Lecture : 6

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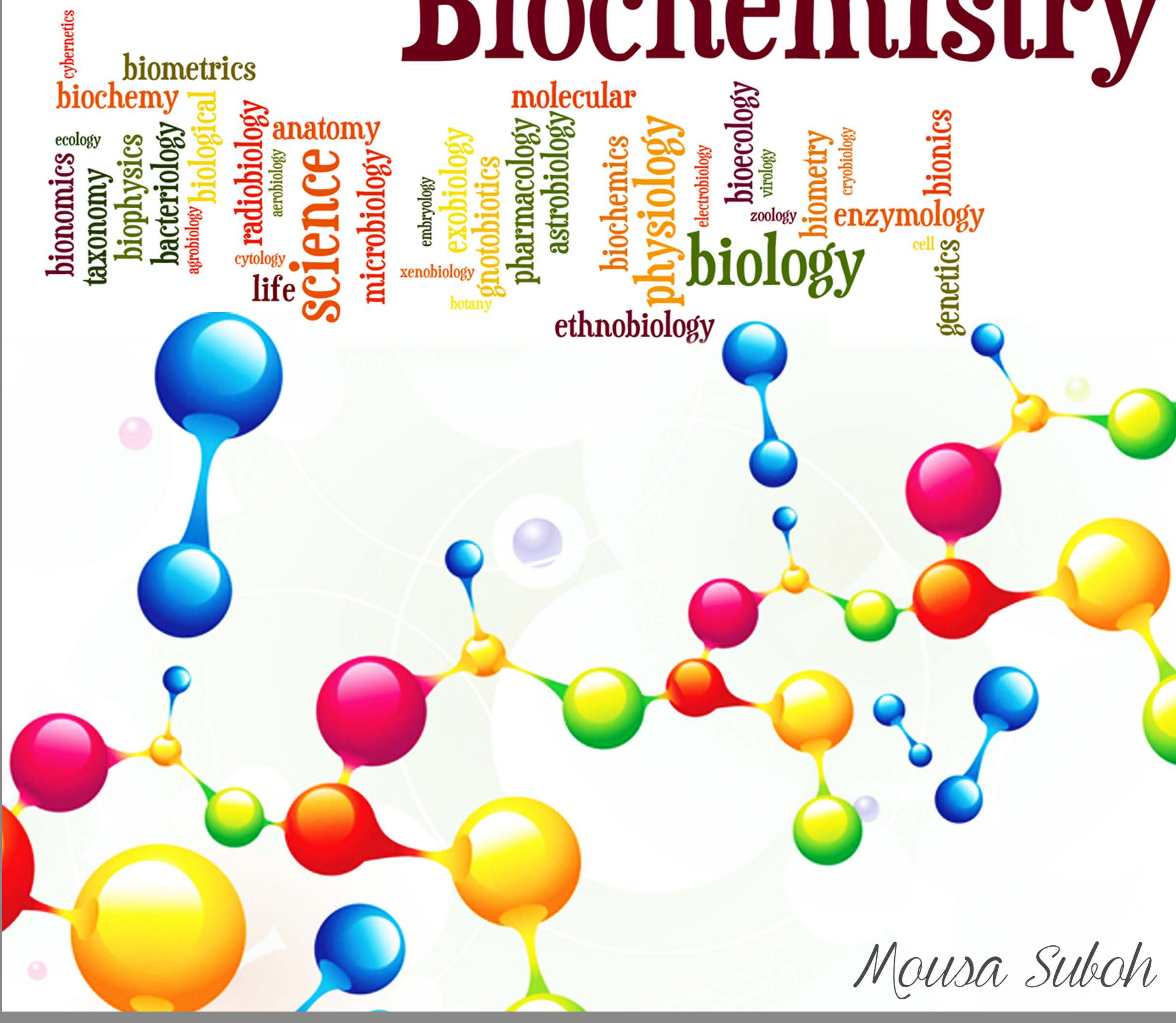
Medical Committee
The University of Jordan

