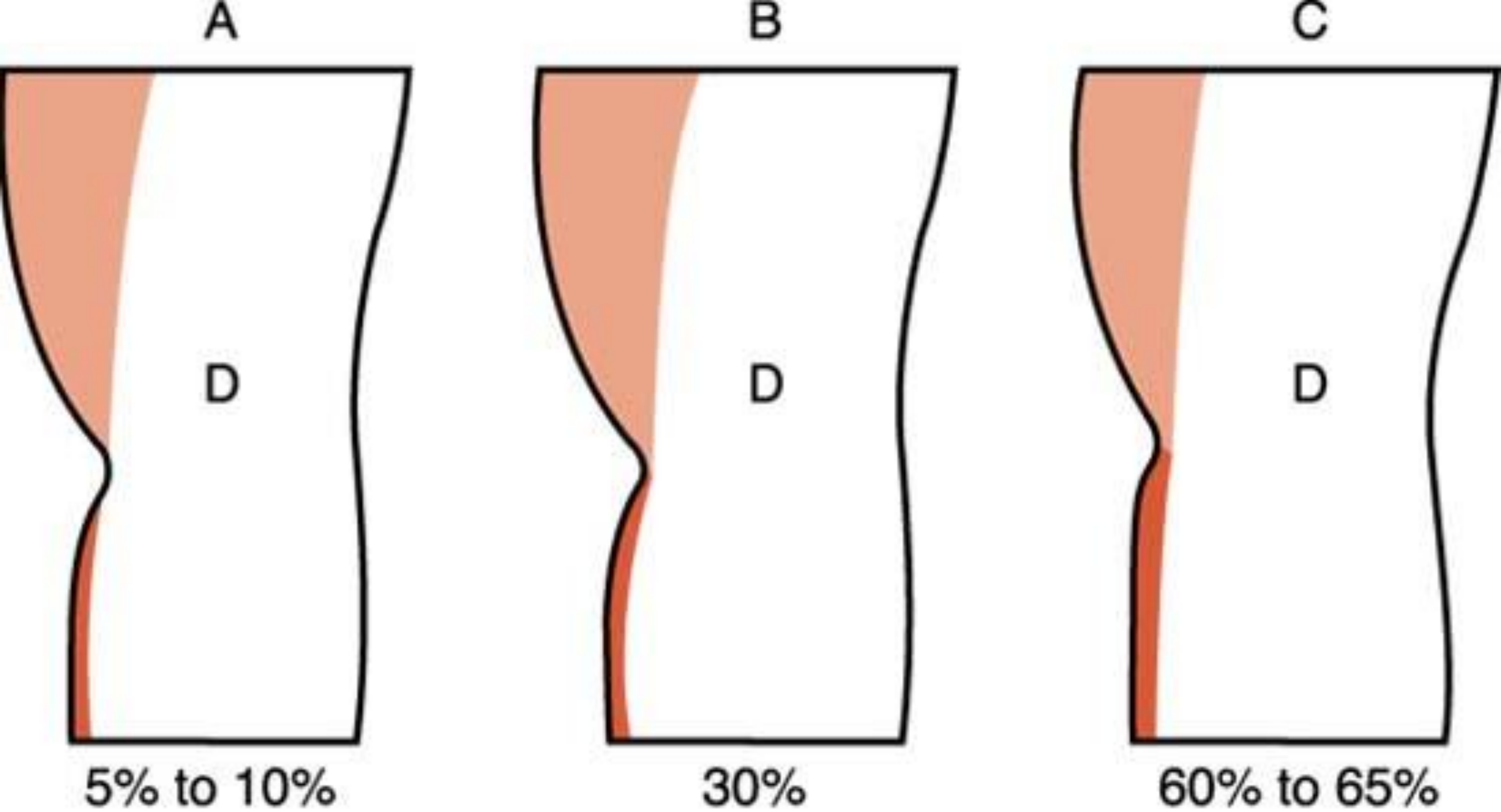
Cementogenesis

Molnár Bálint
2016



Cemento-enamel junction

Classification I

Cementum can be classified based on position, cell-content, fiber-content

Based on position

radicular cementum
coronal cementum

Based on presence of cells

cellular **cementum**
A*cellular cementum*

Based on presence of fibers

Fibrillar cementum
afibrillar **cementum**

Classification II

Acellular cementum doesn't include cellular elements in the matrix.

Cementocytes residing in lacunae can be found in ***cellular cementum.***

Fibrillar cementum is the most important part of cementum, the matrix is based on calcified collagen fibers.

The organic matrix of ***afibrillar cementum*** is based on fine, non-collagenic fibers, there is no contact with the Sharpey-fibers.

Acellular fibrillar cementum

Covers the coronal two-third of the root surface. ***Acellular fibrillar cementum*** is a thin, translucent, non-cellular mineralized tissue.

Histologically, a characteristic lamellar structure (paralell to the root surface) can be seen after dalcination and staining because of the appositional development.

These lines of apposition represent the cyclic, slow appositioning of the cementum. This is a slow process, cells syntethising the matrix stay on the outer surface.

A lot of extrinsic (Sharpey) fibers are integrated into the matrix.

After eruption, the thickness of cementum is increased during lifetime.

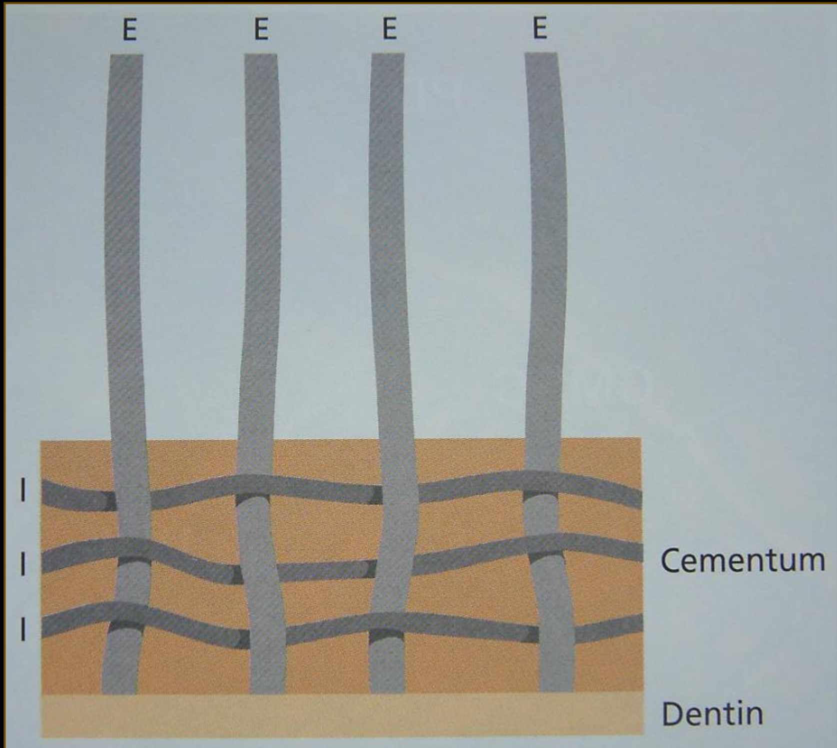
The maximal thickness can reach up to 60-70 microns.

The thickness of cementum decreases coronally, at the cemento-enamel junction.

Collagen fibers are surrounded by a fine, granulated amorph matrix.

Both intrinsic and extrinsic fibers can be found.

The majority of the fibers is directed perpendicularly onto the root surface. These are the main proportion of extrinsic periodontal ligament fibers, anchored into the cementum.



Cellular, fibrillar cementum

Cellular fibrillar cementum covers the apical third of the root surface and the furcations.

Cementocytes can be found in the calcified matrix.

Appositional growth is irregular compared to cellular cementum.

Appositioned layers of cementum are thicker and contain more Sharpey-fibers.

The ongrowth of cementum and mineralization is considerably faster compared to acellular cementum.

Cementoblast synthetising the matrix stay in the matrix and become cementocytes later on.

Secondary cementum
Periodontal ligament
Alveolar bone
Root
Fibrillar cementum

Cementoblasts

The most ancient cementoblat are derived from the ectomesenchymal layer of the developing tooth germ.

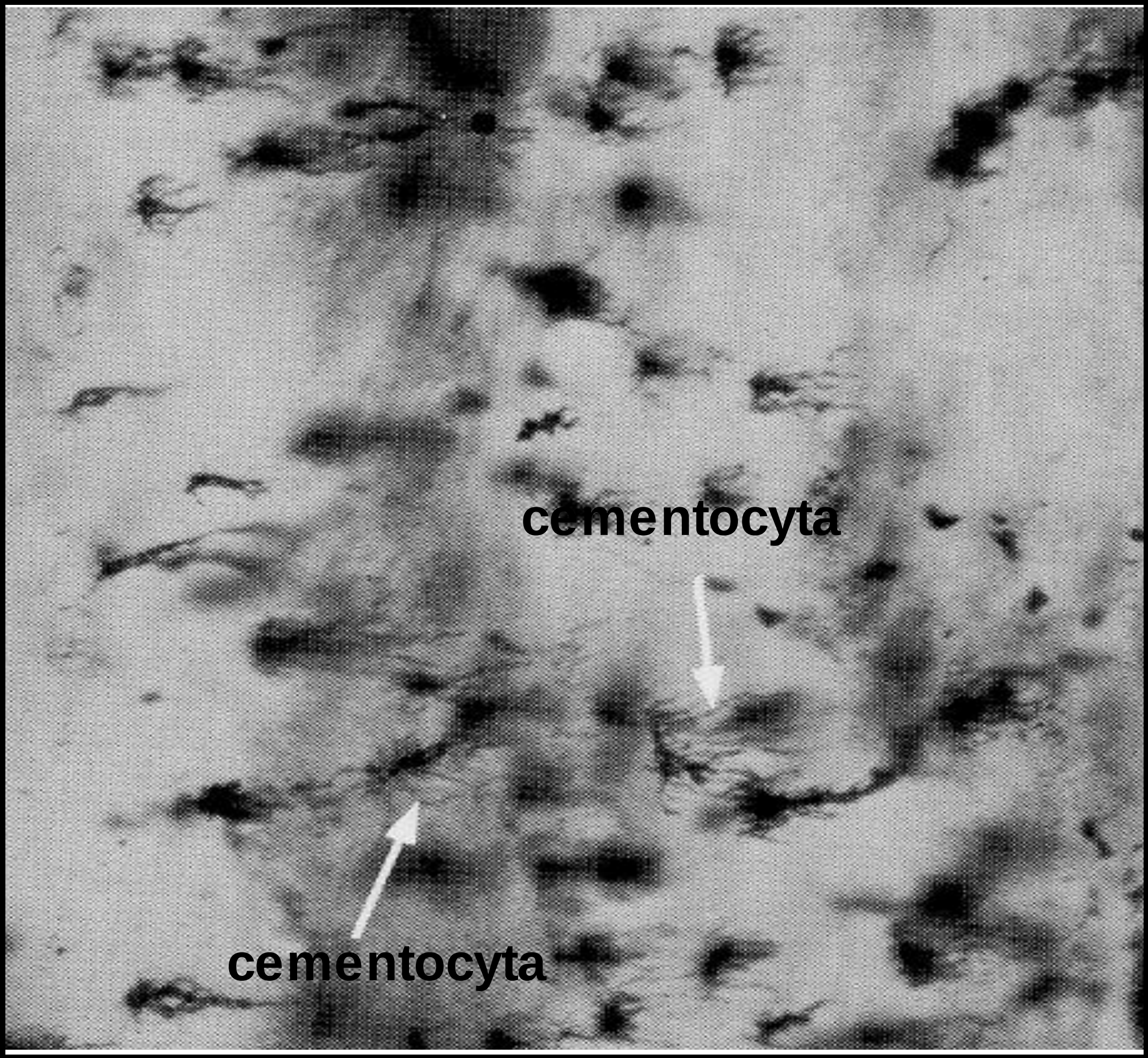
Later, cementoblasts differentiate from the pluripotent mesenchymal cells of the dental follicle.

