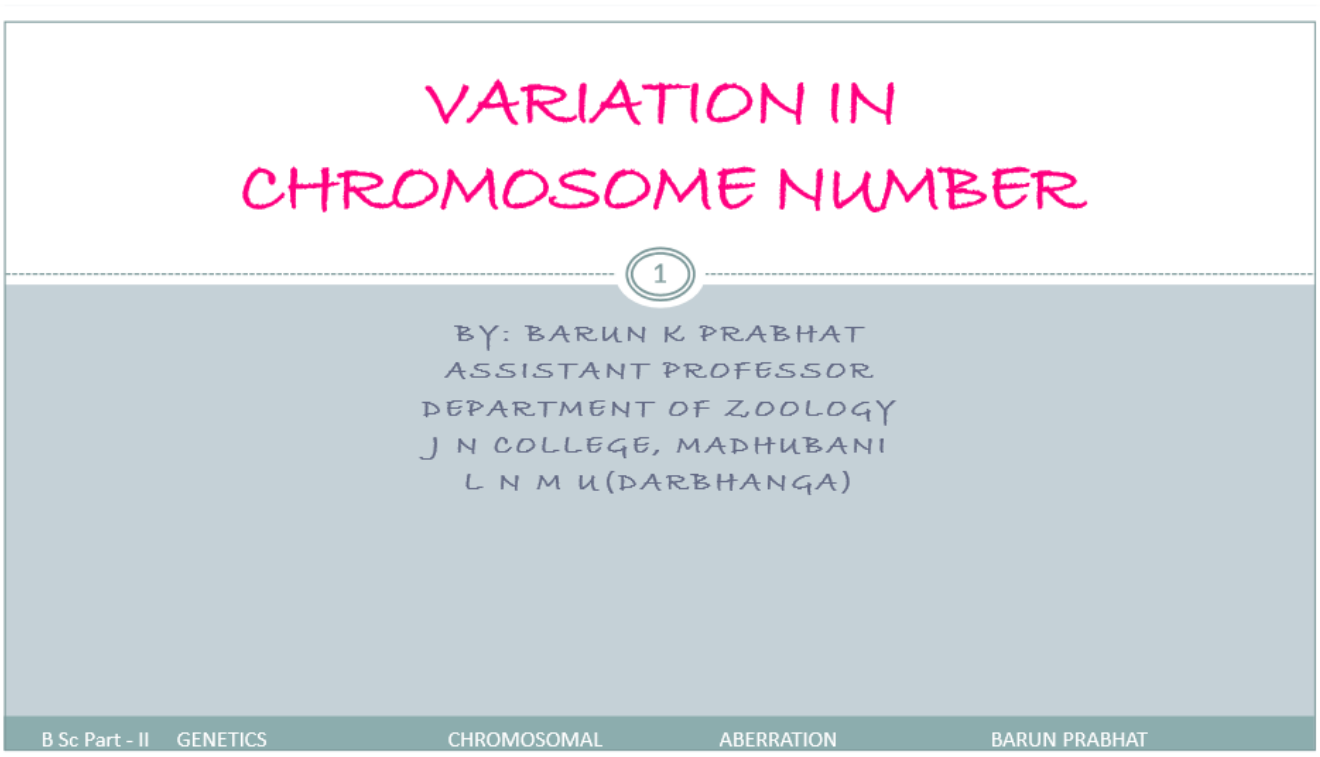
Syndromes due to Variation in Chromosome Number



Chromosome changes are classified in terms of addition or elimination ofparts of chromosomes, whole chromosomes or whole sets of chromosomes (genomes). Two main classes are -

(i) Euploidy: Changes in whole *sets* of chromosomes, i. e. addition or deletion of whole sets of chromosomes

(ii) Aneuploidy: Changes in chromosome *number* by either by additions or deletions of a single chromosome from a set.

