Types of Dentin

- **Dentin**
  - Primary physiologic dentin
  - Circumpulpal dentin and predentin

- **Mantle dentin**
  - Slightly less mineralized than other layers of primary dentin, i.e. circumpulpal dentin.

- **Secondary physiologic dentin**
- **Tertiary dentin or reparative dentin or reactionary dentin and/or irregular secondary dentin**

- **Intertubular dentin**
- **Peritubular dentin**

Tertiary dentin (reactionary or reparative or irregular secondary dentin) is the outcome of odontoblastic response to irritation occurring mainly during secondary dentinogenesis and is caused by dental abrasion, attrition, cavity preparation, erosion or dental caries (Torneck 1994). Lesot et al. (1993) defines

reactionary dentin to be the result of irritation of postmitotic odontoblasts.

whereas

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).

Continued intratubular mineralization of dentin occurs as an age change and may result in complete obturation of the tubules. This process may be accelerated by external stimuli of various types, including certain restorative materials.

Another type of intratubular mineralization 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

Dentin

Pulp

Odontoblast process

Odontoblast cells

Stock et al.

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. Fewer cells than odontoblastic layer. Nerve and capillary plexus located here. Lines the outer pulpal wall and consists of the cell bodies of odontoblast. Secondary dentin may form in this area from the apposition of odontoblast.

<table>
<thead>
<tr>
<th>Zones-from outer to inner zone</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odontoblastic layer</td>
<td>Lines the outer pulpal wall and consists of the cell bodies of odontoblast. Secondary dentin may form in this area from the apposition of odontoblast.</td>
</tr>
<tr>
<td>Cell-free zone</td>
<td>Fewer cells than odontoblastic layer. Nerve and capillary plexus located here.</td>
</tr>
<tr>
<td>Cell-rich zone</td>
<td>Increased density of cells as compared to cell-free zone and also a more extensive vascular system.</td>
</tr>
<tr>
<td>Pulpal-core</td>
<td>Located in the center of the pulp chamber, which has many cells and an extensive vascular supply, similar to cell-rich zone.</td>
</tr>
</tbody>
</table>

CGRP nerve fibers branching peripherally and into dentin, but avoiding reactionary dentin. (Byers et al 1996)

Recent findings have indicated that immune responses are subjected to modulation by the sympathetic nervous system (SNS). Moreover, the findings show that the SNS inhibits the production of pro-inflammatory cytokines, while stimulating the production of anti-inflammatory cytokines. The present review is an attempt to summarize the current results on how the SNS affects inflammation in dental tissues. In dental tissues, it has been found that the SNS is significant for recruitment of inflammatory cells such as CD 4+3+ granulocytes. Sympathetic nerves appear to have an inhibitory effect on osteoclasts, odontoclasts, and on IL-1β production. The SNS stimulates reparative dentin production, since reparative dentin formation was reduced after sympathectomy. Sprouting of sympathetic nerve fibers occurs in chronically inflamed dental pulp, and neural imbalance caused by unilateral sympathectomy recruits immunoglobulin-producing cells to the dental pulp. In conclusion, this article presents evidence in support of interactions between the sympathetic nervous system and dental inflammation.

Fig. 7.1. A. Blood vessels in a healthy, adult pulp. B. Detail (courtesy of Z. H. Perin).
**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 reset 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]

**IL-1α and IL-1β**

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-fibrene funksjon**

Virk A et al, Nature Clinical Practice, 2006

**Perifere nervefibre – tykke og tynne**

<table>
<thead>
<tr>
<th>Axon type</th>
<th>Aα</th>
<th>Aβ</th>
<th>Aδ</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (µm)</td>
<td>13-20</td>
<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>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Pulp protection is prevention of apical periodontitis and spread of oral infection**
Normal and pathological responses

- Normal:
  - Secondary and reactionary dentin formation
  - Pain reactions

- Pathological:
  - Tertiary dentin formation
  - Acute inflammation & pain
  - Chronic inflammation & pain
  - (Productive response)

Reactivity 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 protein-3alpha and beta-defensin-2 stimulate dentin sialophosphoprotein gene expression in human pulp cells. [ie, including odontoblasts]

Biochem Biophys Res Commun. 2003 Jul 11;306(4):867-71

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's 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

The hydrodynamic theory

Bergenholtz et al.
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 phagocytosed 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 constitutes one of the most pleiotropic yet tightly regulated gateways for gene modulation.

Macrophages & dendritic cells

Wikipedia

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 pulpal inflammation and root resorption during orthodontic tooth movement)
  - Chemicals: medicaments, dental materials' components
  - "micro-leakage"; "nano-leakage"

Normal and pathological stimuli

- Age and use, normal wear
- Pathological:
  - http://crobm.iadrjournals.org/cgi/content/full/13/6/509
  - 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.

"micro-leakage"; "nano-leakage"
Total etch issues:
pulp damage or complete control?