FULL SKIN SHEET COVERING ALL SKIN LECTURES

**SKIN TISSUE:**

Role of the skin; its functions in our bodies and its importance:

If you want to know its functions, go to burns unit in Jordan hospital in -1 floor: P

Simply, patients there have no skin in some places of their bodies, probably all places in their bodies

 Patients in pain, because there are free nerve endings inside the epithelium which burn, so they are exposed now, these patients given morphine (sedation)

**Sedation** means that there is pain, and pain means exposure of nerve endings

 Also, they are given *saline* (note that he eats and drinks)  *IV fluid*

Because the skin was preventing water loss in the body and now after it burns, no matter how much he eats and drinks, he is not compensating for the loss in the body so he must be given IV fluid

 Another patient, he is on antibiotics

Skin was protecting under lining structure from the effect of bacteria

Now without skin, bacteria have free access to enter the body so they should be covered by antibiotics

 Sometimes they are covered with a Cardin

* light is turned off, light transmits ultra violet rays

Skin was protecting under lining structure from UV rays

Now and without skin, body must be covered

\*Skin takes the UV rays when it arrives to it, and converts cholecalciferol to dihydrocholecalciferol, which is the precursor of the vitamin D3 helping in the absorbance of calcium from intestine and kidney (now this effect isn't present)

**Skin is a physical Perrier**

 Protection: protects the body from a lot of incoming substances

 Sensation

 Endocrine function**:** skin secretes materials which travel to other places to perform their function (hormones)

-It secretes vitamin D3 which goes to the intestine and kidney to perform its function

 *Thermo regulation*: one of the factors that contribute to the stability of the temperature of the body

**integumentary system:** the largest system in the body consists of the skin and appendages (hair, nail, sweat gland)

Some people consider female breast which a modified apocrine sweat gland, as one of the appendages

a person with a weight of 70 kg, has about 12 kg skin, also the skin covers areas about 1.5 m2 to 2.5 m2

m2 = 10.000 cm2

2 m2 = 20.000 cm2 =

Keeping in mind that the upper layer is stratified epithelium, its thickness might be made up from more than a 100 layer

So the number of cells of this system is laterally a huge number, and it must remain constant all the time

If there is a loss of the cells of the skin at any given time, the cells on the basal layer start to multiply to replace them, and if they fail, ulcers will occur ex: diabetic foot, decubitus ulcers

**Skin is two layers:**

 *Ectodermal* in origin, surface ectoderm form epidermis which is stratified squamous epithelium of the keratinized type

 *Mesodermal* which form the connective tissue

The thickness of stratified epithelium differs from one place to another

**Types of the skin:**

 At the palm of the hand, sole of the foot, there is no hair, and it's impossible to grow under any conditions (thick skin)

Glamorous skin = hairless skin

The thickness of **glamorous skin** is more than the thickness of the skin with hair.

*Exception*: If you look at the skin of the back of the neck (nuchal region), you will see that the thickness of it is greater than the thickness of the palm of the hand and sole of the foot (thick skin)

 Thin skin (with hair)

Anywhere where hair is grown on the skin called *thin skin* even if its thickness was more than the thickness of thick skin

The layer under the **epidermis** is the **dermis,** superficial fascia in the embryo was called binoculars adipose, it's not part of the skin, but we will take about it as **hypodermis**

**3 components of the skin:**

 *Epidermis*: cellular (stratified squamous epithelium of the keratinized type)

 *Dermis*: fibrous, CT, most of its components are dense irregular CT

 *Hypodermis*: yellow adipose tissue

There is a basal lamina, which is important in the skin, it's not a straight line, so the CT must move upward to meet it (the process of the CT is moving upward towards the basal lamina called **dermal papilla**)

On the other hand, the thickness of the epithelium is variable

The thickness of the epithelium over the dermal papilla is less

Indentation of the epithelium into dermis which is moving downwards is called **rete-ridges**

Dermis moving upwards, epidermis moving downwards

-In certain parts of the body particularly at the tips of fingers, this special arrangement makes the finger prints, they are genetically determined, and it's impossible to change them under any conditions

**Layers of the skin:**

Start with the basal lamina

 The first layer above the basal lamina (it's cuboidal - columnar), mitotic activity starts from the basal layer

**Stratum basale**: one row of cells, the cells are connected together by different types of junctions and connected to under lining basal lamina by hemi-desmosomes, the cells on the basal lamina are typical protein synthetic cells, they have large rounded nucleus, its cytoplasm tends to be basophilic, most of time depending on their activity

Stratum basale in both types of skin (thin and thick) is one layer

**The cells change their shape as they move upwards**

 **Stratum spinosum**: Instead of being cuboidal - columnar, they become polyhedral, and they lose all types of junctions except desmosomes which add to their stability in the upper layer, these desmosomes appear under the microscope as s*pines*

Stratum spinosum: its thickness differs from one part to another

Ex: upper eye lid (it's thin) >> 3 – 4 layers

Back of the neck, sole of the foot >> 35 layers (which means that the cell of the stratum basale divide 35 times)

 Why do cells start to lose their junctions??