Biochemistry



Fibrous proteins

Collagens

The collagen are a family of fibrous proteins with 25 different types found in all multicellular animals

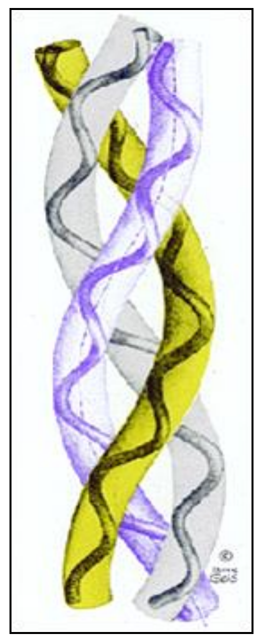
the main function of collagen molecules is to provide structural support to tissues

the primary feature of a typical collagen molecule is stiffness and rigidity

They are the most abundant proteins in mammals, constituting 25% of the total protein mass in these animals.

collagen molecules are named as type I collagen , type II , type III , and so on

the structure of collagen :

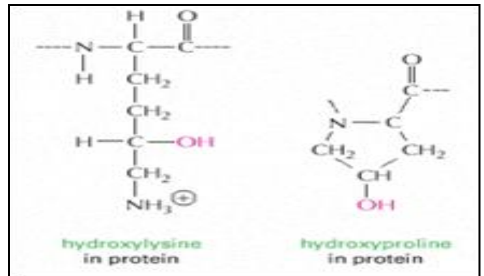


- Left-handed: the direction of rotation is to the left, while the α-helix is right-handed (it rotates to the right).
- Triple-stranded: three strands (collagen polypeptide chains, called α chains) are wound around one another in a rope like superhelix and these strands could be any type of α-collagen I, II, III (different types; each one comes from a specific gene)
- Helical protein: it is **NOT** α helical protein which has its own characteristics
  Ex → collagen helix is much more extended with 3.3 residues per turn so the number of amino acids per each turn is less than α-helix (the Collagen helix turn is smooth whereas the α-helix turn is sharp).
- The basic unit of collagen is called Tropocollagen

Composition of collagens :

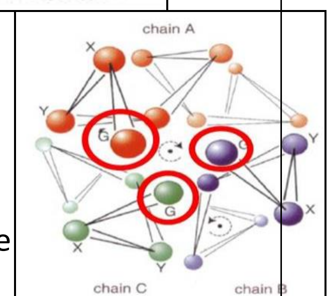
Collagens are rich in glycine (33%) and proline (13%). It is also unusual in containing 4-hydroxyproline (9%) and hydroxylysine

Every third residue is glycine, which, with the preceding residue being proline or hydroxyproline in a repetitive fashion as follows:



- Gly-pro-Y
- Gly-X-hydroxyproline

Functional purpose of amino acids :

