Chromosomal abnormalities

Dr.Sumeya

Obgective

- This lecture explain causes of congenital anomaly which result from chromosomal abnormality either in their number or structure .Also show examples of congenital anomaly

Birth Defects and Spontaneous Abortions: Chromosomal and Genetic Factors

- Chromosomal abnormalities, which may be numerical or structural, are important causes of birth defects and spontaneous abortions.
- It is estimated that 50% of conceptions end in spontaneous abortion and that 50% of these abortuses have major chromosomal abnormalities.
- Thus approximately 25% of conceptuses have a major chromosomal defect.

- The most common chromosomal abnormalities in abortuses are 45,X (Turner syndrome), triploidy, and trisomy 16.
- The most sensitive period for inducing birth defects is the **third to eighth weeks** of gestation, the period of **embryogenesis**.

Numerical Abnormalities

- The normal human somatic cell contains 46 chromosomes; the normal gamete contains 23.
- Normal somatic cells are diploid, or 2n; normal gametes are haploid, or n.
- Euploid refers to any exact multiple of n, e.g., diploid or triploid.
- Aneuploid refers to any chromosome number that is not euploid; it is usually applied when an extra chromosome is present (trisomy) or when one is missing (monosomy).

- Abnormalities in chromosome number may originate during meiotic or mitotic divisions.
- In meiosis, two members of a pair of homologous chromosomes normally separate during the first meiotic division so that each daughter cell receives one member of each pair.
- Sometimes, however, separation does not occur (nondisjunction), and both members of a pair move into one cell .

- As a result of nondisjunction of the chromosomes, one cell receives 24 chromosomes, and the other receives 22 instead of the normal 23.
- When, at fertilization, a gamete having 23 chromosomes fuses with a gamete having 24 or22 chromosomes, the result is an individual with either 47 chromosomes (trisomy) or 45 chromosomes (monosomy).
- Nondisjunction, which occurs during either the first or the second meiotic division of the germ cells, may involve the autosomes or sex chromosomes. In women, the incidence of chromosomal abnormalities, including nondisjunction, increases with age, especially at 35 years and older.

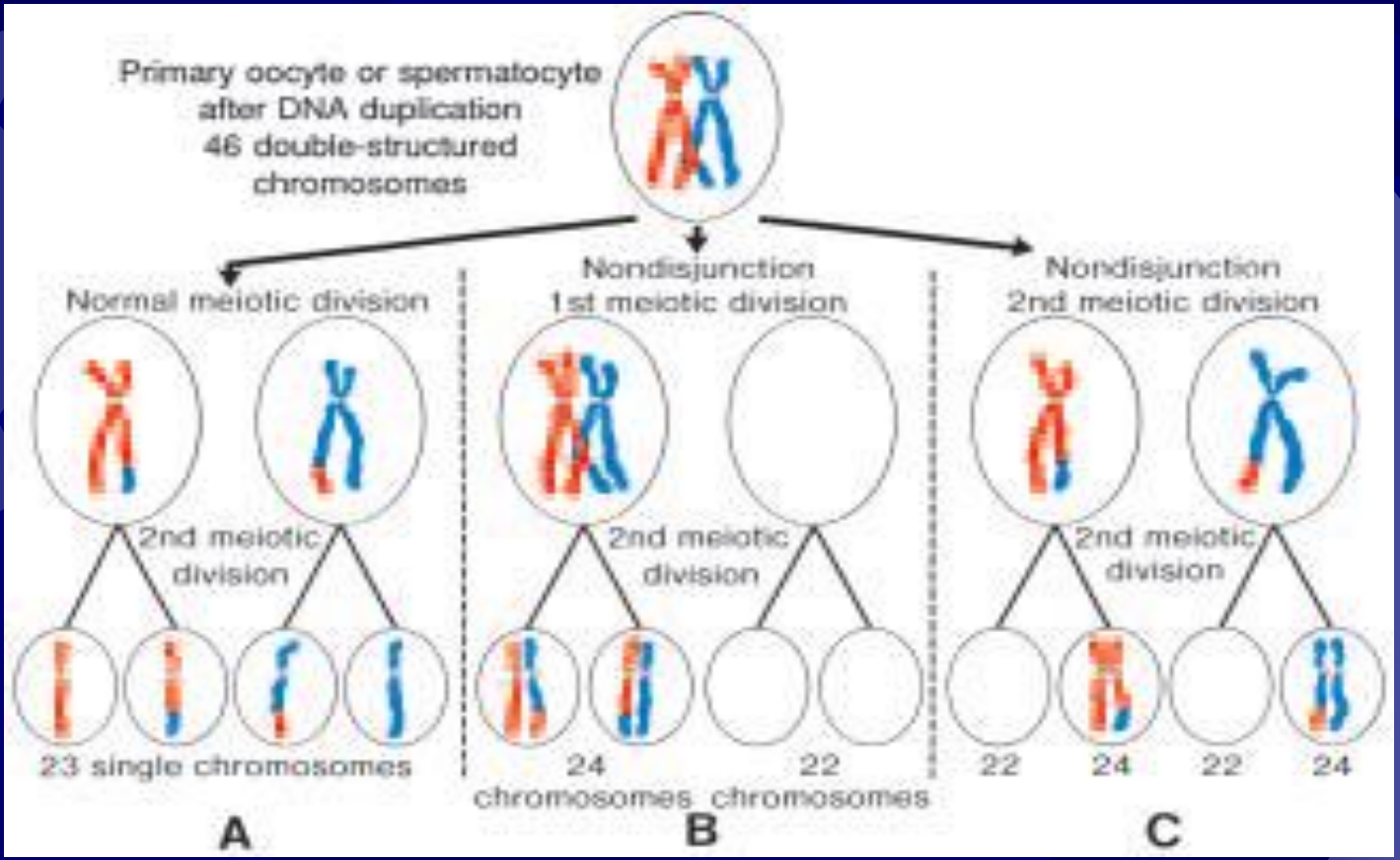
- Occasionally nondisjunction occurs during mitosis (mitotic nondisjunction) in an embryonic cell during the earliest cell divisions.