Cells start to synthesize a material inside it which gradually moves towards the plasma membrane of the cell

In the upper layer of the stratum spinosum (assume that the thickness of stratum spinosum is 30 layers), starting from layer 25 or around that, granules appear inside the cytoplasm of the cell, and these granules start to move gradually towards the plasma membrane

At the layer 25 >> they are close to the nucleus

At the layer 26 >> they become closer to the plasma membrane

At the layer 30 >> they fuse with the plasma membrane

Granules are surrounded by a membrane, and because of that their shape is regular, they are not seen in the light microscope, they can be seen in the electron microscope

When granules fuse with the plasma membrane, they open and empty their content on the surface of the cell

Content of granules >> high amount of phospholipids

So when phospholipids cover the outer surface of the cell >> a sort of barrier protecting the cell

If all cells secrete phospholipids which cover the outer surface of cell, they will create an insulating layer which insulates the above part from contents below

-They were described in 1962 and they were called membrane **coating granules**, then they were called **membrane coated granules**, after that and under the electron microscope, they appear as dark and light areas so they were called them **lamellar bodies**. Finally, and according to the first scientist who discovered and described them, they are called "**odland bodies"**

They are electron microscopic structures

Later on, they managed to take the material which was secreted from these bodies, and they analyzed it, they called the material containing high amount of phospholipids **natural moisturizing factor (NMF**), it's a natural product, re-establishes the softness of the skin

**Changes of the cell as they are moving upward:**

 Their shape changes

 They lose their junctions

 Upper layer starts to show lamellar bodies

 In addition to that, they started to increase their content of cytokeratin

\*Suddenly, in the upper layers of stratum spinosum, dark granules start to appear, they are intensely basophilic in hematoxylin and eosin, they have a high content of sulfur, and they are not limited by a membrane, that's why they appear irregular in shape

 The cytokeratin inside the cell form something called **tonofilaments** which go inside these granules

 We called these granules **keratohyalin granules**

 The layers where keratin hyaline granules appear called **stratum granulosum**

\*\*If the keratin hyaline granules are not formed, it's impossible for epithelium to become keratinized

\*\* keratohyalin granules appear (there is stratum granulosum) but the cytokeratin failed to insert inside the keratohyalin granules, it's impossible for epithelium to become keratinized

**Conditions allowing keratinization:**

 keratin hyaline granules

 cytokeratin must insert inside them

\*both exist but they don't overlap each other, it's impossible for epithelium to become keratinized

stratum granulosum: (1-9 layers)

In thin skin (eye lid), scrotum in males and labium in females, the thickness of stratum granulosum is 1-2 layers, and sometimes they are interrupted (4 cells then a space then 10 cells then space and so on , in horizontal)

\*In thick skin such as the palm of the hand, it might be up to 8-9 layers

The nucleus starts to show signs of degeneration, the cell is dying gradually

 in thick skin there is a layer above stratum granulosum where the nucleus is lost; all organelles of the cell are lost too

\*keratin is not closely packed inside the cell, this area appears as a translucent layer called **stratum lucidum**

It doesn't exist except in thick skin, and its thickness is less than or equals 3 layers

 above the stratum lucidum in thick skin and above the stratum granulosum in thin skin, there is a layer called **stratum corneum**

1. there are no organelles in the cell

2. no nucleus

3. the keratin inside the cell is a very closely packed

4. Its thickness is 5- 55 layers

Most of the thickness of the skin is due to stratum spinosum (35 layers), and stratum corneum (55 layers)

morphologically, stratum corneum is a dead layer

When you take a bath, actually, you are removing millions of cells of stratum corneum, and then they regenerate

\*stratum corneum responds to oils, creams and other things, and cells that respond to a stimulus are living cells

|  |  |
| --- | --- |
| Thick skin | Thin skin |
| stratum corneum | stratum corneum |
| stratum Lucidum |  |
| stratum granulosum | stratum granulosum |
| stratum spinosum | stratum spinosum |
| stratum basale | stratum basale |

Summary of above notes

 Epidermis: cellular, multiplies and divides in basal layer (stratum basal) and contains stratum lucidum (that aren't included in thin skin), granulosa cordum (that don’t contain any granules >>>>>>>>>>>

 Epidermal-dermal junction: finger-liked

 Dermis: fibrous

 Hypodermis: superficial fascia under skin, NOT included in layers of skin

 Adipose tissue: NOT included in layers of skin

>>>>>>>>>

Skin:

 Thin: with hair… all parts of the body can grow hair!

 thick: without hair, restricted into two areas

 sole of the foot

 Palm of the hand

Integumentary system:

Skin, appendages (hair, nails, sebaceous glands, sweat glands), Arrector Pili Muscle (smooth muscle in the skin attach the hair).

Function of the skin:

 Protection

 Sensation

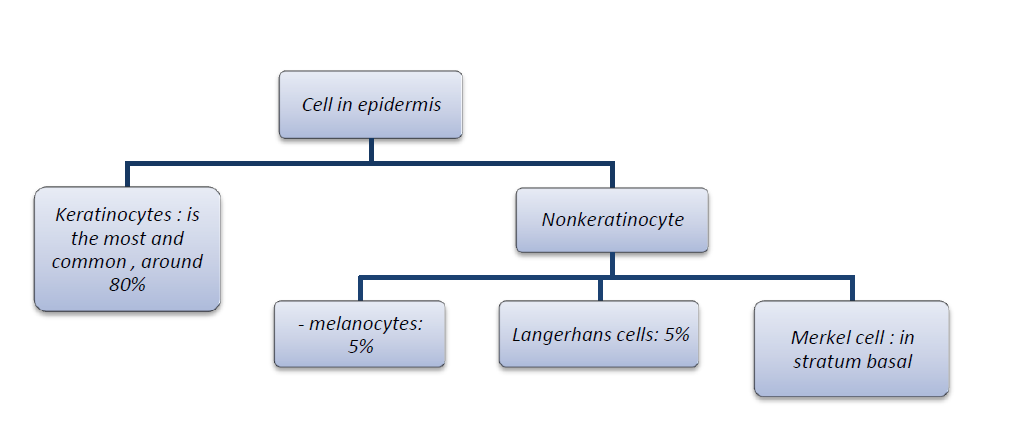
 Secretion

 Regulation the body temperature

The difference between thick & thin skin is that the thin have the hair



The cell coming upward from stratum basale starts to accumulate cytokeratin becomes *keratinized epithelial*. These cells will be called to **keratinocytes.**



**Melanocytes**

 In the nerve there are regions called neural crests, beside it there is a surface ectoderm and between 2 neural crests there is a neural ectoderm (which forms neural tube later on)

In the 10th week of fetal life, the cells start migration from neural crest to epidermis and arrives at the 11th (they need 1 week), they will be larger than nearby cells.

