Introduction and aim of work

New insights into the genetic basis of diseases are being generated at an ever-increasing rate . This explosion of information was ignited by technological advances , such as (PCR) and automated DNA sequencing(**Rehen SK etal , 2005).**

The genetic disorders are divided into chromosomal disorders and gene disorders .

A) Chromosomal disorders are divided into two classes .

1 - Abnormalities of chromosomal number:

These arise from non disjunctions that is from failure of two homologous chromosomes in the first division of meiosis or of two sister chromatids in mitosis or the second division of meiosis to pass to opposite poles of the cell . If non disjunction occurs in gametes the result is abnormal chromosome number (**Rehen SK etal , 2005)** .

2- Abnormalities of chromosome structure :

Result from chromosome breakage and reunion . When a chromosome breaks it can rejoin in its old form (restitutions) or it can rejoin with another broken chromosome (reunion) . Reunion leads to a structural rearrangement that can be balanced or unbalanced . If balanced , the amount of genetic material is identical to that of normal cell . Types of balanced rearrangements include balanced reciprocal translocation , Robertsonian translocations and inversions . If the rearrangement is unbalanced this indicates loss or gian of chromosomal material **(Yang AH et al , 2003) .**

B) Gene disorders are either mendalian monogenic or non mendalian disorders .

1 - Mendalian monogenic disorders are caused by single mutant gene which show on of four simple mendelian patterns of inheritance .

1- Autosomal dominant 2- Autosomal recessive

3- X-linked dominant 4- X-linked recessive

1 - Autosomal dominant traits :

Are fully manifested in the presence of a gene in the heterozygous state that is when only one abnormal gene is present **(Cutting GR etal , 2005)** .

2 - Autosomal recessive disorder :

Autosomal recessive conditions are clinically apparent only in the homozygous state i.e , when both alleles at a particular genetic locus are mutant alleles (**Kristine Barlow , 2007)** .

3 - X-linked inheritance :

Genes located on the x- chromosome are termed x-linked because the female has two x chromosomes she may be either heterozygous or homozygous for the mutant gene and the triat may exhibit recessive or dominant expressions . The male has only one x chromosome and therefore is homozygous for x linked traits **(Laurence D 2000)** .

1 - X-linked dominant traits :

This mode of inheritance is uncommon . Its characteristic features are as follow :

(1) females are affected about twice as often as males .

(2) heterozygous females transmit the trait to both genders with a frequency of 50% .

(3) homozygous affected males transmit the triat to all of their doughters and non of their sons **(Smith CA etal , 2003)** .

2 - X-linked recessive traits :

This mode of inheritance is relatively common . Its characteristic features are as follow :

(1) The disorder is fully expressed only in homozygous affected male .

(2) Heterozygous females are normal accassionaly they may exhibit mild features of the disorder **(Charlesworth B 2003)** .

11 - Non mendilian inheritance :

1 - Polygenic inheritance .

Most phenotypic traits are determined by the collaboration of many genes at different loci rather than by single gene effects . polygenic inheritace is suggested for traits that show continous variations in the form of a normal distribution curve **.** In multifactorial genetic disease there is both a polygenic component and an environmental component of causative factors (**Ricki Lewis 2003)** .

2 - Nontraditional mode of inheritance :

A) Mitochondrial disease are a group of disorders relating to the mitochondria .

B) Trinucleotide repeat disorder are a set of genetic disorders caused by trinucleotide repeats in certain genes exceeding the normal, stable, threshold, which differs per gene.

C) X-inactivation (also called lyonization) is a process by which one of the two copies of the X chromosome present in female mammals is inactivated.

D) Uniparental disomy refers to the situation in which two copies of a chromosome come from the same parent, instead of one copy coming from the mother and one copy coming from the father.

E) Somatic mutation is a mutation that occurs in the somatic (i.e. non-reproductive) cells of an organism **.**

Genetic and chromosomal disorders may lead to diseases .

A) - Chromosomal disorders .

1) - Abnormalities of chromosomal number e.g. Klinefelter syndrome (**Cotran etal , 2005)** , Turner syndrome (**Concha Ruiz M 2006) ,** Down syndrome , Trisome 13 **(Fogu G etal 2008)** and Trisome 18 **(Chen CP. 2006) .**

2) - Abnormalities of chromosome structure e.g. Prader-Willi syndrome **(de Smith AJ etal 2009)** , Wolf-Hirschhorn Syndrome **(Johnston NJ and Franklin DL 2006)** , and DiGeorge Syndrome **(Rommel N etal 2008)** .

B) - Gene disorders

1) - Mendalian monogenic disorders :

1 - Autosomal dominant triats e.g. multiple endocrine neoplasia syndrome **(Carney JA 2005)** , pheochromocytoma(**Szolar DH etal, 2005)** and pseudohypoparathyrodism (**G. Borck etal , 2004) .**

2- Autosomal recessive disorder e.g. Laurance Moon Biedle syndrome (**Moore S et al , 2005)** , Pendred syndrome **(Pearce JM 2007)**, growth hormone deficiency(**James etal , 2005)** and congenital adrenal hyperplasia**(Green-Golan L etal , 2007)** .

3 - X-linked inheritance :

- X-linked recessive triats e.g. androgen insensitivity syndrome **(McPhaul MJ 2002)** , Kennedy disease**(Chen CJ and Fischbeck 2006)** and Diabetes insipidus**(Perkins RM etal , 2006).**

11) - Non mendalian disorders .

- Polygenic inheritance : Diabetes mellitus and polycystic ovary **(Rother KI 2007)** .