Cytogenetics

The microscopic study of chromosomes, blends the skills of cytologists, who study the structure and activities of cells, with those of geneticists, who study genes. Cytologists discovered chromosomes and the way in which they duplicate and separate during cell division at about the same time that geneticists began to understand the behavior of genes at the cellular level. The close correlation between the two disciplines led to their combination.

Plant cytogenetics early became an important subdivision of cytogenetics because, as a general rule, plant chromosomes are larger than those of animals. Animal cytogenetics became important after the development of the so-called squash technique, in which entire cells are pressed flat on a piece of glass and observed through a microscope; the human chromosomes were numbered using this technique.

Today there are multiple ways to attach molecular labels to specific genes and chromosomes, as well as to specific RNAs and proteins, that make these molecules easily discernible from other components of cells, thereby greatly facilitating cytogenetics research.

So cytogenetics is the study of chromosomes and their role in heredity, is the branch of genetics that studies the structure and behavior of chromosomes and their relation to human disease and disease processes.

The goal of cytogenetics:

1. diagnosis of chromosomal abnormalities.
2. localization of any (often abnormal) chromosomal region/DNA sequence.

Basic Cytogenetic Terms

***Chromatin*:** non condensed DNA with proteins attached (interphase of the cell cycle)

***Chromosome*:** condensed DNA with proteins attached (M phase of the cell cycle)Human cells contain 46 chromosome, 44 *autosome* and 2 *sex chromosome.*

karyotype is the number and appearance of chromosomes in the nucleus of a eukaryotic cell. The term is also used for the complete set of chromosomes in a species, or an individual organism.

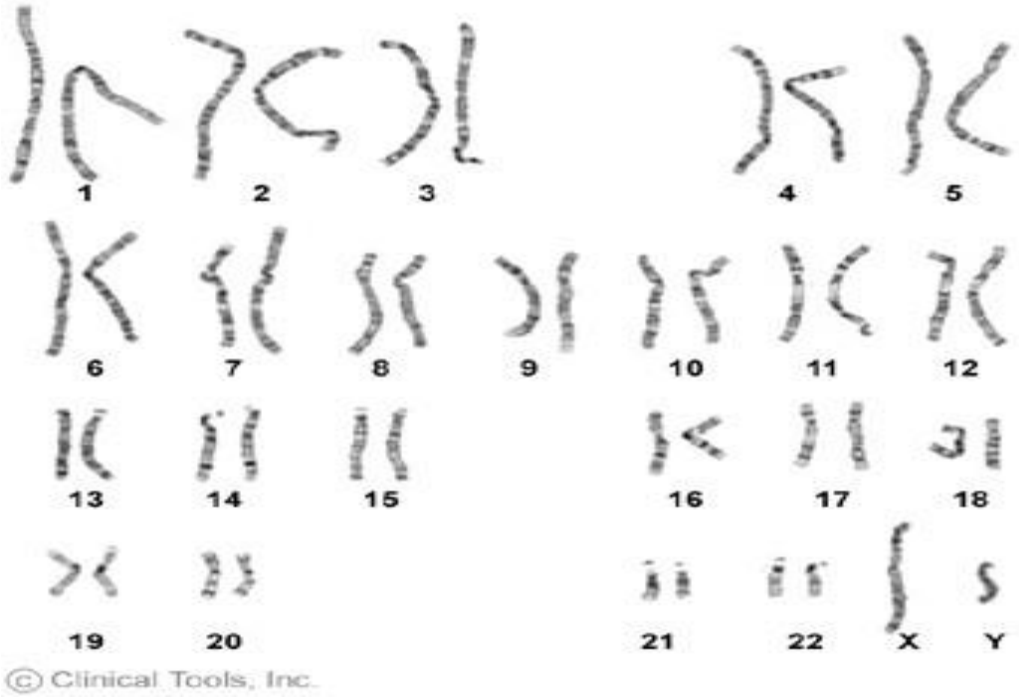
During the past three decades, the importance of clinical cytogenetics to the practice of obstetrics and gynecology has dramatically increased because clinical cytogenetics has a direct effect on the diagnosis, management, and prevention of many disorders that are caused by chromosome aberrations. For many chromosome disorders, physicians face medicolegal responsibilities in the areas of counseling, screening, and diagnosis, and obstetricians and gynecologists therefore must have knowledge about the human chromosome constitution and be able to apply basic principles of chromosome behavior to clinical practice.

A **chromosome** (from ancient Greek: *chromosoma*, *chroma* means color, *soma* means body) is a DNA molecule with part or all of the genetic material (genome) of an organism.

