  - Cause that is easily explainable and well defined.
- Chronic
  - Persists beyond the expected healing time for a particular injury or illness.

Types of Pain

- Nociceptive
  - Somatic:
    - Somatic pain is caused by the activation of pain receptors in either the cutaneous (body surface) or deep tissues (musculoskeletal tissues).
    - bone/soft tissue: "tender, deep, aching"
  - Visceral: "spasms, cramping"
    - Caused by activation of pain receptors resulting from infiltration, compression, extension, or stretching of the thoracic, abdominal, or pelvic viscera.
- Neuropathic
  - Caused by injury to the nervous system
  - "shooting, stabbing, burning"

Primary Afferent Neurons

- A special class of neurons with free nerve endings in the skin and their cell bodies in the dorsal root ganglia
  - A delta
    - fast pain
    - Sharp pain
    - Minimally myelinated
  - C fibers
    - Slow pain
    - Dull, burning pain
    - Non-myelinated


Aδ fiber
C fiber
Subjective pain intensity
First pain
Second pain

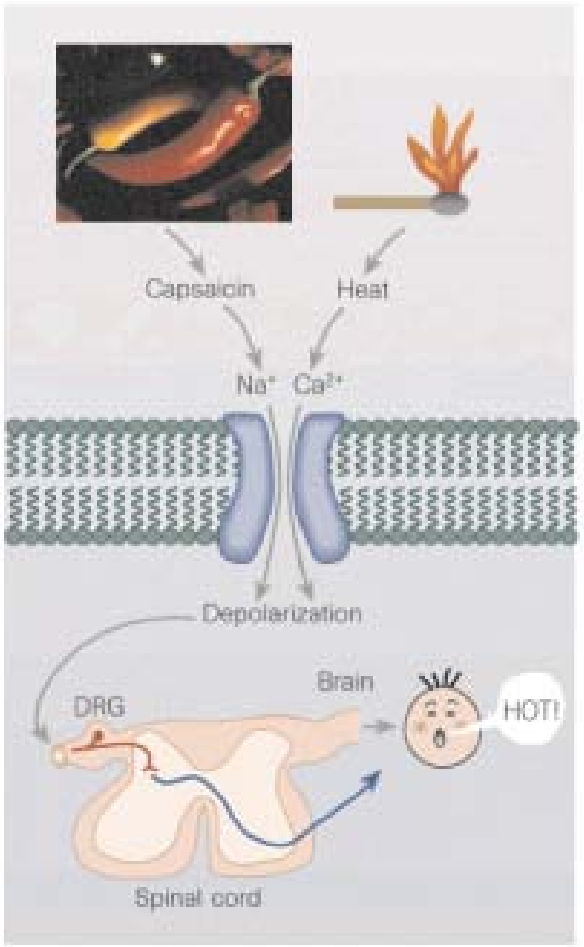
Nociceptors

- Three types
  - Free nerve endings
    - Respond to extremes of heat, acids, and capsaicin
  - Polymodal receptors that react to cold and warm temperatures
  - High threshold nocisensors responding to intensive pressure

- free nerve endings that respond to intense pressure,
  - free nerve endings that respond to extremes of heat, acids, and the presence of capsaicin (the active ingredient in chili peppers),
  - receptors sensitive to ATP, ATP is released when the blood supply to a region is disrupted (ischemia), occurs during spasms of blood vessels that cause angina or migraine, or when a muscle is damaged, also released by rapidly growing tumors,

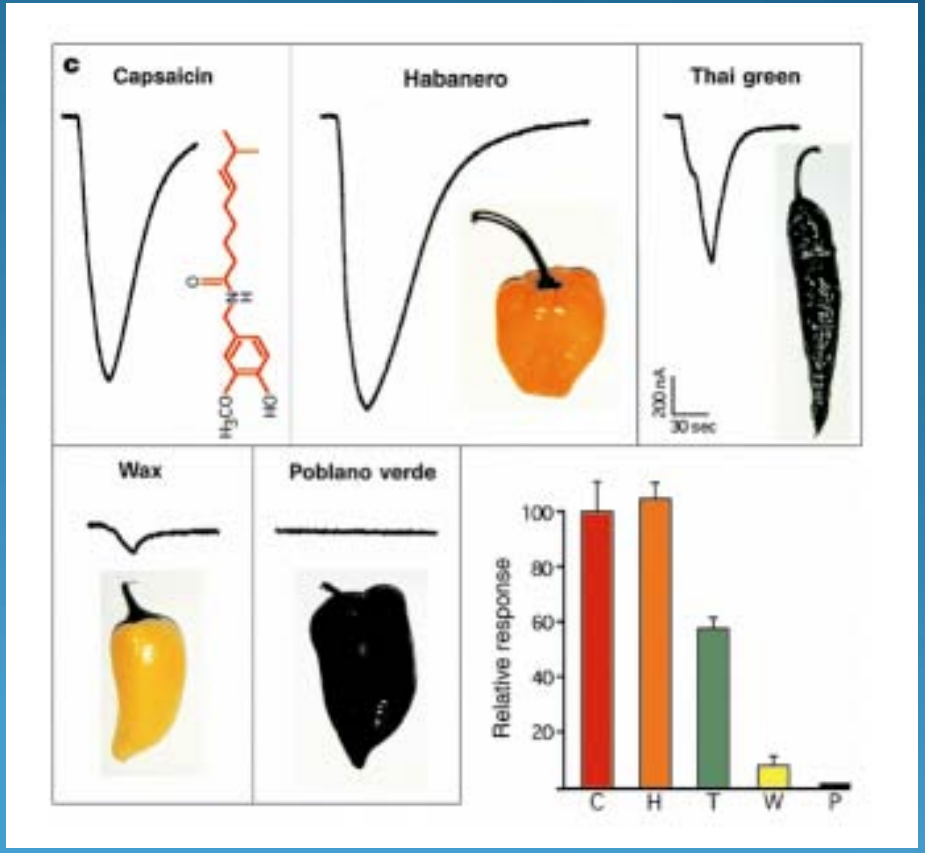
Nociceptors

- Vanilloid receptors, VR1, or capsaicin receptors
- Nonselective cation channels opened by many mediators including heat, low pH, and capsaicin
- Mice without VR1 have impaired sensitivity to pain



Nociceptors

- Chart comparing various peppers activation of VR1.
- Taken from Nature 1997.



