DE- AND REMINERALIZATION OF ENAMEL

ASSOSS. PROF. GATEVA
THE DE- AND REMINERALIZATION

- Of the enamel are dynamical processes
- Health of tooth enamel depends on them.
- They can occur simultaneously or alternately.
DEMINERALIZATION is a process of releasing mineral ions from hard dental structures and their release into the environment.

- Calcium and phosphate are lost from the tooth during the demineralization process.
- May be either precipitated together somewhere else in the tooth or lost to the mouth via the plaque and saliva.
REMINERALIZATION

- Is a process of mineral recovery by penetrating mineral ions into the crystal lattice.

- In the remineralization process, Ca and PO diffuse into the tooth from saliva and/or plaque fluid and precipitate as new material inside the early carious lesion.

- This re-deposited mineral is normal crystal growth on existing partially demineralized crystals but could also be new crystal formation within the subsurface regions of the enamel or dentin.
1. The tooth is attacked by plaque`s acids.
2. During demineralization, calcium and phosphates are dissolved from the enamel.
3. In the process of remineralization, fluoride, calcium, and phosphates are returned to the enamel.
carbohydrates are introduced in the mouth.

Some of them enter the plaque biofilm, and under the action of microorganisms they are broken down into acids.

These acids periodically increase their concentration over the enamel surface, which leads to demineralisation of the stable phase of the enamel. This process is carried out repeatedly during the day.

Parallel with it, the tooth is flushed by the saliva, which has the function of diluting, rinsing out and buffering the plaque acids, and through the calcium and phosphate ions contained in it to compensate periodic partial demineralisation. The caries is caused by the acids that remain in the plaque and are kept for a long time near the enamel surface.
DYNAMIC EQUILIBRIUM

• are in a dynamic equilibrium of moving ions, in which a continuous process of dissolution (demineralization) and recovery (remineralization) is realized.

• For a long time, these two processes happen without causing caries to develop.
CARIOUS PROCESS DEVELOPS:

• To arise, the equilibrium has to be disturbed and the protective saliva qualities are not enough to ensure the process of remineralization.
• Then the periods of demineralization cumulatively accumulate, and the negative mineral balance exceeds the degree of remineralization, which leads to the irreversible degradation of the enamel.
CARIOUS PROCESS

- Dental caries is a consequence of a localized chemical dissolution of the tooth surface caused by formation of acidic by-products from bacterial fermentation of dietary carbohydrates taking place in the dental biofilm covering the affected area.

- The initiation, development, and advancement of the carious process conforms to the laws of chemistry, and it is subject to chemical processes that determine the solubility of substances in liquid and acidic liquid environments.
The solubility of the substances is determined by their structure.

The enamel is built by crystals whose crystal lattice is made up of oppositely charged ions.

According to the science chemistry, any compound formed by positively and negatively charged ions is defined as salt.

This means that enamel is salt, and its solubility will conform to the law of salt dissolution.
SOLUBILITY OF THE SUBSTANCES

Electrolytes

Break down into ions

Acids
Bases
Salts

Non-electrolytes

Do not decompose into ions

Sugar
Starch
Oxides
Alcohol
SOLUBILITY OF THE SALTS:

- When a salt falls into water, reaction of a chemical dissolution or an electrolytic dissociation process occurs.
- As a consequence there is a spontaneous break down of the salt to the ions which leave salt and enter the solution.
The main reason for this dissolution is the property of water molecules. They are highly polar. When a salt is set in an aqueous medium, the water molecules bearing an electrical charge accumulate at one end to the salt ion, with the opposite charge.
PROPERTY OF WATER MOLECULES

- Water molecules attack the electron bonds between salt ions.
- They become weaker than the external attraction,
  - The bond breaks
  - The ion leaves the salt.
- The action of water molecules continues in the solution.
PROPERTY OF WATER MOLECULES

- Each ion is surrounded by many water molecules approaching it with its oppositely charged end.
- Thus, water molecules do not allow the ion to return to the lattice.
- This is possible because the hydration energy around the free ions is much greater than the energy that acts at this point in the crystal lattice. Thus, water appears to be a strong solvent.
The dissolution rate also depends on the concentration of the ions in the solution.

Initially the dissolution rate is high:
- the concentration of the inherent for the crystal ions in the solution is minimal.

In the process of dissolution the inherent for the crystal ions begin to accumulate in the solution and this slows the dissolution rate or rate of ionic movement.
ELECTROLYTE DISSOCIATION IS A REVERSIBLE PROCESS:

- Along with the dissociation of salt to ions, the reverse process of ion-association is carried out.
- Like any reversible process in electrolytic dissociation, equilibrium is established between the two opposite processes.
- This equilibrium is called **dissociation equilibrium**.
When achieved, the proportion of dissociated ions in the solution corresponds to their proportion in salt.

