Annen litteratur for de interesserte:

Tidsskrift: Endodontic Topics 2002 -

Interaktivt: Visual Endodontics, PC-stuen
A skull of a woman from a heathen grave at Hólaskógi in Thjórsárdal. It is probable that a dental infection in the upper jaw was the cause of her death.
Comparison between acute and chronic inflammation:

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<th>Acute</th>
<th>Chronic</th>
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<td>Pathogens, injured tissues</td>
<td>Persistent acute inflammation due to non-degradable pathogens, persistent foreign bodies, or autoimmune reactions</td>
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<td><strong>Major cells involved</strong></td>
<td>Neutrophils, mononuclear cells (monocytes, macrophages)</td>
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wikipedia
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<td><em>Primary mediators</em></td>
<td>Vasoactive amines, eicosanoids (In biochemistry, eicosanoids are signaling molecules made by oxygenation of twenty-carbon essential fatty acids, (EFAs).)</td>
<td>IFN-γ and other cytokines, growth factors, reactive oxygen species, hydrolytic enzymes</td>
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<td>Bradykinin</td>
<td>Kinin system</td>
<td>A vasoactive protein which is able to induce vasodilation, increase vascular permeability, cause smooth muscle contraction, and induce pain.</td>
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<td>C3</td>
<td>Complement system</td>
<td>Cleaves to produce C3a and C3b. C3a stimulates histamine release by mast cells, thereby producing vasodilation. C3b is able to bind to bacterial cell walls and act as an opsonin, which marks the invader as a target for phagocytosis.</td>
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<td>C5a</td>
<td>Complement system</td>
<td>Stimulates histamine release by mast cells, thereby producing vasodilation. It is also able to act as a chemoattractant to direct cells via chemotaxis to the site of inflammation.</td>
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<td>Factor XII (Hageman Factor)</td>
<td>Liver</td>
<td>A protein which circulates inactively, until activated by collagen, platelets, or exposed basement membranes via conformational change. When activated, it in turn is able to activate three plasma systems involved in inflammation: the kinin system, fibrinolysis system, and coagulation system.</td>
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<tr>
<td>Membrane attack complex</td>
<td>Complement system</td>
<td>A complex of the complement proteins C5b, C6, C7, C8, and multiple units of C9. The combination and activation of this range of complement proteins forms the <em>membrane attack complex</em>, which is able to insert into bacterial cell walls and causes cell lysis with ensuing death.</td>
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<td>Plasmin</td>
<td>Fibrinolysis system</td>
<td>Able to break down fibrin clots, cleave complement protein C3, and activate Factor XII.</td>
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<td>Thrombin</td>
<td>Coagulation system</td>
<td>Cleaves the soluble plasma protein fibrinogen to produce insoluble fibrin, which aggregates to form a blood clot. Thrombin can also bind to cells via the PAR1 receptor to trigger several other inflammatory responses, such as production of chemokines and nitric oxide.</td>
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Bioprosesser i pulpa
sekundær dentin, reactionary dentin
annen hårdvevsdannelse
betennelse
Vital, inflamed: reversible-irreversible pulpitis

Microabscesses can heal
Mjør & Tronstad 1972
Fig. 1.3. Breaks in the muco-cutaneous barrier associated with teeth. (a) Attrition (A), abrasion or trauma exposes the pulp. (b) Dental caries (C) reaches the pulp with subsequent infection of the pulp and periapical tissues. (c) Dental plaque (P) penetrates the gingival cuff and bacteria invade the gingival and periodontal tissues.
Periapical diagnoses

- Transient AP
- Incipient AP
- Condensing AP
- Acute apical periodontitis AAP
- Chronic apical periodontitis CAP
  - Dental granuloma
  - Cyst: true cyst or bay cyst
- Exacerbating CAP
Adielsson et al 2003
Success = absence of apical periodontitis: clinically, radiographically, histologically

Prevention: vital, inflamed

Treatment: necrotic, infected

Fig. 1.1
Tooth characteristics in relation to endodontic diagnosis

- Caries
- Erosion/abrasion/attrition
- Defective fillings/margins
- Tooth fractures
Fig. 1.6
Fig. 3.1. Pathways of periapical inflammation and bone destruction.
Activation of Phagocytes

Activation

IL-1, TNF
Endothelium activation
Leukocyte adhesion

PAF
Leukocyte adhesion

IL-8, LTB4
Increase of Vascular Permeability

Chemotaxis

LPS
Peptidoglycan
LTA
Fimbriae
Metabolites

Acute aspects; Siqueira & Barnett 2004
Activation of the Complement System

Complement Activation

C3a → Mast Cell Histamine
C4a → Increase of Vascular Permeability
C5a

Chemotaxis

LPS
Peptidoglycan
LTA
Fimbriae

Neutrophil

Acute aspects; Siqueira & Barnett 2004
Chemotaxis

Phagocytes

IL-8, LTB4

Complement Activation

C5a

Neutrophils
Elastase
Collagenase
Gelatinase
Oxygen radicals

Tissue Damage
Abscess formation

Acute aspects; Siqueira & Barnett 2004
Acute aspects; Siqueira & Barnett 2004
Bacterial components