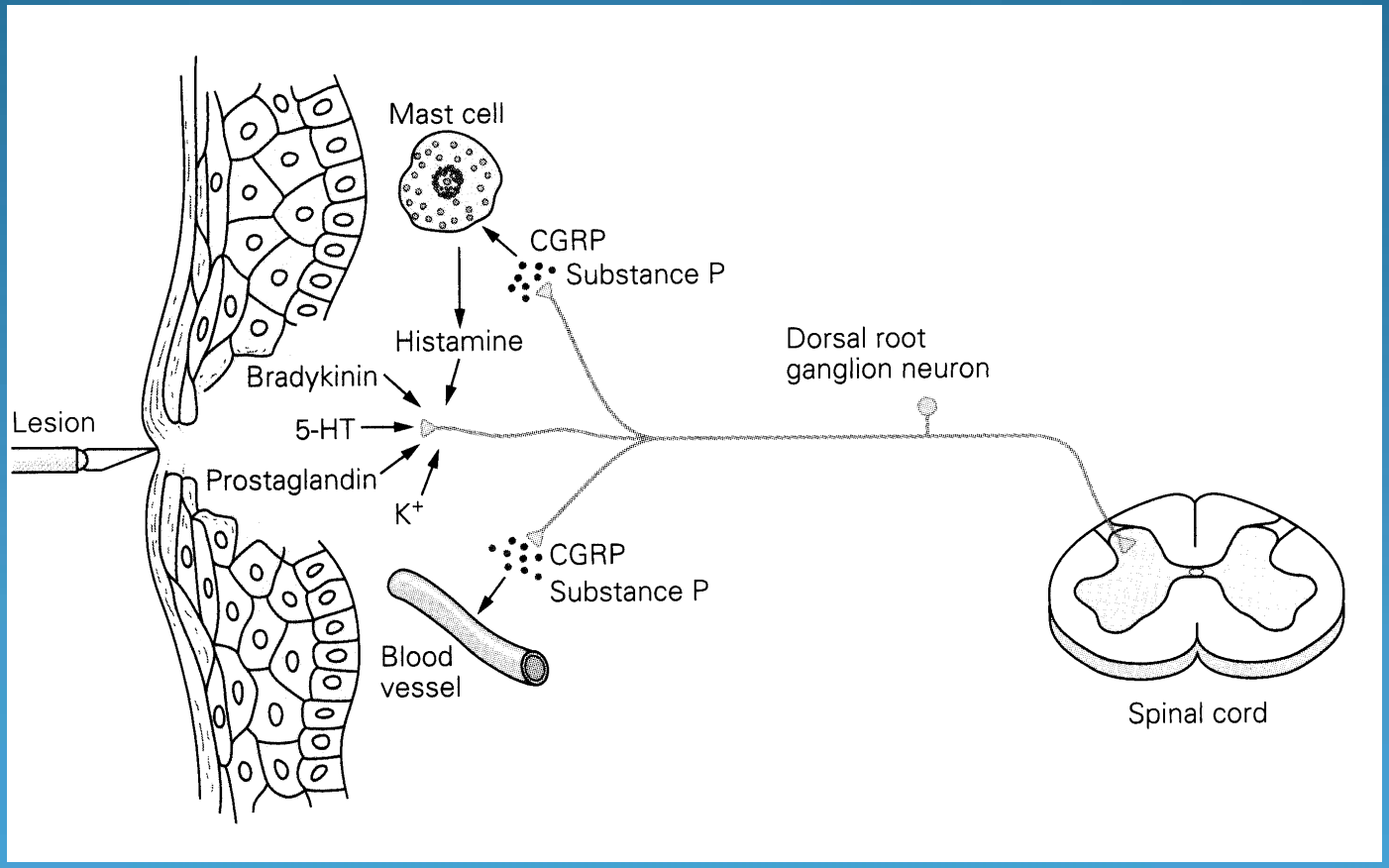
Different substances can activate or sensitize nociceptors (lower pain threshold)

Inhibited by COX inhibitors

Substance	*Source*
Potassium	Damaged cells
Serotonin	Platelets
Bradykinin	Plasma
Histamine	Mast cells
Prostaglandins	Damaged cells
Leukotrienes	Damaged cells
Substance P	Primary afferent fibers

Source: Modified from Fields, 1987.

