

Pharmacological treatment of pain

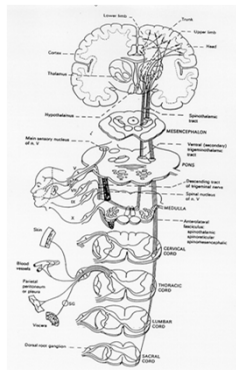
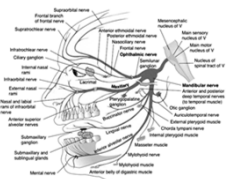
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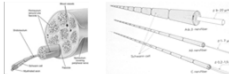
Diagnostic measures of pain

- Anamnesic: *Listen to the patient!*
- Clinical examination
- X-ray and/or CT-scanning
- Laboratory tests
- Biopsy
- Referral to other specialties: Neurology, neurosurgery, ENT, psychiatry, psychology etc.

Pain pathway from the face Trigeminal nerve



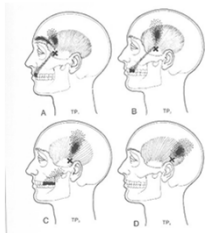
Peripheral nerves



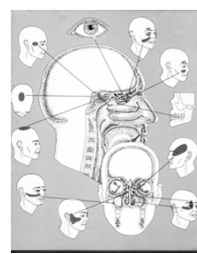
Fiber	Diameter μm	Lednings-hastighed (m/s)	Innervation
A α A β	12-20	70-120	Mekanoreceptorer
A δ	2-7	10-30	Kraftigt tryk Kulde Smerte viscera
C	1-5	<2-5	Varme Smerte viscera

Referred pain in the face

M. Temporalis



Sinus



Pain control = no pain

- **Pain prophylaxis:**
Prevent pain before they arise
("preemptive analgesia")
- **Pain therapy:**
Treat existing pain:
 - a) symptomatic treatment (reduce/remove smerte)
 - b) causal treatment (eliminate the cause)

Effect of af pain prophylactics

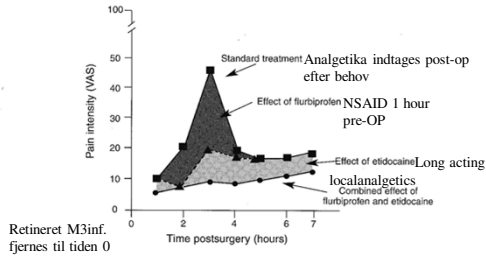
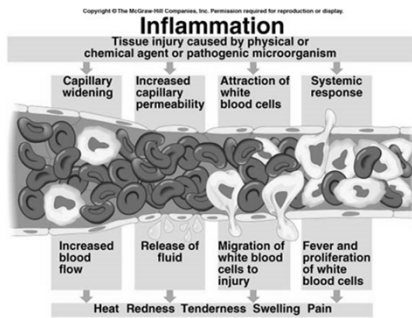


Fig 19-3 The suppression of postoperative pain by the combination of an NSAID, flurbiprofen, and etidocaine, a long-acting local anesthetic. The contribution of each drug to the total effect is shown.

Inflammation



The five cardinal symptoms:

1. Calor = heat
2. Rubor = redness
3. Tumor = swelling (oedema)
4. Dolor = pain
5. Functio laesa = impaired function

The five cardinal symptoms:

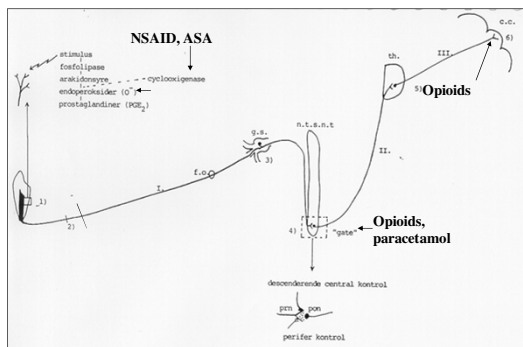
- Heat, redness and swelling:
vasodilatation