\* The melanocytes insinuate themselves among the cells of stratum basale and push the basal lamina down because of their size.

 Most of the cells that originate from neural crest are dendritic thus the melanocytes are dendrites, and they send dendrites to nearby cell (the cells nearby it in stratum basal) Each melanocyte sends 3-30 processes. Each melanocyte is in contact with 3-30 keratinocytes



\*\* **Epidermal melanin unit**: melanocyte, its dendrites and keratinocytes which are in touch with them.

\*\* **Nevus:** are the spots which appear when melanocytes rest during their migration then they secrete a specific substance

**The nevus is:**

- Viable extent: they appear a lot in sacrum and coccyx (called it Mongolian spots)

\*Density of secretion: (light color and dark)

 The melanocyte takes amino acid “**TYROSIN** “from circulation and starts to form melanin which passes in different stages during formation, the first stage is that when melanin is very close to nucleus it gradually starts to migrate into the dendrites tip of it which is the last stage. Then melanin becomes darker. The melanin becomes multicolored; dark and light areas, and appearance similar to the lamellar bodies. \*\* **NMF** (**Natural Moisturizing Factor)** they cover the surface of the epithelium sort of protection.

 Appearance of melanocyte : melanin in dendrites is limited which indicates that melanin isn't mature, when it arrives the tip of dendrites it appears extremely dark and attaches with keratinocytes, keratinocyte is going to phagocytose the melanin by lysosomes. Lysosomes from the melanocyte phagocytose the melanin from the tips of the dendrites.

 The melanin covers the upper part of the nucleus of keratinocytes to form a **supranuclear cap,** which protects the nucleus from ultraviolet waves.



Exposure to UV waves results in extensive formation of keratinocytes so the melanocyte cannot form melanin for all cells to cover all the areas ,so in the new cells (keratinocytes) there are no supra-nuclear cap thus the nuclei are exposed directly to UV waves = CANCER . People spending more time under the sun are most likely to get cancer; they were advised to wear suitable clothes to protect themselves from the sun.

 **The most important factor to determine the color of the skin is the melanocytes** but there are other factors, the number of melanocytes is the same in all people no matter what the color of the skin is.

- *Carotene pigment*: It is a genetically determined secretion. Carotene pigment in hypodermis mainly, is responsible for the yellow to reddish tones people of Asian and American-Indian ancestry have more carotene in the stratum corneum. - Hemoglobin is in red blood cells within the capillaries in the dermis. The thickness of the skin differs from one person to anther and from females and males (thinner in females) it reflects the color of blood vessels in dermis e.g. when shy = red, cold = blue

Anyone whether black or white or albino has the same number of melanocyte = 800 -1000 cell/ mm.

\* Skin color cannot be identical to mother or father unless it’d pure

 And it is **fully differentiated** (don’t divide) so any abnormal division causes cancer ‘melanoma‘is the most dangerous type of cancers.

 Activity of melanocyte is **genetically determined.**

\***Tyrosinase** is the enzyme fully essential for the formation of melanin

If it absent, its **albinism**

\*Insufficiency of the enzyme is the reason for the white color

 Action of melanocytes is flexible, but the color will not change; except under certain drugs which are used in cancer as [cytoscreen], which result in the inhibition of melanocytes and conversion of the color of skin from black to white.

\*UV Waves stimulate the melanocyte to secrete more melanin, but if it is stimulated for a long time keratinocytes keep their color for 28 days. (Which is the time that needed for keratinocytes to migrate from basal lamina)?And when the skin is being under sun exposure for a long time that means it needs more than 28 days before converting back to its normal color.

 Melanocytes are closer to blood vessels than epithelia because they are in the lower part of lamina, and the cancer may transmit to blood vessels. And when the **Nevus** becomes darker, prominent, and itchy or becomes protruding out of the skin and blood vessels are coming towards them, it should be surgically removed as melanocytes are fully differentiated and resistant to all types of chemical and biological treatment. If it is kept, melanoma spreads to other parts of the body. Melanoma is one of the worst types of cancer.

**Langerhans**

Paul Langer Hans's story: Paul Langerhans, a German physician and anatomist, who discovered the cells at the age of 21 while he was a medical student

When he stained the skin with special staining which has gold. The staining is already intercellular which means it can’t be removed even by washing .It appeared as dark spots within dendrites

Paul’s conclusions were wrong about the cell. He concluded some stuff depending on the shape.

Langerhan’s cells:

 Located in epidermis

 Have dendrites  Origin from bone narrow from differentiation of monocytes. Part of MPS  Antigen-presenting immune cells

 It is clear cell (don't stain by H &E) in addition to melanocytes



To distinguish between melanocyte and langerhans:

**By location** Langerhans: stratum spinosum. In epidermis monocytes: Cannot be directly above stratum basale

**Merkel cells**

 It is a clear cell

 Located on the basal lamina (there are also melanocytes but they are dendritic and it’s between stratum basale at lower level, however merkel cells are not dendritic and aren't on the same level of the stratum basale)

 With special stain the neurotransmitter will appear. Related to the nervous system.

 Origin from neural crest

**\*\* desmosomes** between adjacent analogical cells

- Melanocyte + basal lamina = hemidesmosome

- Melanocyte + keratinocyte = no desmosome

- Keratinocyte + merkel cell = desmosome [that mean they are analogical]

 All cells on stratum basale are dividing but we don’t know when they will stop. When keratinocytes stop dividing they are going to become merkel cells

Merkel cells are retired keratinocytes that stopped dividing

 Basal aspect of keratinocytes some of them have something fork-like, they are stem cells which divide into keratinocytes. If they lose their ability to divide their basal part becomes straight. Once they lose the ability to divide they become merkel cells… this theory states that merkel cells are not of a neural crest origin. Under these cells there is nerve, when it reaches the basal lamina it is unmyelinated and it forms a disk right under the cell. This is called a **merkel disc.** This nerve is said to have came to a keratinocyte and inhibited it, and turned it into a merkel cell. The function of a merkel cell is most likely to be for receiving sensation (receives low sensations).