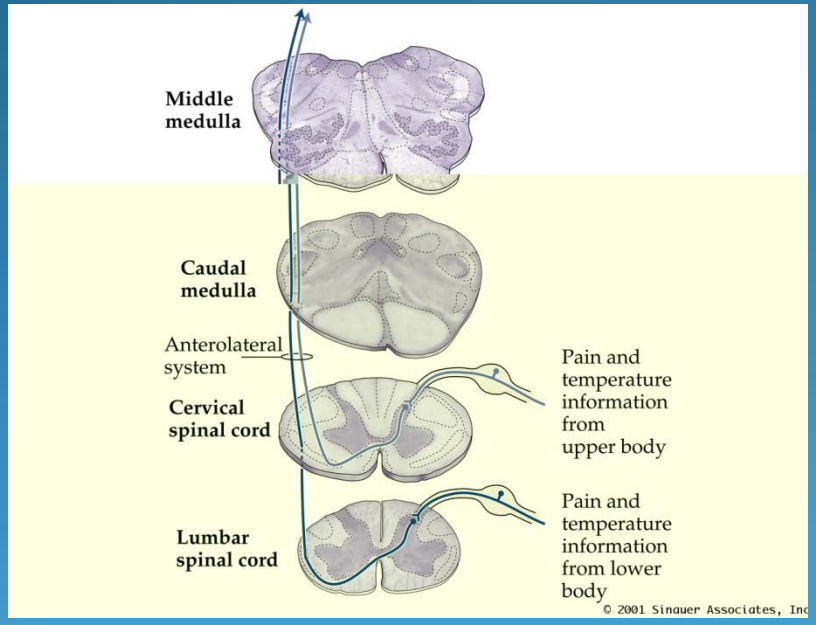
- Nociceptors release mediators
  - Substance P
- Causes depolarization
- This results in positive feedback



Pain Pathways

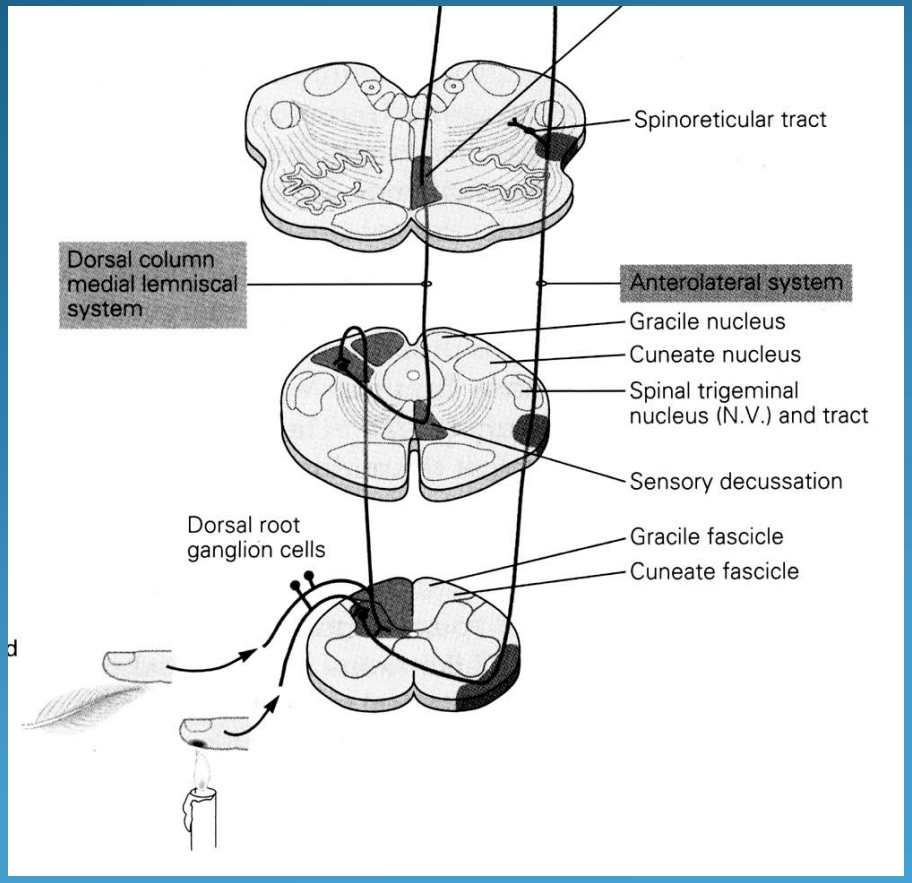
- **Spinothalamic**
- Spinomesencephalic
- Spinoreticular
- Spinolimbic
- Spinocervical
- Postsynaptic dorsal column pathways

Spinothalamic Tract



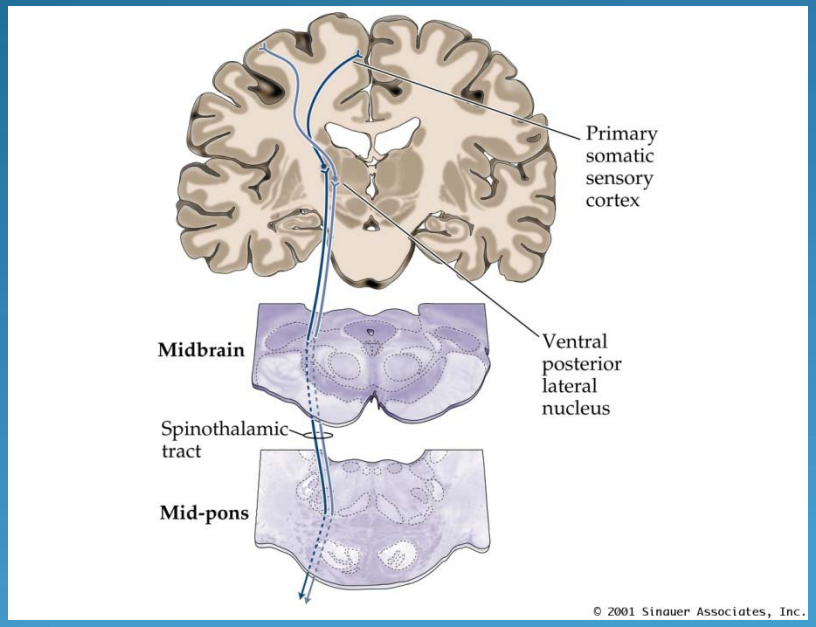
- Afferent fibers end in the substantia gelatinosa in the dorsal horn of the spinal cord.
- Cross in anterior white commissure
- Form antero-lateral system and head up through the brainstem to thalamus via spinothalamic tract.

