Sheet no : 8

Refer to slide no : 8

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This sheet will be written as extra information on each slide

Slide#2
inborn errors of metabolism: the infant at birth, or shortly after, will have certain diseases concerning the metabolic activities of the body.

Slide#3
as known, each enzyme is controlled by a gene.

Slides#4
food consumed by human beings consists of carbohydrates, lipids, and proteins. So after eating the food it will be metabolized starting from the mouth “where there are certain proteolytic enzymes”, then it’ll go to the stomach, where the food will be broken to large molecules, then it’ll go to the intestines where the food will be broken into smaller compounds “the basic compounds (proteins into aminoacids, carbohydrates into monosaccharide’s, lipids into glycerol and fatty acid chains) and these components will be absorbed.
If there is a deficient enzyme at any stage of any metabolic chain, then a certain disorder will result.

Slide#5 same.

Slide#6
deficiency in an enzyme means that the gene controlling this enzyme has a mutation, this mutation can be autosomal recessive, autosomal dominant, or X-linked.
All metabolic disorders are single gene disorders.

Slide#7 same.

Slide#8
example on “deficiency in end product” is sickle cell anemia, here hemoglobin is the end product, and because not enough hemoglobin will be produced sickle cell anemia will result.

Slide#9
excess is like deficiency, because these products will be accumulated in the body.

Slide#10
this slide shows what happen if there is a deficiency in an enzyme controlling certain step in glycogen metabolism.

Slide#11
organelle diseases, here there is accumulation of metabolic compounds in these areas and storage diseases will result.

Slide#12
example on amino acid disorder is phenylketonuria.
Fatty acid disorders include both the cell and the mitochondria, because metabolism of fatty acids happen in the mitochondria in addition to the cell.

Slide#13 same.

Slide#14 the doctor didn’t read it.

Slide#15 same.

Slide#16 same.

Slide#17
MR: mental retardation.

Slide#18 , #19, #20, #21 just for more understanding.

Slide#22
G6PD deficiency is mainly present in males, in females it might be present as a very mild disease.

Slide#23 same.

Slide#24
diagnosis may be done by looking for disaccharides in urine.

Slide#25
the first two disorders will be discussed only.

Slide#26 has not been discussed.

Slide#27
PKU test must be done in each newborn in addition to galactosemia, and TSH “thyroid problems”.
Developmental delay happens due to accumulation of PA “phenylalanine” in the liver and the brain.
The patients should be diagnosed as early as possible to prevent them from taking milk with PA in it.
AR: autosomal recessive.

Slide#28
the picture here is very important study it carefully.
In general, three different diseases can be generated by deficiency in PA metabolism, PKU due to problem in PA hydroxylase D, Alkaptonuria, and Albinism.
There are two types of albinism, complete albinism and sex-linked type of albinism (where the male has pink eyes while the female has some black spots due to X-inactivation “it has been discussed in a previous lecture”).

Slides#29, #30 haven’t been discussed.

Slide#31
the concentrations in this slide are used to diagnosis and to follow up the patient.

Slide#32
Guthrie test is used to detect PKU, this test is done by streaking E.coli bacteria on a PA deficient media “PA is essential for the growth of the bacteria”, then drops from the patient’s blood are added on the media, then the media will be autoclaved, if the bacteria has grown around the blood drops then the patient has PA in his blood and he has the disease. This test can be done for many metabolites.
Guthrie test is a qualitative test, so a quantitative test must be done to determine the level of PA in the patient, this is done by “chromatography” test.
PA can be taken from the blood, urine, or CSF, but the easiest way to collect it is from the blood.

Slide#33 same.

Slide#34
PKU happens due to more than 70 mutation. The gene consists of 13 exons.

Slide#35 same.

Slide#36
diagnosis of this disorder is easy, it’s done by taking a urine sample from the patient and after a while it’ll become black in color, also the patient may have black spots under the skin.

Slide#37 same.

Slides#38-#41 have not been discussed.

Slide#42
If a disorder happened in the metabolism of the branched amino acids then ketosis “ketone bodies accumulation will result” and it’s very serious disease, the breath of the patient will smell like acetone, and it results from disorders in the enzymes transporting amino acids into the mitochondria.

Slide#43 same

Slide#44
the main products of urea cycle is Nitrogen and carbon dioxide.
Urea cycle disorders result from deficiency in different enzymes along the urea cycle.

Slide#45 same.

Slide#46
note: in urea cycle disorders ketone bodies are not found.

slide#47 hasn’t been discussed

slide#48
lipids are included in all steroid hormones and in the plasma membrane of all cells.

Slide#49
metabolism of many fatty acids happens in the mitochondria, and they are very important source of energy.

Slide#50
diagnosis: chromatography can be used to determine the number of carbons in the fatty acid chain.

Slide#51 same.

Slide#52
LDL receptor disease is a type of autosomal dominant disease, the disease can be present at 5 levels, either at the level of synthesis in the endoplasmic reticulum, or during transportation to Golgi apparatus, or during binding with cholesterol, or during clustering, or during recycling inside the endosome.
People with this disorder usually die due to heart attack because of the accumulation of cholesterol and lipids in the circulation. If they have homozygous form of the disease they will die at early ages, but if they have heterozygous form then they will live until they are 40-45 but eventually they will die from heart attack.

Slide#54
usually, the acidity of the urine is about 6-6.5, but with this disease it can become 3-3.4

Slide#55, #56 the doctor just read them without focusing on something specific.

slide#57
usually anything enters the cell through phagocytosis will go to the lysosome, like viruses, bacteria, glycoprotiens, etc.

 Slide#58
if there is a problem in hydrolysis of any of these things inside the lysosome, then they will accumulate in the cell, then organelle type of disease will result

Slide#59
glycoseaminoglycans = mucopolysaccharides (MPS), they are about 7 disorders.

Slide#60 same.

Slide#61, #62 have not been discussed

 Slide#63
these are the 7 disorders regarding (MPS), hunter syndrome is x-linked but the others are autosomal recessive.

Slide#64 hasn’t been discussed.

Slide#65
Lesch-Nyhan disease: the problem is due to accumulation of certain nucleotides

Slide#66 same.

Slide#67
as mentioned, steroids are synthesized from cholesterol, and many enzymes are included in the synthesis of steroids “testosterone, androgens, etc”.
The most common disorders regarding steroids are:
-17-hydroxylase deficiency
-3 b dehydrogenase
-11b dehydrogenase
-androgen insensitivity

Slide#68 hasn’t been discussed.

Slide#69
if these symptoms are present without explanation, then we should suspect that the patient has metabolic disorder.

Slide#70
if the skin is used for diagnosis we usually culture the skin to generate fibroblasts, and we look for the deficient enzyme inside these fibroblasts

Slide#71
macrophages are important to determine what kind of storage disease is present because they are responsible for phagocytosis.
-urine analysis is the most important test “in the doctor’s opinion”, because we can look for chemicals, bacteria or even viruses in the urine, the color and the smell of the urine are also important.
-urine reducing substances are: disaccharides; lactose “the doctor also mentioned galactose and fructose even though they are monosaccharides”.
-from plasma ammonia we can detect problems of the urea cycle.