\*When aging or under solar effect, the skin becomes straighter because the quality of collagen & elastic fibers which were formed by fibroblast is going to be weaker.

Earlier signs of ageing are appearing.

 There is unmyelinated nerve passes through trends of basal lamina **inhibits** the growth of **keratinocytes.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Features** | **Melanocyte** | **Langerhans cell** | **Merkel cell** |
| **Is it a clear cell** | **Yes** | **Yes** | **Yes** |
| **Has dendrites** | **Yes** | **Yes** | **No** |
| **Location** | **Stratum basale** | **Stratum spinosum** | **Stratum basale** |
| **Origin from** | **Neural crest** | **Bone marrow** | **Neural crest/unknown origin** |
| **Function** | **Physical protection by melanin** | **Immune system** | **Mechanical receptor for pain** |

**\*notes**

- Nonkeratin cells form 10% of skin cells in epidermis

- Skin surface = 2.5 m2 (as what dr. said)

- The skin loss is 1000 cells/ hour/ 1cm2 >>> when the cells are protected

\*Unprotected cells lose more than protected (in showering or under sun exposure)

- at any time stratum basale must be divided (mitosis) to compensate for the lost cells

**\*\* dermal-epidermal junctions**

The dermal-epidermal junction in the skin is very important because everywhere in the skin there are antigenic cells of substances for specific site i.e. the substance in the site cannot be in other places.

The body forms antibodies for these substances.

The antigen anti body reaction will disturb the function of the basal lamina. Basal lamina prevents substances from passing through. When it is disturbed substances go through to the epidermis and epidermal cells get separated.

\*As we age, the basal lamina becomes straighter. The more we get exposed to sun more, the basal lamina gets straighter. A person who is aging and is exposed to a lot of sun, will age faster.

Protection might delay aging! People who cannot afford good quality protection creams tend to age faster. As we grow older fibroblast increase their production of collagen and elastic fibers, but at a lower quality.

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**The dermis**

- papillary dermis: right under epidermis

o Loose connective tissue.

 Superficial dermis.

 Under epidermis immediately.

 Contain: WBCs, mast cells (with certain numbers if it increase it will be pathological), fibroblasts.

- reticular dermis: nearer to the blood vessels

o Dense irregular connective tissue.

 Deep dermis.

 Deep to papillary dermis.

**No. of Reticular fibers in papillary dermis > No. of Reticular fibers in reticular dermis**

**DERMIS IS OF VARIABLE THICKNESS.**

**\* In papillary dermis there are lots of type of cells including fibroblasts and mast cells. If mast cells increase they might be pathological.**

Dermis is different in its thickness, this is why the skin is thin, like eyelid or thick like back and all sides of neck, (DERMIS IS WHAT MAKES THE SKIN LOOK THICK OR THIN) but it is the thin skin whereas the thick skin is in the sole of the foot and Palm of the hand.

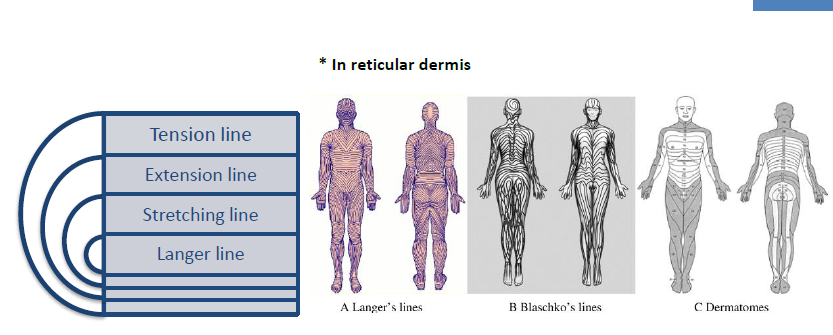
-Collagen fibers are anchoring dermis into basal lamina so the lamina densa is closer to CT anchoring fibers is type 6 &7 of collagen.

The number of projections in the papillary dermis is a big number when the person uses his hands more while working.

This is the sort of protection (mechanical protection) is to keep the dermis and epidermis contacted with each other all the time (in females the number is small because of the manual work).

The number of projection will increase by using our skin. E.g. hands

**Reticular Dermis**



As the name implies it is made of dense irregular connective tissue.

These tension lines are present in the same direction of collagen fibers. For example, in the chest area the collagen fibers are diagonal in direction; the lines are diagonal there. In the face and the upper limp these lines take the shape of a large hemi circle.

\*What is their importance?!

In surgical injury

 Perpendicular to the fibers:

 It cuts the fibers

 The fibroblast takes a long time to form collagen … it stimulates the fibroblast to produce collagen fibers and form “keloid**”**

 It takes more time to recover

 Parallel to the fibers:

 It separates the fibers

 Quick recovery

When Langer described this area… he said although this is dense irregular connective tissue, it has a sort of regular irregularity. Bundles form a network but within the bundle the fibers.

**Note**

\* The doctor insisted that melanocytes are only attached by hemidesmosomes with the underlying basal lamina and they are not attached by desmosomes with the nearby structures (the nearby keratinocytes).

\*Why does the skin/the hair appear sometimes dark and sometimes appear blond? , what are the factors that make the hair differ in color?

1) Everybody has got two types of melanin : a) Pheomelanin which appears brown to black , b) Eumelanin which appears lighter in color , so **depending** in which one of those types is existed more the color of the skin will differ .

2) Depending on the **concentration** of melanin in the keratinocytes so whenever this concentration increases the color will be darker in color.

3) The **activity** of melanocytes , for example at old age this activity decreases so the color of the hair specifically will be affected ( it will be light in color ) , at late level of life the melanocytes stop secreting melanin in hair and this happens gradually ( so the color of this hair will change gradually from gray to white ) .

