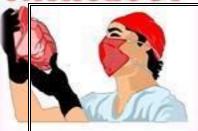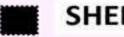# PATHOLOGY

■ SHEET

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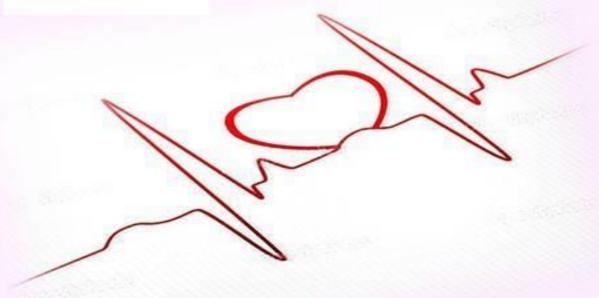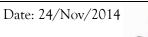
Lecture Number: 17

Doctor: *Dr.Mazen*
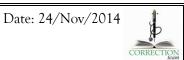
DONE BY: Saeed Ismail

Designed By: Majida Al-foqaraa'

Review:

- In the previous lecture we talked about classifications/naming of tumors into benign and malignant and characteristics of each.
- A student asks for more clarification of **Cancer stem cell theory**.

-It is mainly one of two things; either the tissue stem cells themselves have been insulted, there is been a genetic mutation, so they themselves have transformed, and therefore by definition stem cells can replicate indefinitely. And that's what makes these cancer cells that have resulted from transformed from stem cells able to replicate indefinitely.

-On the other hand, the tissue somatic cells cannot replicate indefinitely. So for them to become immortal (to replicate indefinitely), they need to gain stem like functions. So they will dedifferentiate from their differentiated states to a stem cell-like state by expressing genes that are known for stemness. And on of the mechanisms of dedifferentiation is gaining telomerase activity.

-Both hypotheses have been found to be valid in acute and chronic leukemia; acute for dedifferentiation and chronic for the stem cell transformation.

—Therefore, the theory is that cancer stem cells arise out of normal stem cells or the precursor cells that normal stem cells produce.

-Another question...We have not heard about heart cancer or skeletal muscle cancer...Why?? Maybe because that there is not a lot of transformation that occurs in cardiac tissue or it's just resistant to the insults. Actually the exact reason is unknown.

Epidemiology

<u>-**The numbers mentioned in our book are U.S data, and we will be looking at Jordanian numbers and rates, even though they are not in the book but they are required.**</u>

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- The doctor said that he is NOT going to ask about percentages and numbers, all you need to know are the trends: what is common, uncommon, the reason this type is common and why this is more lethal than the others.

-You need to look at the slides while studying this sheet.

The U.S data: Slide #2

Cancer **incidence** by site and sex:

Males: prostate cancer is #1, followed by lung and colorectal.

❖ Female: breast cancer is #1, followed by lung and colorectal.

- Example: In the U.S prostate cancer is #1 incidence in males, whereas, breast cancer is #1 incidence in females, followed by lung and bronchus cancer in both sexes.
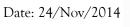
Now according to the *mortality* rates Lung cancer takes first place then comes prostate and breast cancers in males and females respectively, but why?
(How questions might come in the exam)
*you have to think of appropriate *hypothesis*, like:

- Prostate and breast cancers are more **treatable** and we have better treatments for them.
- Lung cancer has more advanced **severity** or early metastasis.
- Early diagnosis (due to **awareness** and **education** which are the best tools you have for diseases) and **screening** (prostate and breast screening), most females check their breasts regularly after a menstrual cycle to look for lumps.
- We don't have screenings for lung cancer

This is the type of thinking you need to do, not blindly memorize numbers, try to come up with the hypothesis on molecular, genetic, behavioral and environmental basis. So a question in the EXAM may come on these, for example, why is lung cancer responsible for most deaths? All of the following hypotheses apply EXCEPT; reasonable question!

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**Incidence is the percentage of new cases.