- Such conditions produce mosaicism, with some cells having an abnormal chromosome number and others being normal. Affected individuals may exhibit few or many of the characteristics of a particular syndrome, depending on the number of cells involved and their distribution.

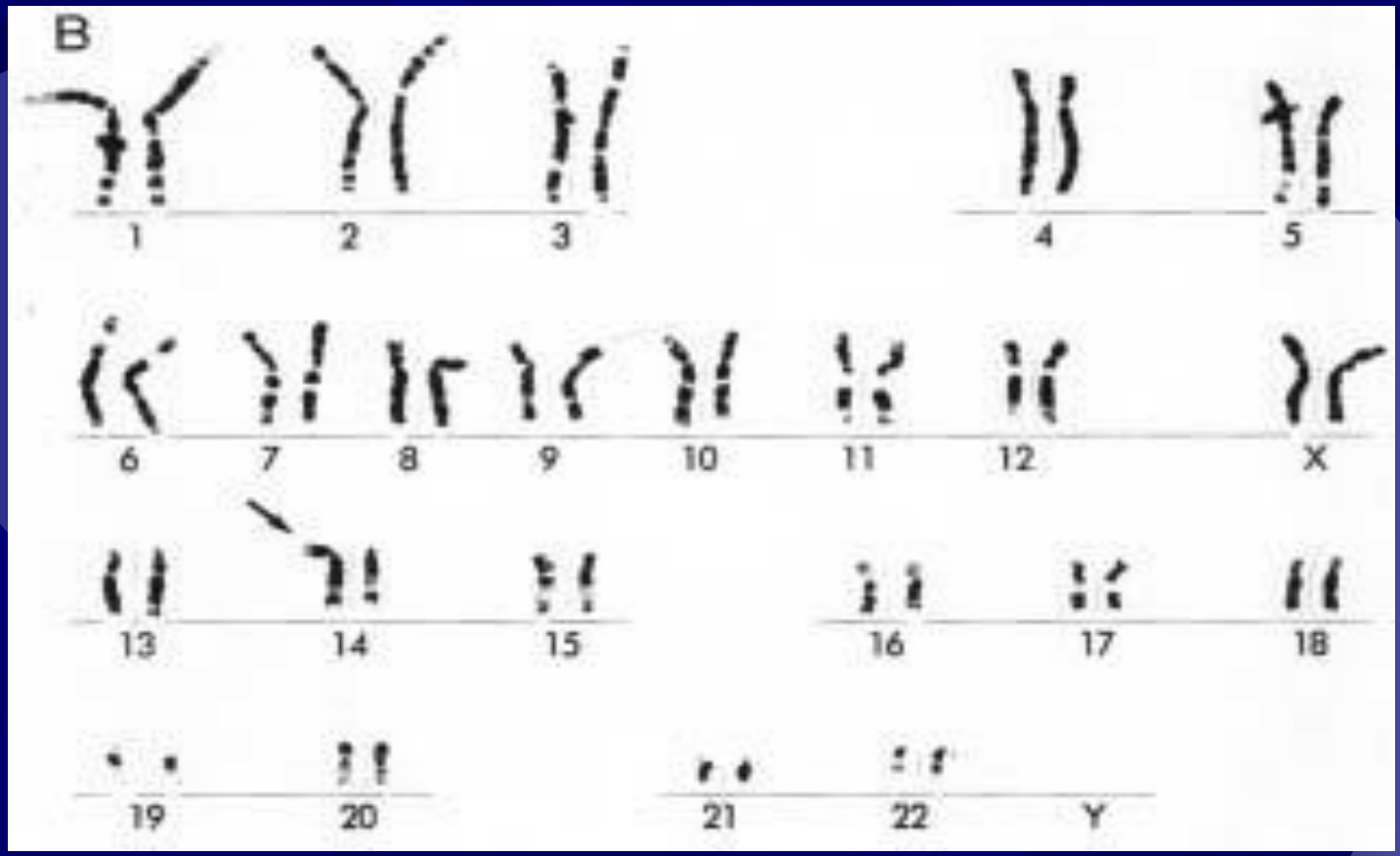
- Sometimes chromosomes break, and pieces of one chromosome attach to another.
- Such **translocations** may be balanced, in which case breakage and reunion occur between two chromosomes but no critical genetic material is lost and individuals are normal; or they may be unbalanced, in which case part of one chromosome is lost and an altered phenotype is produced.

- For example, unbalanced translocations between the long arms of chromosomes 14 and 21 during meiosis I or II produce gametes with an extra copy of chromosome 21, one of the causes of Down syndrome.
- Translocations are particularly common between chromosomes 13, 14, 15, 21, and 22 because they cluster during meiosis.