Cementoblast synthetise low-density fibers and the proteoglycan-containing amorph matrix incorporating the Sharpey fibers of the periodontal ligament.

Cementocytes

Cementocytes can only be seen in cellular cementum. These cells with numerous pedicles reside in the lacunae of cementum.

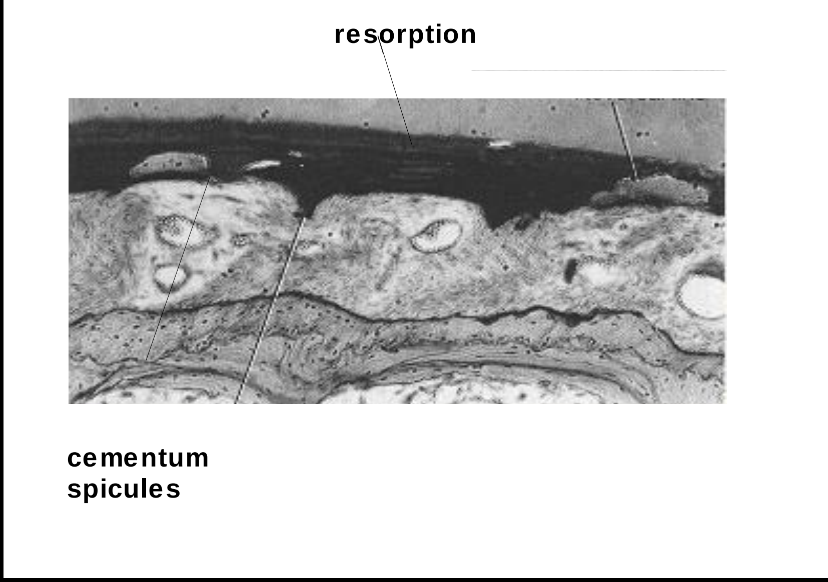
Cementum micro-tubules around the pedicles are orientatated towards the root surface.



Cementoclasts (odontoclasts)

Multinuclear cells morphologically similar to osteoclasts

These cells are responsible for the rapid resorption of the roots of deciduous teeth and for the localised cementresorption in adults.



Calcified component of cementum

Contains hidroxiapatite cristals, this makes 50- 60% of the hole cementum.

The rest of the cementinal tissue is 27% collagen and 13% water.

The main proportion of collagen is type I collagen (90%), type III and XII collagen fibers can also be found.

Beyond these, a munber of non-collagenic proteins are present, e.g. glycosaminoglycanes, chondroitin-sulfates.

Non-collagenic proteins

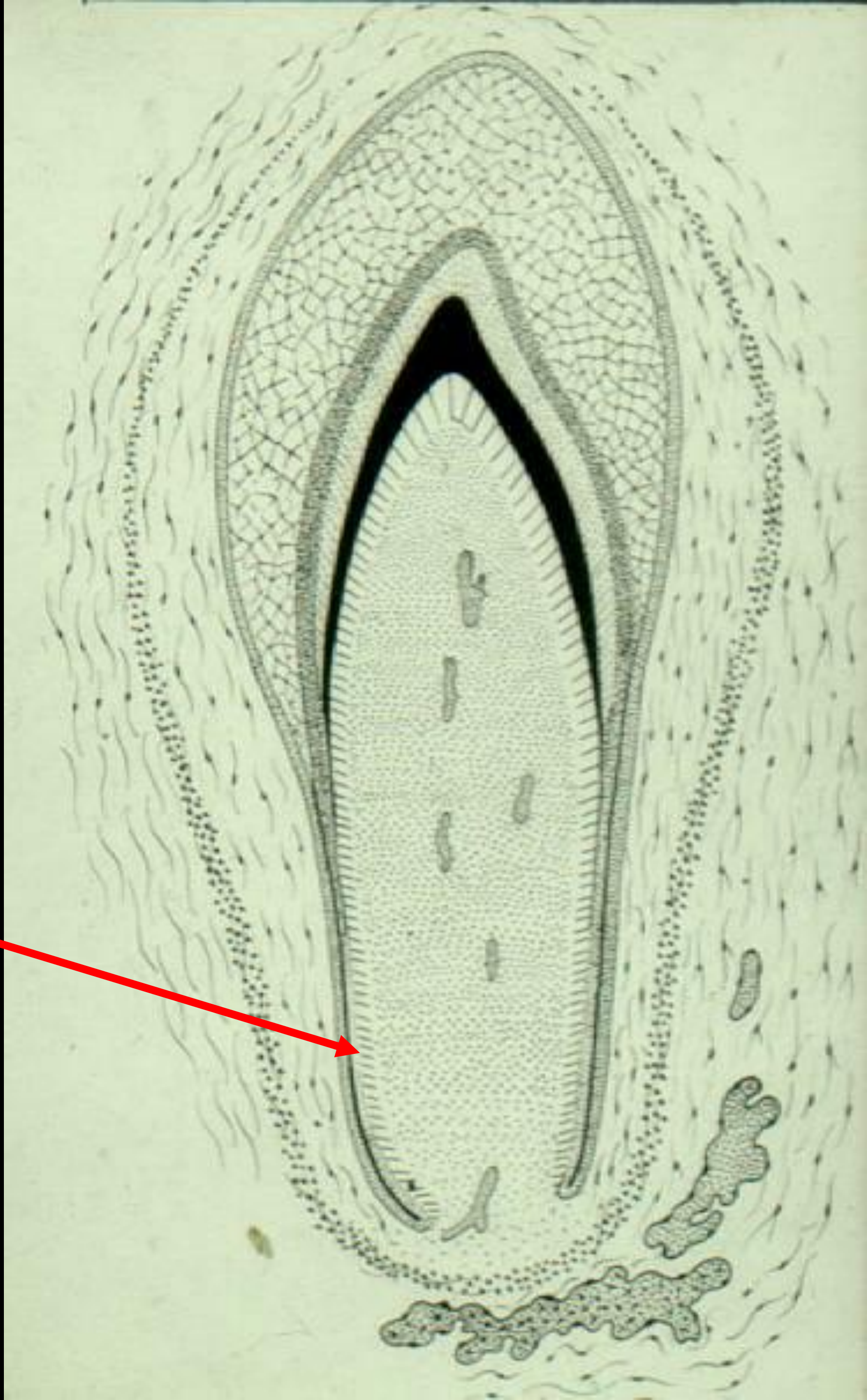
- Bone sialoprotein
- Dentin matrix protein
- Enamel matrix protein (Amelogenin)
- Fibronectin
- Osteonectin
- Osteopontin
- Tenascin
- Proteoglycanes
- Growth factors