Chromosomes are normally visible under a light microscope only when the cell is undergoing the metaphase of cell division. Before this happens, every chromosome is copied once (S phase), and the copy is joined to the original by a centromere, resulting either in an X-shaped structure . During metaphase the X-shape structure is called a metaphase chromosome. In this highly condensed form chromosomes are easiest to distinguish and study. In animal cells, chromosomes reach their highest compaction level in anaphase during segregation. Chromosomal recombination during meiosis and subsequent sexual reproduction play a significant role in genetic diversity. If these structures are manipulated incorrectly, through processes known as chromosomal instability and translocation, the cell may undergo mitotic catastrophe and die, or it may unexpectedly evade apoptosis, leading to the progression of cancer.

Human beings have 46 chromosomes, consisting of 22 pairs of **autosomes** and a pair of **sex chromosomes**: two X sex chromosomes for females (XX) and an X and Y sex chromosome for males (XY). One member of each pair of chromosomes comes from the mother (through the egg cell); one member of each pair comes from the father (through the sperm cell).

A photograph of the chromosomes in a cell is known as a **karyotype**. The autosomes are numbered 1-22 in decreasing size order.



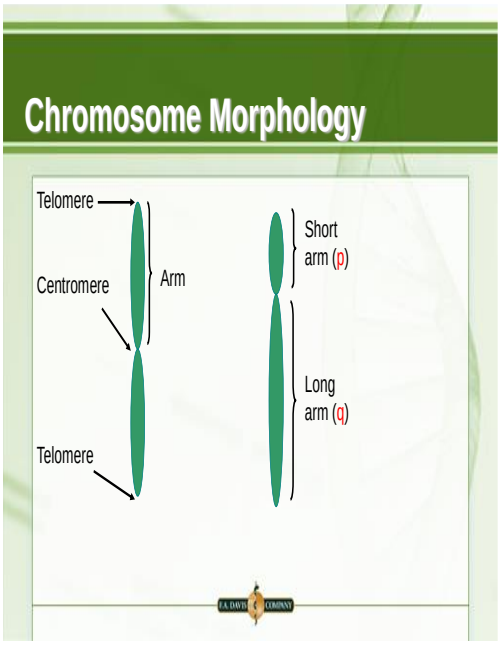
Chromosome morphology

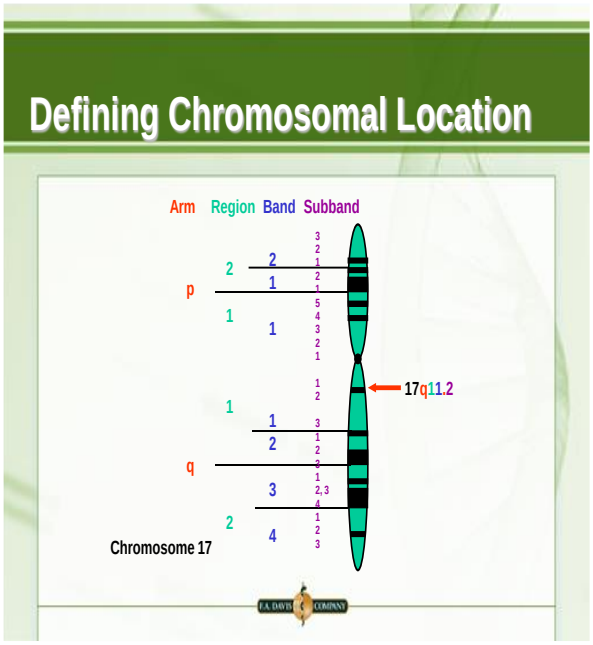
Before 1970 was limited to the relative length and the position of the centromere. The centromere, or primary constriction, is the site of attachment of the spindle fibers essential for the orderly segregation of chromatids (duplicates of each chromosome) into daughter cells during mitosis and meiosis. At the metaphase of mitosis, chromosomes are already duplicated and the duplicates are held together by the centromere. The chromosome number of a cell is actually a count of the number of centromeres. When the centromere divides, each chromatid with its own centromere becomes a chromosome.