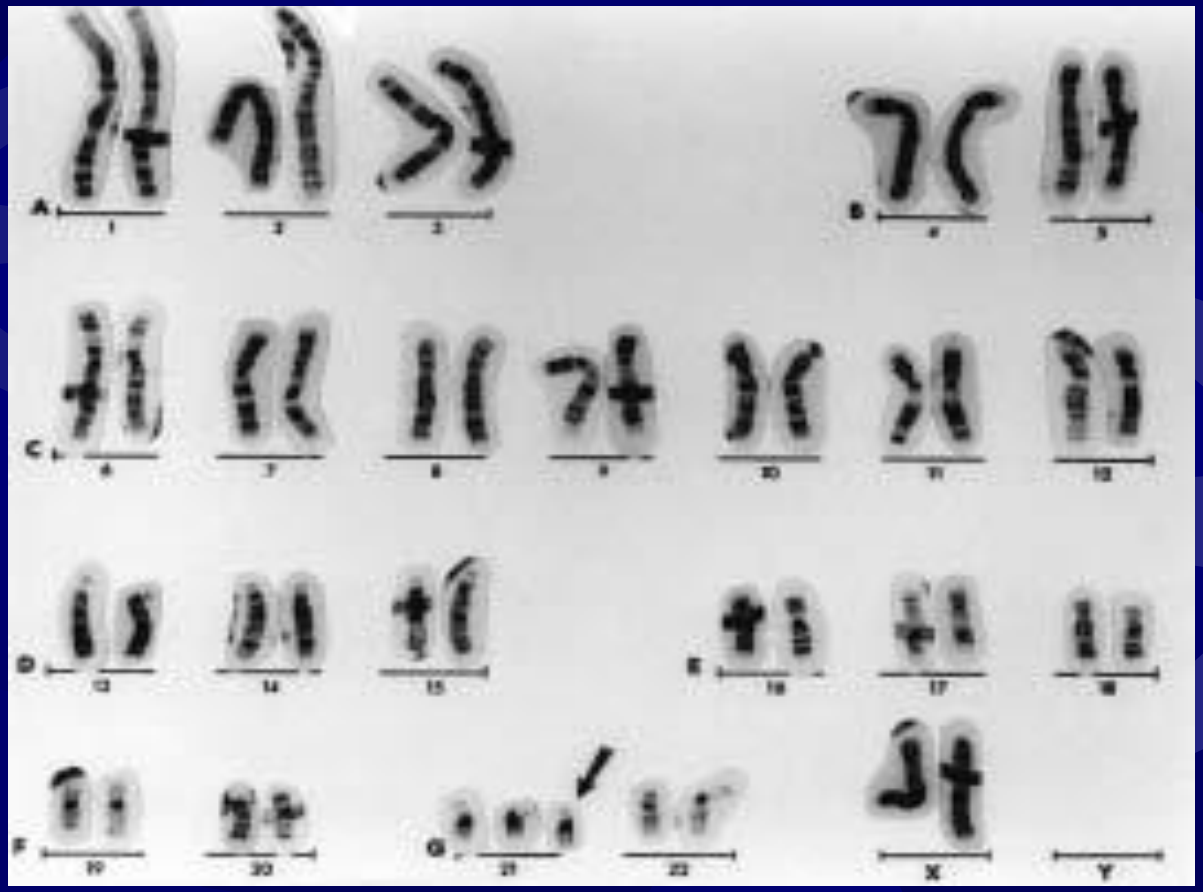
A. Normal maturation divisions. B. Nondisjunction in the first meiotic division.
C. Nondisjunction in the second meiotic division.



Karyotype of translocation of chromosome 21 onto 14, resulting in Down syndrome.



Karyotype of trisomy 21 (arrow), Down syndrome



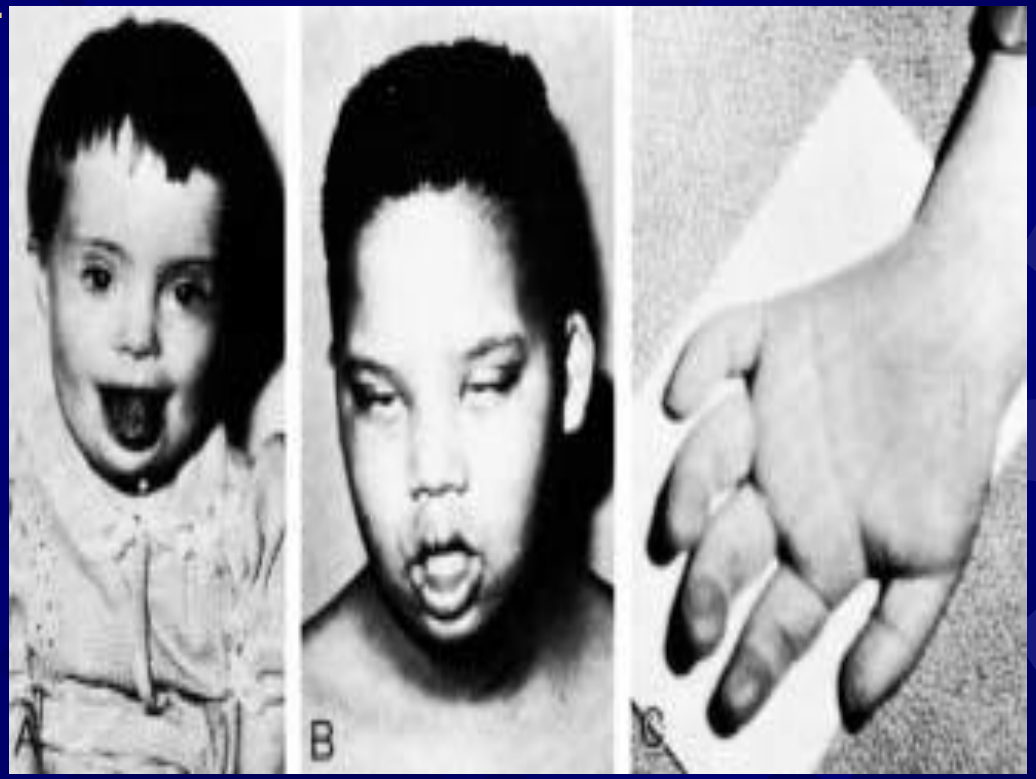
TRISOMY 21 (DOWN SYNDROME)

- Down syndrome is usually caused by an extra copy of chromosome 21.
- Features of children with Down syndrome include growth retardation; varying degrees of mental retardation; craniofacial abnormalities, including upward slanting eyes, epicanthal folds (extra skin folds at the medial corners of the eyes), flat facies, and small ears; cardiac defects; and hypotonia
- These individuals also have relatively high incidences of leukemia, infections, thyroid dysfunction, and premature aging.