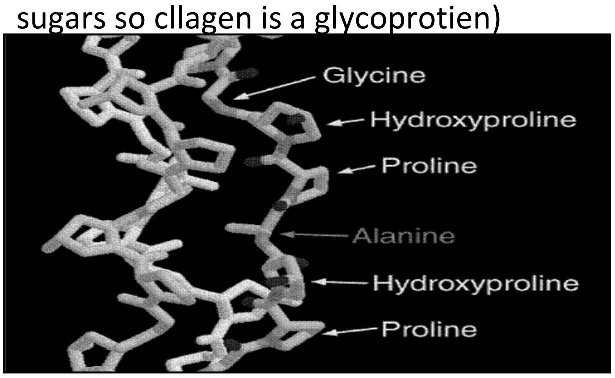


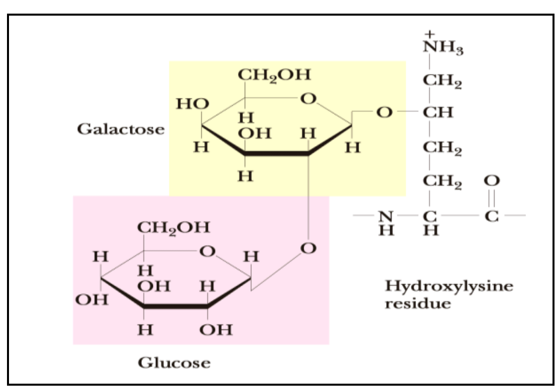
Glycine → It is a very small amino acid and the R group of it is not charged so it fits and allows the three helical a chains to pack tightly together (this makes the collagen rigid) to form the final collagen superhelix so If we look at the helix from above we will see that the position of glycine in the middle not to outside.

Proline → we said before that Proline disrupts α-helix while collagen is a helical protein rich in Proline, how is that?

Proline creates the kinks (that make the sharp turns) and stabilizes the helical conformation in each a chain. Proline is a rigid amino acid which makes the collagen a rigid protein.

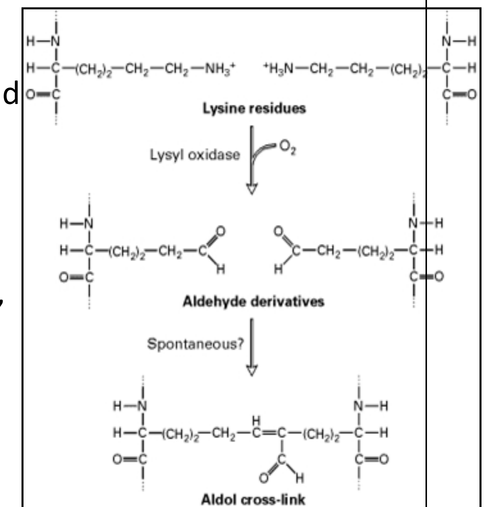
Hydroxylysine →serves as attachment sites of polysaccharides making collagen a glycoprotein. Sugars attach to the hydroxyl group (Lysine is a positively charged amino acid that is hydroxylated to get a hydroxyl group for the attachment of the sugars so cllagen is a glycoprotien)





Lysine → Some of the lysine side chains are oxidized (the amino groups is removed and there is an addition of an aldehyde group) to aldehyde derivatives. Covalent aldol cross-links form between hydroxylysine residues and lysine or another oxidized lysine, (this increases the rigidity).

These cross-links stabilize the side-by-side packing of collagen molecules and generate a strong fibril making collagen more rigid



If cross-linking is inhibited, the tensile strength of the fibrils is drastically reduced and becomes less rigid;

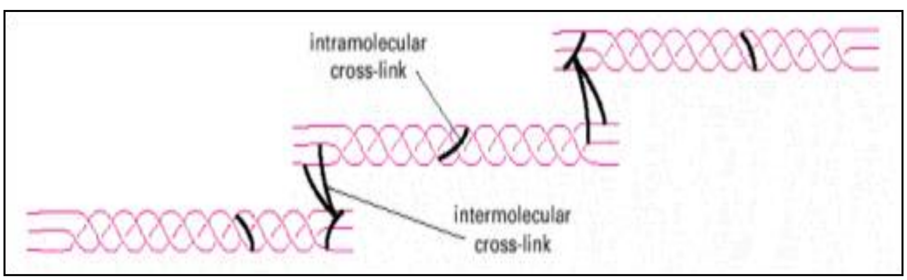
collagenous tissues become fragile, and structures such as skin,

tendons, and blood vessels tend to tear.

The amount of cross-linking in a tissue increases with age. That is why meat from older animals is tougher than meat from younger animals.