There is a situation where a balance occurs between the ions in the salt and the ions in the solution.

The solution is then saturated with respect to the solid phase ions.
ELECTROLYTIC DISSOCIATION:

- The equilibrium thus obtained is **dynamic**

- since, at any change in the medium, the reaction can be drawn in one of both directions.

- This means that one particle at a one moment may be in ionic form, and in another it may be in the crystal.

- By state of equilibrium, the number of ions in the solution and in the crystal will be constant.

The solution is then saturated with respect to the solid phase ions.
THE SOLUBILITY OF A SALT

- Means the rupture of the bonds between the opposite charged ions.
- In specific conditions its determination is based on the chemical principles and constants.
- Is sensitive to the conditions of the environment.
- In order to understand the solubility of a salt (crystal), some basic concepts, such as an ionic product, a solubility product, ionic activity, have to be known.
THE IONIC PRODUCT ($Q_{SP}$)

- is the concentration of all ions present in the solution.
- A laboratory-made electrolyte dissociation of salt in water (ideal condition), ionic product will be equal of the concentration of salt and water ions.
THE IONIC PRODUCT \((Q_{sp})\)

- In biological conditions, when it comes to dissolving of the enamel crystals – in oral environment.
- The saliva as well as the plaque fluid in which the process is carried out primarily contain a variety of ions.
  - They may be calcium, phosphate, fluoride, and are **inherent** to the crystal,
  - But may be sodium, potassium, and other, which are **not inherent** to the crystal.
- In these cases, the ionic product will be **larger** than the ions resulting from the dissolution of the crystal.
THE SOLUBILITY PRODUCT

- Ksp - characterizes the ions, which are only obtained by dissolving the crystal.
- The ionic product (amount of all dissolved ions) will be equal to the solubility product - when a solution is saturated.
- In any other situation, the ionic product will differ from the solubility product.
- The solubility of the salt is changed by the presence in the solution of inherent for it ions.
- If such ions are present in the solution, the solubility of the salt decreases.
ACTIVITY OF THE SOLUTION

- The ability of the dissolved ions to interact with each other determines the *activity* of the solution.
Factors, which can influence solubility

- Common ion effect
- Temperature changes
  - Effect of transformation
  - Effect of particle size
SOLUBILITY IS PRIMARILY MANAGED BY

The common ion effect

In equilibrium, the concentration of ions in the solution is equal to the concentration of the ions in the crystal.

Any change in ion`s concentration will affect the equilibrium.
THE EQUILIBRIUM IS AFFECTED

- If additional amount of ions inherent for the crystal are added to the solution, it becomes super saturated
  - becomes unstable and prone to precipitation - formation of new crystals from the available ions
- If in the solution are present substances, which can play role of nucleation's centers, precipitation immediately begins.
  - This principle is especially important for understanding the processes of remineralization.
- Precipitation under these conditions occurs to equalize the ionic product with the solubility product.
- If the solution is not super saturated, precipitation cannot be performed and then the solubility product (Ksp) is greater than the ionic product (Qsp).

- If the solution is super saturated with ions, the ionic product (Qsp) is greater than the solubility product (Ksp).

\[ Qsp < Ksp \text{ – unsaturated solution, enhancing solubility;} \]
\[ Qsp = Ksp \text{ – saturated solution, equilibrium;} \]
\[ Qsp > Ksp \text{ – super saturated solution, predisposing to precipitation.} \]
FACTORS, WHICH CAN INFLUENCE SOLUBILITY

- **Effect of transformation.** Another change in solubility may occur if dissociated ions in the solution are altered after equilibrium. This can be done by changing the medium (e.g., changing the pH or other ions in the solution), and forming another ion. Then the solubility of the crystal increases without changing the solubility product.

- **Effect of particle size.** The larger the crystals, the weaker their solubility. This is because the increase of the crystal size decreases the surface energy.

- **Temperature changes** - can influence solubility. There are salts which can dissolve faster by temperature increases and others, which slows their solubility by same conditions.
THE SOLUBILITY OF THE ENAMEL

- a variety of ions and proteins
- as well as microorganisms and their products
- in every act of eating and drinking - continuous intakes of various substances and their ions.

Dental biofilm

The plaque fluid is even more varied in composition and causes changes in solubility. Acids introduced with food and acids produced by microbial metabolism in it are retained for much longer, and the protection qualities of saliva are hard to be manifested.

