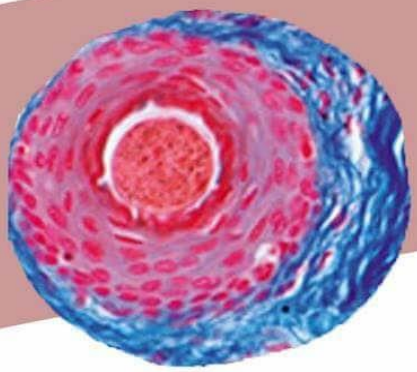
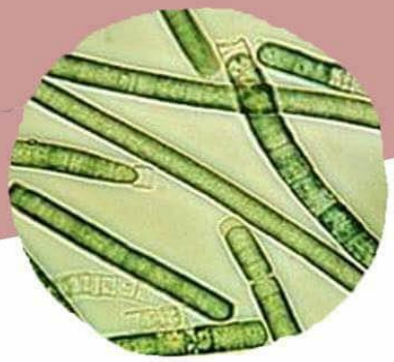
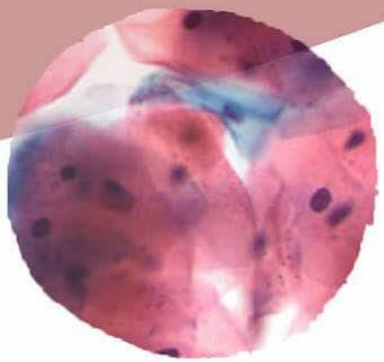
INTRODUCTION TO PATHOLOGY

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Sheet# 1

INTRODUCTION TO PATHOLOGY

*prof has expatiated in some details, you have just to understand the core of lecture.

- What is Pathology ?

Pathology is the study of disease,

Pathology is your bridge to the tree of medicine, everything you have took in your basic medical science will be converted to clinical knowledge through pathology. Pathology is also the basis of medical research; so without pathology the basic scientific research won't be turned into clinical application, also without pathology basic sciences won't be able to understand disease.

Studying pathology requires strong knowledge in histology; **because pathology is the study of disease, by investigating the causes of the disease and the associated changes in stages of cells, tissues, organs.**

- What is Etiology ?

*** is the science of searching the origin of the disease, including the causes and the modifying factors; which is a combination of genetic (inherited & acquired) and environmental triggering factors.**

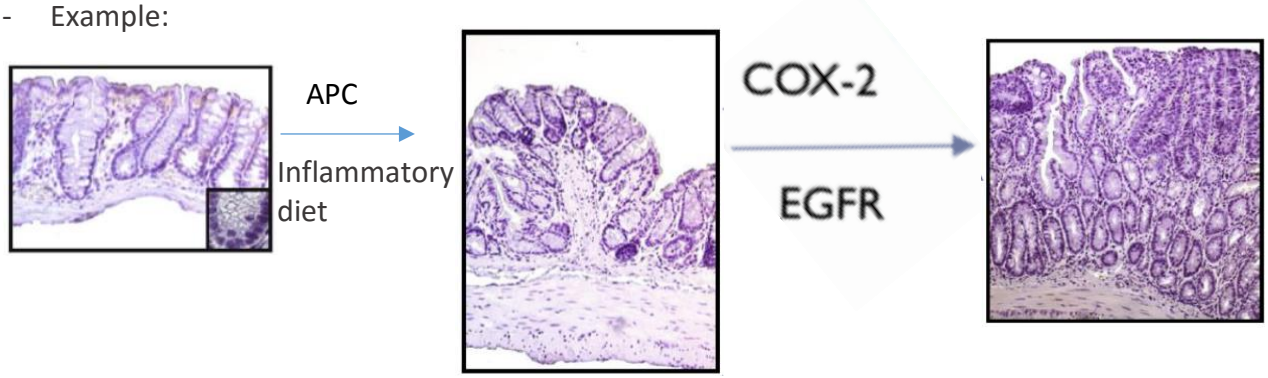
*Etiology refers for WHY a disease arises.

- What is Pathogenesis ?

Refers to the steps in the development of disease (how the etiological factors trigger: Molecular and cellular changes that give rise to functional "biochemical" and structural "morphological" abnormalities that are characterize a disease.

*Pathogenesis describes HOW a disease develop.
*Functional & Structural abnormalities affect organ's physiological functioning.

- Example:



The first slide represents normal column epithelial layer with normal crypts and basement membranes. The second slide represent polyp "abnormal growth of tissue projecting from mucus membrane"; this abnormality occurs due to a mutation in APC gene; if you inherited this mutation you will have thousands of polyps in your intestine. Unfortunately, one of the most frequent polyps is "adenomatous polyps" which carry a high risk of Cancer (third slide); (how?) polyps cause the push of mutations that activate EGFR receptors resulting in cancer.
These are the Etiology of polyps' cancer, and by studying that we understand the pathogenesis.

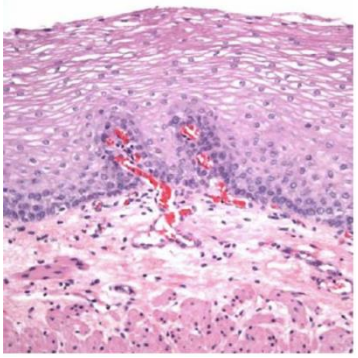
- This is all (last example) is Knowledge we taken for granted (true or for sure).

How did we can for this knowledge?
How did we know that the first slide is normal, second is a polyp, and the third is cancer?