Spinothalamic Tract



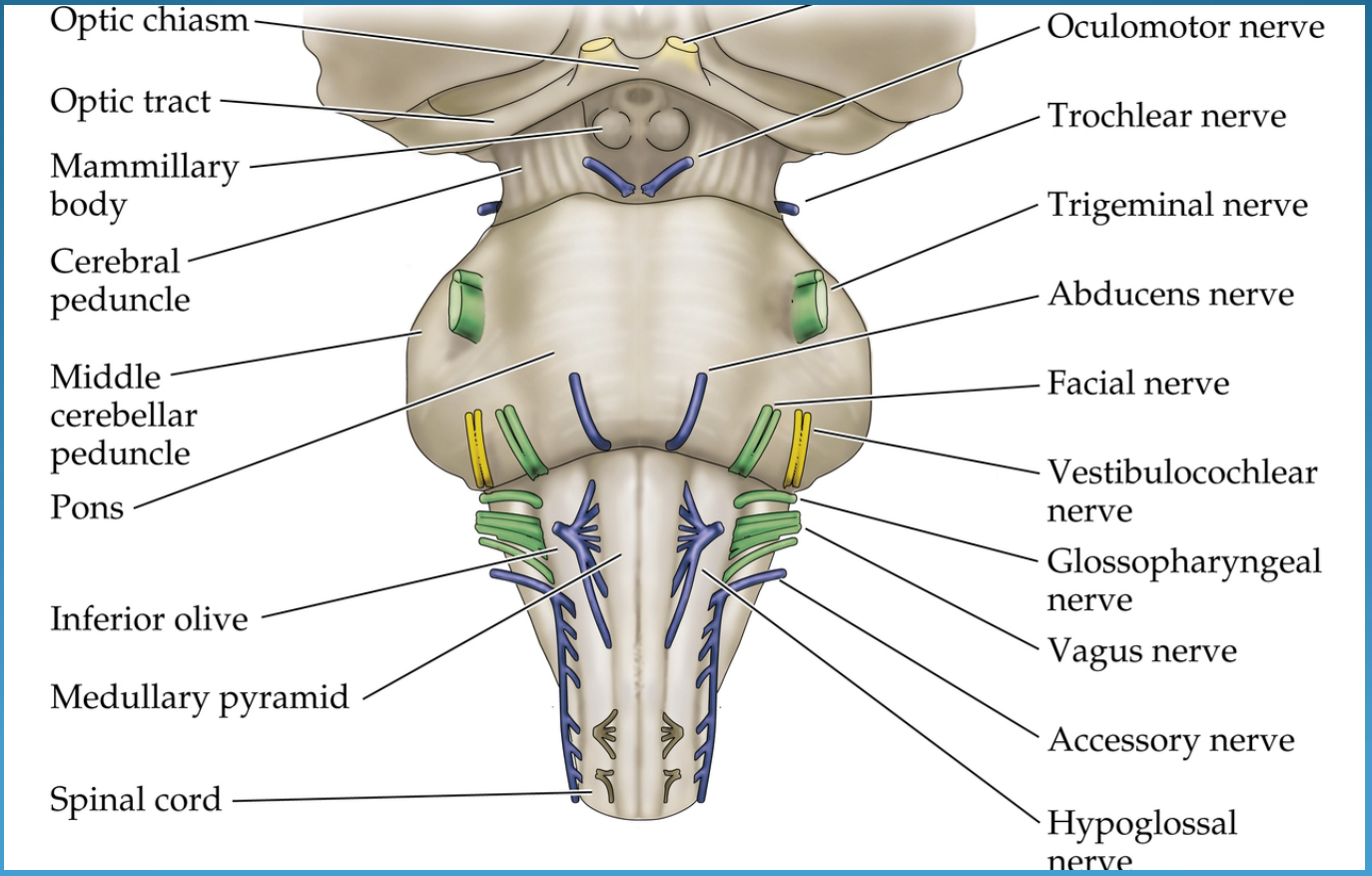
- Touch and pain are on opposite sides below medulla.
- Touch and pain are on the same side above the medulla.

