The title of the lecture : **Immunodeficiency and Tumour Immunology.**lecture # : 14  
refer to the slides i only wrote what the doctor said.  
 **Part 1 : Immunodeficiency**

when you think about immunodeficiency , you should think about the development of the new systems ( the development of the stem cells ) until we got production of the Ig's and other cells , so immunodeficiency might happen at each stage of these developments.  
 Clinically we can divide the immunodeficiency into 2 groups :  
-**Primary** : it's about the interesting defects , missing enzymes , missing cell types ( ex. no T helper cells ) , non-functional components , and congenital problems.  
-**Secondary [ acquired ]** : it's about underlying diseases , chronic infections , lymphoid malignancy , leukaemia , malnutrition , and immunosuppression.

* We know that some stem cells go to the thymus and others go to the BM, so if we had stem cells deficiency we would have T and B cells deficiency too , or we could have a selective deficiency in B or T cells , here we have stem cells but the problem happened at later stage.   
  We said before that some B-cells need T-cells in order to produce antibodies ,that means if we don't have T-cells the B-cells won't be able to produce those antibodies.  
    
  Classification of the **primary** IDDs  
    
   **Primary B-cells immunodeficiency** ; we have two types :-  
  1. Bruton X-linked agammaglobulinaemia ( the gene is the X-chromosome ).  
  no B-lymphocytes production , hence no Ig's production.   
    
  2.common variable immunodeficiency ( selective IgA and IgG deficiency )   
  mature B-cells failed to differentiate to mature plasma secreting cells, here we'll have some typical infections like pneumonia and fibrosis ( upper respiratory tract diseases )   
  \*Treatment : giving the patient Igs [ passive immunity ].  
    
  **Primary T-cells immunodeficiency :-**   
  Di George syndrome , and heart diseases .. etc -Check slide #5  
   **Severe combined immunodeficiency diseases SCID** :-  
  no stem cells , no T-cells , no B-cells , and no antibodies.   
  generally the patient doesn't survive unless we do BM transplantation , giving him/her IV Ig's , or gene therapy which is not that successful.  
    
  -Note : we can have a deficiency in the molecules not only in the cells like growth factors , IL , and other.  
    
  We could also have a deficiency in the phagocytic system [ *phagocytic dysfunction* ], here some chronic , severe infections might happen , we can see abscesses on the skin or in the oral cavity.  
  \*Treatment : giving the patient T o B lymphocytes.  
   *Chediak-Higashi Syndrome*here there is a phagocytosis but the microorganisms inside the phagosome can't be killed, and it's an Autosomal recessive.  
    
    
   *Leukocyte adhesion deficiency*i'ts an Autosomal recessive too   
  Group of disorders in which the leukocyte interaction with vascular endothelium is disrupted  
  - beta subunit of integrins   
  -selectin ligands  
     
  The doctor didn't say that much about these subjects , you have to go back to the slides for more details.  
    
  **Complement system deficiency**   
  The function of the complement system ( we mentioned that before ) :  
  destruction of the target cells , eliminate the immune complexes , and recognition of certain cells.   
    
  each complement will be degraded , and those degraded materials if they're not metabolised , they will cause severe diseases.   
    
  C1, C2 , C3 ( classical pathway ) any deficiency could lead to autoimmunity infections.  
  C3b , B , P ( alternative pathway ) any deficiency could lead to pyogenic infections, deficiency in C3 also could lead to pyogenic infections.  
  C5-C9 ( late components ) any deficiency could lead to recurrent neisserial infections.  
  Check the table slide #29.  
    
   Now after we finished talking about the **primary** immunodeficiency let's talk about the **secondary** one [ the acquired one ].  
  The doctor just mentioned the causes , and they are : acute or chronic infections , metabolic disorders , Thalassemia , chronic GIT infections , drug induce immunodeficiency , analgesic agents , immunity diseases , post-operative status , malnutrition , malignancy , and deliberate immunosuppression.   
    
  An example of a secondary Immunodeficiency : **AIDS  
  HIV** virus infects the helper T-cells , leading to destruction in the immunity system.  
  **-The ways of the virus transmission :**sexual transmission , tissue transplantation , by blood , from the mother to the fetus , or by breast feeding which is very rare to happen.  
    
  **-What will happen when the virus enters the human body ?**  
  HIV has a long incubation period ( several weeks ) , after the incubation period there will be an immune response production, as the viruses increase in number , T-lymphocytes will decrease in number , and when the virus enters the cell ( stop replicating ) the number of T-lymphocytes will increase again and go the normal level , and again when the viruses start to increase the T-lymphocytes decrease [ almost zero ] , then we can see the infection. Antibodies will be produced but they won't prevent the infection ( there is no cure for such a disease ).  
  -How to diagnose immunodeficiencies   
  **Medical history :** Age at onset (age is very important )  
  Vaccines   
  Family history  
  severity of illness   
  **Physical Exam :** Tonsils , organomegaly .palpate lymph nodes , chart growth , and chest X-ray.