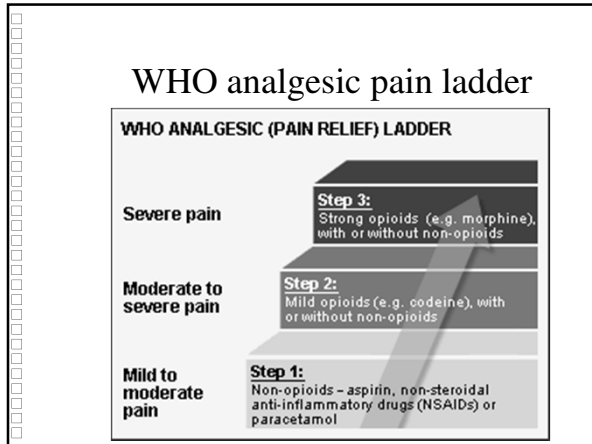
Purpose: More blood to the tissue:
Oxygen, leukocytes, antibodies and proteins
to defend against infection og promote
healing

The five cardinal symptoms:

- Pain induced by biochemical, *algogene substances* → stimulation of nociceptors
- Algogene substances: prostaglandines, noradrenalin, serotonin, histamine, bradykinin, K+, H+

Pain control with analgetics



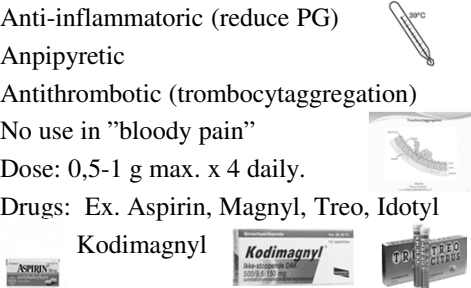


- Primary analgetics:**
- Strong opioids (ex. Morphine)
 - Weak/mild opioids (ex. Tramadol and Codeine)
 - NSAID (nonsteroid antiinflammatoriske stoffer)
 - Paracetamol
 - Acetylsalicylic acid (ASA)

- Secondary analgetics:**
- Ex.:*
- Psychopharmacological drugs (ex. TCA, Anafranil)
 - Antiepileptic drugs (Gabapentin)
 - Glucocorticoids (ex. Dexametason)

Acetylsalicylic acid (ASA)

- Weak to moderate pain
- Anti-inflammatory (reduce PG)
- Antipyretic
- Antithrombotic (trombocyttagregation)
- No use in "bloody pain"
- Dose: 0,5-1 g max. x 4 daily.
- Drugs: Ex. Aspirin, Magnyl, Treo, Idotyl

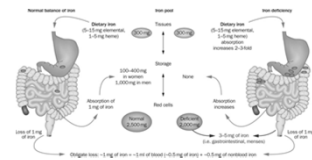


Acetylsalicylic acid (ASA)


- OBS:
 - Pregnancy (1.+3. trimester)
 - Anticoagulation therapy
 - GI problems (peptic ulcer, Mb. Chron)
 - Allergy (crosslink allergy to NSAID)
 - Thrombocytopenia

Acetylsalicylic acid (ASA)

- OBS:
 - Asthma (allergy)
 - Liver/kidney disease
 - Risk of occult blood loss at longterm use




Paracetamol




- Approved 1974 (DK)
- Large packages on receipt 1/10-2013
- Consumption decreased 6 %
- Admission due to poisoning decreased 31 %
- Suicide attempts (15-24 år – 11000/år – 650 "successful") using weak analgetics reduced 58 %

Paracetamol



- Weak to moderate pain
- Very few side effects
- Antipyretic
- Weak anti-inflammatory
- Suitable for children
- Different medication forms:
 - Tablets, mixture, suppositories
- Dose: 1 g 3-4 x daily. Children: 50 mg/kg/døgn in 3-4 doses daily
- Drugs: Paracetamol, pamol, panodil, pinex

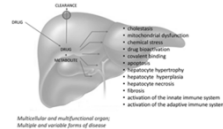
Paracetamol



- OBS: - Pregnancy OK (obs cryptorchidism)
- Anticoagulation therapy using K-vitamin antagonists
- Risk of occult blood loss at longterm use
.....and OBS!→