\* The first part of the body will be affected by this is the region of sideburns because of this they are called the gray line.

4) The melanocytes are under the effect of the **sympathetic** system: so whenever it becomes overactive, the melanocytes will be inhibited so the color of either the skin or the hair will be affected, however the color of the skin is going to be fixed (will not be affected considerably), on the other hand the color of the hair will be affected more.

\*\* The activity of the melanocytes is the same in the hair and in the skin, this activity (the secretion of melanin) is not continuous, but it happens in cycles (they secrete melanin then they stop then they secretes then stop and so on)

This activity is stopped by the sympathetic effect (the cycles will stop and the color of the hair will be changed to gray then to white)

**Blood vessels of dermis**

\* The blood supply of the skin comes from the muscles, the vessels that supply the skin are called the cutaneous blood vessels which pass to the dermis and then they form two arterial plexuses:

1) Superficial which comes to the junction between papillary (superficial) and reticular (deep) dermis.

2) Deep at the junction between reticular dermis and hypodermis.

\* those two arterial plexuses are **interconnected** with each other (so there is an artery leaving from the deep towards the superficial part, and another which comes from the superficial towards the deep).

\* There are three venous plexuses, two of them are at the same level of the arterial plexuses in dermis and the third one in between, and they are:

1) Superficial

2) deep

3) intermediate: lies in the middle of dermis.

**Arteriovenous anastomoses (or shunts)**

\* at the normal state in the body the artery forms capillaries at its end and those capillaries gather to form vein (the arteries are connected with veins via capillaries).

\* However in many places in the skin the artery is directly terminated into vein by passing the capillaries at that place. At this case the artery comes in contact directly with the vein, so there must be a smooth muscle at the junction encircling the site of anastomoses, *this muscle is called Glumas*

\* This smooth muscle is contracted into its normal state in order to prevent the passage of the blood from the artery towards the vein , however when the temperature of the body is raised, the glumas relaxes , this allows the passage of arterial blood directly toward the venous circulation , this accelerates the blood circulation , and this in turn accelerates the heat loss of the body , however this smooth muscle will reconstruct whenever the temperature of the body becomes normal or close to normal .

\*\* Note that when the smooth muscle is contracted the blood passes from the artery to vein indirectly through capillaries, however when it relaxes the blood passes from artery to vein directly without passing the capillary.

\* At the normal conditions 5% of the circulation is opened and 95% is closed in capillaries and they are alternating (changing so that the 5% will be opened and another 5% will be closed and so on)

\* those 5% are overlapped: there is a connection between the first opened the 5% and the next 5% and this part will still gain its blood supply

\*The blood supply of the skin is *profuse*: At the time when the body is affected by a shock (the volume of blood in the circulation is changed) for example when exposed to an antibody which the body is in sensitivity towards e.g. a bee sting or snake venom and so on, in these cases toxins enter the circulation and they open the collateral circulation, so whenever the open circulated blood increases for example by 1% then we need more blood.. and this blood that is needed is going to be shifted from cutaneous tissues (the skin) to pass toward the vital organs, and that's why when the circulation is opened further, the individual gets dizzy and then this person falls because the blood is being pumped towards brain against the gravity

\* Falling on the ground is a defensive mechanism that makes the heart and the brain at the same level so we canceled the gravity effect, the skin of this patient will be cold because the blood moved from the skin toward vital organs.

- The first aid of this case is to pull the patient legs up so that will make the blood moves toward brain and the upper structures of head and neck.

**Types of sweat glands**

**1) Merocrine (eccrine)**

\* Merocrine glands in skin in particular are called *eccrine glands*

\* They are *simple tubular*, because their length is longer than the area that they are located in, so the secreting part becomes coiled

\* The secreting part and the duct are continuous with each other but we are going to deal with them as two separate entities

\* the secreting part shows three types of cells: Dark, clear, myoepithelial cells

\*: Dark cells and clear cells are over riding each other: the dark is over the clear area so it gives you the impression that they are stratified cuboidal epithelium.

the clear area is in touch with the basal lamina and it doesn't reach the lumen.

The dark area reaches the lumen but it's not in touch with the basal lamina

\* their colors differ because the presence of granules in dark cells and due to the lack of granules in clear cells.

\* Those granules are apical in position, and they contain a lot of glycoprotein

\* Those two cells (dark and clear) are surrounded from the external side by the myoepithelial cells which were described as "basket cells": it surrounds the secreting part from the external side.

\* this cell contains actin and myosin and cytokeratin (thus it owns the properties of muscles and epithelium)

\* myoepithelium was thought to be contractile due to the presence of actin and myosin and it was thought that its contraction causes the evacuation of the eccrine contents , that was believed to be true until a scientific called Szato who set the records straight as he designed an experiment focused on degeneration the myoepithelial cells by stimulating it by electricity . He discovered that the gland which he degenerated its myoepithelial cells still has its secretion activity normally however the secreting part became dilated.

\* He concluded that: the function of myoepithelium is not to evacuate the secretion but it's only to support the secreting part.

However the secretion is secreted by the capillary phenomena because the secreting part is wider than the duct system

\* the products of secretion are composed by the eccrine glands which are similar to those in plasma. The plasma contains 140 mEq Na+/L

\* we can find 140meq Na+/L at the secreting part o0f the sweat gland

so if this secretion and loss of sodium continues the level of sodium will decrease in the blood, however when we analyzed the sweat from the skin surface we found that the sodium content is less than 140mEq Na+/L

\* the conclusion : the secreting part of eccrine secreted140 mEq Na+/L but during the passage of the sweat in the duct system the duct reabsorbed part of the sodium back to the circulation and this justifies why we find only 85 mEq Na+/L (less sodium ions) in the skin surface

\*the beginning of the duct system is simple cuboidal , then the cells get bigger gradually , but in the end the duct will go through the epidermis , here the lining of the duct will be stratified squamous keratinized epithelium , this indicates that whenever the sweat reaches the epidermis its composition will never change because the keratinized stratified squamous epithelium will never absorb anything " (not part of its function), however its function is just ensure that the sweat reaches the surface

\* Acrosyrengium : is a part of the duct of eccrine sweat gland that projects inside the epidermis , it's related with a cancer-related sweat gland and it's called acrosyrengiuma ( cancer in the duct of sweat gland inside the epidermis)

\*Eccrine sweat glands are innervated by cholinergic fibers

\*the secreting products of sweat glands are odorless , but what makes the odor is the fermentation of bacteria that are found in the surface of the skin , they produce fermentation due to the presence of glycoproteins.