Spinothalamic Tract

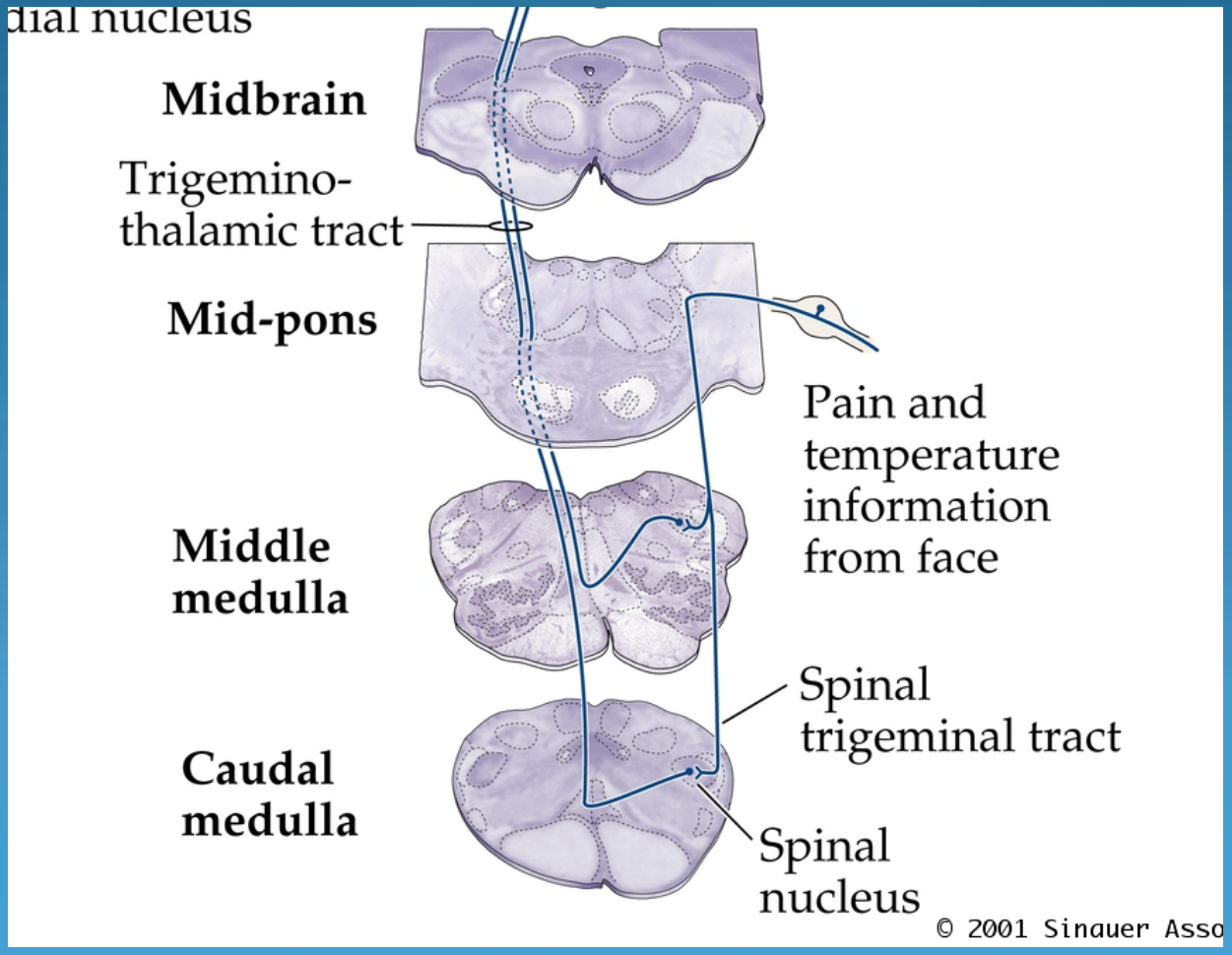


- Neurons synapse in the ventral posterior lateral nucleus.
- They then transverse to the primary somatic sensory cortex.

Trigeminal pain and temperature



Trigeminal pain and temperature

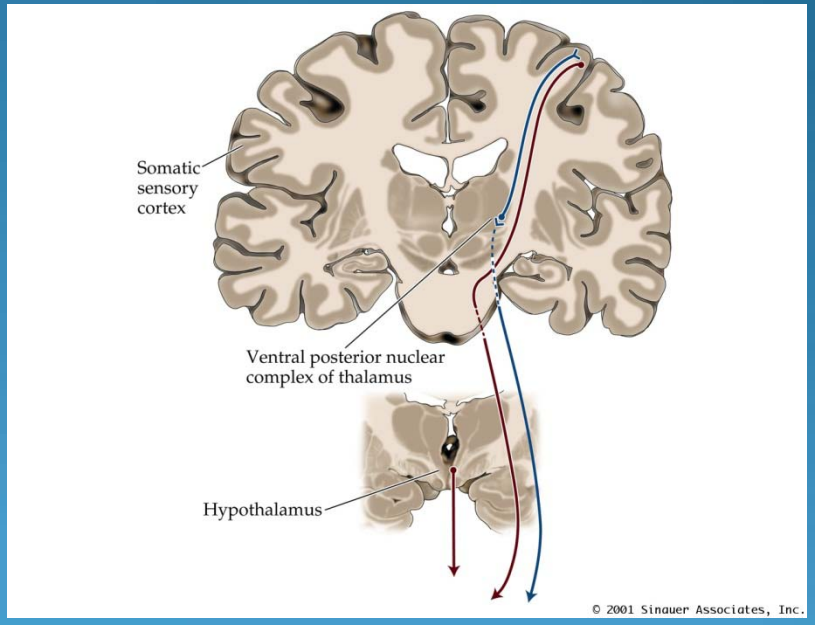


Trigeminal pain and temperature

- Pain and temperature in the face are carried via sensory neurons with cell bodies in the trigeminal (V) ganglion.
- They enter the mid pons and descend to the medulla in the spinal trigeminal tract.
- They then synapse at the spinal nucleus and cross over to form the trigemino-thalamic tract.

