The formation of primary dentin continues until the tooth becomes functional (Linde & Goldberg 1993) or until the root apex is closed (Torneck 1994). Therefore, dentin formation proceeds at a slower rate after this point. Odontoblasts die off in the region of their cell bodies as well as in the region of their termini in the dentinal tubules. This results in the formation of reactionary dentin as an age change during dentinogenesis. Tertiary dentin formation occurs from irritation that occurs during secondary dentinogenesis and may be caused by dental abrasion, attrition, erosion or dental caries (Torneck 1994). Lesot et al. (1993) defines reactionary dentin as the result of irritation of postmitotic odontoblasts.

Reparative dentin is formed by odontoblasts or odontoblast-like cells which differentiate from pulp cells after the cell death of primary odontoblasts (Magloire et al. 1992, Magloire et al. 1996). The continued intratubular mineralization of dentin may occur as an age change and may result in complete occlusion of the tubules. This process may be accelerated by external stimuli of various types, including certain restorative materials. Another type of intratubular remineralization includes precipitation of mineral salts within the tubules, for example, as found in the “transparent zone” of dentin subjacent to a slowly progressing caries lesion. Both types of intratubular remineralizations are collectively referred to as sclerotic dentin.
Odontoblasts and process

Odentoblasts process

Odentoblast cells

Microcanals connecting dentine tubules

Dentin penetration: to and from the pulp

The three (mechanisms of protection by dentin) described:
1) diffusion limitation;
2) limited wetness for hydrolysis; and
3) buffering by dentinal hydroxyapatite,

appear to allow the relatively safe use of a wide range of tooth restorative materials.


1) Microbial pathways in tubules
2) Antigenic diffusion in all directions
Located in the center of the pulp chamber, which has many cells and an extensive vascular supply, similar to cell-rich zone.

Increased density of cells as compared to cell-free zone and also a more extensive vascular system.

Cell-free zone

Fewer cells than odontoblastic layer. Nerve and capillary plexus located here.

Cell-rich zone

Increased density of cells as compared to cell-free zone and also a more extensive vascular system.

Pulpal-core

Located in the center of the pulp chamber, which has many cells and an extensive vascular supply, similar to cell-rich zone.

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CD43 is a cell surface-associated mucin that is abundantly expressed by most leukocytes, and that appears to function as a negative regulator of cell surface interactions, providing a repulsive barrier around cells. [1995]

IL-1α and IL-1β
Both IL-1α and IL-1β are produced by macrophages, monocytes, and dendritic cells. They form an important part of the inflammatory response of the body against infection. These cytokines increase the expression of adhesion factors on endothelial cells to enable transmigration of leukocytes, the cells that fight pathogens, to sites of infection and re-set the hypothalamus thermoregulatory center, leading to an increased body temperature which expresses itself as fever. IL-1 is therefore called an endogenous pyrogen.

The increased body temperature helps the body’s immune system to fight infection. IL-1 is also important in the regulation of hematopoiesis. IL-1β production in peripheral tissue has also been associated with hyperalgesia (increased sensitivity to pain) associated with fever.[6]

For the most part, these two forms of IL-1 bind to the same cellular receptor. This receptor is composed of two related, but non-identical, subunits that transmit intracellular signals via a pathway that is mostly shared with certain other receptors. These include the Toll family of innate immune receptors and the receptor for IL-18. IL-1α .... is produced by many cell types but is only secreted by monocytes and macrophages.

Aδ- og C-fibrenes funksjon

<table>
<thead>
<tr>
<th>Muscle control</th>
<th>Touch, vibration</th>
<th>Cold perception, pain</th>
<th>Warmth perception, pain</th>
<th>Heart rate, blood pressure, appetite, G.I.T functions</th>
</tr>
</thead>
<tbody>
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<td>Touch, vibration, position, nociception</td>
<td>Cold perception, pain</td>
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<td></td>
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Perifere nervefibre – tykke og tynne

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<thead>
<tr>
<th>Axon type</th>
<th>Aδ</th>
<th>Aβ</th>
<th>Aδ</th>
<th>C</th>
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<tbody>
<tr>
<td>Diameter (µm)</td>
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<td>6-12</td>
<td>1-5</td>
<td>0.2-1.5</td>
</tr>
<tr>
<td>Hastighet (m/s)</td>
<td>80-120</td>
<td>35-75</td>
<td>5-35</td>
<td>0.5-2.0</td>
</tr>
<tr>
<td>Forekomst</td>
<td>1 : 4</td>
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Pulp protection is prevention of apical periodontitis and spread of oral infection

Perifere nervefibre – tykke og tynne

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Responses of the Pulp

- Productive
- Nervous
- Cellular
- Vascular
- Inflammatory
- Degenerative
  (Molecular mechanisms)