Nerve stimulation

Parasympathetic Sensory Sympathetic
VIP CGRP SP NPY

Permeability

Chemotaxis

Phagocytosis

Permeability

Vasodilatation

PGE2

BRADYKININ

HISTAMINE

Met-enk Leu-enk

PMN Mono
cyte

SP

CGRP

VIP

Parasympathetic

CGRP Sensory

SP

NPY Sympathetic

Nerve stimulation

Bacterial components

Fig. 3.6
Infection, not necrosis, is essential for development of AP

Ørstavik, Essential Endodontology 1998; courtesy of Lambjerg Hansen
Bacterial components

Th1 cells

Macrophages

Th2 cells

Osteoclastic bone resorption

IFNα, GM-CSF, TNFα

IL-1, TNFα, IL-11

IL-4,-6,-10,-13

IL-10

IL-10

Fig. 3.7
The resorptive process

- Denudation:
  - Cementum
  - Predentin
- Remodelling:
  - Deposition
  - resorption
- Infectious/pathological
  - Internal inflammatory
  - External inflammatory
- Physiological/protective
  - Pressure induced
  - Surface repair
  - Replacement/ankylosis
PU.1 regulates cytokine-dependent proliferation and differentiation of granulocyte/macrophage progenitors

A mononuclear phagocyte colony-stimulating factor (M-CSF) synthesized by mesenchymal cells

Receptor activator of nuclear factor- B ligand (RANKL) is a critical cytokine for osteoclast differentiation and activation and an essential regulator of osteoblast-osteoclast cross-talks (4). RANKL activates its receptor RANK, which is located on osteoclastic lineage cells, and this interaction is prevented by osteoprotegerin (OPG), which acts as an endogenous receptor antagonist and blocks the effects of RANKL (4). While RANKL enhances bone resorption and bone loss and promotes osteoporosis, OPG has opposite effects (5).
Hvordan oppstår odonto/osteklaster?

• Osteoclasts formation requires the presence of RANK ligand (receptor activator of nuclear factor κβ) and M-CSF (Macrophage colony-stimulating factor). These membrane bound proteins are produced by neighbouring stromal cells and osteoblasts; thus requiring direct contact between these cells and osteoclast precursors.

• M-CSF acts through its receptor on the osteoclast [precursor], c-fms (colony stimulating factor 1 receptor), a transmembrane tyrosine kinase-receptor, leading to secondary messenger activation of tyrosine kinase Src. Both of these molecules are necessary for osteoclastogenesis and are widely involved in the differentiation of monocyte/macrophage derived cells.

Hvordan oppstår odonto/osteklaster?

• **RANKL** is a member of the tumour necrosis family (**TNF**), and is essential in osteoclastogenesis. RANKL knockout mice exhibit a phenotype of **osteopetrosis** and defects of tooth eruption, along with an absence or deficiency of osteoclasts. RANKL activates NF-κβ (nuclear factor-κβ) and NFATc1 (nuclear factor of activated t cells, cytoplasmic, calcineurin-dependent 1) through **RANK**. NF-κβ activation is stimulated almost immediately after RANKL-RANK interaction occurs, and is not upregulated. NFATc1 stimulation, however, begins ~24-48 hours after binding occurs and its expression has been shown to be RANKL dependent.

• Osteoclast differentiation is inhibited[/regulated] by **osteoprotegerin (OPG)**, which binds to RANKL thereby preventing interaction with RANK.

Figure 2. Mode of action and biological effects of RANKL, RANK, and OPG on bone metabolism and the immune system. (1) RANKL is expressed by osteoblastic lineage cells (cell-bound RANKL) and activated T lymphocytes (soluble RANKL). A truncated ectodomain form of RANKL is derived from the cell-bound form after cleavage by the enzyme TACE. (2) All three RANKL variants stimulate their specific receptor, RANK, which is located on osteoclastic and dendritic cells and thus modulate various biological functions. (3) OPG is secreted by osteoblastic lineage and other cells and acts as a soluble receptor antagonist which neutralizes RANKL (black), and thus, prevents RANKL-RANK interaction. (4) OPG also blocks the pro-apoptotic cytokine TRAIL (white).

OSTEOBLAST

1. Differentiation
2. Activation
3. Fusion
4. Survival

OSTEOCLAST

DENDRITIC CELL

1. Survival
2. Immunostimulatory activity

OPG  •  RANKL  △  RANK  ○  TRAIL  ▲  TACE
Lesion capsule
Cyst epithelium

Bay cyst
True cyst
- Dentin protection
- Pulp capping
- Partial pulpotomy
- Pulpotomy
- Pulpectomy
- Disinfection
- Pain control
- Antibiotics
Vital Infected pulp; apical periodontitis Instrumentation & irrigation Dressing

Filled & healing Complete healing

Root canal infection Time
Sublethal cellular damage

Damage to Blood Vessels
Activation of Hageman Factor

Kinin system
Clotting system
Fibrinolytic system

Bradykinin
Fibrinopeptides
Fibrin products

Inflammation

Sensory nerve endings
Substance P
CRF P

Siqueira & Barnett 2004
Apical root resorption

Traumatic; aseptic

Traumatic; infective
Side diagnoses: Vertical fracture