\* another point: many of the products that we usually eat are going to be secreted by sweat such as: onion carry, alcohol... ETC, And that will make an odor for the sweat

\* Diabetic patients; whenever the level of their blood sugar increases too high which causes ketoacidosis, their sweat odor smell like acetone

\* the patients who suffer from kidney (renal) failure their sweat odor contains urea

-the urea tries to find alternative ways to be secreted out of the body, so it will be secreted with sweat.

**2) Apocrine sweat gland**

Apocrine glands are said to be apocrine because they are similar to those in animals, however their secretion differs from those "apocrine in animals" because they don't have an odor.

\* the doctor said that their secretion is merocrine

\* it's found in axilla region, around the nipple, around the umbilicus, and in genetal-urinoary regions.

\*the ducts opens in hair follicles , its secreting part is wider than the secreting part of eccrine sweat gland , the cells are large and pyramidal . Also the cells are relatively bigger.

\* the sweat of animal contains an odor

\* the secretion of apocrine is nearly viscous; however the secretion of eccrine (merocrine) is watery. Both their sweat is odorless.

\* modified apocrine sweat gland: they are apocrine but their secretion is merocrine the gland opens on hair follicle but the secretion is a merocrine, they are found in : female breast , moll's glands (found in eye's lid edge) and ceruminous glands which are found in the ear ( they secrete the yellow-brown wax in the ear )

**Sebaceous Glands**

\* it's simple , it opens on a hair follicle “ it owns one duct” , the secreting part of it is dilated , *so it's a acinar holocrine gland*

\*\*remember eccrine are simple tubular coiled

\* the C.T which surrounding them contains undifferentiated cells , because their secretion is holocrine , the cell which dies will be replaced by an undifferentiated cell

\* People suffering from "acne" they notice a swelling in the site of acne then they press it in order to squeeze the sebum out , by this way we squeeze it externally , however the normal way for squeezing the sebum is proceeded internally : the sebum then moves towards the hair to be eliminated .

\* what produces acne ? : the site where sebum is squeezed out normally is blocked , the sebaceous gland is being formed continuously from the undifferentiated cells from the surrounding C.T and it will secrete but again the site of normal elimination is blocked .. so the sebum will collect and fill this area to form the acne

\* you are not going to get rid of acne unless you get rid of this block

\* the skin of new born babies is oily due to the secretion of sebaceous glands which were encouraged from hormones that passed from the mother towards the fetus

however after birth there will be no hormones (from the mother) so the sebaceous gland will shrink and they stop secreting until the age puberty , at this age the female will secret estrogen and progesterone , the male will secrete testosterone , at this age(puberty) the sebaceous secretions are at a level of imbalance , so the sebaceous glands will secrete again and squeeze their secretions , the secretions at the beginning will be thickened , which blocks the ducts , and that will cause acne vulgaris

\* doctors recommend people who suffer from Acne Vulgaris to wash their face by water and medical soup , why ?

When you wash your face with soup actually you are massaging for your face (massage to the sebaceous glands and the hair of face ) which helps to eliminate the substance that blocks the duct from the outside.

\*Another point : the medical soap contains substances that resist bacterial attack

\* the sebum is bactericidal , i.e. it can destroy some types of bacteria

\* every single hair has got one or more sebaceous glands , however sebaceous glands are not only associated with hair , it could be found on another regions , for example : at the oral cavity on the surface of the cheek you can feel an elevated region ,, this elevation is sebaceous glands opening in the mucosa of the oral cavity , they are called **Fordise spots** in respect to the person who described them , they are yellow in color.

**Hair**

\* hair growth is periodical, happens in patches : the hair grows longer in the spring and in summer more than winter and autumn

\* there are three stages of hair growth

1) Anagen : the hair grows at this stage

2) Catagen : quiescence stage

3) Telogen : the fall of the hair

\* these stages are genetically determined , differ from individual to another( for example the Anagen (hair growth stage) can be 3 or 4 or 5 months whatever it was it’s genetically determined and you can do nothing with it .

\* shampoo can do nothing with those stages ( there is no shampoo that can make your hair longer .. it's just commercial business )

\* the hair must pass those 3 stages , in fact every hair follicle is going fall , because the hair follicle is parallel to keratin in skin , the keratin will fall after 28 days , so the hair follicle behaves at the same way

if we removed the hair from its place , another hair will be formed after 28 days , at the beginning hair follicle growth it will be friable but after a while there will be a condensation for the keratin , this hair follicle will be thicker and darker in color after a while .

\* the duration of hair growth differ from region to another of the body , for example : usually the Anagen reaches three months on females hair , the catagen 1- 2 months , telogen 2-3 weeks , then the hair will fall , if more than hair follicle reached the time that they will fall at the same time , you are going to wake up and find a group of hair follicles over your pillow.

\* the hair of eyebrows is genetically determined , the Anagen of it is one month , the catagen is 4 years !! , , but they must fall at last as all hair do.

\* the sex hormones are responsible for the normal distribution of the hair . So the distribution of hair differ from males and females

\* thyroid gland patients ; their hair falls more.