Non-collagenic proteins

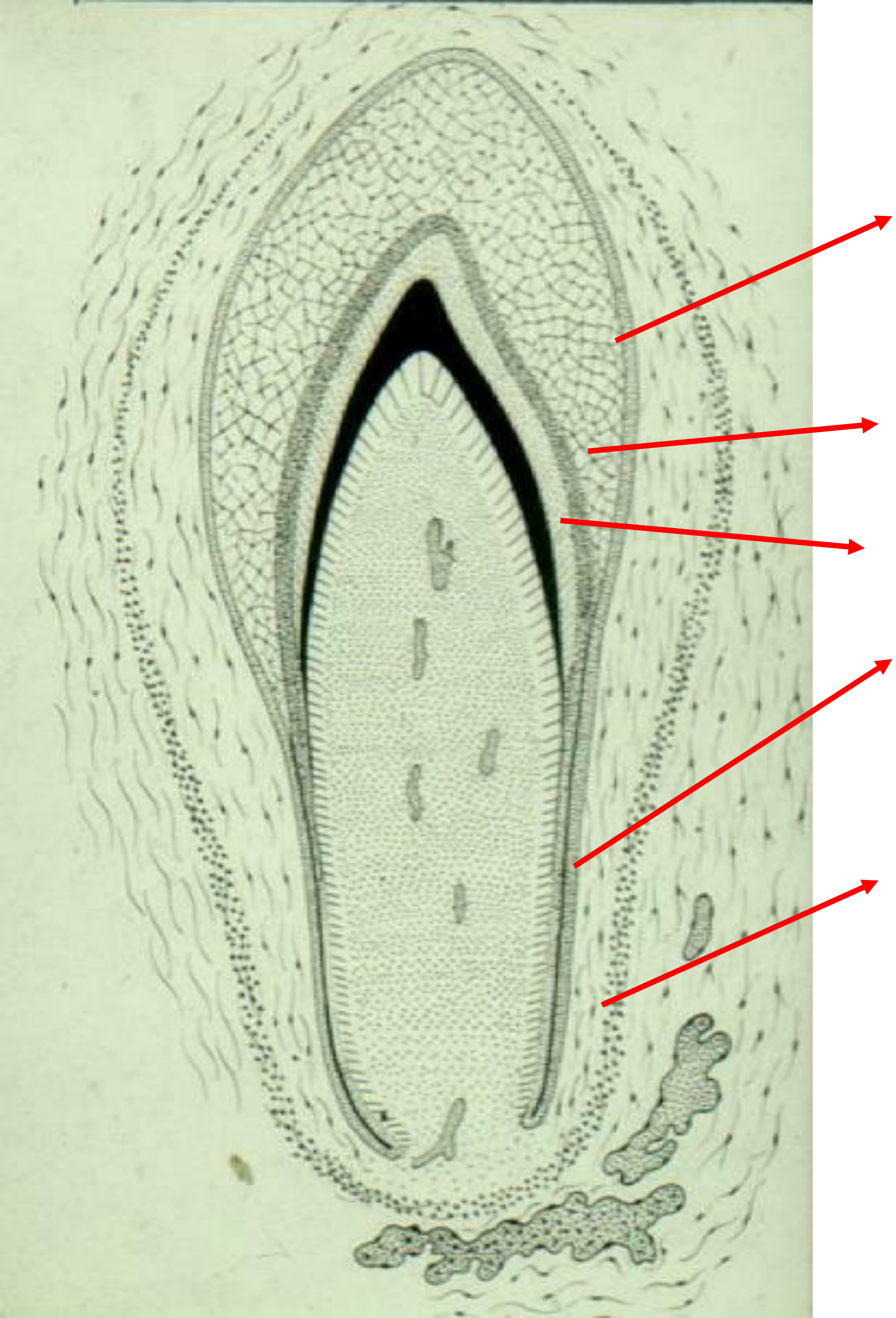
- **Enamel matrix protein (Amelogenin)**
  - Epithelial cells of the Hertwig's root sheath synthetise EMP-s, which precipitates onto the developing dentin surface before cemetum formation.
  - It seems altough that this only occurs at the most coronal part of acellular cementum.

CEMENTOGENESIS

- Cementum formation occurs during lifetime throughout the whole root suface.
- However, at the beginning this happens only at the deepest margin of Hertwig's epithelial root sheath



Development of the attachment apparatus



Cementogenesis

During development of the attachment aparatus mineralised dentin is separated from mesenchymal celles of the dental follicle by Hertwig's epithelial root sheath, which coordinates root morphogenesis.

The inner layer of the epithelial sheath consists of modified ameloblast secreting an enamel-matrix-like protein layer (hyalin) onto the root surface. (*MacNeil et al., Lindskog,a,b,*)

During eruption, the proliferation of Hertwig's epithelial sheath cells is not apically orientated, but results in the eruption of the crown. Proliferation of these cells only turns apically after the crown has almost reached occlusion.

Hertwig' epithelial sheath is responsible for root morphology, it also separates the dental pailla from the dental follicle.

The developing predentin is covered by a 10um thick, hyalin-like layer.

This hyalin-like layer is amelogenin -or enamel matrix protein- secreted by the reduced ameloblasts of the Hertwig's epithelial sheath.

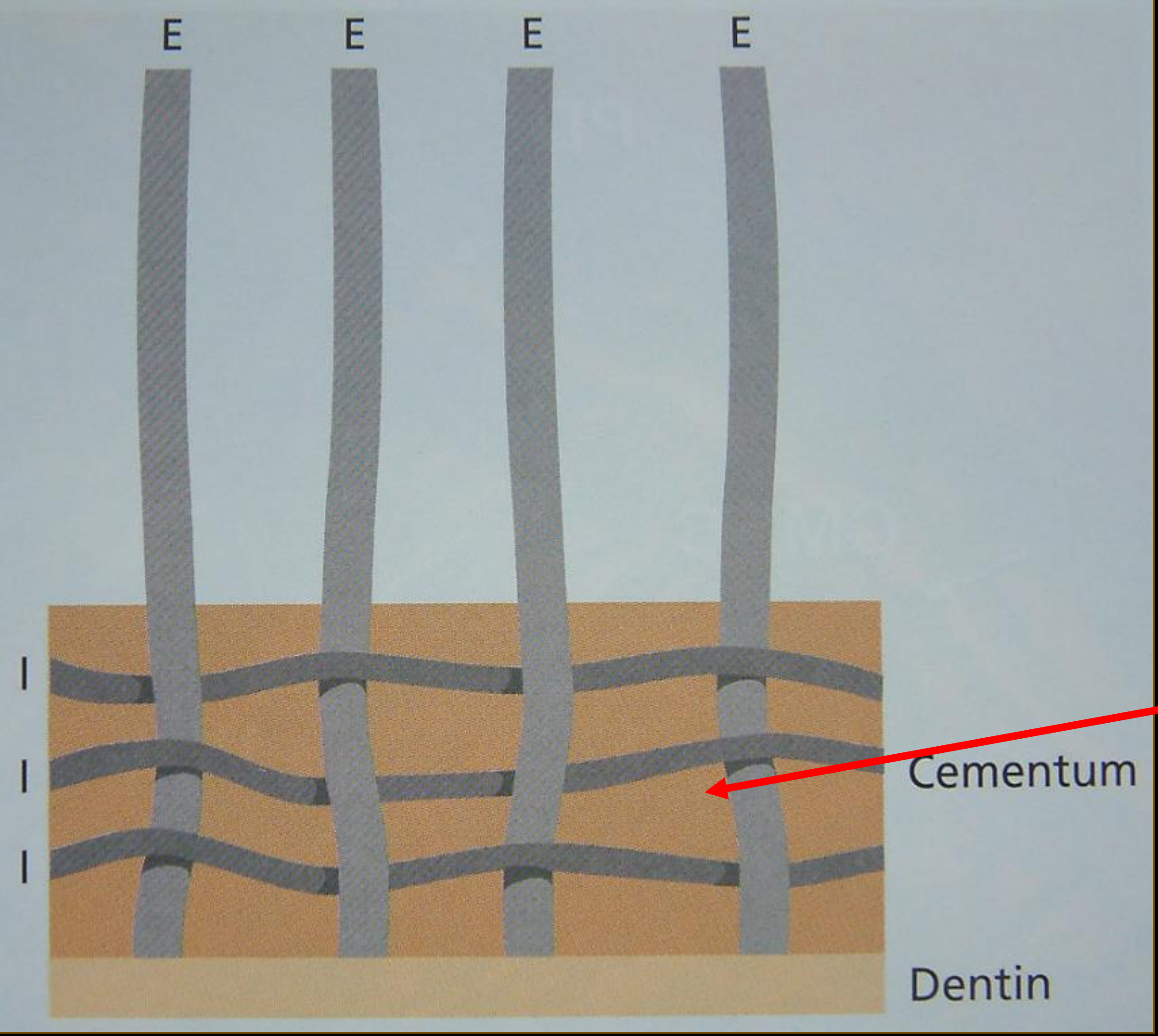
Thereby the differentiation of the mesenchymal cells of the dental follicle is initiated, which become cementoblats and start to synthetise acellular cementum.

Important fact is that before development of root cementum always a precipitation of enamel matrix protein layer occurs. This layer contains proteins secreted from enameloblasts. (*Slavkin 1976, Slavkin 1989, Hammarstrom és mts)*

These proteins seem to play a major role in

iniating the differentiation of ectomesenchymal pulp cells and the development of root predentin

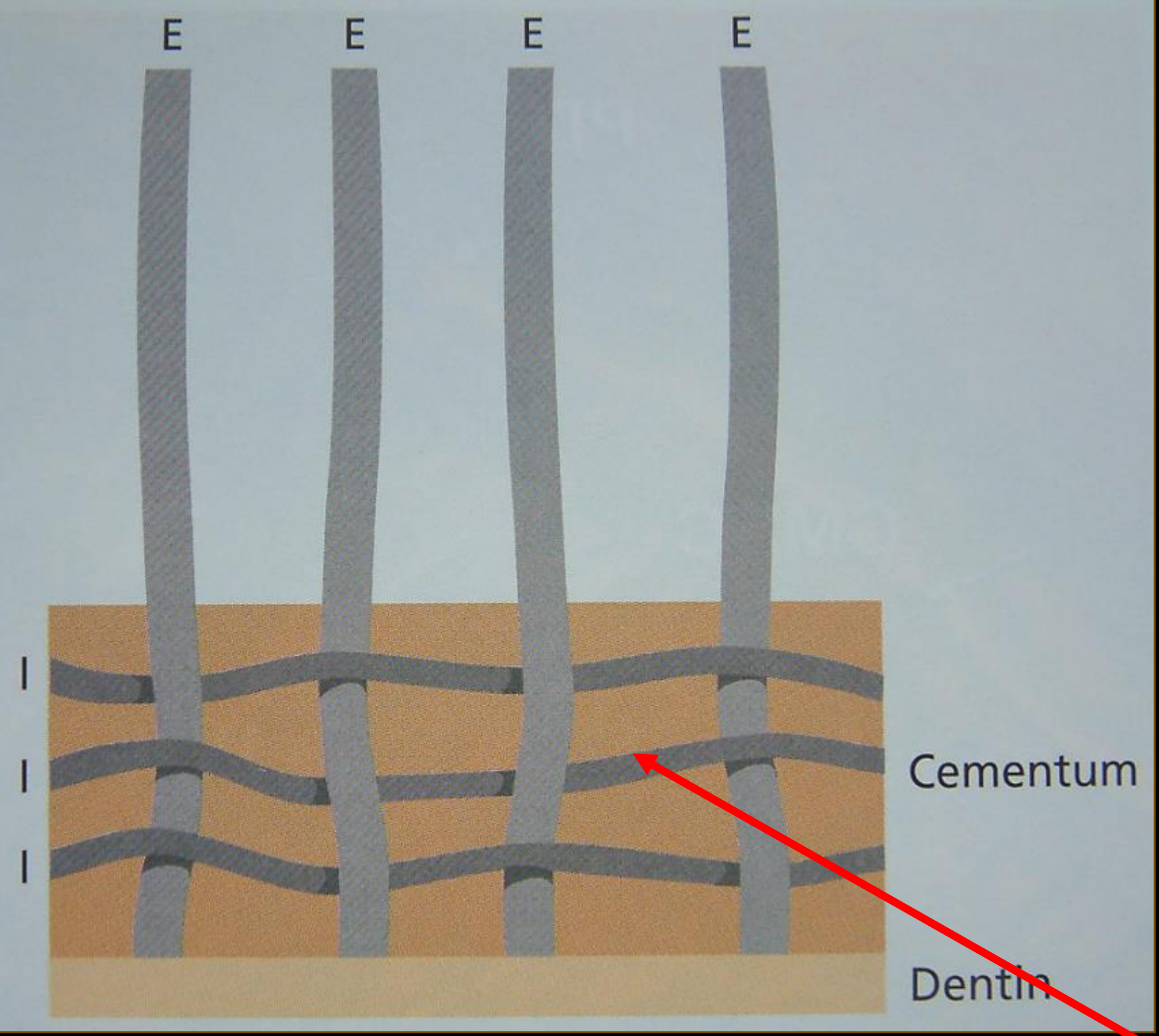
the later initiation and regulation of normal cementogenesis



Cemento-dentinal junction I

The first mesenchyamal cells of the dental follicle are fibroblast-like cells, attaching tot the non-mineralised dentin matrix.