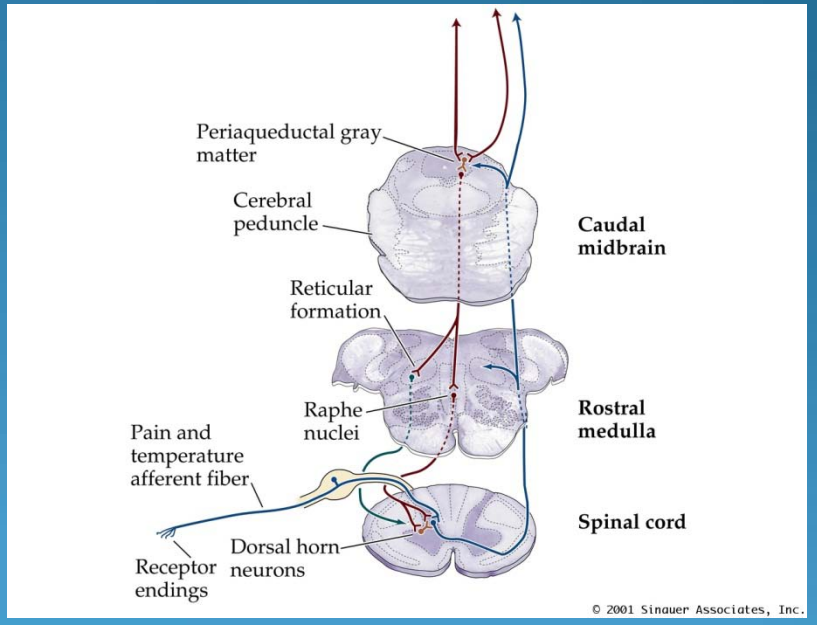
Central Control of pain

- Melzack and Wall theory of pain
  - Existence of a “gate” which prevents excess pain stimulation from entering the brain.
  - Gate localized in the dorsal horns and substantia gelatinosa
  - Substantia gelatinosa controlled centrally.



Central Control of pain

- T cells (central transmission cells) in substantia gelatinosa receive input from the skin and other cells of SG
- Afferent fibers excite T cells and other SG cells
- Output from SG is via T cells by spinothalamic tract and determines degree of pain felt.



Central Control of pain

- The central input to the T cells comes from the periaquaductal gray and rostroventral medulla.
- Stimulation of these areas reduce pain by reducing activity in the spinothalamic tract.
- These fibers secrete enkephalin or serotonin that activates local cells to produce enkephalins.
- The input from C and A delta fibers to T cells is inhibited by enkephalin.
- Output from T cells also goes to midbrain to activate the descending inhibitory control.
- It is thought that opioids act here.

Narcotic analgesics

- Affect opioid receptors (spinal and cerebral)
  - Mu
  - kappa
  - delta
  - Sigma
  - Each is specific for different drugs

Narcotic Analgesics

- Three types of opioids
  - Opiate agonists
  - Mixed agonists/antagonists
  - Antagonists
- Analgesic and euphoric effects

Narcotic analgesics

- Mechanisms of Opioid analgesia
  - Segmental control (Gate Control)
    - Inhibition of second order neuronal transmission (spino-thalamic tract) in the dorsal horn
    - Acts at rostroventral medulla and periaquaductal grey
    - Inhibits substance P

Narcotic analgesics

- Side effects of opioids
  - Dose dependent respiratory depression
  - Euphoria
  - dependence
  - Increased ICP
  - Bradyarrhythmias
  - N/v
  - Sedation/excitation
  - pruritus
  - Vagal effects
    - Miosis, urinary retention, initially defacation then constipation

Opioid duration of action

- Fentanyl: 45-60 minutes
- Codeine: 4-6 hours
- Morphine, oxymorphone, hydromorphone: 2-4 hours
- Butorphanol: 30-60 minutes
- Buprenorphine: 8 hours

Why use preanesthetic medications?

- Decrease anxiety
- Provide chemical restraint
- Decreased doses of other drugs (local anesthetic)
- Provide analgesia

Preoperative evaluation

- Type and length of procedure
  - Small procedures such as biopsies rarely require adjunctive agents except in those very anxious
  - Those procedures anticipated to be:
    - longer than 90 minutes
    - On the head and neck
    - Use of large amounts local anesthetics
  - Better tolerated with adjunctive agents

Preoperative evaluation

- Do a good H&P
  - Pay attention to liver and kidney dysfunction
  - Elderly patients should have dose reduction of medications
  - Hx of alcohol or sedative use
  - ? Pregnant
  - Ask about allergies and adverse reactions to sedatives and pain medications
  - Any drug-drug interactions

Intraoperative monitoring

- Degree depends on medication used, dosage, route, and status of patient
- Get baseline resting BP, HR, and RR
- Check vital signs periodically
- Talk to the patient (the best was to evaluate alertness and signs of distress)
- ECG monitoring, pulse ox, and ACLS

Preoperative sedatives and analgesics

- Routes
  - Oral is preferred
    - Oral offers certain degree of safety, but decreased effectiveness and slower onset of action
    - If using oral need to give 30-60 minutes before the procedure
  - IM offers more rapid onset with higher blood levels
    - Absorption from the deep muscle mass is usually slow and continuous, however, can be erratic
  - IV is the most effective method
    - Most rapid onset
    - Have finer control over desired level of sedation and analgesia
    - Complications from overdosing more likely
    - Need closer patient monitoring
    - Safer to do intermittent dosing than continuous drip in the office

Opioid Agonist	Potency compared to morphine
Morphine	1
Oxycodone (Roxicodone, Percodan, Percocet)	1
Hydrocodone (Lorcet, Lortab, Vicodin)	1
Methadone (Dolophine)	1.5x
Hydromorphone (Dilaudid)	5x
Levorphanol (Levo-Dromoran)	7.5x
Oxymorphone IV (Numorphan)	10x
Fentanyl	100x
Codeine	- 5x
Meperidine (Demerol)	- 10x

Preoperative opioid analgesics

- Morphine
  - Opiate agonist
  - Acts at mu receptors in spinal cord
  - Inhibits substance P release
  - Raises pain threshold
  - Produces euphoria
  - Dose dependent respiratory depression peaking 30 minutes after IM and 90 minutes after SQ
  - Pupillary constriction, bradyarrhythmias