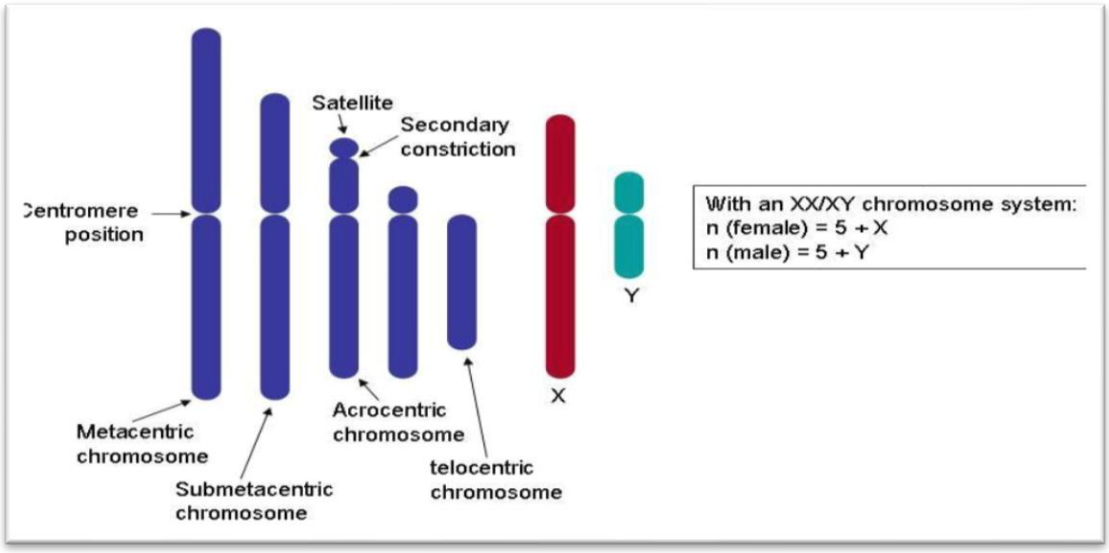
The location of the centromere divides each chromosome into a short arm, designated *p* for petite, and a long arm, designated *q.* Chromosomes are *metacentric* if the centromere is located in the middle of the chromosome (*i.e.* the arms are of approximately equal length), *submetacentric* when the centromere is located away

from the center, and *acrocentric* when the centromere lies close to one end of a chromosome. The ends of the short arms of acrocentric chromosomes often exhibit *satellites,* which are portions of the ends of chromosomes that seemingly are separated from the main body and apparently represent an altered coiling pattern of the chromatin. These satellite regions are associated with nucleolar formation

An *acentric chromosome* is one without a centromere and, lacking a site for spindle fiber attachment, is not passed to the daughter cells of the next cell generation. A *dicentric chromosome* has two centromeres that can produce a cycle of chromosome breakage if the two centromeres simultaneously move toward different daughter cells during cell division.







Size of Chromosome:

The length of chromosome ranges from 0.25 µm (fungi and birds) to 30 µm (Trillium, Liliaceae). It does not include salivary gland chromosomes of diptera which may be 2 mm long. All the chromosomes of a species are of similar size (symmetrical karyotype). In the asymmetrical case there may be two size groups e.g., Yucca or a gradual series of different sizes e.g., man.

Size differences may be found in the different species of a genus. For example, the chromosomes of Allium porum are half the size of the chromosomes of Allium sativum. Chromosome size may also vary within the species or in different varieties. In the plant Mediola, for example, the chromosomes of root tip are 50% longer than the chromosomes of shoot tip.

Function of a Chromosome

1-The chromosome holds not only the genetic code, but many of the proteins responsible for helping express it.

2-Its complex form and structure dictate how often genes can be translated into proteins, and which genes are translated. This process is known as *gene expression* and is responsible for creating organisms.

3-The chromosomes carry genes or DNA molecules, hence are carriers of heredity.

4- During total life of any organism chromosomes preserve or maintain their identity and continuity.

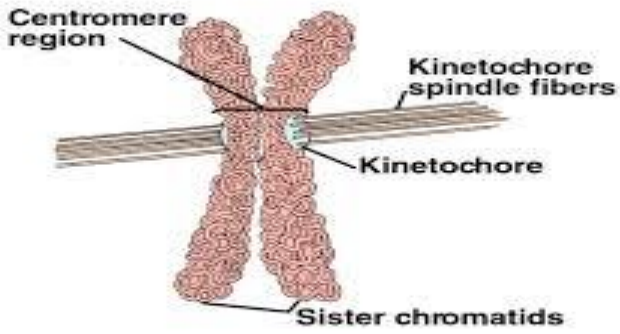
5-It indirectly helps in protein synthesis. Nucleolus contains RNA and this serves as a means of transmission of genetic information's of cytoplasm.

6- The sex chromosomes or allosomes decide the sex of the individual.

7- The number of chromosomes always remain constant for a particular species.

8- One chromosome is related with only one set of physiological functions while other chromosomes will have other pairs of other character. The autosome may under go any change but sex chromosome or allosome will remain unchanged. Sex chromosome, if changed by mutation or aberration, will give rise to intersex or gynandrosporous individual.

Chromosome Related Nomenclature



Chromatin: the complex of DNA,histones, and nonhistone proteins within the nucleus of a eukaryotic cell (DNApersistence length ~50nm). The material of which chromosomes are made.

• **Chromatid:** one of the two copies of a replicated chromosome that is joined at the centromere to the other copy. The two identical chromatids are called sister chromatids.