Paracetamol - Hepatotoxicity

- Single dose > 4 g → hospital for antidote treatment (N-acetylcystein)
- Liverdamage single dose > 10-15 g.
- Death single dose > 25 g (3-4 dage)
- Liver tranplantation



NSAID

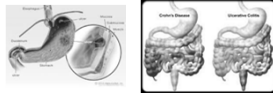
- Weak to moderate pain
- Originally developed to treat rheumatic diseases (anti-inflammatory effect)
- Anti-inflammatory (reduce PG in CNS)
- Anipyretic
- Antithrombotic (trombocyttaggregation)
- Dose: 400-600 mg x 3-4 daily (Ibumentin)
50 mg x 3 daily (Voltaren)
500 mg x 2 daily (Naproxen)

NSAID + paracetamol

- A very effective pain relief treatment
- Ex. 400-600 mg ibumentin 3-4 x dgl. + 1 g paracetamol daily
- Attack the pain at two sides:

NSAID

- OBS: - Pregnancy (1.+3. trimester)
- Anticoagulation therapy
- GI problems (peptic ulcer, Mb. Crohn

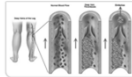


- Allergy (crosslink allergy to NSAID)
- Thrombocytopenia

NSAID and thromboembolism

- Risk of thromboembolism with the use of high doses (> 1600-1800 mg/daily) for a long period (weeks/months)

- DVT



- AMI



- Apoplexy



NSAID – COX 2 inhibitors

- Drugs: Ex. Celebra® (Celecoxib)
- Great risk of thromboembolism
- Only with great risk of GI bleeding
- Lowest dose for a short period
- Very rare use in dentistry
- Specialist treatment between cardiologist and ex. Rheumatologist (R.A.)

Strong opioids

- Strong/severe pain
- Analgetic
- Euphoric
- Anxiolytic
- Sedative
- Respiratory depressant (antidote: Naloxone)
- Many adverse effects

Strong opioids

- Drugs: Morphine, pethidine
- Dose: Ex. tbl. Morfin 10 mg x 4-6 daily
- Only ordained by the pt.'s physician

Strong opioids

- OBS:
 - Caution by pregnancy
 - No use in lactating women
 - Nausea/vomiting
 - Obstipation
 - Tolerance
 - Itching
 - Hallucinations
 - Xerostomia!

Weak opioids - Codeine

- Analgetic
- Antitussive effect
- Often combined with ASA, paracetamol, NSAID
- Tablet á 25 mg
- Dose: 25-50 mg max. x 4 daily

Weak opioids – Codeine

- OBS: - Pregnancy
- Respiratory insufficiency (ex. severe asthma/KOL)
- No effect on 10 % of the population (prodrug, 5-10 % converted to morphine in the liver)

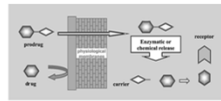


FIGURE 2 - Representation of a prodrug design to enhance bioavailability

Weak opioids - Tramadol

- Tramadol: fx Nobligan®: 50-100 mg 3-4 x dagl.
- OBS: - Anticoagulation therapy
- Pregnancy
- Not in lactating women
- Obs alcohol, psychopharma
- Xerostomia
- Nausea
- Dizziness

Combination of analgetics

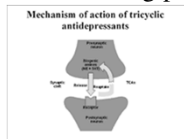
Paracetamol (400-500 mg) + codeine (30 mg),
ex. Kodipar®, Fortamol® eller Pinex
Comp.®

Antiepileptic drugs

- Used in neuralgic pain Anvendes ved neuralgiforme smerter, ex. trigeminal neuralgia
 1. Karbamazepin (Tegretol®) 200-800 mg daily
 2. Gabapentin 300-400 mg 3 x daily
 3. Fenytoin + clonazepam (Rivotril®)
- Often in collaboration with neurologist

Tricyclic antidepressants (TCA)

- Increases serotonin in the descending pain control (CNS level)



- Use in chronic pain ex. clomipramin (Anafranil®) 25-50 mg x 3 dagl. eller amitriptylin (Saroten®)
- Obs LA with adrenaline (hypertensive crisis)