Preoperative opioid analgesics

- Morphine
  - Can get histamine release after IV use leading to pruritus and urticaria
  - Constipation, n/v
  - 2-4 hour duration of action
  - cheap
  - 10 mg IV/SC/IM q 3-4 hours for adults
  - 30 mg po q 3-4 hours for adults
  - .1 mg/kg IV/SC/IM q 3-4 hours pediatrics
  - .3 mg/kg po q 3-4 hours pediatrics

Preoperative opioid analgesics

- Meperidine (Demerol)
  - Opiate agonist
  - Binds to kappa receptors
  - Short duration of action of 1-3 hours
  - Less sedation and nausea than morphine
  - Does cause histamine release
  - Adult dose 50-100 mg IM or SQ q 3-4 hours

Preoperative opioid analgesics

- Meperidine
  - Pediatric dose is .75 mg/kg q 2-3 hours
  - Analgesia begins in 15 minutes and peaks at 45-60 minutes
  - Respiratory depression max at 1 hour on IM and lasts up to 4 hours
  - IV administration can produce tachycardia (mild atropine like effects)
  - can depress cardiac contractility
  - Toxic metabolite→normeperidine→seizures
  - Only effective IM or IV
  - 50mg demerol po = 625 mg ASA

Preoperative opioid analgesics

- Fentanyl (sublimaze)
  - Opiate agonist
  - Binds to kappa receptors
  - 100x more potent than morphine
  - little sedative activity at low doses (1-2 ug/kg)
  - Less likely for n/v than morphine or meperidine
  - Analgesic effect rapid in onset
  - short duration of action 45-60 minutes
  - No histamine release

Preoperative opioid analgesia

- Fentanyl
  - Can stimulate strong cholinergic action leading to bradycardia
  - Get respiratory depression more rapidly, though it is of shorter duration
  - Adult IM dose 50-100 ug with analgesia beginning in 7-8 minutes and lasting 1-2 hours
  - Adult IV starting dose 50-100 ug q 1 hour with almost immediate analgesia and can be repeated every 30-60 minutes
  - Not recommended for pediatric patients.

Sedatives

- The goal of sedative preoperatively is to provide:
  - Anxiety relief
  - Some degree of amnesia
- The level of anxiety relief and amnesia depends on
  - Agent used
  - Dosage
  - Route administered

Sedatives

- Benzodiazepines
  - The preferred preoperative sedative
  - Provides some degree of amnesia depending on dose
  - Very safe and well tolerated
  - Contraindications include narrow and open angle glaucoma

Sedatives

- Diazepam (Valium)
  - Agonist at GABA receptors
  - Preferred agent if oral or sublingual route desired
  - Sublingual route has quicker onset of action
  - Can raise seizure threshold
  - Thus good for procedures that require larger amounts of local anesthesia
  - Usual dose .1-.2 mg/kg or 5-10 mg

Sedatives

- Diazepam
  - Give 30-60 minutes prior to procedure
  - Will last up to 3 hours
  - Peds use 1-2.5mg (.2 mg/kg)
  - If more intense levels of sedation then use IV diazepam
  - IV administration is more likely to cause respiratory depression

Sedatives

- Midazolam (Versed)
  - More potent than diazepam
  - More rapid onset and shorter recovery time
  - Effects begin in 15 minutes and peak in 30-60 minutes
  - Cleared by liver
  - Dose is .07-.08 mg/kg IM (adult and pediatric)
  - Begin with 1 mg IV slowly q 2-3 min up to 5 mg
  - Dose of 1 to 2.5 mg of IV versed equivalent to oral dose of 5-10 mg of diazepam

Sedatives

- Barbituates
  - Causes degrees of hypnosis and drowsiness
  - Anxiety reduction with some respiratory depression
  - Pentobarbital or secobarbital preferred due to short onset and duration
  - Usual onset 20-60 minutes and lasts 3-4 hours
  - Oral dose adults 100-200 mg (1.5mg/kg)
  - Oral dose children 2 mg/kg

Sedatives

- Pentobarbital (Nembutal) and secobarbital (Seconal)
  - available as 50-100 mg caps
  - Pentobarb longer duration of action than secobarbital
  - Do not use IM secondary to erratic absorption
  - Can get paradoxical excitement in elderly and children

Sedatives

- Chloral hydrate
  - Best sedative for infants and small children
  - Rarely produces paradoxical excitement
  - Well tolerated
  - High degree of safety
  - Syrup 500mg/5cc
  - Rectal dose 20-40mg/kg onset in 30-60 min
  - 25-50 mg/kg up to 1000 mg po/pr
  - Adult dose 500-1000 mg
  - Can last up to 5-6 hours
  - Use cautiously in those with liver and renal disease

Sedatives

- Methoxyflurane (Penthrane)
  - Produces sedation and analgesia when breathed by hand held inhaler
  - Do not exceed 15 cc
  - Dose dependent nephrotoxicity
  - Fatal renal toxicity in those on TCN
  - Hepatic toxicity possible

Sedatives

- Nitrous oxide-oxygen sedation
  - 20% nitrous oxide/80% oxygen mixture
  - Equivalent to 15mg morphine
  - Eliminated by lungs
- Advantages
  - Safe
  - Nonallergenicity
  - No preop fasting or medicine
  - Rapid onset of sedation
  - Rapid recovery
  - Low cost

Sedatives

- Disadvantages
  - Inconsistent pain control
  - Respiratory depression
  - Middle ear expansion
  - Pneumothorax
  - Intestinal distention
  - N/v
  - Headache
  - Excessive talking
  - Vivid dreams
  - Induced Sexual fantasies