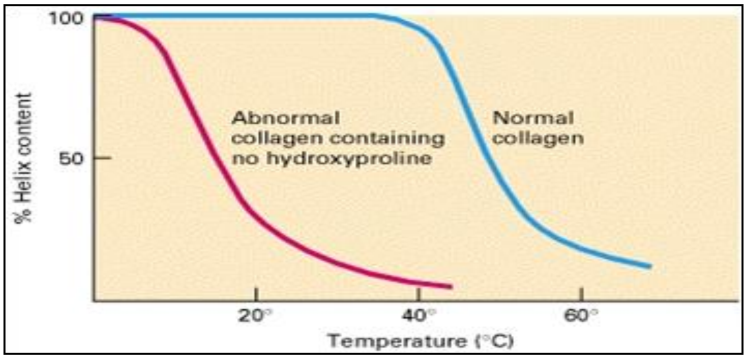
So there is two types of cross linking :

- **Intermolecular:** cross-linking **in between** tropocollagens.
- **intramolecular:** cross-linking **within** the the three strands that make up the tropocollagen (within the one tropocollagen)
  This is facilitated by oxidized by lysine.



Hydroxyproline → it makes the structure rigid and **provides stability** , it makes collagen very stable even at 40 °C. Without hydrogen bonds between hydroxyproline residues (the hydroxyl group of hydroxyproline creates hydrogen bindings (if there is a mutation in the enzyme that cuases hydroxylation of proline), the collagen helix is unstable and loses most of its helical content at temperatures above 20 °C.

The normal collagen is stable at 40 °C but the mutated one (without hydroxyproline) at 40 °C is denaturated; the three strans of tropocollagen become far away from eachother.

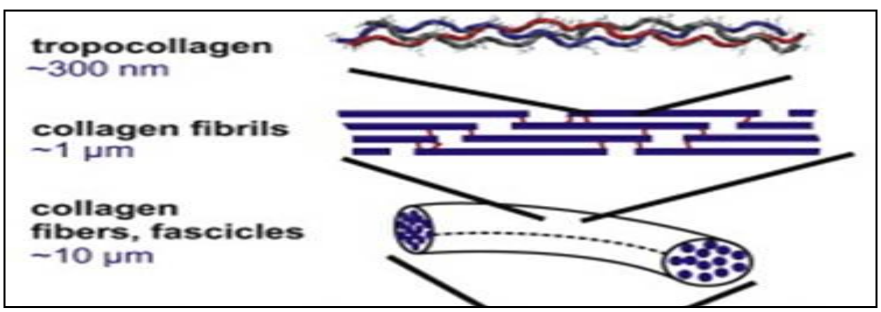


Formation of collagen fibers :

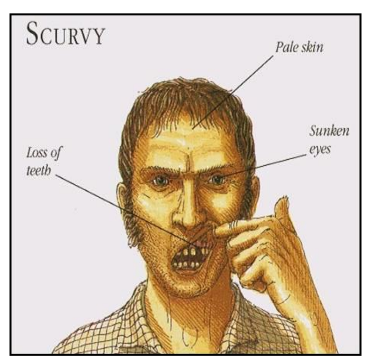
Following cellular release of **protocollagen**, **5** of them into a **microfibril**, which are connected with each other via **aldehyde links** (oxidize lysine).

Microfibrils align with each other forming **larger collagen fibrils**, which are strengthened by the formation of covalent cross-links between lysine residues.

Microfibrils assemble into **collagen fibers**. Microfibrils can be seen with electron microscope and the collagen fibers can be seen with light microscope.



Scurvy - الاسقريوط



Scurvy is a disease is caused by a dietary deficiency of ascorbic acid (vitamin C). Deficiency of vitamin C prevents proline hydroxylation (the enzyme that catalyze the hydroxylation of proline becomes inactive). The defective pro-α chains fail to form a stable triple helix and are immediately degraded within the cell.

Blood vessels become extremely fragile, teeth become loose in their sockets and the skin rupture easily .

That's why sailors who don't eat fresh food that contain vitamin C suffer from scurvy.