- The syndrome is caused by trisomy 21 resulting from meiotic nondisjunction, and in 75% of these instances, nondisjunction occurs during oocyte formation.
- The incidence of Down syndrome is approximately 1 in 2000 conceptuses for women under age 25.
- This risk increases with maternal age to 1 in 300 at age 35 and 1 in 100 at age 40.

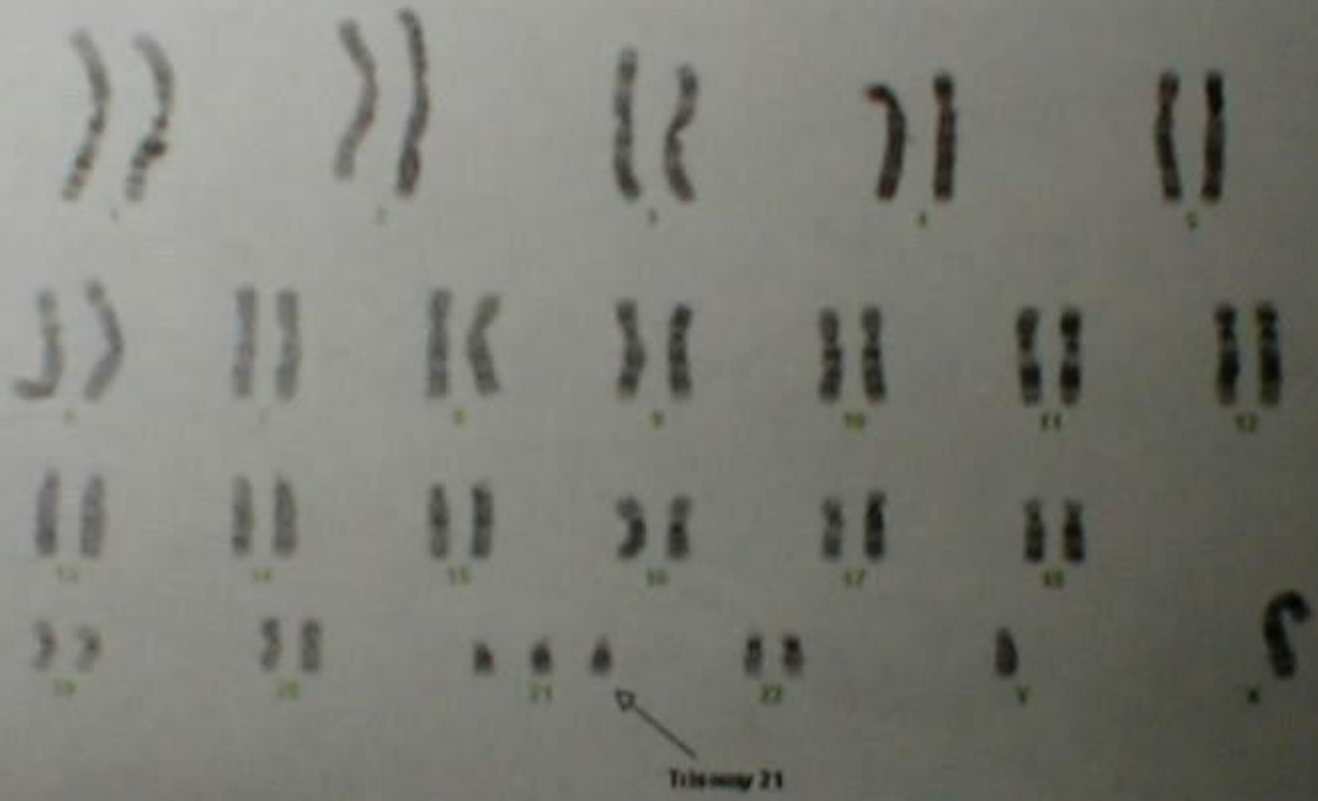
- In approximately 4% of cases of Down syndrome, there is an unbalanced translocation between chromosome 21 and chromosome 13, 14, or 15
- The final 1% are caused by mosaicism resulting from mitotic nondisjunction. These individuals have some cells with a normal chromosome number and some that are aneuploid.
- They may exhibit few or many of the characteristics of Down syndrome.

A and B. Children with Down syndrome, which is characterized by a flat, broad face, oblique palpebral fissures, epicanthus, and furrowed lower lip. C. Another
characteristic of Down syndrome is a broad hand with single transverse or simian crease.
Many children with Down syndrome are mentally retarded and have congenital heart
abnormalities.



photographed.