These cells secrete a collagen matrix around the non-mineralised collagen fibers.

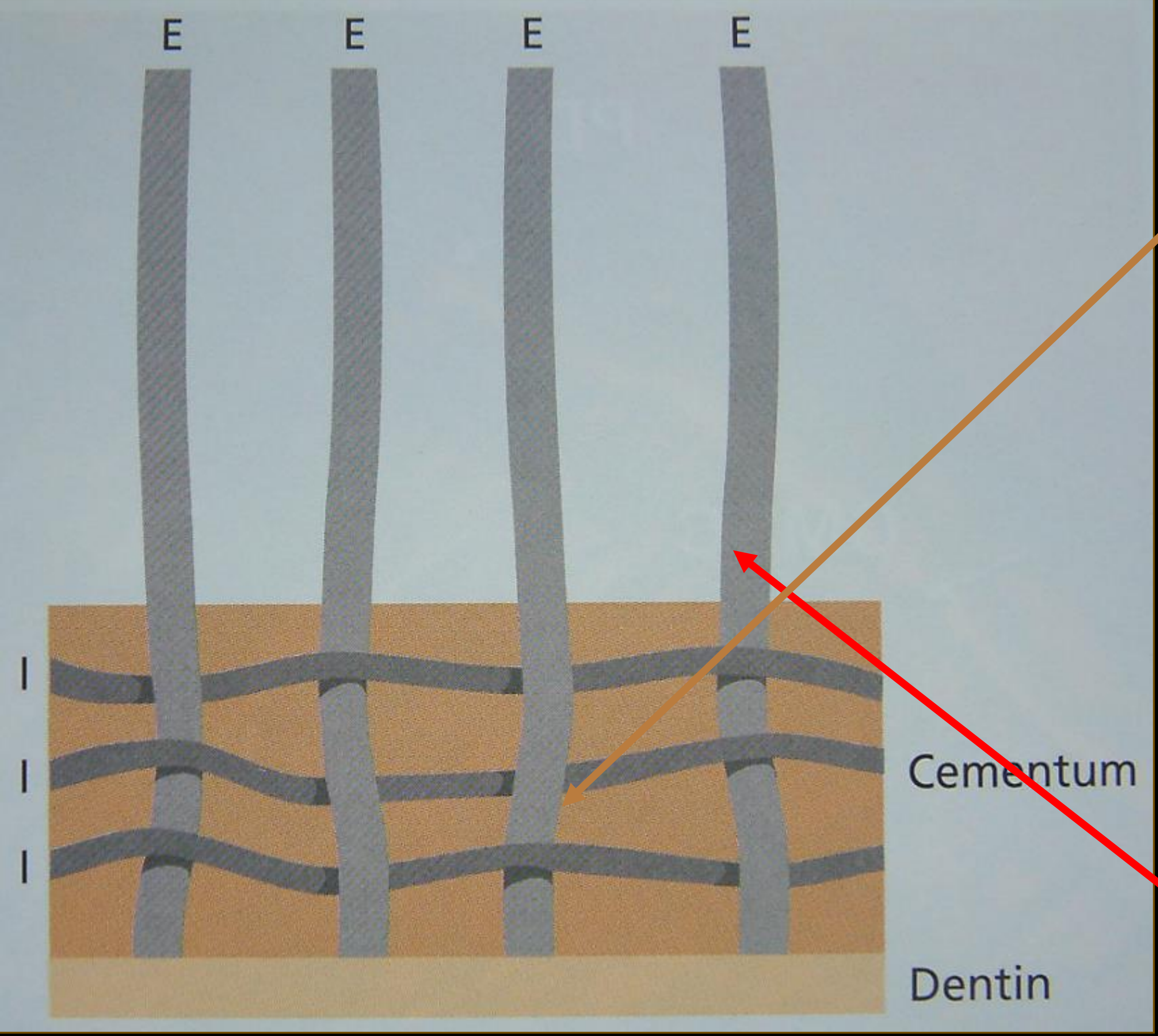


Cemento-dentinal junction II

Initial dentin mineralisation starts from the direction of the pulp and is only finished once the most superficial dentin-derived collagen fibers and the deepest dental follicle-derived collagen fibers have interdigited.

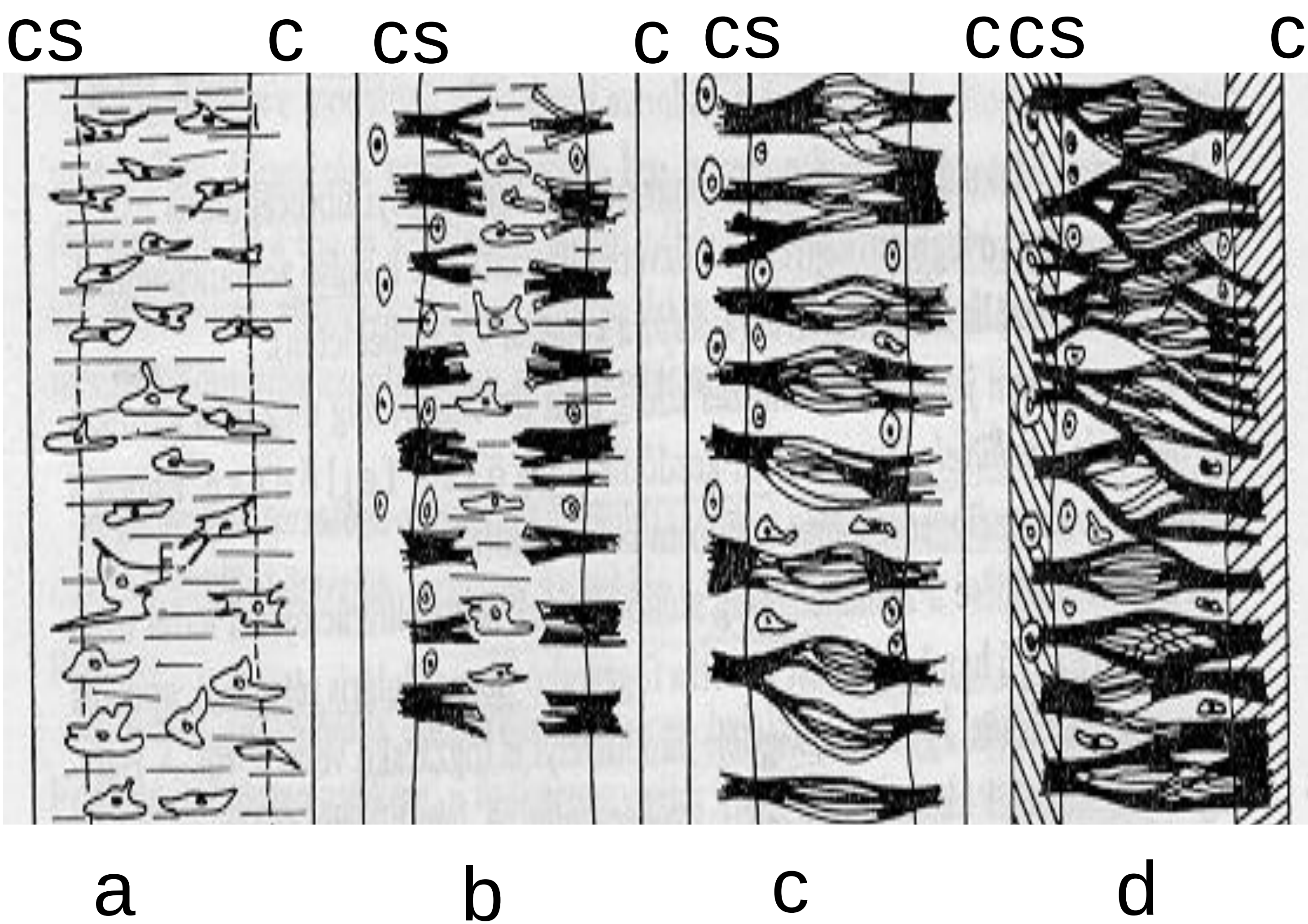
Thus a very strong dentin-cementum junction is created. This junction is covered by peripheric, intrinsic fiber containing cementum layers during later cementogenesis.