Elastins

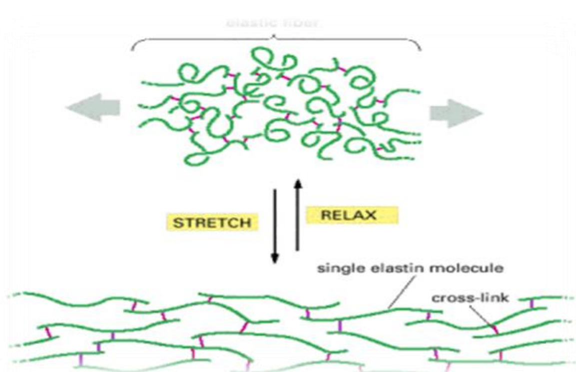
Elastins are fibrous proteins that are mixed with collagen, many tissues, such as skin, blood vessels, and lungs, need to be both strong and elastic in order to function.

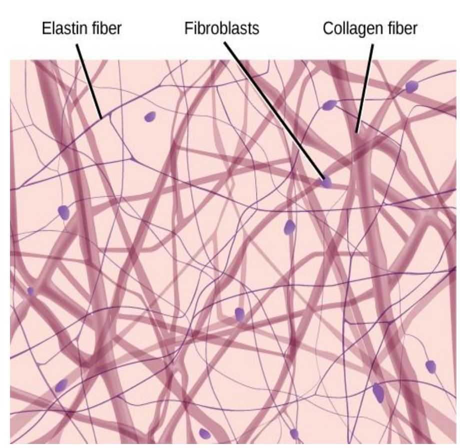
→ Collagen provides rigidity (strength)
→ Elastin provides flexibility to the tissue so it can be stretched.

So we can pull (tug) our skin becaause of elastin and but we can't tear it because of collagen.

((long inelastic collagen fibrils are interwoven with the elastic fibers to limit the extent of stretching and prevent the tissue from tearing))

Elastin is a coiled protein; a network of elastic fibers in the extracellular matrix of these tissues gives them the required resilience so that they can recoil after transient stretch.





The main component of elastic fibers is elastin, which is a highly hydrophobic protein and is rich in (proline and glycine) → they help packing the protein and creating kinks .

* hydrophobic nature gives the elasticity

It contains some hydroxyproline but **No** hydroxylysine → so it is not glycosylated (doesn't get polysaccharides attached to it , so it's not a glycolprotein)

Remember : Hydroxylysine serves as attachment sites of polysaccharides making protein a glycoprotein, which is found in collagen

The primary component, tropoelastin molecules, is cross-linked between lysines to one another, so there is a cross-linking but there is no glycosylation.

The elastin protein is composed largely of two types of short segments that alternate along the polypeptide chain:

- Hydrophobic segments, which are responsible for the elastic properties of the molecule.
- Alanine- and lysine-rich α-helical segments, which form cross-links between adjacent molecules

Keratins

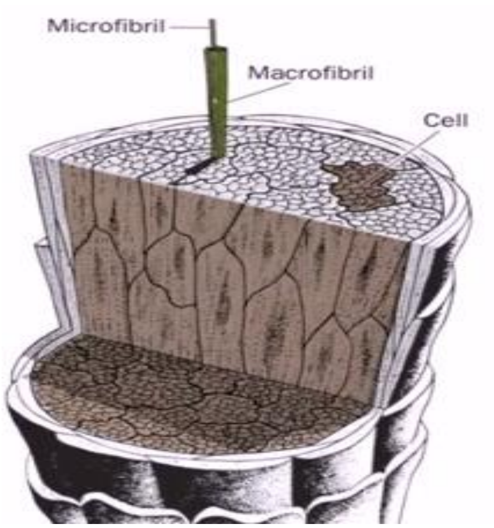
Fibrous protein , we have two types of keratin **α-keratin** and **β-keratin** which as members of a broad group of intermediate filament proteins