Enamel - biological apatite

All this adds specifics of ongoing processes such as:
- dissolving of the enamel
- achievement of equilibrium with the fluid environment.
ENAMEL

- Is a salt formed from calcium phosphates.
- The basic calcium phosphate in it is the hydroxyapatite, simply called apatite.
  - Other calcium phosphates in the enamel are brushit $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, $\beta$-tricalcium phosphate $\text{Ca}_3(\text{PO}_4)_2$, octacalcium phosphate - $\text{Ca}_8(\text{PO}_4)_4(\text{HPO}_4)_2 \cdot 5\text{H}_2\text{O}$.
- The most stable of all calcium phosphates are apatite crystals.
- Many of the properties of the enamel are similar to those of apatite.
- The most important distinctive features of enamel apatite from pure apatite are: crystallographic differences - enamel apatite has a wider A-axis than pure apatite. This makes the enamel easier to dissolve.
- The presence of different ions in its crystalline lattice - non-apatite substitutions as well as the different calcium-phosphorous ratio (in pure apatite, the Ca/P ratio is 1.67 while in enamel it is 1.64) determines different solubility.
COMPOSITION OF HYDROXYAPATITE

- Hydroxyapatite is made up of calcium, phosphate and hydroxide ions arranged in a precise manner in the crystal lattice.

- If during the enamel histogenesis different ions such as Na, Mg, K, Sr and others are present in the tissue fluid, they could be incorporated into the crystal lattice and this leads to formation of non-pure hydroxyapatite crystals.

- Hydroxyapatite - \((Ca, W)_{10} (PO_4, X)_6(OH, y)_2\)

- Where:
  - \(W = Na, Mg, K, Sr\)
  - \(X = CO_3\) or \(HPO_4\)
  - \(Y = Cl\) or \(F\)
VARIETIES OF APATITE

- Depending on the type of ions entering the crystal lattice there may be different varieties of apatite.
  - Carbonat apatite - (Ca\(_{10-x}\)Na\(_x\))(PO\(_4\))\(_{6-x}\)(CO\(_3\))\(_x\)(OH)\(_2\)
  - Fluorhydroxyapatite - Ca\(_{10}\)(PO\(_4\))\(_6\)(F, OH)\(_2\)
  - Fluorapatite - Ca\(_{10}\)(PO\(_4\))\(_6\) F\(_2\)
THE SOLUBILITY OF THE ENAMEL

- Each type of apatite crystal has a different solubility degree.
- **Fluorapatite** is most resistant
  - its amount is relatively small in enamel.
- **Hydroxyapatite** has a higher solubility and a higher solubility product.
  - It is the most common apatite in the enamel.
- **Carbonapatites** have the highest solubility and greatest solubility product.
- **Brushit** is also very soluble.
THE SOLUBILITY OF THE ENAMEL

- At pH=7.4 - the hydroxyapatite is extremely stable.
- At pH<5.5 - determined as critical
  - The hydroxyapatite loses its resistance and starts to dissolve actively.
  - The fluorapatite is stable at this pH level,
- At pH = 4.5 FA begins to dissolve.
THE SOLUBILITY OF THE HYDROXYAPATITE

- In a liquid medium the hydroxyapatite as any salt is subjected to electrolytic dissociation.
- Its dissolution is subject to the law of mass action.
  - According to this law, the dissociation rate is proportional to the product of the masses of the involved substances.
- When one unit of hydroxyapatite is dissolved into the solution are released
  - 10 calcium,
  - 6 trivalent phosphate and
  - 2 hydroxide ions:
  \[ \text{Ca}_{10}(\text{PO}_4)_6(\text{OH}) \rightleftharpoons 10\text{Ca}^{2+} + 6\text{PO}_4^{3-} + 2\text{OH}^- \]
THE SOLUBILITY OF THE HYDROXYAPATITE

- The loss of mineral from the tooth is controlled by the ionic product of the corresponding ions in the solution.
- In HA these are calcium, phosphate and hydroxide ions.
- The product of the hydroxyapatite ionic activity ($\text{PIA}_{\text{ha}}$) is equal to the product of the calcium ion concentration to the times of 10, the phosphate ions to the times of 6 and the hydroxide ion concentration to the times of 2.

$$\text{PIA}_{\text{ha}} = (\text{Ca}^{2+})^{10} \times (\text{PO}_4^{3-})^6 \times (\text{OH}^-)^2$$
THE SOLUBILITY OF THE HYDROXYAPATITE

- $\text{PIA}_{\text{ha}} = (\text{Ca}^{2+})^{10} \times (\text{PO}_4^{3-})^6 \times (\text{OH}^-)^2$

- In this process the most important are phosphate ions.