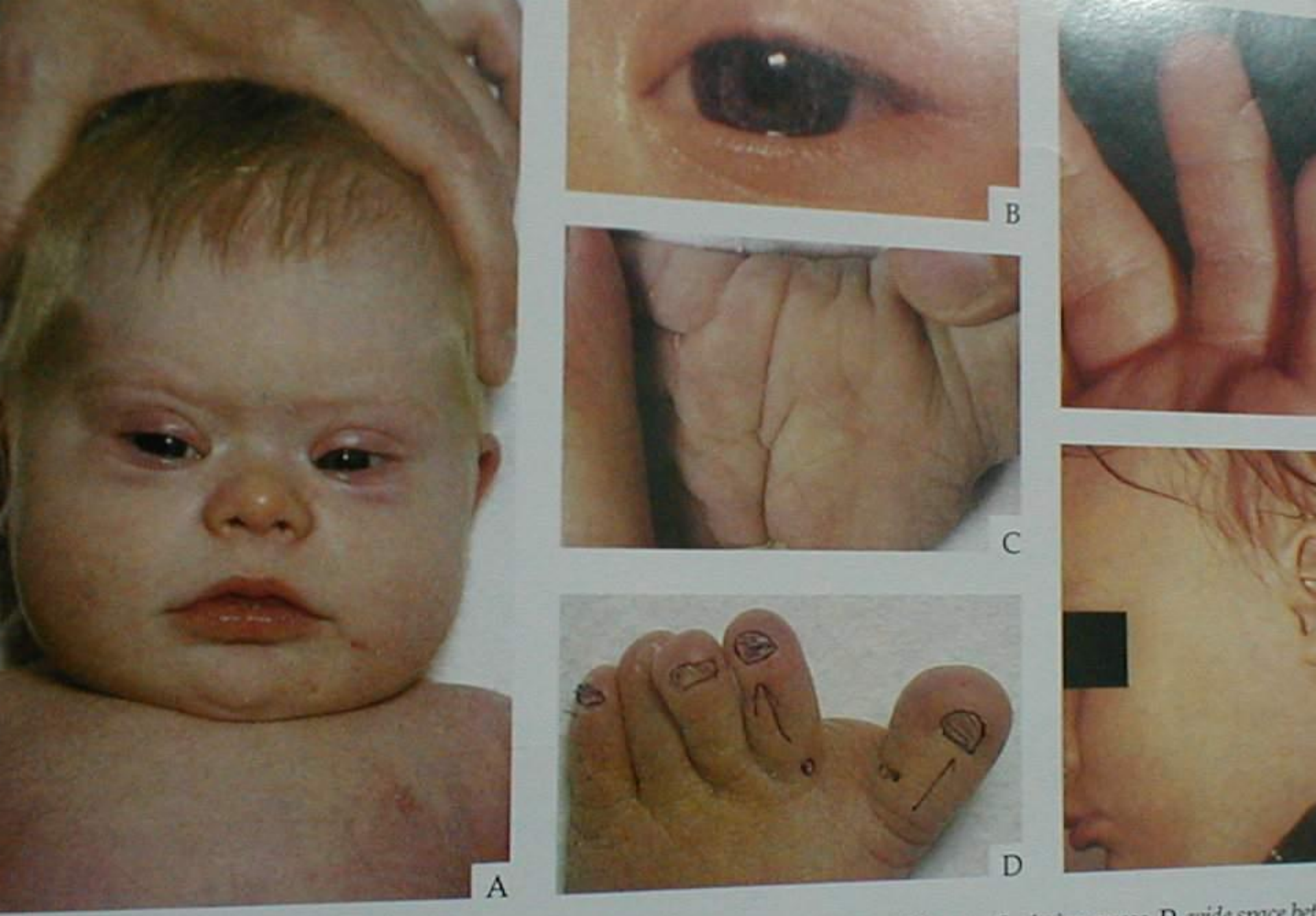
Result: 47, XY,+21



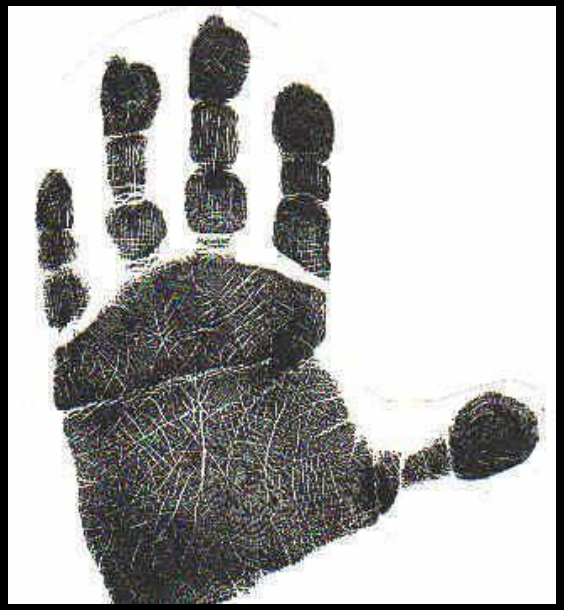
Comment: **The karyotype is consistent with Down Syndrome (trisomy 21) male.**