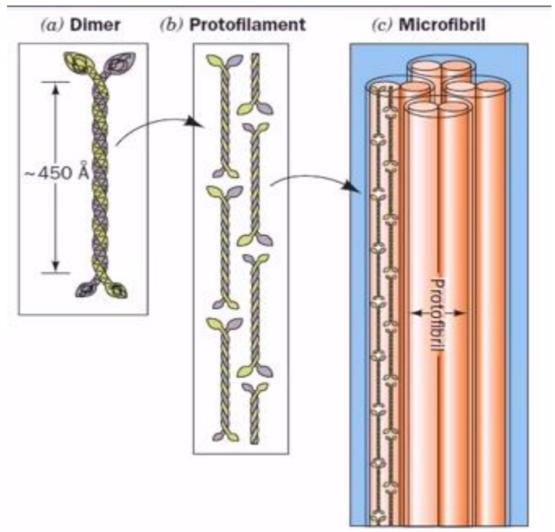
- α–keratin is the major proteins of hair and fingernails as well as animal skin
- α–keratin has unusually high content of cysteine → disulfide bonds

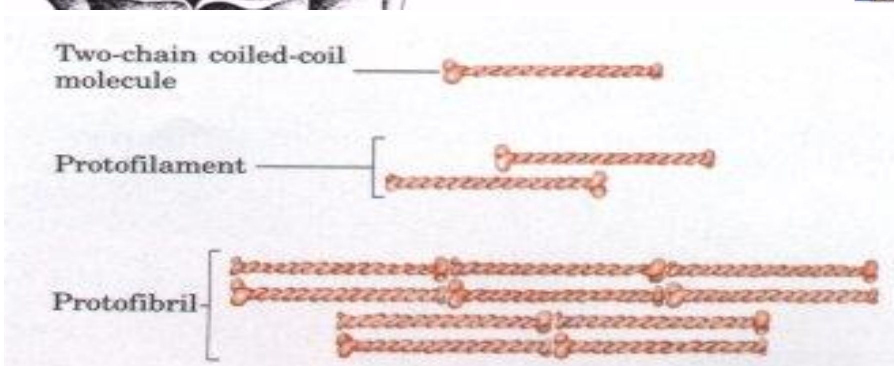
α –keratin structure :

- **two helical α –keratin molecules interwine**
- two dimmers twist together to form a **4-molecule protofibril** .
- **eight protofibrils** combine to make the **microfibril**
- **hundreds of microfibrils** are cemented into a **macrofibril**

- α-keratin is hardened by the introduction of disulfide cross-links specially in finger nails
  there are α-keratins in hair and nails but the α-keratin in nails have a lot of disulfide bonds because of that nails are hard while in the hair it's different it doesn't have that much

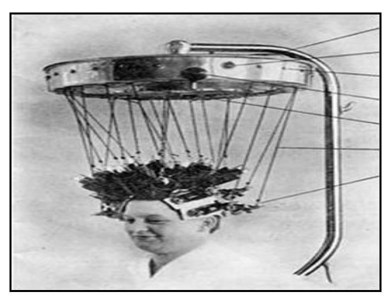






How is a perm done?

A basic reducing substance (usually ammonium thioglycolate) is added to reduce and rupture some of the disulfide cross-links



Temporary Wave

(by reformation of hydrogen bonds) when the hair gets wet, water molecules intrude into the keratin strands disrupting some of the hydrogen bonds between microfibrils , which help to keep the alpha-helices aligned. When hair is dried up, the hair strands are able for a short time to maintain the new curl

Permanent wave

(by re formation of disulfide bonds) The hair is put on rollers or curlers. The alpha-helices can shift positions. An oxidizing agent, usually a dilute solution of hydrogen peroxide, is added to reform the disulfide bonds in their new positions. The permanent will hold these new disulfide bond positions until the hair grows out
(reduction of disulfide bonds so they are broken, then they roll the hair, after that reoxidation is done to reform the new disulfide bonds)

***Important notes the doctor mentioned about previous lecture**

When pH < pKa the group is protonated (abundance of protons)

When pH > pKa the group is unprotonated

When amino group protonated → ionized

When carboxylic group protonated → unionized