**Prevalence is the overall load of the disease, new and old cases for a particular time period.

Slide #3: This is just a snap shot for the U.S in the 2010; let's take a look at time trends (which gives us a clue about what is going on):

- There is a big growth in lung cancer deaths in males from 50's to the 80's (more smoking), whereas, "female-smoking" was less acceptable sociably in the 50's and 60's than the 80's; as more females started to smoke, more females are dying from lung cancer.
- Breast cancer: there was a slight increase in trend but it is *plateaued* recently, because of better treatments, screening and more awareness.
- Cervical cancer: it is fairly low but it's getting lower as we move on the years, because married females get internal examination, cytologic smears for early detection of this tumor (using a microscope and looking for any abnormal changes especially dysplasia). And the development of the human papillomavirus (HPV) vaccine may eliminate this caner {HPV induces transformation in cervical cells}, and it is found that this virus is more common in societies where they start their sexual life earlier and have more sexual partners because it's a sexual transmitted virus, so the vaccine is cost-effective in these societies with earlier sexual life unlike our society.

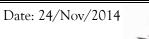### Now type trends and population trends are also based on:

    I.   **Geography (environment)** (slide 4-6)

These are all standardized age and population rates because we compare different population, so you don't need to worry about the number of people in Japan or US.

Breast cancer deaths (USA vs. Japan), It is more lethal in the U.S, hypotheses:

    ✓ Genetics.

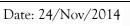Written by   **Saeed Ismail**

✓ Type of food that affect estrogen levels (because some breast cancers are estrogen dependent).

✓ Environment.

✓ Better awareness and screening in Japan.

✓ Japanese women are usually skinnier so they have smaller breasts in which it is easier to detect a lump.

✓ Maybe breast cancer is less severe in Japan or metastasize less.

Stomach cancer deaths, it is more lethal in Japan (the hypothesis now is flipped).

If a Japanese person migrates to the U.S and reproduces; the second generation children have a risk of getting stomach cancer that is halfway between the risks of the U.S population and the Japanese population, so genetics seems like a less likely factor, maybe the environment has something to do with it or the type of food.

So the environment has a big impact on whether someone gets cancer, the severity of the cancer and which type of cancer, certain groups of the population get specific cancer (e.g. coal miners get coal miner's lung "anthracosis" because they are not protected from the carbon dust they found anthracotic pigment in their hilar lymph nodes) (look at table 5-2):

➢ *Asbestos*: it was used in ceiling, insulation and brake linings then it was found that it is related to **mesothelioma.**

➢ *Vinyl chloride:* "that new car smell we all love" has a lot of organic solvents, it is used in the front of the car and studies say that these are toxic levels through the first 3 months and some studies say through the first 3 years of the car's age, and they are more toxic in the summer (more temperature more volatile).

➢ *Radon and its decay products:* from decay of minerals containing uranium (USA and its allies dropped depleted uranium ignitions in Afghanistan and Iraq even though it is called depleted it still has radioactive particles in it), and multiple studies have been done in public about the massive increase in rates of child leukemia, lymphomas, birth defects, etc..

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Saeed Ismail

Now let's talk about Jordan: "all world maps in the slides"

The most common cancer (incidence) excluding sex-specific cancers is **colorectal** cancer; our society is heterogeneous with people coming from around so it is harder to find out a reason why but you can still make some hypotheses:

Our diet; more fat less fiber (Russia and Scandinavian countries where they have high fat diets; colorectal cancer is #1 cancer excluding sex-specific cancers)

–A student asks "Is the only cause of colorectal cancer not eating fibers? No, fiber is one of the things that may correlate. There is a difference between correlation and causation. **Causation** means that something causes something else. **Correlation** means that with this, something else is also present. A correlation could be either positive or negative. A positive correlation is when you have a curve moves the same direction as the other curve. If it moves in the opposite direction, that will be a negative correlation.

-So, fat has a positive correlation with colorectal cancer, and fiber has a negative correlation with colorectal cancer.

II.   <u>Age</u> **slides (22-23):** Age distribution is different in our countries from age distributions in Europe countries for example; we are a young population. And we said that age is one of the most important risk factors in several diseases including cancer. So that means if we want to compare our population with other populations, we have to do an **Age Standardized Rate (ASR)**, and then we can compare.

❖ **Males:** prostate cancer is #1 in the U.S and colorectal cancer is #1 in Jordan.