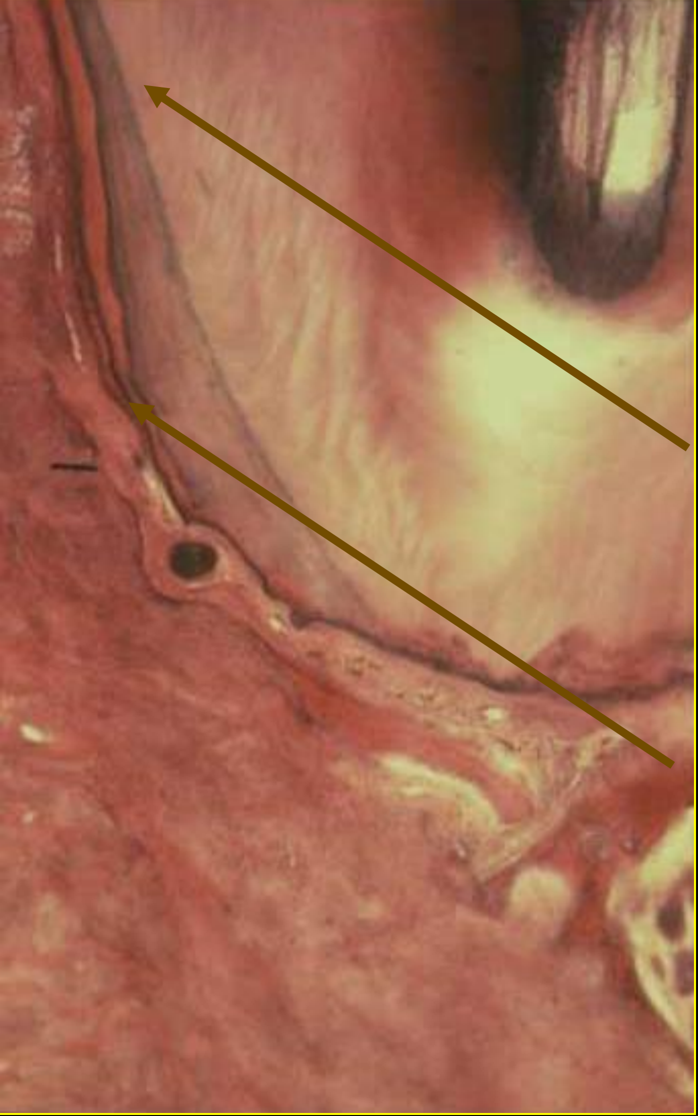
Cemento-dentinal junction III



Once the layer incorporating intrinsic paralell fibers reaches a thickness of 15-20 µm, comes in contact with collagen fibers of the developing periodontal ligament. Later these layers become the greatest proportion of the collagen matrix of acellular cementum.

Extrinsic fibers – Sharpey fibers

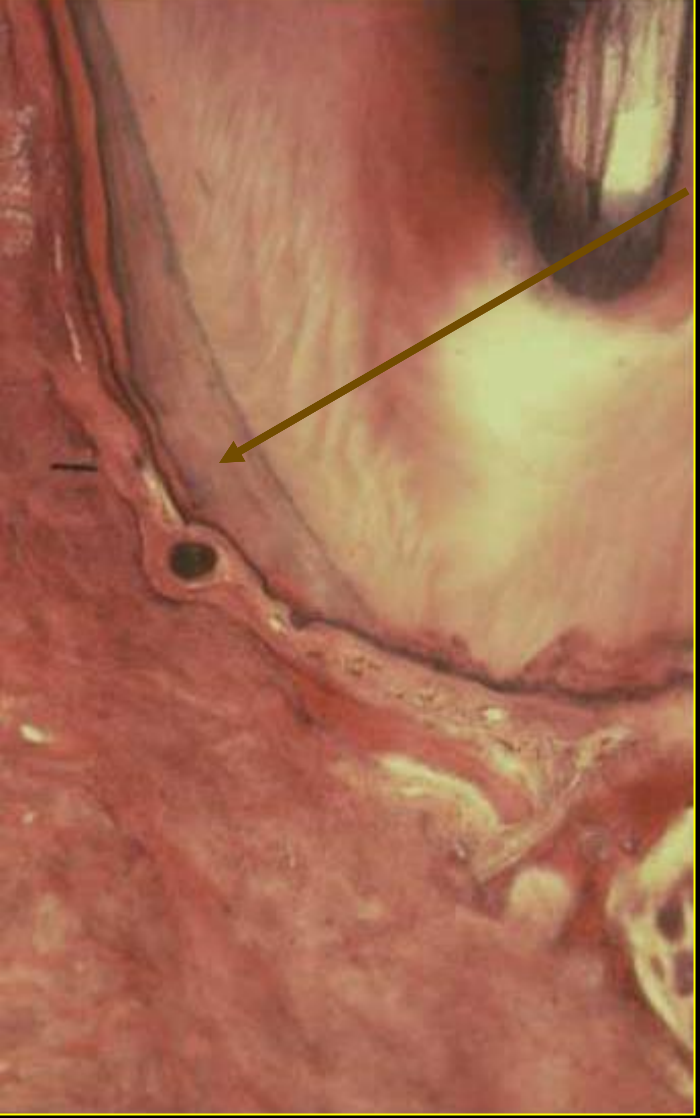

cs
c
cs
c
cs
c
cs
c
a
b
c
d



CELLULAR INTRINSIC FIBRILLAR CEMENTUM

- **Otherwise than in acellular cementum, where the matrix is screted by fibroblasts,**
- **the matrix of cellular cementum is secreted by differentiated odontoblast cells.**
- **The first layer is secreted around collagen fibers of non-calcicfied dentin.**
- **Numerous non-collagenic proteins are synthetised, which regulate matrix mineralisation.**
- **On the surface, a non-mineralised cementoid layer can always be found.**

CELLULAR EXTRINSIC FIBRILLAR CEMENTUM



- **Secondary cellular cementum, containing extrinsic fibers develops as a result of incorporation and calcification of Sharpey fibers.**
- **This type of cementogenesis is irregular, occurs in discrete time intervals, thus resulting in an „annual ring”-like histological picture.**

Experimental evidences of cemento-dentinal morphogenesis and bilateral induction

Molar dental papilla + incisor enamel organ – development of molar root and crown

Molar enamel organ + incisor dental papilla – development of incisor root and crown

Dental papilla + extraoral epithelium – ectopical enamel organ development

Pluripotent mesenchymal cells of the dental papilla seem to carry the genetic code determining tooth morphogenesis and the number of roots

Molecular regulation of cementogenesis

- Bone morphogenetic proteins - BMP
- Matrix proteines
- Epithelial factors
- Osteocalcin
- Transcriptional factors

Molecular regulation of cementogenesis

- **Bone morphogenic proteins - BMP**

BMP-2,-4,-7 facilitates the differentiation of preosteoblasts and precementoblasts

In in vitro animal studies, increased periodontal regeneration was shown after BMP treatment

Molecular regulation of cementogenesis

- **Matrix proteines**
- SIALOPROTEIN
- Facilitataes surface mineralisation
- OSTEOPONTIN
- Regulates mineralisation, cell adhesion
- ENAMEL MATRIX PROTEINES - EMP
- Only a minimal amount can be found in the cementum
- Facilitates acellular and cellular cement formation and cell differentiation
- Inhibits apical migration of the epithelial cells

Molecular regulation of cementogenesis

- **EPITHELIAL FACTORS**
- ENAMEL MATRIX PROTEINS – EMP
- BASAL MEMBRANE PROTEINS
- PTH RELATED PROTEIN

Molecular regulation of cementogenesis

- OSTEOCALCIN
- marker of osteoblast, cementoblast and odontoblast maturation and regulates mineralisation
- TRANSCRIPTION FACTORS
- gene expression

Molecular regulation of cementogenesis

OTHER MOLECULAR FACTORS

TGF- beta

PDGF

PROTEOGLYCANS

ALCALIC PHOSPHATASE (hypophosphatasia)

PATIENTS WITH hypophosphatasia: SEVERE CEMENOGENESIS-DEFECTS

CEMENTO- NEOGENESIS

REGENERATION

ONCE DEMAGED PERIODONTIUM HAS A LIMITED REGENERATIVE CAPACITY →

DURING ORTHODONTIC TOOTH MOVEMENT A TOTAL REMODELLING OF THE WHOLE PERIODONTAL SUPPROTIVE TISSUE TAKES PLACE

IN DISEASE NORMAL REGENERATION OCCURS JUST IN THE VERY INITIAL STAGE OF INFLAMMATION →

CEMENTO- NEOGENESIS

REGENERATION

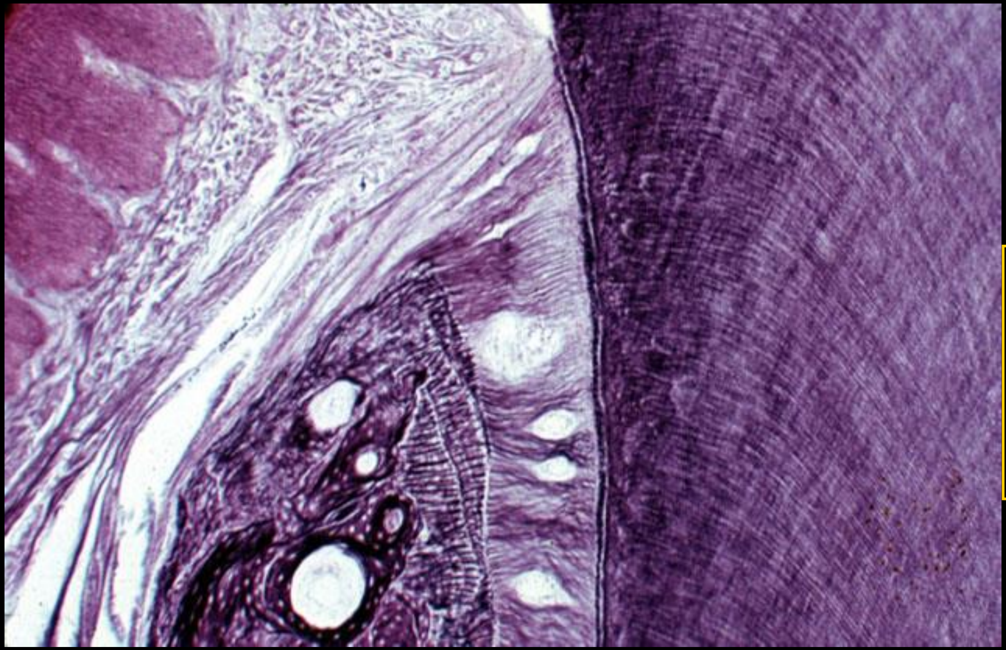
REGENERATION INVOLVES:

RECRUITMENT OF LOCALLY AVAILABLE PROGENTOR CELLS TO THE SITE OF DAMAGE

- DIFFERENTIATION ITNO PERIODONTAL LIGAMENT-FORMING CELLS
- MINEARAL FORMIN CEMENTOBLASTS
- BONE FORMING OSTEOBLASTS

CEMENTO-NEOGENESIS

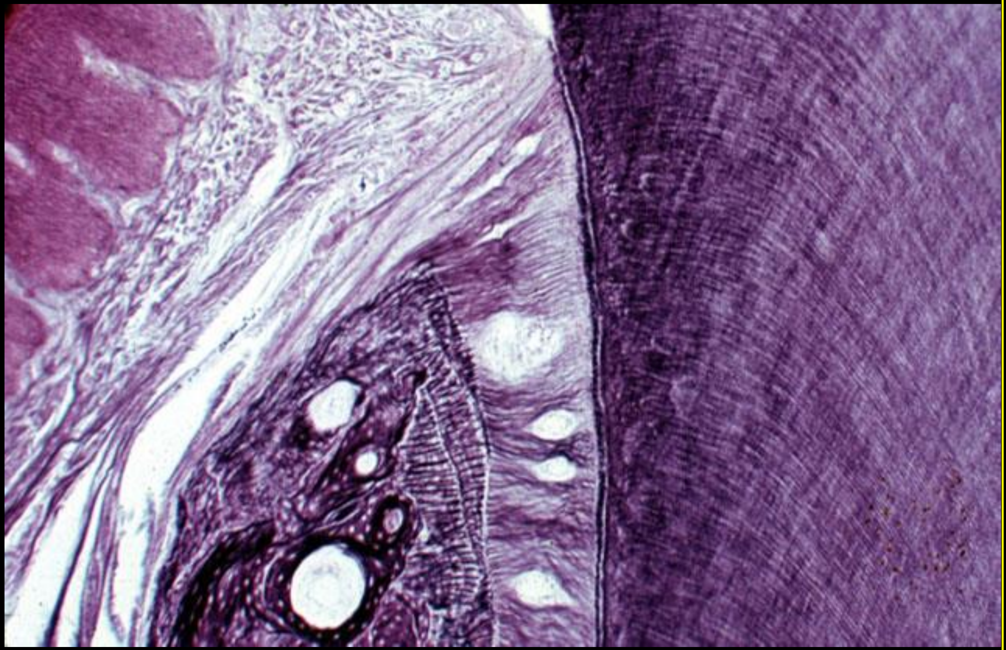
REGENERATION



PDL HAS ONE OF THE HIGHEST RATE OF CELLULAR TURNOVER IN THE BODY

CEMENTO-NEOGENESIS

REGENERATION

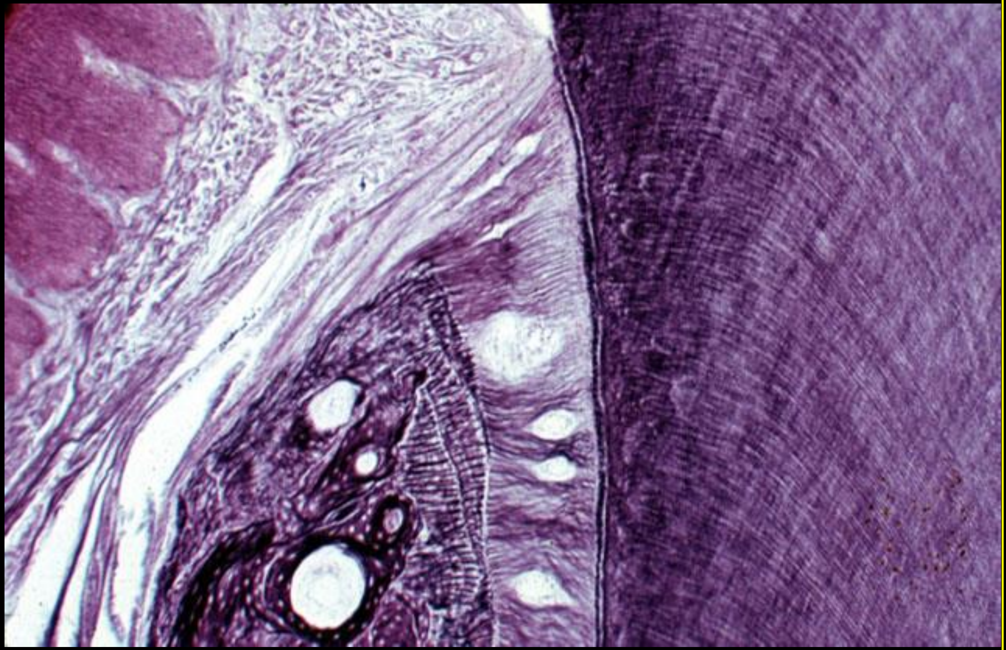


CELLS IN THE PDL:

- CEMENTOBLASTS
- FIBROBLASTS
- OSTEOBLASTS
- MYOFIBROBLASTS
- ENDOTHELIAL CELLS
- EPITHELIAL CELLS (MALLASEZ)
- NERVE CELLS
- PROGENITOR (STEM CELLS)

CEMENTO-NEOGENESIS

REGENERATION



PROGENITOR (STEM CELLS)

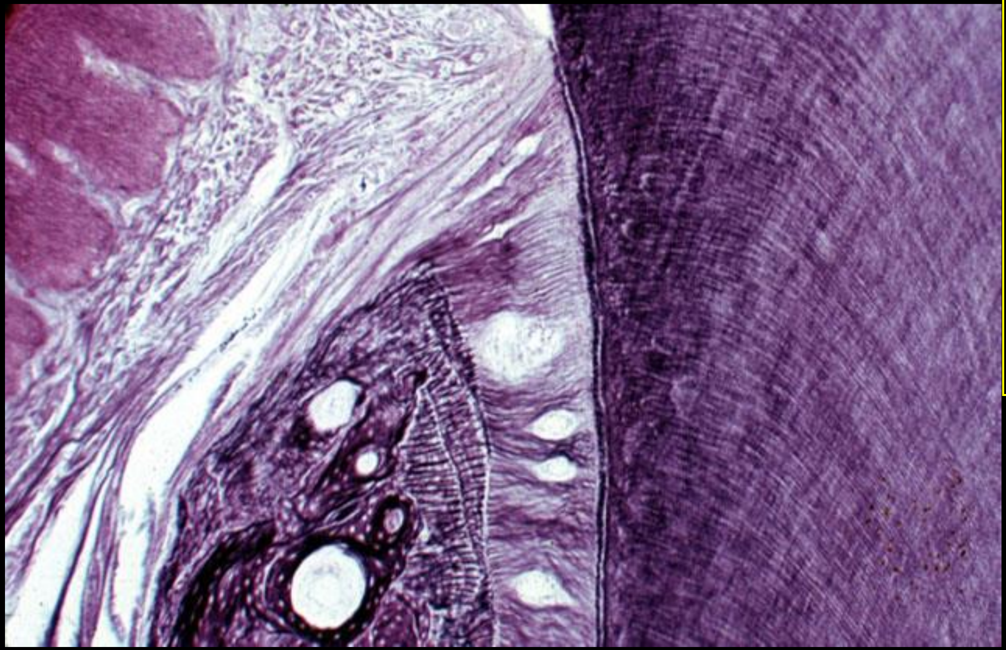
WITHIN THE PERIVASCULAR TISSUE OF PDL

MORPHOLOGIC CHARACTERISTICS:

- SMALL SIZE
- RESPONSIVENESS TO STIMULATING FACTORS
- SLOW LIFE CYCLE
- UNDIFFERENTIATED AND PLURIPOTENT

CEMENTO-NEOGENESIS

REGENERATION



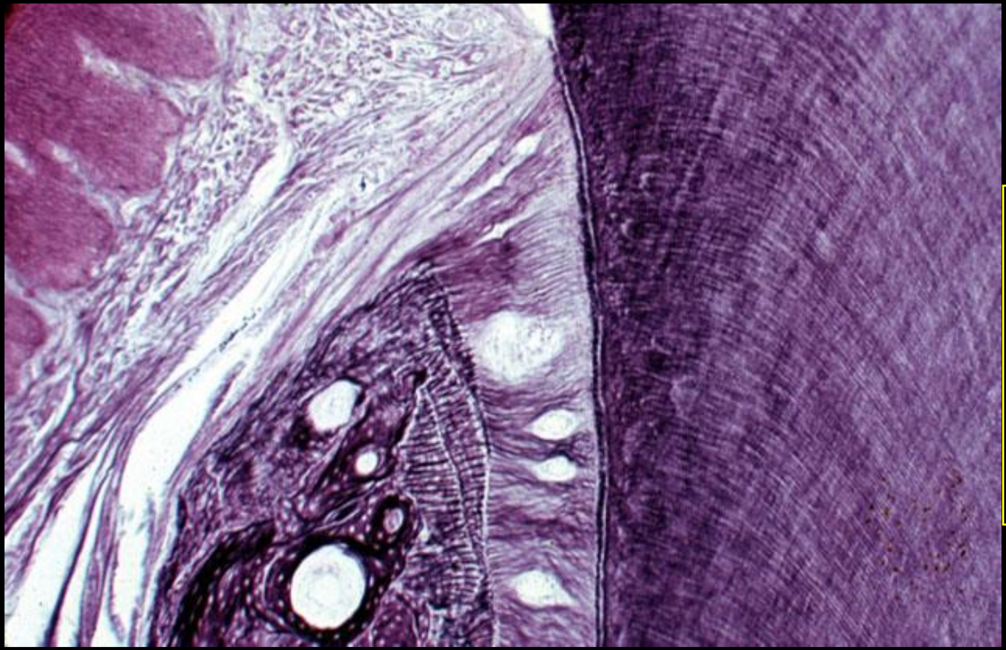
PROGENITOR (STEM CELLS)

IT WAS FIRST PROPOSED BY MELCHER IN 1976 INDICATING THAT THE THREE STROMAL CELLS IN THE PDL ARE DERIVED FROM THE SAME PRECURSORS ANCESTOR (STEM) CELL

Melcher AH. Cells of periodontium: their role in the healing of wounds Ann R Coll Surg Engl 1985:67: 130-131