Partial List of Terms to Describe Aneuploidy, Using *Drosophila* as an Example (Eight Chromosomes: X, X, 2, 2, 3, 3, 4, 4)

Type	Formula	Number of Chromosomes	Example
Normal	$2n$	8	X, X, 2, 2, 3, 3, 4, 4
Monosomic	$2n - 1$	7	X, X, 2, 2, 3, 4, 4
Nullisomic	$2n - 2$	6	X, X, 2, 2, 4, 4
Double monosomic	$2n - 1 - 1$	6	X, X, 2, 3, 4, 4
Trisomic	$2n + 1$	9	X, X, 2, 2, 3, 3, 4, 4, 4
Tetrasomic	$2n + 2$	10	X, X, 2, 2, 3, 3, 3, 3, 4, 4
Double trisomic	$2n + 1 + 1$	10	X, X, 2, 2, 2, 3, 3, 3, 4, 4

Aneuploidy

Monosomic: A diploid cell missing a single chromosome

Nullisomic: A cell missing both copies of that chromosome

Double Monosomic : A cell missing two non-homologous chromosomes

For Extra Chromosomes

Trisomic: a chromosome is present in triplicate (cell has $2n + 1$ chromosomes)

Tetrasomic: a diploid cell with an extra chromosome

Double trisomic: 2 chromosomes are present in triplicate in the zygote (so that the cell has $2n + 1+1$ chromosomes)

Cause of Aneuploidy:

Nondisjunction in meiosis or by chromosomal lagging whereby one chromosome moves more slowly than the others during anaphase

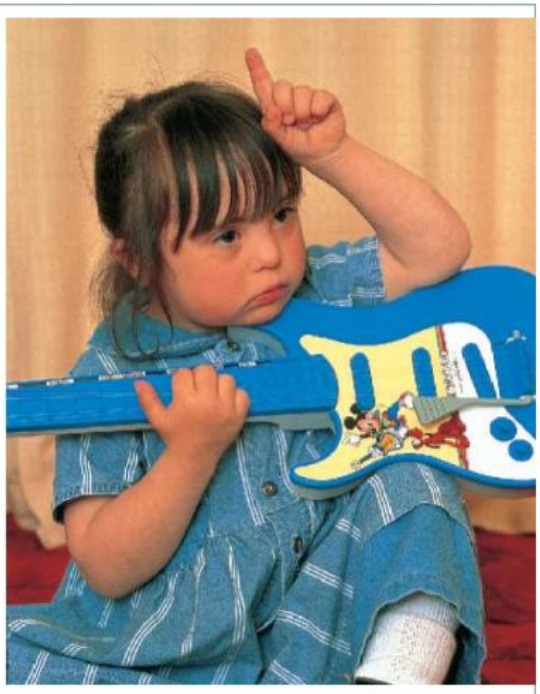
Aneuploidy Resulting from Nondisjunction in Humans