\* the patients who take cortisone suffer from problems in the hair and pigmentation (the activity of melanocytes all over the body )

\* the hair only gets its nourishment from inside , so the health of hair will be affected by the way of eating ( deficiency of vitamin b or zinc etc will affect the hair)

\* the shampoo which contains vitamin b or zinc is useless , because the keratin of the hair is made of dead cells so the nourishment of hair from shampoo is something impossible.

\* the most important factor of hair growth is the blood supply , so the permanent hair removal depends on its mechanism , by cutting blood supply from the hair follicle, because the blood supply is important for the vitality of hair follicle.

**More notes on hair**

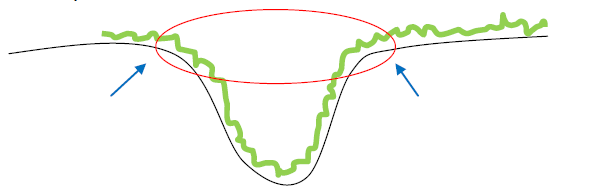
- **Surface epithelium cells**: Stratified squamous epithelial cells of the keratinized type.

- **Epidermal adnexa** (appendages/derivatives): are not skin (when we refer to skin we usually refer to the dermis and the epidermis)  They are located within the *dermis*, but they originate from the *epidermis*.

- During embryonic life, the hair invaginates downward:

 First layer to descend  **Stratum Basale**

 If the outer surface of skin is removed, a part of the Stratum Basale still invaginates downward (deep), so after some time you will find that these cells have proliferated and have replaced the surface cells.



\*\*This is seen in some burn victims. If the burn is superficial, and the area of the burn was surrounded by a shield (This experiment is usually performed on rabbits): An area of the skin is removed, and is replaced by a stainless steel chamber. This is done so that the surface Stratum Basale cells at areas to the left and right are prevented from covering the entire area of the burn. After a while, the wound heals  the Stratum Basale cells migrate from the hair, present deeper down, and replace surface cells. (remember when we studied glands, we mentioned that there are certain stem cells present at invaginations which replace damaged surface cells, and how they are present deep down so that they are protected, it's the same case with hair.)

 The **Depth** that the Stratum Basale cells reach is genetically determined.

 **Hair Follicles** are present at different levels. A hair follicle is the invagination of the epidermal epithelium containing the root of a hair.

 **Laser Hair Removal**: More than one session, during each session the laser destroys hair follicles at a certain depth, and destroys deeper layers depth during the following session.

 Some hair follicles penetrate through the **Hypodermis** (Superficial Fascia), this is an indication that even if we reach the reticular dermis during Hair Removal, some hair cells could still grow, this is a reason why we might, in some cases, accept the Hypodermis as a part of the skin (even though it is actually **not**).

**Hair Follicle – Parts**

 **Dermal Papilla:** the base of the hair bulb (terminal dilated part of a hair follicle) is evaginated by connective tissue**;** this evagination is referred to as the dermal papilla. It is similar to that found in the papillary dermis.

- There are mitotically active cells present above the dermal papilla, this is where hair growth starts**.**

- Contains both a nerve and an arterial-venous plexus.

- Therefore, it is painful to remove a hair from its root. Severity of pain felt decreases as the hair is removed from the same place frequently (threshold increases, higher tolerance).

- The epithelium is avascular. Blood supply to the root of the hair is of great importance as growth and mitotic activity occurs there, if blood supply is cut  hair follicle will die**.**

- If a hair is pulled too strongly and bleeding occurred (indication that the plexus is injured) hair will never grow back since loss of blood flow results in death of the follicle.

 The epidermal cells covering this dermal papilla are very active and form a keratinized structure - the **Hair Root,** which produces and is continuous with the **Hair Shaft** protruding beyond the skin surface. The hair is made up of **Keratin**.

 **Medulla**: it is noticed that the medulla gets thinner as you move along the hair towards its ends. This is especially seen in females. When the medulla is absent, the ends of the hair become split and curl; this is an indication that the hair has finished the growth phase (anagen) and is now in the 2nd phase (catagen). It will eventually reach the telogen phase and fall off. Hair grows in patches and falls in patches as well. Hair falling increases due to stress/menstrual cycle.

 **Cortex:** a layer of cells directly over the medulla.

 **Cuticle**: a layer cells directly over the cortex. This is the layer we feel when we touch our hair. Each cuticle cell (equivalent to Stratum Corneum) overrides adjacent or under/overlying cells, and there are oblique sulfur bonds between them

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 **Melanocytes:**

- Closer to the vascular supply.

- Large cells, so lie a bit deeper than nearby cells.

- Closer to the nerves as well.

- Sympathetic stimulation  melanocytes will be depleted. Sometimes, loss of function is permanent. How this happens: as cells containing melanin migrate upward, they become widely separated  only very few cells have melanin  the black color is less dark than it once was  hair color turns gray  move even farther apart  gray color gets lighter melanocytes are fully differentiated, so no melanin is released again  the gray color is permanent.

 **Internal Root Sheath**

- Outermost root cells, disappears at the level of the sebaceous gland.

 **External Root Sheath**

- Covers the internal root sheath and extends all the way to the epidermis, where it is continuous with the basal and spinous layers. There is a condensation of Connective Tissue at the area surrounding this sheath, named: the **Glassy**

**Membrane** (it is not a membrane and it is not glassy, though). This is the site of insertion of the *Arrector Pili muscle*.

 **Arrector Pili Muscle**

- A "bulge" found directly below the sebaceous gland.

- When it contracts  messages the wall of the sebaceous gland  increased Sebum release (more cells will rupture to release sebum). This is especially noticed in females, when under stress (sympathetic overstimulation) hair is oilier, more frequent washing needed.

- Contraction of this muscle pulls the hair shaft to a more erect position. In humans, this isn't of great use, but in some lower animals such as polar bears, this is important. The air coming in contact with the skin is warmer, so when the muscle contracts, the hairs are erect (skin make dimples, gooseflesh skin), and the upper parts of the hair curl and trap the air for a longer duration. The air is then released gradually.