Adjunctive Agents

- Hydroxyzine (Vistaril, Atarax)
  - Frequently slight decrease in HR and may potentiate opioids
  - 50-100mg adults and .6 mg/kg po in children

Adjunctive Agents

- Atropine
  - Competitively blocks the action of acetylcholine on postganglionic parasympathetic cholinergic receptors.
  - Occasionally used to reduce salivary and bronchial secretions
  - Helps with over stimulation of vagus reflexes induced by preop agents (opioids)
  - Causes mydriasis, blurred vision, dryness of mouth, and tachycardia
  - Dose .3-.6 mg 30-60 minutes before surgery
  - Duration of action 60-90 minutes
- Glycopyrrolate (Robinul-V) is less arrhythmogenic and lasts 2-4 hours

Opioid antagonist

- Naloxone (Narcan)
  - Used to reverse opioid overdose
  - Displaces receptor bound opioids
  - Good for overcoming respiratory/CV depression
  - IV adult dose is .2-.4 mg titrated at rate of .2 mg q2 minutes until response

Benzodiazepine Antagonist

- Flumazenil
  - Benzo receptor antagonist
  - Used to reverse overdose of benzos
  - .2 mg IV every 60 seconds to max of 1 mg
  - Contraindicated in patients on benzos for seizures

Combined drug regimens

- Drugs can have synergistic effects so use caution
- Diazepam 5-10 mg sl 30-60 minutes before surgery with morphine 30 mg and hydroxyzine 25-50 mg IM 20-30 minutes before surgery.

Postoperative Analgesia

- Postoperative pain is inevitable
- Severity depends on complexity and location of surgery
- Also depends on personality of patient
- Pain can occur from
  - Tissue injury
  - Edema or bleeding
  - Ischemic tissue
  - infection

Postoperative analgesia

- Good postop wound care is important
- Ice bag during the first 24 hours is good adjunct in reducing post-op pain.

Postoperative Analgesia

- Acetaminophen
  - Works well for minor procedures and mild to moderate pain
    - Punch bx, excisions, etc.
  - Adults 325-1000mg po q 4-6 hrs do not exceed 4g/day
  - 10 g is the lethal dose
  - Pediatrics 10mg/kg po q 4-6 hours (160mg/5cc)
  - No increased risk of bleeding that can be seen with NSAIDS
  - Inhibits PG synthesis in CNS
  - Few side effects
  - Large doses can damage the liver

Postoperative Analgesia

- NSAIDS
  - Inhibit prostaglandin synthesis by inhibiting COX
  - Differ from acetaminophen by their anti-inflammatory properties
  - Increased risk of bleeding operative and post-operative
  - Adults ibuprofen 200-600mg po q 4-6 hours
  - Do not use with renal failure, GERD, PUD

Postoperative Analgesia

- Opioids
  - If opioids used parentally during the preop period, then reduce postop dose to ¼ the usual dose to decrease risk of overdosage
- Don't worry about addiction
- If people are in severe pain they need the medications!!

Postoperative Analgesia

- Codeine
  - Analgesia begins in 20 minutes and lasts 4-6 hours
  - Adult dose 15-60 mg q 4-6 hours
  - Tylenol #3 (325 mg of Tylenol with 30 mg of codeine)
  - 1-2 po q 4-6 hours
  - Pediatric elixir of 12 mg codeine and 120 mg Tylenol per 5cc→.5-1 mg/kg q 4-6 hours
  - Less euphoria

Postoperative Analgesia

- Oxycodone
  - Derivative of morphine
  - Equipotent to morphine and 10 times more potent than codeine
  - Relief of moderate to moderately severe pain
  - Do not use in those intolerant to codeine as it is partially metabolized to codeine
  - 5 mg po q 6 hours
  - Percocet (5mg oxycodone with 325 mg Tylenol)
    - 1-2 po q 6 hours

Postoperative Analgesia

- Hydrocodone
  - Semisynthetic opioid
  - Vicodin, Lorcet, and Lortab (5 mg hydrocodone and 500 mg Tylenol)
    - Has multiple strengths
  - Vicoprofen (ibuprofen with hydrocodone)

Postoperative Nausea

- It is common after extensive surgery of face or scalp
- Adequate postop analgesia control will reduce potential nausea
- Opioids can induce nausea
- Prochlorperazine (compazine) and promethazine (phenergan)
  - Can use rectally 25 mg q 12 hours and 5mg in children
  - Compazine 5-10 mg po tid-qid prn
  - Phenergan 25 mg po q4-6 hours prn

Discharge criteria

- Need an adult escort present
- Vital signs stable for at least 1 hour
- No respiratory depression
- Oriented to PPT
- Able to walk unassisted
- Take fluids and void
- No n/v present
- No excessive pain
- Bleeding stopped

Other opioids

- Methadone
  - Works on mu receptors
  - Produces less euphoria

Other opioids

- Pentazocine
  - Mixed agonist-antagonist
  - Agonist for kappa receptors
  - Antagonist for mu, delta receptors
  - For moderate pain
  - 1-2 hour duration of action
  - Less euphoria

Other opioids

- Oxymorphone (Numorphone)
  - Mu agonist
  - Similar to morphine
  - 10 times as potent
  - Less vomiting and better sedation
  - Does not cause histamine release
  - Slightly shorter duration of action
  - More expensive than morphine

Other opioids

- Butorphanol
  - Kappa partial agonist, mu antagonist
  - 5-10x as potent as morphine
  - Minimal sedative effects
  - Minimal cardiopulmonary effects
  - 3-4 hour duration of action