-What we will do at the lab ?   
we do the CBC test [ complete blood count ].  
proteins concentration to know where exactly the deficiency is [ Ig's are proteins ]  
cells function.  
antibodies level.  
we can look for natural killer cells if they do their job normally or not.  
skin injection.  
  
**part 2 : Tumour Immunology**Tumor is a major problem , has many features , (the doctor said you took that in pathology, so he supposed that we already know them ) anyhow , you have to know that if anything happens to the control mechanism this will lead to abnormalities in the body.  
Tumors express antigens that are recognized as foreign substances by immune system.   
When immunosuppressers failed to prevent the growth of the tumor , the tumor will grow very rapidly. In tumor the antibodies won't react with the antigens on the cells because it's already consumed by the circulating ones [ immunoglobulins shading ].  
The immune system can be activated externally; if we take tumor cells in vitro and we add some T-cells , they'll respond and when we increase the response by adding interleukins.  
  
**-Causes of Tumor :**Spontaneous , UV and ionizing radiation, Genetic abnormalities , Immunosuppression ,   
 Virus-induced (HepC, EBV, HPV) , Chemical carcinogens.  
  
**Host Defense Against Tumor** **Tumor Immunity**  
-Tumor specific antigens **( TSA )**  
*Present only on tumor cells* and not on any normal cells and can be recognized by cytotoxic T-lymphocytes.  
and they are :  
Cancer testis antigen ,Viral antigen , Mucin , Oncofetal antigens , Antigens resulting from mutational in protein, and B catenin, RAS, P53,CDK4.  
  
**Oncofetal antigens** ; we have proteins that only present in fetal life they are important to the development of the fetus and after delivery the synthesis of those proteins will stop and they will be find in a very very low concentration in the body , but in tumor those proteins will start to be synthesized even after birth , still we can't use them as a tumor markers , we can use them only for treatments , except for Prostasin.  
  
-Tumor associated antigens **( TAA )**   
*Not unique to tumors and are also see on normal cells.[ originally found in the host cells but they'll increase if there's a tumor].*go back to slide #6 , 7 , 8 , and 11 the doctor didn't add any extra thing he just read those slides*.*  
Normally if we have mutant self proteins , the immune system will recognize them , if the causatives of mutation were carcinogens or because of radiation , those proteins will survive and the immune system can't control them or if there is a production of oncogene and we have 2 types ; 1.oncogene ( protosomal dominant disease, we need only one allele to be mutated ) 2.suppresser gene (autosomal recessive disease , two alleles should be mutated).Oncogene is either virual induced or cellular induced.  
  
-What will the immune response be ?   
the antigens will be processed by antigen presenting cells APC, it's like the way we mentioned in the previous lectures[normal response] hope you memorized them, remember that tumor specific T-cells will recognize the cytotoxicity, some antibodies will produce antibodies depending cytotoxic cells , now natural killer cells will be activated by gamma interferons that have been produced by T-lymphocytes , they are extremely important, They can recognize the APCs with class I.  
sometimes with NK cells there will be certain suppressors molecules in the tumor and they will prevent the 2nd signal which is coming from class I , so we will only have first signal and tumor will survive and grow more and more.  
so normally the immune system should recognize the tumor either by NK cells , non-specific immunity , or  
 T-lymphocytes.  
If the immune response equals the proliferation of the tumor , that would give us what's called static problem which is not a real problem, but if the proliferation is more the tumor will escape the immune response.  
  
-How that escape happen ?  
if we're talking about cytotoxic lymphocytes , in this case MHC expression on cytotoxic lymphocytes will be suppressed , but if you have a low expression , you can't present that antigen , so here the tumor will produce some antigens , and those antigens will go to the circulation and react with the Ig's or the T-lymphocytes.  
if we're talking about T-lymphocytes, MHC2 will be suppressed.  
if the antigens were week , they wouldn't be able to escape.  
and if there's a regulatory problem this could increase the growth of the tumor.  
  
 **Immunoediting [ the great escape ] :**Strong evidence that IR ( immune response ) controls and eradicates nascent cancer cells , “Immunoediting” eventually produces low antigenicity tumour cells , so they will not be recognized in a strong way. Pressure from immune system coupled with genomic instability selects for escape , with each new mutation , we will have new antigens and that would give the tumor the great escape too.  
  
**Treatment :**we can take cells from the patient and add IL-2 to the tumor target cells , after activating certain number , i give them to the patient to treat the tumor , theoretically is possible but it's very very difficult to treat a tumor.   
radiation and transplantation, we can destroy all the ''lymphoid system'' for example by radiating the whole body , then after that we can do the transplantation from a matching donor.  
allogeneic transplantation , now we have ''international BM banks''.  
  
  
  
 Farah Habasheneh  
sorry for any mistake.