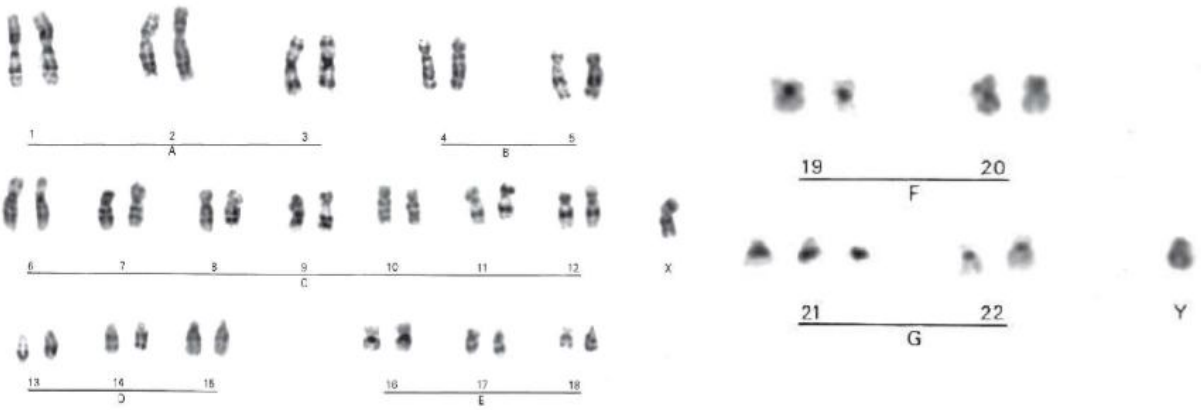
Karyotype	Chromosome Formula	Clinical Syndrome	Estimated Frequency at Birth	Phenotype
47, +21	$2n + 1$	Down	1/700	Short, broad hands with palmar crease, short stature, hyperflexibility of joints, mental retardation, broad head with round face, open mouth with large tongue, epicanthal fold.
47, +13	$2n + 1$	Patau	1/20,000	Mental deficiency and deafness, minor muscle seizures, cleft lip and/or palate, cardiac anomalies, posterior heel prominence.
47, +18	$2n + 1$	Edward	1/8000	Congenital malformation of many organs, low-set, malformed ears, receding mandible, small mouth and nose with general elfin appearance, mental deficiency, horseshoe or double kidney, short sternum; 90 percent die within first six months after birth.
45, X	$2n - 1$	Turner	1/2500 female births	Female with retarded sexual development, usually sterile, short stature, webbing of skin in neck region, cardiovascular abnormalities, hearing impairment.
47, XXY	$2n + 1$	Klinefelter	1/500 male births	Male, subfertile with small testes, developed breasts, feminine-pitched voice, knock-knees, long limbs.
48, XXXY	$2n + 2$			
48, XXYY	$2n + 2$			
49, XXXXY	$2n + 3$			
50, XXXXXY	$2n + 4$			
47, XXX	$2n + 1$	Triplo-X	1/700	Female with usually normal genitalia and limited fertility, slight mental retardation.

Aneuploidy in Human Beings

About one in 160 live human births has some sort of chromosomal anomaly; most are balanced translocations, autosomal trisomics, or sexchromosomal aneuploids.

Down Syndrome: Trisomy 21 (Down Syndrome), 47,XX or XY,21





Karyotype of an individual with trisomy 21, Down syndrome

Down syndrome

Frequency: about one in seven hundred (1/700) live births.

Features: mildly to moderately mentally retarded

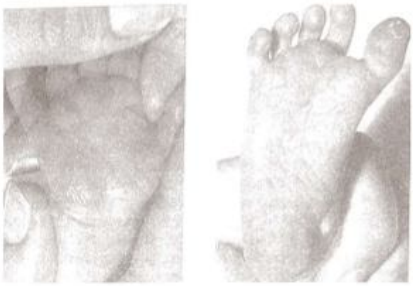
congenital heart defects

a very high (1/100) risk of acute leukemia.

are short and have a broad, short skull; hyperflexibility of joints

excess skin on the back of the neck.

Physician John Langdon Down first described this syndrome in 1866.



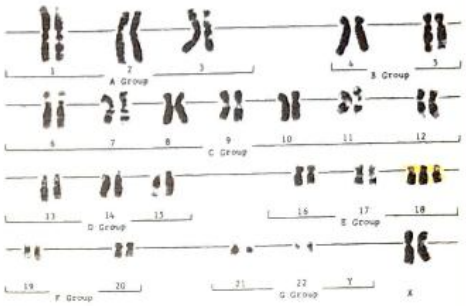
Hand and foot of child with Down Syndrome

child with Down Syndrome Facial expression

Trisomy 18 (Edward Syndrome), 47,XX or XY,18

Described by J.H. Edwards in 1960

Frequency: one in ten thousand (1/8,000) live births.