CEMENTO- NEOGENESIS

REGENERATION



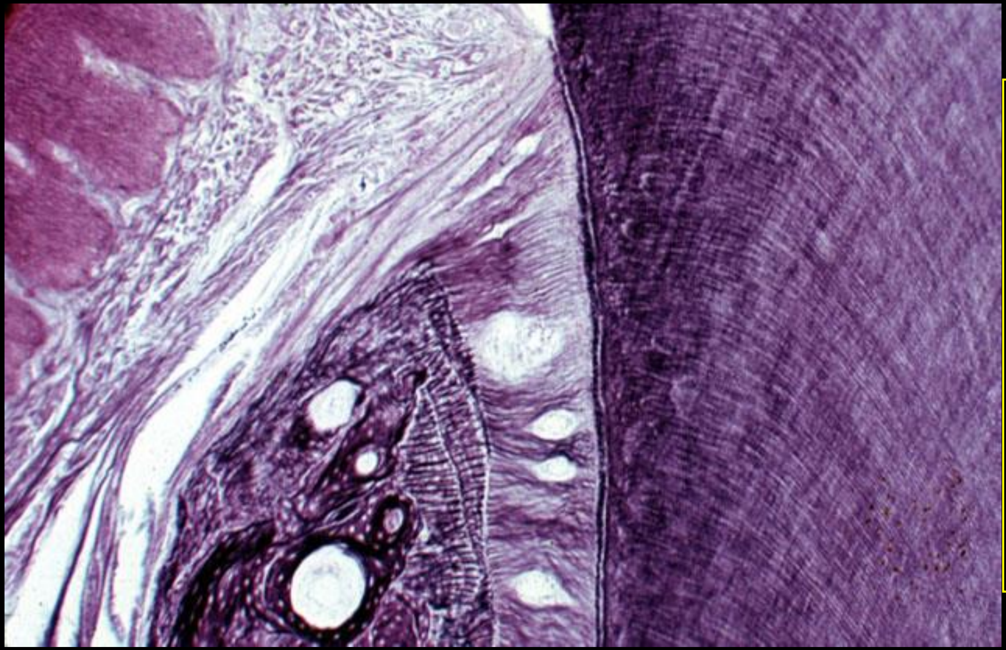
PROGENITOR (STEM CELLS)

THE FIRST HISTOLOGICAL EVIDENCE OF PDL STEM CELLS ARE PROVIDED BY THE WORKS OF McCULLOCH

McCulloch CA. Progenitor cell populations in the periodontal ligament in mice Anat Rec 1985; 221: 258-262

CEMENTO- NEOGENESIS

REGENERATION



PROGENITOR (STEM CELLS)

DURING THE MORHOGENESIS SOME PLURIPOTENT PROGENITOR CELLS REMAIN UNDIFFERENTIATED WITHIN THE PDL AND CAN MAINTAIN NORMAL TISSUE HOMEOSTASIS

McCulloch CA. Progenitor cell populations in the periodontal ligament in mice Anat Rec 1985; 221: 258-262

CEMENTO- NEOGENESIS

REGENERATION

CELLS IN
DENTAL
FOLLICLE

GROWTH FACTORS

PRECEMENTOBLAST → CEMENTOBLAST
PREFIBROBLASTS → FIBROBLASTS
PREOSTEOBLAST → OSTEOBLAST

EXTRACELLULAR MATRIX+
CELL ADHESION MOLECULES

STEM CELS IN
PERIVASCULAR
PDL TISSUE

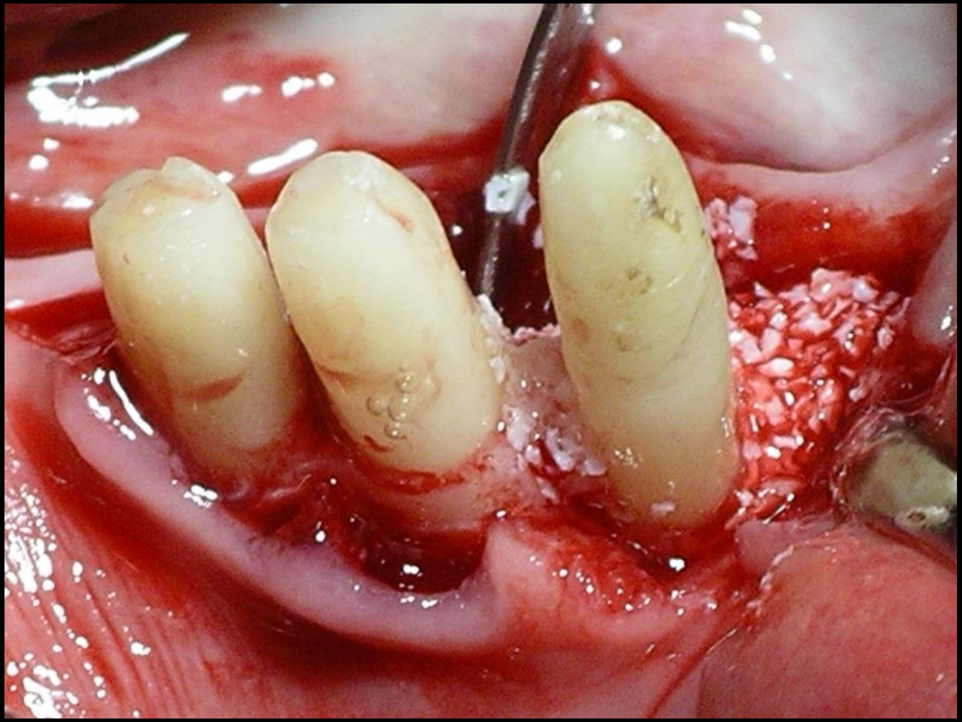
GROWTH FACTORS

PRECEMENTOBLAST → CEMENTOBLAST
PREFIBROBLASTS → FIBROBLASTS
PREOSTEOBLAST → OSTEOBLAST

EXTRACELLULAR MATRIX+
CELL ADHESION MOLECULES

CEMENTO- NEOGENESIS

REGENERATION



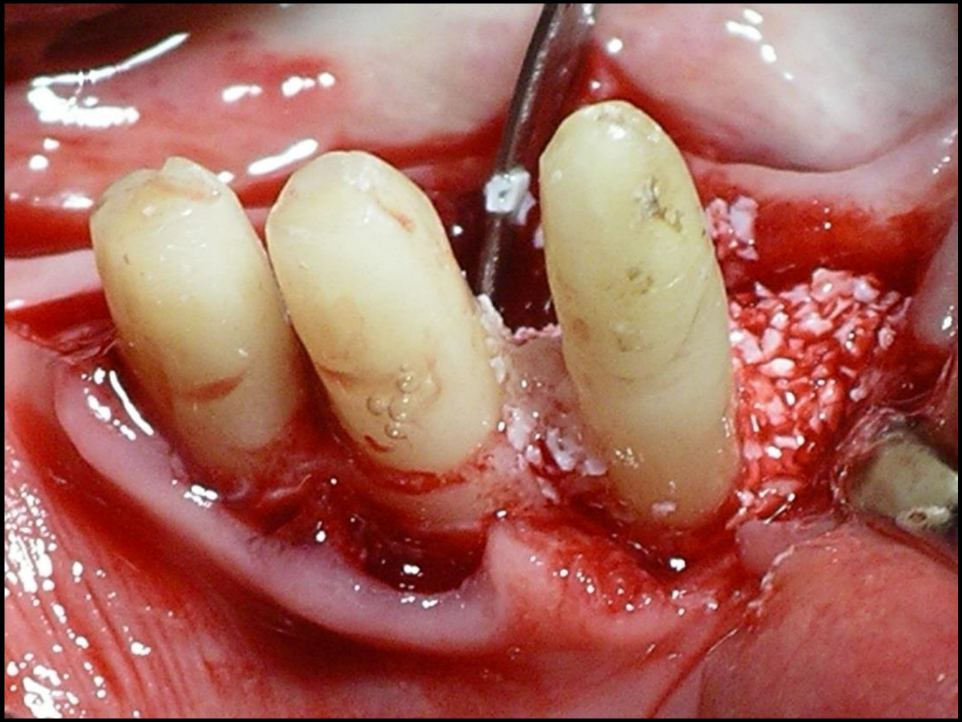
DURING TISSUE INJURY

THE STEM CELLS CAN
BE ACTIVATED
TOWARDS TERMINAL
DIFFERENTIATION

AND TISSUE REPAIR
OR REGENERATION

CEMENTO- NEOGENESIS

REGENERATION



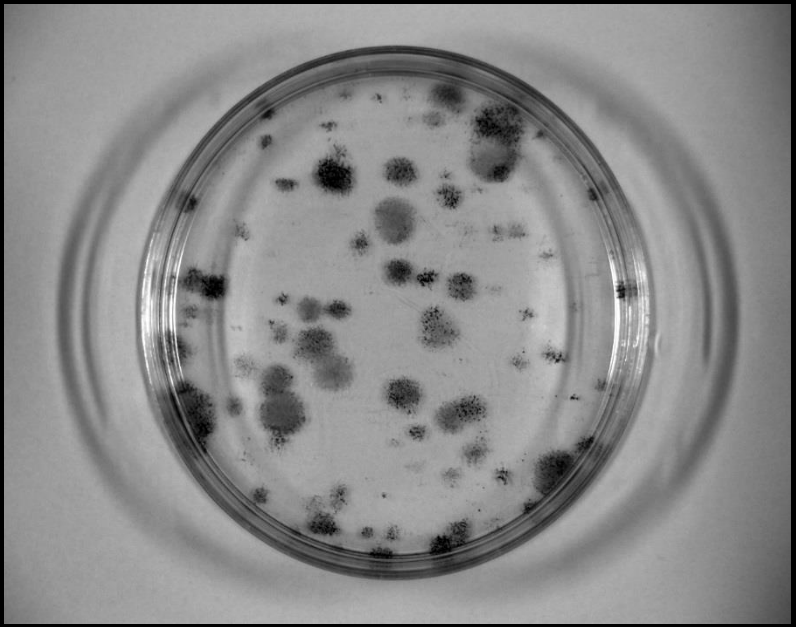
PERIODONTAL LIGAMENT STEM CELLS

HAVE THE CAPACITY TO FORM CLONOGENIC ADHERENT CELL COLINIES

LIKE THE BONE MARROW STROMAL STEM CELLS

CEMENTO- NEOGENESIS

REGENERATION



ONE ISOLATED PDL STEM CELL CREATED 170 ADHERENT COLONY FORMING UNITES MUCH MORE THAN THAT OF THE BONE MARROW STEM CELLS

170VS. 50 per 100000 cells plated

Seo BM et al: Investigation of multipotent postnatal stem cells from human periodontal ligament Lancet 2004; 364: 149-155