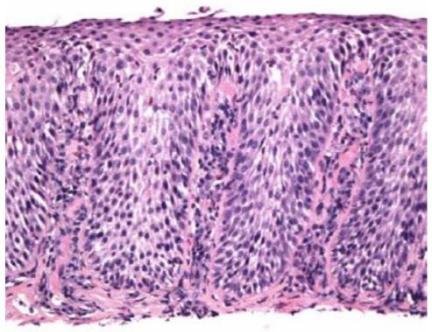
"The Morphological Knowledge Database"
is the first method used to relate the pathologic structural features with pathologic complains.
And by contrast to relate the non-disease structural features with normality.

Virchow's Theory of Cellular Pathology;
-Virchow took hundreds of samples from normal people and patients.
-he linked the view of the cellular nature of all vital processes with both physiological or pathological one.

For example:
We took esophageal tissue samples from people who complain nothing and others who complain heartburn.



The vast majority of patients who do not have a disease had an esophagus that looked like this



The vast majority of patients who complained about heartburn had an esophagus that looked like this

Therefore

The next patient with an esophagus that looks like this should have no heartburn

The next patient with an esophagus that looks like this should have or had heartburn.

- Along with a thorough history and clinical examination a pathological examination will result in:
  1- Diagnosis
  2- Disease's **grade**: Degree of deviation from the physiological normal, low-grade means that it grows slowly, high-grade means that it grows more rapidly.
  3- Disease's **stage**: The stage of a cancer describes the size of a tumor and how far it has spread from where it originated.

You have to use everything you know in histology to understand how normal is different from abnormal. However, this way is very old knowledge, we don't depend on this in pathology any more. Why?
Because morphology tells us tissue organization changes but nothing about molecular changes.
Multiple tissues affected by the same disease may look alike, but the molecular basis may different; therefore, the treatment should be different.

- **Knowledge that we are developing is the <u>Molecular knowledge database.</u>**

Molecular techniques are used;
1-karyotype test:
we look at the karyotype trying to detect any molecular abnormalities in chromosomes' <u>number</u> or <u>appearance</u>.

For example, "Philadelphia chromosome" which is an abnormal exchange in the genetic material between chromosome 9 and 22,
vast majority of patients who have this transportation between the 9 and 22 chromosomes have leukemia;
*this chromosomal abnormality leads to wide prognosis (very good- very bad /less, or more aggressive)

- Just extra info about about leukemia, that there are degrees of leukemia from high aggressive to low ones, both patients' who had less and more aggressive leukemia <u>tissues look alike under MC</u>. <u>But under molecular basis they are not alike</u>; less aggressive have kind of proteins that are absent in more aggressive that improve medications.

2-fluorescent hybridizations.

You don't have to do karyotype to figure out Philadelphia chromosome anymore; you can do fluorescent hybridizations. By using green dye for chromosomes number 9, and red dyes for chromosomes number 22.
In normal, we must have two 9 chromosomes (green fluorescence) in one place and two 22 chromosomes (red fluorescence) in other place, BUT if we find red & green fluorescence at the same position that means we have Philadelphia chromosome.

3-Microarrays data analysis.
Any change in sequence of nucleotides is considered as mutation.
Microarray is a method used to figure out any change in nucleotides sequence.

Microarray is essential built chip that has many spots with either DNA or RNA, <u>as we know that DNA strands has complementary structure</u>; now as we look for mutations we have to put on the chip the normal sequence & whole set of sequence that have the mutation on it. By washing up any nucleotide that doesn't stick to the chip we can figure the mutations because it not complementary with the normal sequence.

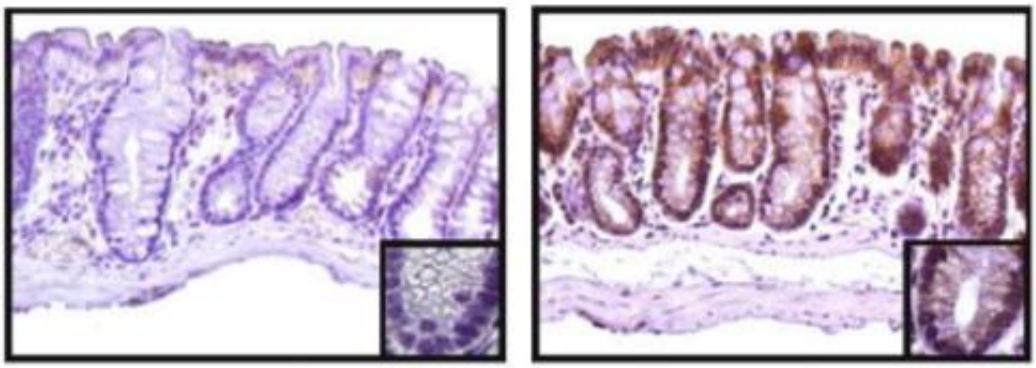
Microarray can be used also <u>indirectly</u> for proteins, by looking in mRNA, in this case rather than having

little bits of DNA on the chip, we have the complementary of DNA which is reversible of mRNA stuck on the chip.

4-Reverse transcription PCR:
In this method do use some enzymatic reactions, to transcribe mRNA chain to a copy of DNA.
Then *polymeric chain reaction* PCR is done to amplify & to know how much starting material you have so you will get more of one type of mRNA compared to other types.

This tells you in other terms how much of this mRNA you cell is producing.
*enzymes we have used for reverse transcription of mRNA is actually from viruses called “retro-virus”.
*retro-viruses are called like that because they have reverse transcript.

5-Histochemistery:
this method is used so we can look at proteins,



Normal (left) produces little COX-2 proteins.
Where the trans genic mouse(right) that has modified to over production of COX-2 proteins.

Look morphologically normal but molecularly abnormal.