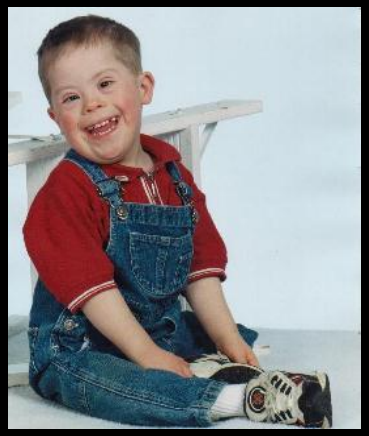
Geneticist: Ala' Hejazi, MSc

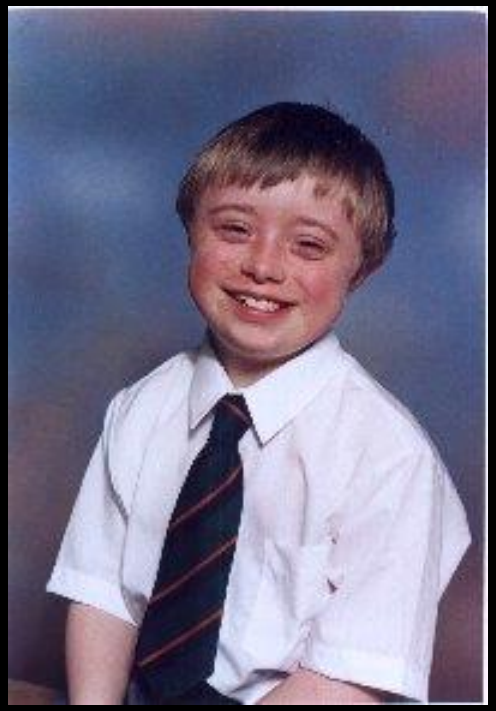
Hat ejazi

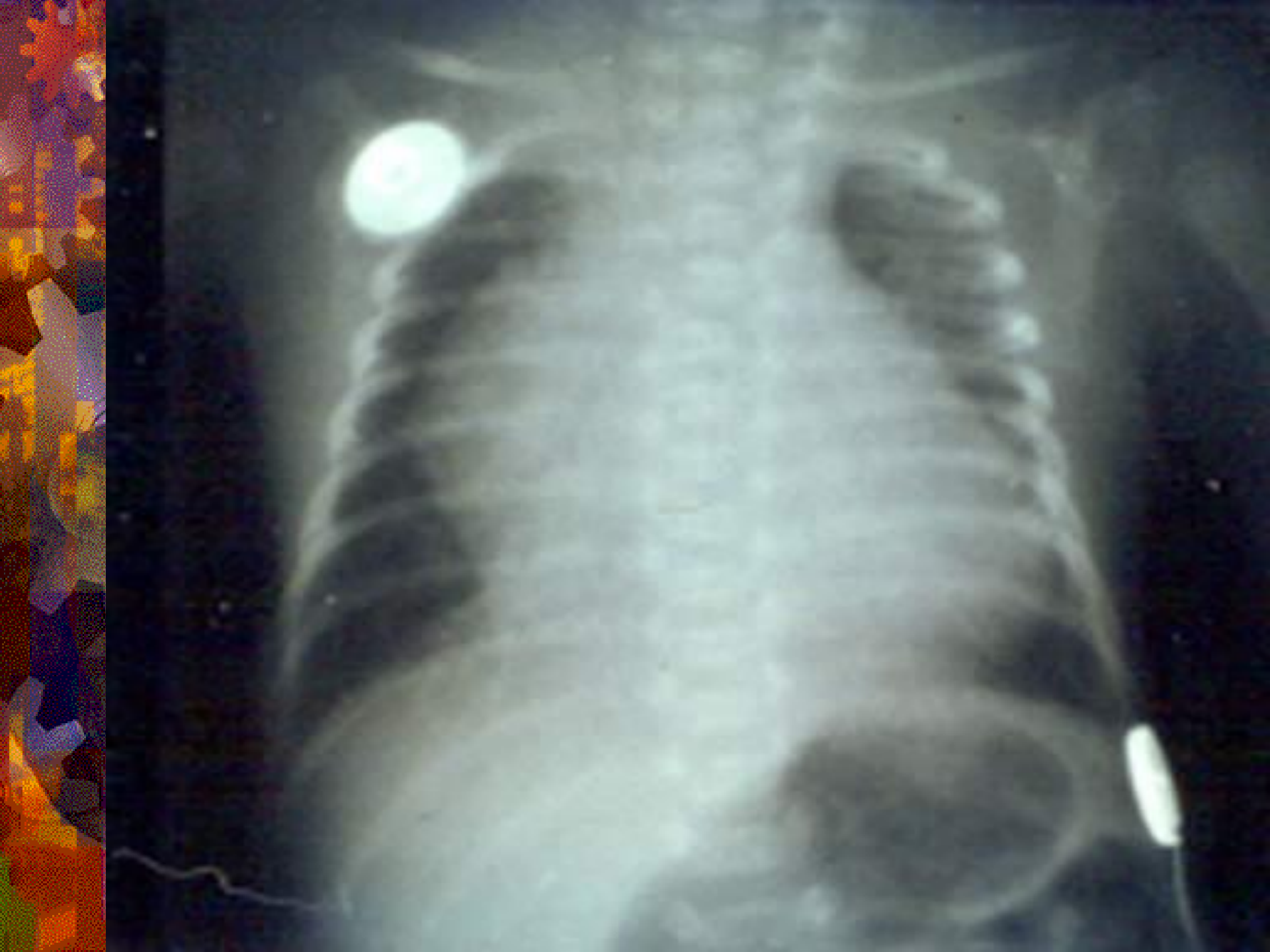


IG. 1.14 Clinical photographs show several minor anomalies associ-
Brushfield spots. C, simian crease. D, wide space bet
second toes. E, short fifth finger. F, small ears.