CEMENTO- NEOGENESIS

REGENERATION

THE PDL STEM CELLS ALSO UNDERGO SENESCENCE AND HAVE LIMITED LIFE SPAN

UNLIKE FOETAL STEM CELLS THAT PRACTICALLY IMMORTAL - THAT IS RELATED TO ITS HIGH ACTIVITY OF THELOMERAZE ENZYME THAT MAINTAN DNA LENGTH AND CHROMOSOMAL STABILITY

STROMAL STEM CELLS ACTIVITY CAN BE EXTENDED BY TELOMERAZE ENZYME STIMULATION

CEMENTO- NEOGENESIS

REGENERATION

THE PDL STEM CELLS UNDER CERTAIN CIRCUMSTANCES CAN DIFFERENTIATE INTO CELLS FORMING ORGANIZED TISSUE IN VIVO

THEY NEED AN INORGANIC SCAFFOLD – LIKE HYDROXYAPATIT CRYSTAL OR BETA TRICALCIUM PHOSPHATE

TO BE INDUCED AND GET MORPHOGENIC POTENTIAL AND TO DIFFERENTIATE TO CEMENTOBLASTS, OSTEOBLASTS AND FIBROBLASTS

Seo BM et al: Investigation of multipotent postnatal stem cells from human periodontal ligament Lancet 2004; 364: 149-155

CEMENTO- NEOGENESIS

REGENERATION

THE PDL STEM CELLS UNDER CERTAIN CIRCUMSTANCES CAN DIFFERENTIATE INTO CELLS FORMING ORGANIZED TISSUE IN VIVO

THIS CAN BE INDUCED BY BIOLOGICAL SUBSTANCES

AMELOGENIN (EMDOGAIN) ENAMEL MATRIX PROTEIN DEPOSITED

- •ON THE SURFACE OF THE NEWLY FORMED CEMENTUM DURING TOOTH DEVELOPMENT
- •OR ON THE SURFACE OF THE CEMENTUM DURING WOULD HEALING

CAN FACILITATE THE ATTACHMENT OF THE MULTIPOTENT MESENCHYMAL PROGENITOR CELLS AND THEIR FIFFERENTIATION TO CEMENT MATRIX FORMING CELLS

CEMENTO- NEOGENESIS

REGENERATION

THE PDL STEM CELLS ARE DERIVED FROM THE ECTOMESENCHYMAL CELLS OF THE DENTAL SACC

THE KEY ELEMENT IN REGENERATION:

TO ATTARCT AND RECRIUT THE PROPER PROGENITOR CELLS

THE PRODUCTION OF THE PROPER EXTRACELLULAR MATRIX CONSISTENT WITH THE ORIGINAL PERIODONTAL TISSUES

CEMENTO- NEOGENESIS

REGENERATION

CELL SEEDING AND TISSUE ENGINERING

PERIODONTAL LIGAMENTAL STEM CELLS CAN BE TRANSPLANTED INT PERIODONTAL DEFECT WITHOUT ANY ADVERSE EFFECTS

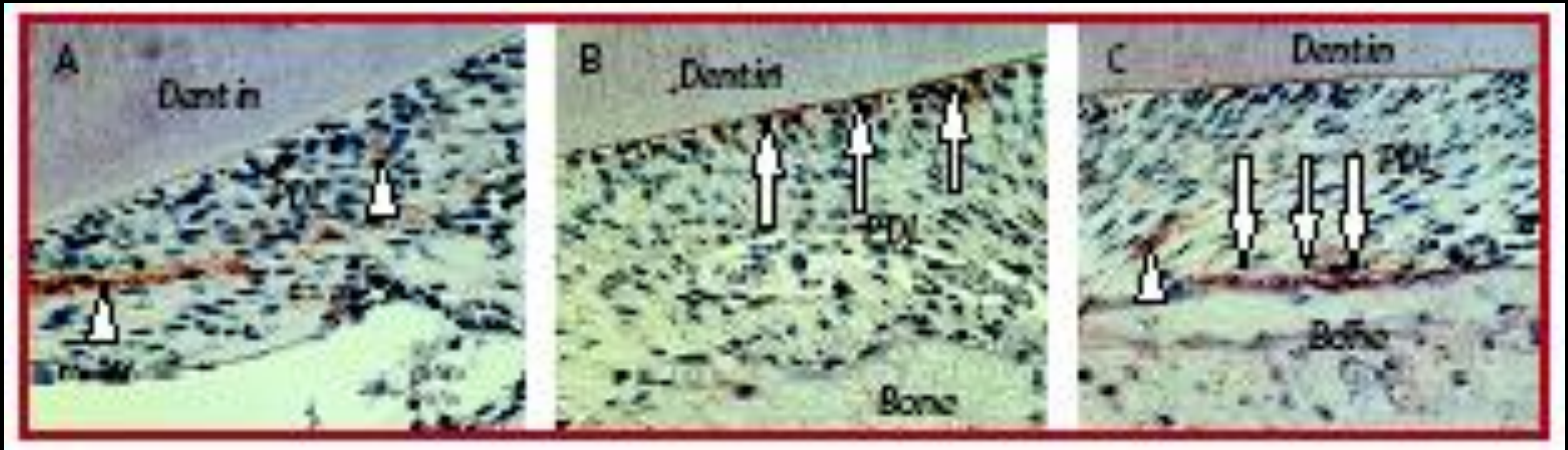
Lang H et al. Attachment formation following replantation of cultured cells into periodontal defects J. Dent Res 1998; 77: 393-398

CEMENTO- NEOGENESIS

REGENERATION

CELL SEEDING AND TISSUE ENGINERING

IMPLANTED PERIODONTAL LIGAMENTAL STEM CELLS ATTACHED BOTH TO ALVEOLAR BONE AND CEMENTUM SURFACE AND FORMED PERIODOTNAL LIGAMANET IDENTICAL TO THE SHARPEY'S FIBERS



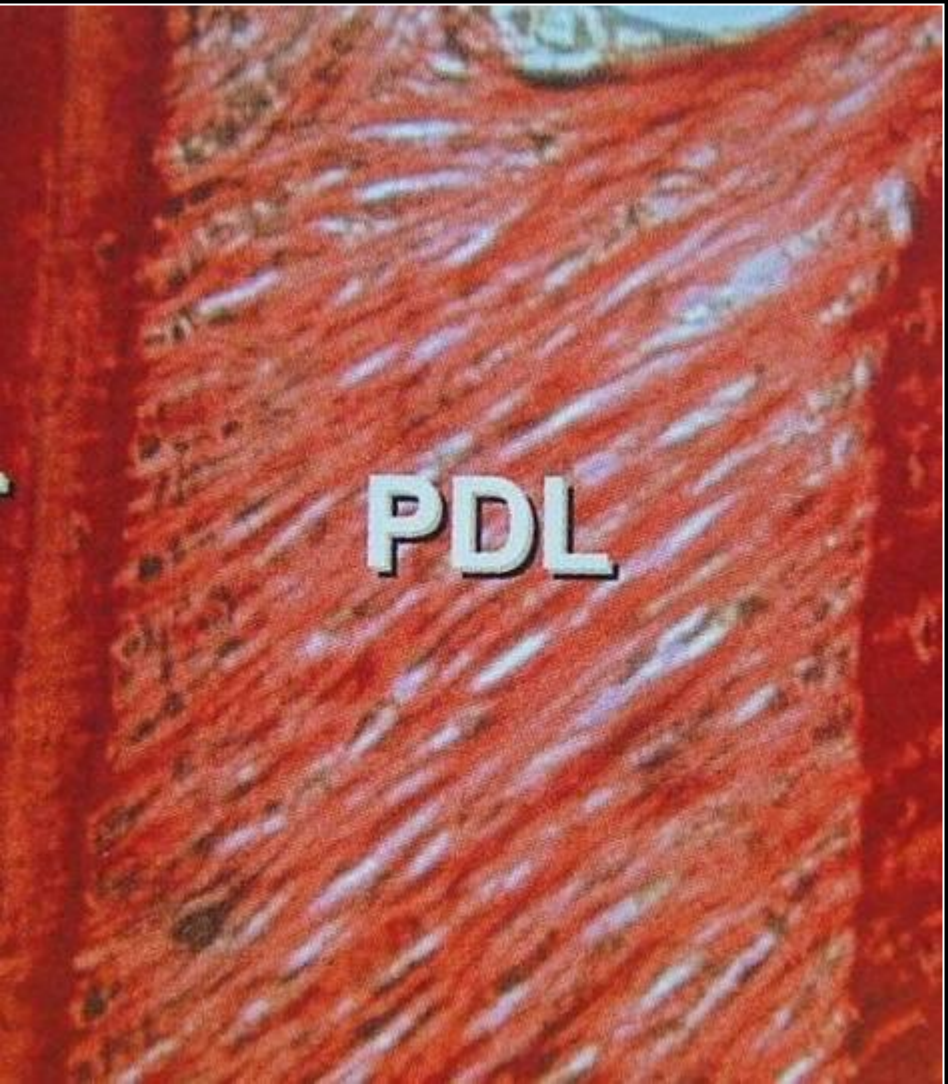
A – PDL **B** – Cementum **C** – Alveolar bone

Seo BM et al: Investigation of multipotent postnatal stem cells from human periodontal ligament Lancet 2004; 364: 149-155

CEMENTO- NEOGENESIS

REGENERATION

CELL SEEDING AND TISSUE ENGINERING



FURTHER STUDIES ARE NEEDED TO DETERMINE THE EFFICACY AND SAFETY OF THE EX VIVO EXPANDED STEM CELLS TO REPAIR PERIODONTAL DEFECTS

SUITABLE CARRIES AND INDUCTIVE BIOLOGICAL AGENTS SHOULD BE DETERMINED AND SAFELY USED

Thank you for your attention!