❖ **Females:**

Whenever there is an exception in the epidemiologic data we start wondering either the data is wrong or there is something unique that particular population that causes increase in rates of a specific cancer over another (for example: eating

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certain type of nuts that have aflatoxins like in south east Asia, increase their incidence of liver cancer so there is correlation between nuts, aflatoxins and liver cancer, so studies for the underlying mechanism that could lead to it are now in progress.

"So epidemiologic data also directs scientific inquiry"

**Jordan is in the middle between countries with high cancer rates and low cancer rates (we are average).

****Colorectal cancer**: we are a little bit above average, and it is poorly treated

****Breast cancer:** we are a bit above average, and we are not doing very well in treatment and that could be a whole matter of awareness.
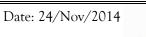
All of the former are about **INCIDENCE.

Mortality: colorectal cancer is the most killer (again excluding sex-specific cancer), but if you look specifically at males you will find that lung cancer kills more males than colorectal cancer, even though, colorectal cancer incidence is higher; hypotheses→awareness, screening, severity, treatment and specialized doctors.

For females breast cancer is #1 cause of mortality.

**The doctor should no set behind the desk when treating patients in order not to create a barrier between the doctor and the patient, or the doctor doesn't have his job manners and doesn't bother his self to stand up and do physical examination (physical examination is the #1 tool for diagnosis) they just ask you to do tests, and then people will not be happy visiting doctors and some of them will not come back (and that's another hypothesis).

This is a snapshot in 2010 that shows where cancers occur in Jordan; and you can see that the older you get the more cancer rates till 75 because there are less people above the age of 75, so age is a risk factor.

Most cancer deaths occur between 55 and 75 (older → more death).

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As population develops➔ age gets longer because of better health care system provided.

III.   Heredity   (slides 24-26)

Only 5%-10% of all cancers are inherited, but still we study them because they give us the molecular basis for studying the sporadic "non-inherited" cancers.
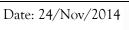
Inherited cancers are Divided into 3 groups:

    A. **Autosomal Dominant**: one copy is required; if you have a parent with a mutated gene your chance is 50% to get that mutated gene (inherited retinoblastoma is by lateral, whereas, sporadic cases present with one).

    B. **Autosomal Recessive**: it means that you need two copies, and the percentage would be 25% if you 2 parents with one copy each, now if you have a parent with the disease and the other parent is a carrier the percentage would be 50%.

    C. **Familial**: present with a second primary cancer, because not only they have gained a retinoblastoma mutation in the retina they have a mutation the entire body and the most common cancer is osteosarcoma.

Autosomal dominant diseases also have Marker phenotypes; APC (adenomatous polyposis coli) gene they present with hundreds of polyps or adenomas in their colon, and when you see that, it is a good indication that the patient has a certain mutation specially if you look at the family medical history and the genetic tree.

Not all of marker phenotypes are related to where the cancer occurs; NF1 (neurofibromatosis 1) present with "lisch nodules" (nodules on the iris) and "café-au-lait spots" looks like Nescafe with milk on multiple spots over the patient's body.

All the sporadic cancers from 90% to 95% there is substance where you can find the familial inheritance and maybe dominant or recessive but it's not the classic dominant or recessive i.e. they get the gene but they don't necessarily get the disease.

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Or it could be more complicated where it is related to the environment, for example; polymorphisms in the P450 system may allow certain toxins to accumulate ; polymorphisms of the nicotinic acid receptors make certain people more addictive to cigarettes so they smoke more and are at higher risk for lung cancer.

Acquired Preneoplastic Lesions (slide 27)

**These are not inevitable to turn into malignant cancers, we already mentioned some of them like; metaplasia, dysplasia and endometrial hyperplasia these are ground for transformation to occur

**Are benign tumors going to turn to malignant tumors??

The answer is yes and no; it depends on the organ for example; 50% of the adenomas in the colon turn to carcinomas, whereas, leiomyomas in the uterus rarely change into malignant tumors.

This is common in tissue injury if you're exposed to inflammatory mediators, accumulating damage, and increasing proliferation or if exposed to inflammation byproducts potential mutations.

Please refer to the book if you don't understand something, as there are weird sentences in the sheet that I didn't understand until reading from the book.

Best wishes,

   Saeed Ismail

Written by   **Saeed Ismail**