- In an alkaline environment they give off hydrogen.

- In acid environment - they accept hydrogen.

- The coefficient determining the ionic strength of the solution depends on
  
  - the pH of the solution, the $t^0$, the addition of new ions in the solution, and the formation of complex ions.
From the etiology of the caries process

When eating in the mouth carbohydrates come in:
- some of them enter the plaque biofilm and under the action of MO they break down to acids.
- acids periodically increase their concentration above the enamel surface - demineralization of the enamel repeatedly during the day.

The tooth is flushed by saliva:
- saliva dilutes, rinses and buffers plaque acids;
- $Ca^{2+}$ и $PO_4^{3-}$ ions contained in saliva compensate this partial demineralization.
Caries lesion is caused by the acids that remain in the dental biofilm and stay for a long time near (white contact) the enamel surface.
The solubility of calcium phosphates is very strongly altered by the pH of the solution.

The most destabilizing situation for the crystal is the change in pH (occurs when acids are added to the solution).
SOLUBILITY OF HYDROXYAPATITE IN ACID MEDIUM

- Since the acid is also electrolyte,
- when it falls into a liquid medium, just like the crystal, it begins to dissociate itself.
- According to the law of Arenius,
- acids are dissociated to hydrogen ions and an acid anion.
  - $\text{H}_n\text{A} \rightarrow n\text{H}^+ + \text{A}^{n-}$
  - $\text{A}^-$ is an acid ion.
THE STRENGTH OF ACIDS

- Is related to the proportion by which it reacts with water to form ions.
- Is measured with the concentration of hydrogen ions.
- The more hydrogen ions there are in the acid, the stronger it is.
- The hydrogen ion is the most special ion. Hydrogen has only one proton in its nucleus and one electron in its shell and is at the top of the periodic table. By giving its only electron it becomes an ion, but in practice this ion is a proton. Therefore, in chemistry, the hydrogen ion is called proton and its inclusion in other ions, as is the case with phosphate ions in the dissociation of hydroxylapatite, is called protonation.
THE HYDROGEN ION

- Is the most special ion.
- Hydrogen has only:
  - 1 proton in its nucleus
  - 1 electron in its shell
  - is at the top of the periodic table.
- By giving its only electron it becomes an ion, but in practice this ion is a proton.
- Therefore, in chemistry, the hydrogen ion is called proton
- Its inclusion in other ions, (as is the case with phosphate ions in the dissociation of hydroxylapatite), is called protonation.
When acid is dissociated in the solution around HA, the active action of hydrogen ions begins.

Hydrogen ions are:
- the smallest,
- most mobile
- most reactive ions.

Active protons come in contact with HA and immediately combine with phosphate and hydroxide ions from the crystal by protonating them to form monohydrogenphosphate ion ($\text{HPO}_4^{2-}$) and water ($\text{H}_2\text{O}$).
- They quickly leave the crystal and move into the solution:
SOLUBILITY OF HYDROXYAPATITE IN ACID MEDIUM

- In its dissociation, hydroxyapatite releases two types of anions - phosphate and hydroxide

\[
\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \rightleftharpoons \text{Ca}^{2+} + 6\text{PO}_4^{3-} + \text{OH}^{-} \\
\downarrow \quad \text{H}^+ \\
\text{Monohydrogen phosphate ion}
\]

\[
\text{HPO}_4^{2+} + \text{H}_2\text{O} \rightleftharpoons \quad \downarrow \quad \text{H}^+ \\
\text{Dihydrogen phosphate ion}
\]

\[
\text{H}_2\text{PO}_4^{-}
\]
The more often acid is introduced, the more actively the crystal dissolves.

1. Addition of acids, the activity of the ionic product in the solution increases.

2. It becomes unsaturated.

3. In order to be saturated, new amounts of HA should be dissolved.

4. This process continues until a new level of equilibrium is obtained.

5. It is obtained due to the dissolution of crystal.

6. The more often acid is introduced, the more actively the crystal dissolves.
At pH=5.0 - the solution is unsaturated (the ionic product of HA is much < than the solubility product.

- The unsaturated solution requires a new portion of calcium and phosphate ions, extracted from crystal.

The moment when the solution is again saturated with mineral ions is called "critical pH".

- For hydroxyapatite, this value is 5.5
- Above it, parallel to the demineralization of the crystal, the reverse process is performed, although dissolution still dominates.