- NOT an epidermal derivative.

- It is a part of the dermis and not the epidermis.

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 Notes:

 **Hair Oils**: (example: coconut oil) claim to make the hair "stronger" and "thicker". What this oil actually does is simply elevate the hair, thus increasing the distance between each two cuticle cells  the oblique sulfur bonds are farther apart  give the impression that the hair is thicker and its color seems darker. When hair oil is no longer used and the hair is frequently washed, hair returns to normal.

 Periods of hair growth are **genetically determined**; you cannot speed up the hair growth phases (anagen). Each hair is programmed to reach a certain length and then fall off, this cannot be changed by the use of any type of hair products.

 A permanent change in hair color/growth is never possible.

 For normal hair growth, a **balanced diet** is needed. Vitamins and other nutrients must be received through diet; they could never be passed along to hair through shampoos or hair products.

 **Thyroid disease**: Hair of the patient indicated whether they have hyper/hypothyroid.

- *Hyperthyroid*  frequent hair loss, aggressive behavior  this indicates that Thyroxin has something to do with the growth of the hair.

- *Hypothyroid*  thick, oily, friable hair + disorientation  indicates a less active thyroid gland

 Some **toxins** remain in the hair indefinitely:

- Example: Mummies, Arsenic remains in their hair for extremely long periods of time (7000 years).

 Certain **drugs** could leave traces in hair; those traces could remain even if the person has stopped taking the drugs for a long time.

- Example: Morphine, Heroine. Some Analgesics: Tramedol  remains in hair for 20 years.

 Hair remains a very long time without decaying.

 If a laser overdose is given due to malpractice/misuse of equipment by Hair Removal Centers  leads to severe burns.

 Some hair salons claim to have products which permanently dye the hair, this is not possible though since the hair inside the dermis is not colored and will eventually grow again. The hair color after dying is never the same as that seen on the package since the color on the package was tried out by dying white hair.

 **Hydrogen Peroxide** is used to remove the dye from the hair, the concentration used for this purpose is 25% while the concentration of it used for sterilizing purposes at hospitals is 1-5% only. Hair salons place aluminum foil on the hair to "protect" the skin, though this is not sufficient since it burns skin if it comes in contact with it, and if the contact lasts long  reaches dermis and epidermis  it reaches the hair  hair dies  never grows back.

 Rate of hair growth can only be temporarily accelerated.

- Example: **Minoxidil**: initially was released as a treatment for high blood pressure. All Angiotensin-converting enzyme inhibitors (including Menoxidil) lead to abnormal hair growth occasionally. Therefore, companies started marketing it as a treatment for Baldness. The minute you stop using this drug, hair falls off again.

 Hair character can be changed temporarily. Example: **By heat**  hair drying/straightening. **Hair perms**  burn the hair.

 **Hair transplants**: either synthetic (very dangerous), or hair is taken from a different part of the body and transplanted. Either way, it is not permanent.

 Patients receiving chemotherapy suffer hair loss. Two common treatments are Methotrexate and Adriamycin, those drugs attack the hair during the S phase (when DNA is being synthesized) so this process is arrested, and hair falls. Hair grows back as treatment is stopped.

**Clinical Cases**

**1) Skin Cancer**

 **Basal Cell Carcinoma**

- Picture taken from the Ala (side) of the nose, this is a very common site.

- Another common site is between the eyes and above the nose (continuous friction from glasses could lead to it).

- It is considered to be *locally malignant*: if it is surgically removed  does not return or returns also locally. No need for a follow up after surgery.

 **Squamous Cell Carcinoma** -

- Picture taken from the dorsum of the nose.

- The shape of the cancer is "dirty", described as having a "dirty floor".

- Invasive; may penetrate through to deeper structures

- In need of close, regular follow up.

- Squamous cells are differentiated  surgery is the only option.

**2) Vitiligo** *-*

- Depigmented sections of skin, appear as patches.

- Some areas are pigmented, some not.

- An *autoimmune* disease  Antibodies for melanocytes form in specific areas  Prevent melanin secretion. (if they stop secreting they won't work again)

- Some drugs are taken to mask the color of the skin in order not to see the discrepancy between the two types; pigmented & not pigmented (not really a treatment it is closer to be make up).

**3) Albinism**

- Previously discussed. Albinos have the same number of melanocytes as normal people, but tyrosine is deficient.

**4) Psoriasis** *-*

- Common in the Middle East.

- An autoimmune disease  acceleration of growth of keratinocytes  they reach upper layers in a relatively very short period of time (1 week instead of 2- 4 weeks)

- Scaly skin (like the fish peels )

- No Stratum Granulosum  no Keratohyalin granules  abnormal Keratinization

- What prevents the production of stratum granulosum is the accelerated movement of the epidermal cells from the basal lamina upward.

- Treatment: must slow down their movement, to give the cells a chance to get mature enough upon reaching the upper surface.

**5) Melanoma** *-*

- Worst type of cancer: *well-differentiated* melanocyte  only hope is through surgery  unguaranteed since cells could have moved from the basal lamina to anywhere else**.**

- Melanocytes present at a lower level than the nearby keratinocytes so they are closer to blood vessels.

- The patient first comes with an itchy mole  after a while it begins to ulcerate (epithelium is disrupted)  patient will come with symptoms in places far from the site of the mole.

- *Prognosis* (life expectancy) decreases as symptoms are less related to site of the mole; because this probably means that the cancer reached these fare sites.

**6) Acne Vulgaris**

- Extreme case.

- During puberty, almost all females and males suffer from acne but to different extents.

- Could be due to psychological reasons.

- Treatments:

 Retinoids: most frequently used to treat it.

- Those are *hepatotoxic*: affect the liver, so a liver function test must be performed periodically. In the case of a deviation from the base line  the dosage must be reduced or the treatment must be stopped.

**Best of Luck =)**