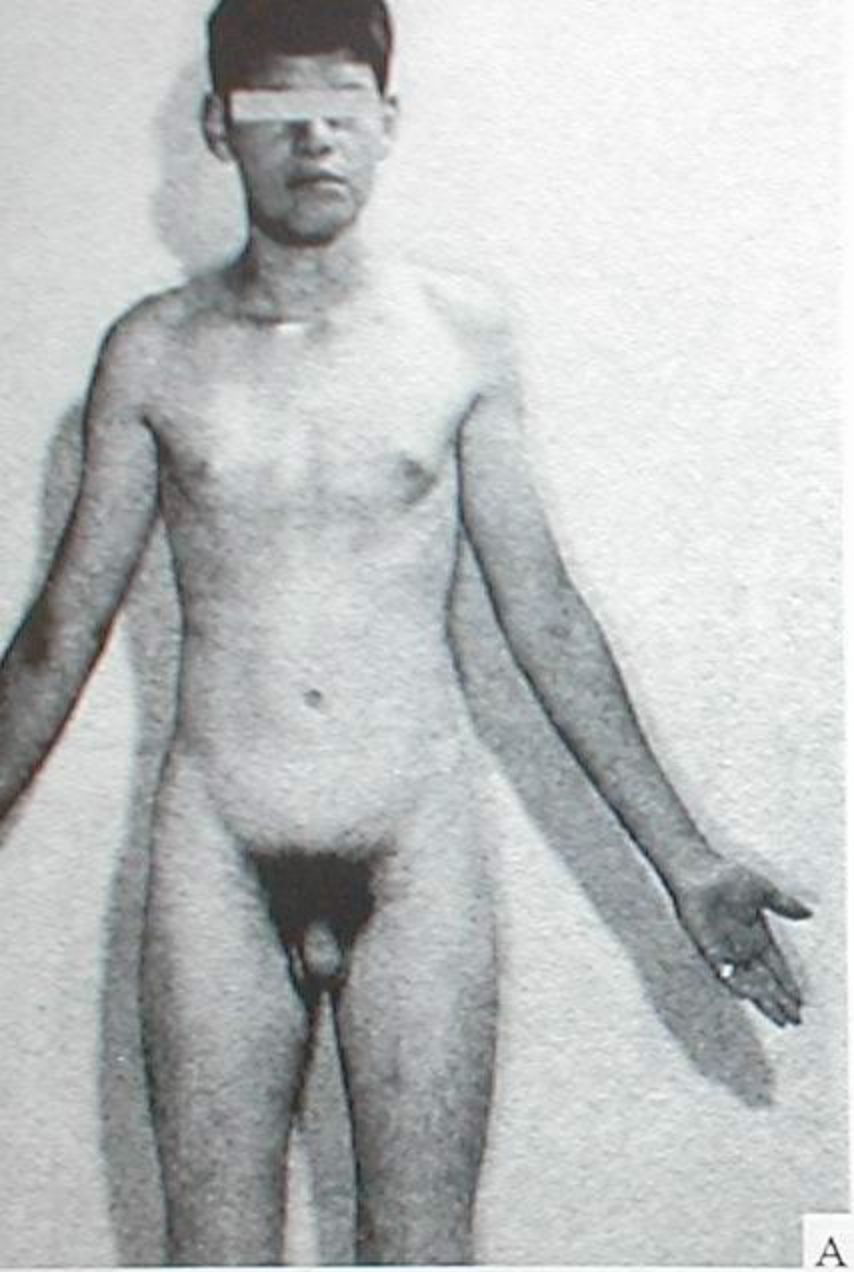


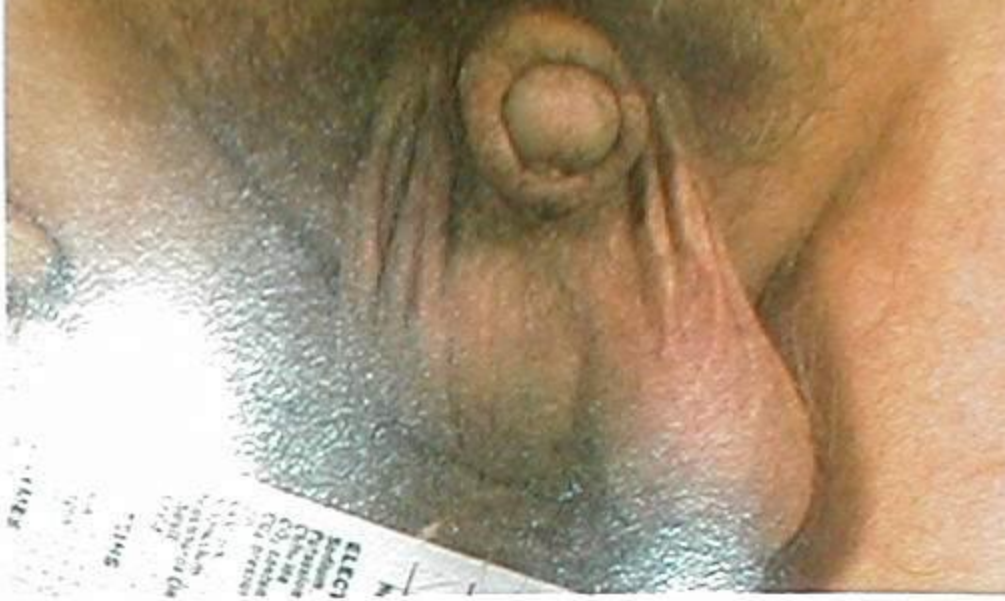
KLINEFELTER SYNDROME

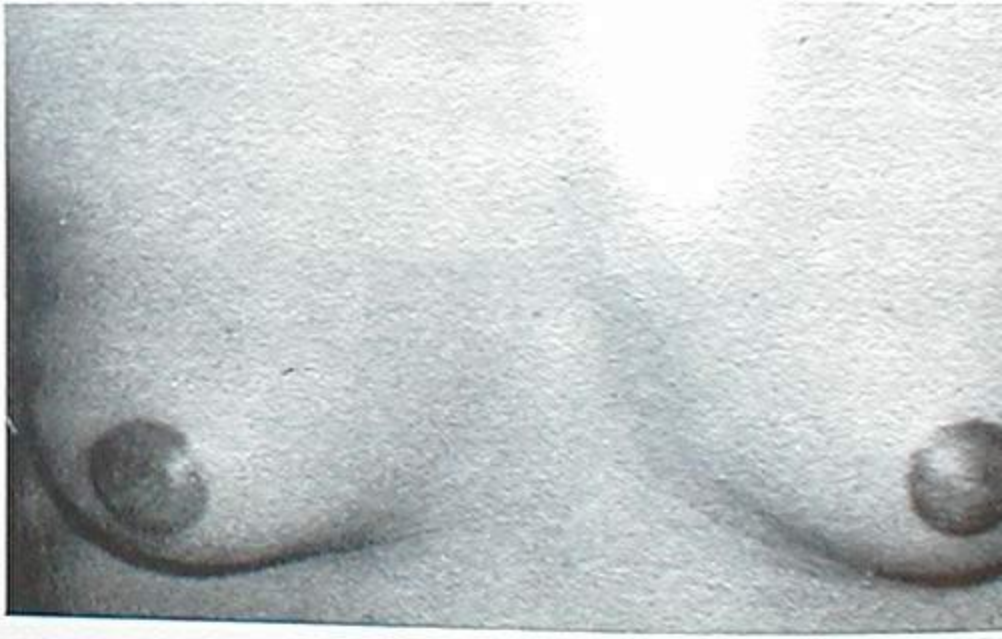
- The clinical features of Klinefelter syndrome, found only in males and usually detected at puberty, are sterility, testicular atrophy and usually gynecomastia.