Only at pH about 7 the ionic product of hydroxyapatite in the solution is equal to the solubility product and equilibrium occurs in the process.

- At pH=7.0 the solution is saturated
- the ionic product is equal to the solubility product (there is mistake in the book)
PROCESS OF ENAMEL DE- AND REMINERALIZATION

- The enamel is constantly flushed by the saliva.
- Concentration of calcium and phosphate ions in saliva is constantly variable
  - but under normal conditions, their amount is about 1.5 mmol/l.
- At neutral pH - the amount of calcium and phosphate ions is sufficient to saturate the medium.
- These conditions ensure equilibrium among de- and remineralization processes and there is no substantial ionic movement.
PROCESS OF ENAMEL DE- AND REMINERALIZATION

- Under physiological conditions, saliva and oral fluids are saturated with hydroxyapatite and fluorapatite.
- This is a prerequisite for the existence of enamel apatite in the mouth.
- If oral fluids are not saturated with these apatites, the hard dental structures will dissolve without other reason.
- The higher the saturation of the environment with respect to an apatite, the greater the tendency for its formation.
By acidification of the environment, its saturation with inherent for apatite ions decreases sharply.

A level is reached in which the environment is not saturated with these ions.

This requires a quick extraction of new ions from the enamel to saturate it.

The direction of ions movement exists only in the direction from the enamel to the solution - critical pH 5.5.

This is the moment when only a process of demineralization occurs.
PROCESS OF ENAMEL REMINERALIZATION

If Ca or PO ions are added to the solution, their concentration rapidly increases, and this helps equilibrium to occur again.

No further extraction of the ions from the enamel is necessary and its solubility decreases or stops.

An excess of only one type of ion in the solution can lead to equilibrium even if the other ions are few.

It is enough for the solution to be saturated with only one type of the inherent ions to stop enamel dissolving.

Due to this phenomenon there is a possibility for enamel remineralization with the addition of calcium, phosphate or fluoride ions in solution.
Repeatedly throughout the day a partial demineralisation is performed on the enamel surface, followed by remineralization. Between the enamel and the saliva is the plaque biofilm that mediates these processes.
PROCESS OF ENAMEL DE- AND REMINERALIZATION

- At each meal, acids come in the plaque and others are formed by microbial metabolism.
- They dissociate to $H^+$ ion which diffuses into the enamel.
- Calcium and phosphate ions released from the enamel to buffer the medium fall into the plaque.
- From there, some of the ions can be released into the physiological content, and other ions can be reintroduced into the enamel when the medium is alkalinized.
- A carious process will develop when this dynamic equilibrium is won by the process of demineralization.
- Then the direction of the acid ions is towards the enamel, and the inherent for the apatite ions move toward the plaque.
In order to buffer the resulting acidity on the enamel surface, under the plaque biofilm, apatite dissolution begins.

As a result, the concentration of Ca$^{2+}$, Mg$^{2+}$, PO$_4^{3-}$, HPO$_4^{-}$, as well as carbonate/bicarbonate ions in the solution over the enamel is increased.

Such ions also come from saliva.

After the primary demineralization, as a result of the action of the saliva the alkalization of the medium begins.
PROCESS OF ENAMEL DE- AND REMINERALIZATION

- Then the ions, that saturated the environment of the enamel (the plaque liquid) are directed to the enamel and entering it can precipitate to dicalcium phosphate dihydrate or octacalcium phosphate.
- If the favorable environment continues to exist, they can be transformed to hydroxylapatite, and in the presence of fluoride ions to fluorohydroxyapatite.
- Thus remineralization of the enamel occurs
Fluorapatite (FA) or fluorhydroxyapatite (FHA) can be directly formed by alkalizing the medium and in the presence of a low concentration of F-.
By alkalisation of the medium and high concentrations of F-, CaF$_2$ is initially formed. CaF$_2$ in the presence of HPO$_4^{2-}$/PO$_4^{3-}$ can be hydrolyzed secondary to FXA. Thus formed apatite will have smaller amounts of CO$_3^{2-}$ и Mg$^{2+}$ making it much more resistant to subsequent acid exposure. This is one explanation for the greater resistance of remineralized enamel in comparison to primary mineralized enamel.
Remineralization occurs when the solution is supersaturated with inherent for the crystal ions or the ionic product is greater than the solubility product.

The possibility of remineralization and repair of partially demineralized enamel surfaces is the basis on which the contemporary respect to the carious process is built and allows the introduction of a new therapeutic approach - non-operative preventive treatment.