Affected individuals - mostly **female**, with 80 to 90% mortality by two years of age.

usually has *elfin appearance*

small nose and mouth,

a receding lower jaw, abnormal ears

receding mandible, creases on the fingers

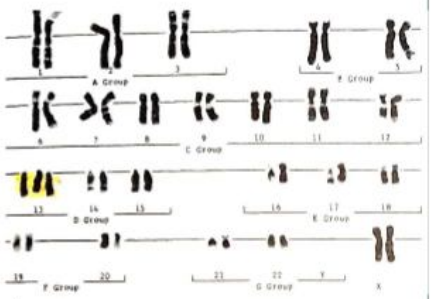
right club foot, left rockottom foot

overlapping of little and index fingers

severe mental retardation

Trisomy 13 (Patau Syndrome), 47, +13; XX or XY,13,

Described by Patau in 1960



Frequency: one in twenty thousand (1/20,000) live births.

Features: cleft palate, cleft lip, con-genital heart defects,

polydactyly, and severe mental retardation.

Mortality is very high in the first year of life.

Non-existent in adults as severity results in early death

Most of the death within 3 months

Other autosomal trisomics are known but are extremely rare.

These include **trisomy 8** (47,XX or XY,8) and **cat's eye syndrome**, a trisomy of an unidentified, small acrocentric chromosome (47,XX or XY,[acrocentric]).

Several aneuploids involving sex chromosomes are also known.

Turner Syndrome, (45, X)

Described by H. H. Turner

Chromosome complement: 44 autosomes + one X chromosome

1/2500 live female births; in population 1/5000

More than 90% abort spontaneously

virtually no ovary, Sterile

limited secondary sexual characteristics

Ovaries have fibrous streak of tissues

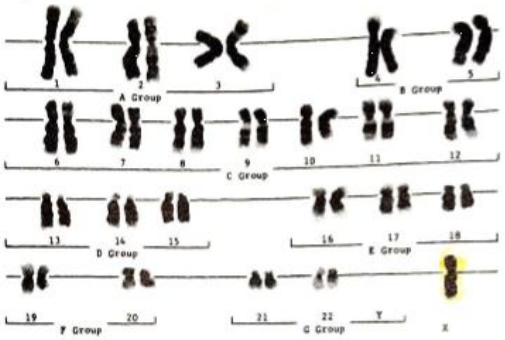
Short stature, low set ears,

Webbed neck

Shield like-chest

Mental deficiency not associated

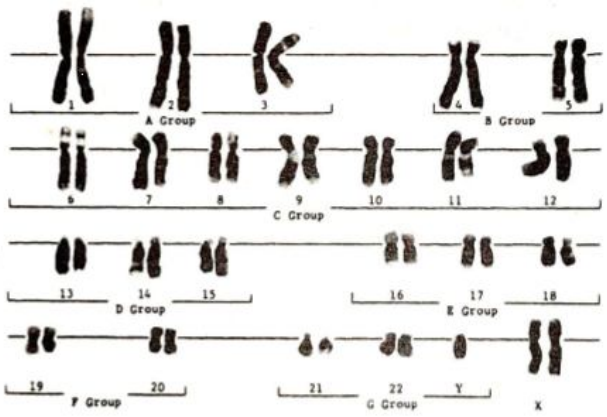
X chromatin negative



Origin: probably, from eggs or sperm with no sex-chromosome or from loss of sex chromosomes in mitosis during early cleavage after formation of an XX or XY zygote.

Klinefelter Syndrome (47, XXY)

Described by : H. F. Klinefelter in 1942
Frequency: 1/500 live male births
Features: Enlarged breasts,
underdeveloped body hair,
small testis, small prostrate glands
One or more chromatin body
Karyotype: XXYY, XXXY, XXXYY, XXXXY, a
XXXXXY
Mental retardation if more than
2 X chromosomes present



Note: Turner and Klinefelter syndrome indicate that sex in human is determined by Y chromosome

Thanks

Suggested readings: various books on Genetics, online study materials