- The cells have 47 chromosomes with a sex chromosomal complement of the XXY type.

- The incidence is approximately 1 in 500 males. Nondisjunction of the XX homologues is the most common causative event.
- Although mental retardation is not generally part of the syndrome, the more X chromosomes there are, the more likely there will be some degree of mental impairment





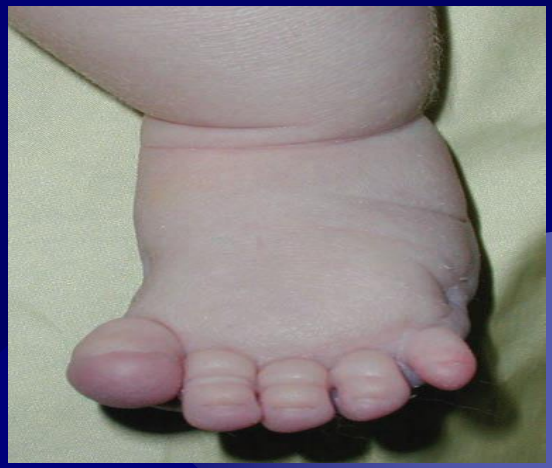


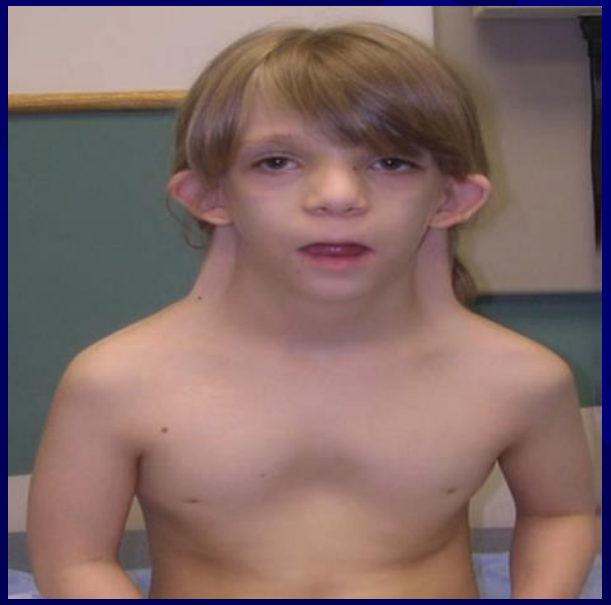
ical photographs show several physical manifestations yndrome. A, eunuchoid body habitus, relatively narrow eased carrying angle of arms, female distribution of

small testes and penis. C, gynecomastia. (B, courtesy of Dr. Pe University of Pittsburgh School of Medicine C, reproduced by sion from Gardner LI (ed): Endocrine and Genetic Diseases

TURNER SYNDROME

- Turner syndrome, with a 45,X karyotype, is the only monosomy compatible with life. Even then, 98% of all fetuses with the syndrome are spontaneously aborted.
- The few that survive are unmistakably female in appearance and are characterized by the absence of ovaries (gonadal dysgenesis) and short stature.
- Other common associated abnormalities are webbed neck lymphedema of the extremities, skeletal deformities, and a broad chest with widely spaced nipples.

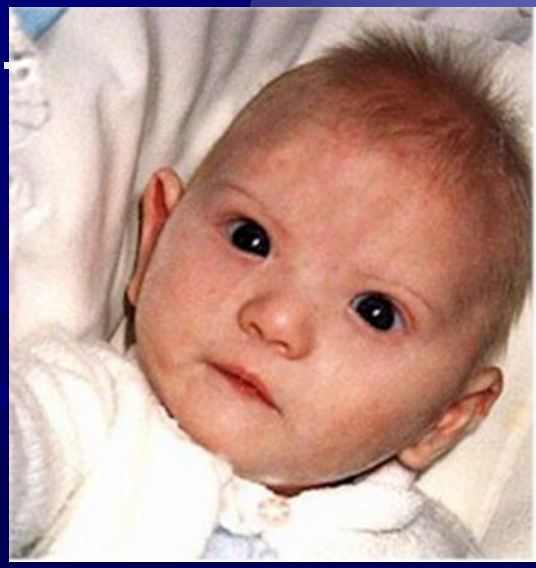




Structural Abnormalities

- Structural chromosome abnormalities, which involve one or more chromosomes, usually result from chromosome breakage.
- Breaks are caused by environmental factors, such as viruses, radiation, and drugs.
- The result of breakage depends on what happens to the broken pieces.
- In some cases, the broken piece of a chromosome is lost, and the infant with partial deletion of a chromosome is abnormal.

- A well-known syndrome, caused by partial deletion of the short arm of chromosome 5, **is the cri-du-chat syndrome.**
- Such children have a cat like cry, microcephaly, mental retardation, and congenital heart disease.
- Many other relatively rare syndromes are known to result from a partial chromosome loss.



Cri du Chat

Cry of the Cat individuals sound like cats crying.

Why?

The larynx of the child is improperly developed.

triploidy

- Complete extra set of chromosomes
- Mostly miscarriages
- Large hydatidiform placenta
- VSD(Ventricular Septal Defect), ASD(Autism Spectrum Disorder),
- Genital and CNS abnormalities

THANK YOU