• **Centromere:** the chromosomal region that holds sister chromatids together and

where the kinetochore forms.

Kinetochore: the centromeric substructure that binds microtubules and directs chromosome movement in mitosis.
• **Gene**: a segment of DNA encoding a functional RNA or protein product.

Chemical Composition of Chromosome:

1. DNA — 40%

2. RNA — 1.5% (Helps in synthesis of chromosomal fibres)

3. Histone (Protein) — 50%.

4. Non-Histone (Protein) — 8.5%;

5. Some amount of calcium which is attached with DNA. DNA is the chief and most significant part of chromosome)

According to Mirsky and Ris (1945), the chemical composition of an isolated chromosome is as follows:

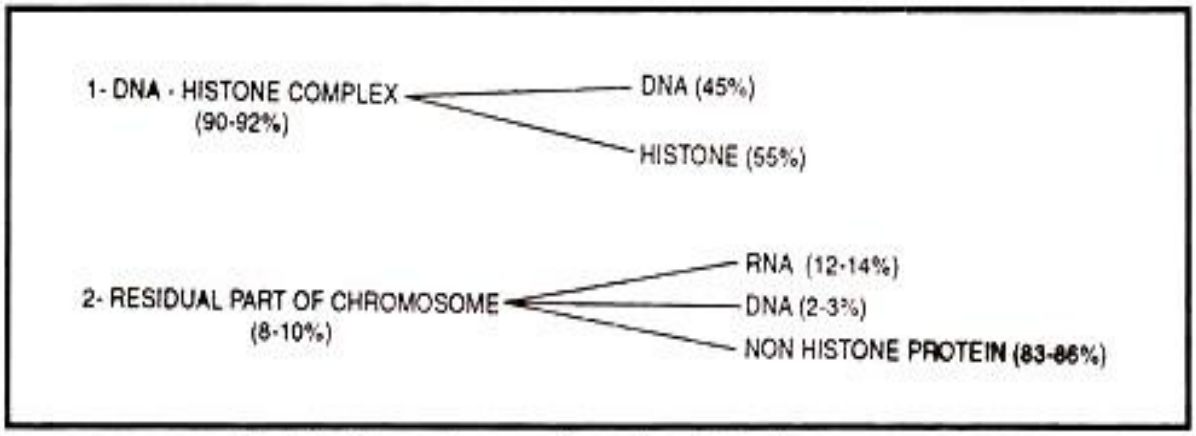


Fig. 50. Chemical composition of an isolated chromosome.

Protein in the chromosome probably acts as a framework to which the different nucleic acids are attached. The electron microscopic studies of chromosomes demonstrated that chromosomes contain very fine threads having a thickness of 2nm-4nm.

It can be considered that the thickness of a chromosome is usually hundred times more than that of DNA and the length of DNA present in chromosome is many hundred times more than the length of chromosomes themselves.

The major chemical components of chromosomes are DNA, RNA, histone proteins and nonhistone proteins. Calcium is also present in addition to these constituents. The relative proportions of different components are given in Table 6.1 for a variety of organisms, which suggest that there is more protein than DNA in chromatin in all cases.

Table 6.1. **Chemical composition of chromatin (per cent) from various sources.**

Source	DNA	Histone	Nonhistone	RNA
Pea embryonic axis	39.0	40.0	11.0	10.0
Pea vegetative bud	40.0	52.0	4.0	4.0
Pea growing cotyledon	43.5	34.5	16.0	6.0
Rat liver	37.0	37.0	25.0	1.0
Cow thymus	40.2	46.0	13.5	0.3
Sea urchin blastula	39.2	41.0	19.0	1.0
Sea urchin larva	33.4	29.0	35.0	2.6

DNA. As we know, DNA is the most important of chemical components of chromatin, since it plays the central role of controlling heredity. The most convenient measurement of DNA is picogram (10^{-12} g) which is equivalent to 31 cm of double helical DNA (for details of the double helical structure of DNA, consult .It has been found that quantity of DNA varies greatly in cells from different kinds of organisms. The haploid genome of mammals usually contains 1000 times DNA content of bacteria. Other eukaryotes may similarly have 10 to 100 times the bacterial DNA content. It is interesting to note that a human diploid cell has 174 cm (5-6 picograms) of DNA, so that all cells in a human being may have DNA equal to 2.5 x 10^{10} km (100 g), a length which is equal to 100 times the distance from earth to sun. Similarly a diploid cell of *Trillium* has 37 meters (120 picograms) and that of *Drosophila* salivary glands has 91 meters (293 picograms) of DNA. In comparison of these enormous lengths, the DNA of bacteria measures only 1.1 mm-1.4mm.