Normal and pathological responses

- Normal:
  - Secondary and reactionary dentin formation
  - Pain reactions
- Pathological:
  - Tertiary dentin formation
  - Acute inflammation & pain
  - Chronic inflammation & pain
  - (Productive response)

Reactive dentinogenesis during dental caries may result from the solubilization of growth factors, **transforming growth factor-beta (TGF-beta)**, from the dentin matrix which initiate the stimulation of odontoblasts (Smith et al. 1995, Sloan et al. 2000a). It has been demonstrated that TGF-beta 1 and beta 3 may have inductive effects on pulpal cells (Sloan & Smith 1999). Recent studies show that dentin and bone matrix contain various **angiogenic growth factors** (Roberts-Clark & Smith 2000), **bone morphogenic proteins** (Sloan et al. 2000b), **bone sialoproteins and osteopontin** (Qin et al. 2001), which may be beneficial to the reparative response of the dentin-pulp complex.

**beta-defensin-2**
**macrophage inflammatory protein-3alpha**

**TRANSFORMING GROWTH FACTOR-BETA (TGF-beta)** is a biological protein. TGF beta controls proliferation, differentiation, and other functions in most cell types. It can also act as a negative autocrine growth factor.
Macrophage inflammatory proteins (MIP) belong to the family of chemokines known as chemotactic cytokines. In humans, there are two major forms, MIP-1α and MIP-1β, that are now officially named CCL3 and CCL4 respectively. Both are major factors produced by macrophages after they are stimulated with bacterial endotoxins. They activate human granulocytes (neutrophils, eosinophils and basophils), which can lead to acute neutrophilic inflammation. They also induce the synthesis and release of other pro-inflammatory cytokines such as interleukin 1 (IL-1), IL-6 and TNF-α from fibroblasts and macrophages. The genes for CCL3 and CCL4 are both located on human chromosome 17.

Defensins are small (29-51 residue) cysteine-rich cationic proteins found in both vertebrates and invertebrates. They are active against bacteria, fungi and enveloped viruses. They consist of 28-42 amino acids including six to eight conserved cysteine residues. Cells of the immune system contain these peptides to assist in killing phagocytized bacteria, for example in neutrophil granulocytes and almost all epithelial cells. Most defensins function by penetrating the microbial cell membrane by way of electrical attraction, and once embedded, forming a pore in the membrane which allows efflux.

Dentin (hyper)sensitivity

- Pain elicitation
- Differential character
- Mechanisms
- Treatment

Nervous response
Defensins are small cysteine-rich cationic proteins found in both vertebrates and invertebrates. They are active against bacteria, fungi, and many enveloped and nonenveloped viruses. Cells of the immune system contain these peptides to assist in killing phagocytized bacteria, for example in neutrophil granulocytes and almost all epithelial cells. Most defensins function by binding to microbial cell membrane and once embedded, forming pore-like membrane defects that allow efflux of essential ions and nutrients.

Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. They are single membrane-spanning non-catalytic receptors that recognize structurally conserved molecules derived from microbes. Once these microbes have breached physical barriers such as the skin or intestinal tract mucosa, they are recognized by TLRs which activates immune cell responses.
In all, thousands of genes are activated by TLR signaling, and collectively, the TLRs constitute one of the most pleiotropic yet tightly regulated gateways for gene modulation.

**Normal and pathological stimuli**

- **Age and use, normal wear**
- **Pathological:**
  - Attrition (*normal* tooth on tooth: the act of wearing or grinding down by friction), erosion (to eat into or away by slow destruction of substance (chemical: as by acid, infection, or cancer), abrasion (pathological mechanical: a wearing, grinding, or rubbing away by friction), gingival recession
  - Caries and infection
  - Mechanical: orthodontics
  - Mechanical: preparation
  - Chemicals
  - “micro-leakage”; “nano-leakage”
Normal and pathological stimuli

- Age and use, normal wear
- Pathological:
  - Attrition, erosion, abrasion, recession
  - Caries and infection
  - Mechanical: orthodontics (EGF released following orthodontic force application plays a part in the angiogenic response of the pulp; SP stimulates the production of PGE2 and RANKL and promoted bone resorption, and may be involved in pulp inflammation and root resorption during orthodontic tooth movement)
  - Mechanical: preparation
  - Chemicals: medicaments, dental materials' components
  - "micro-leakage"; "nano-leakage"

ANALYSIS OF PULPAL REACTIONS TO RESTORATIVE PROCEDURES, MATERIALS, PULP CAPPING, AND FUTURE THERAPIES.

Peter E. Murray*, L. Jack Windsor, Thomas W. Smyth, Abeer A. Hafez, Charles F. Cox

Murray et al 2002

Cordeiro et al 2008

Bergenholtz et al.
Total etch issues:
pulp damage or complete control?


Clearfil 5 d
Ca(OH)2 180 d
Clearfil 180 d