The Cytology

Nucleus

Dr.Emad Al-Radhi

Ph.D. Molecular cytology

Definition *Lec.1*

The nucleus is the largest cellular organelle in animal cells that found in eukaryotic cells, its acts like the brain at the cell, because it contains most at the cells genetic material which organized as multiple long linear DNA molecules in complete which a large variety of proteins such as histones to from chromosomes.

Shape of nucleus

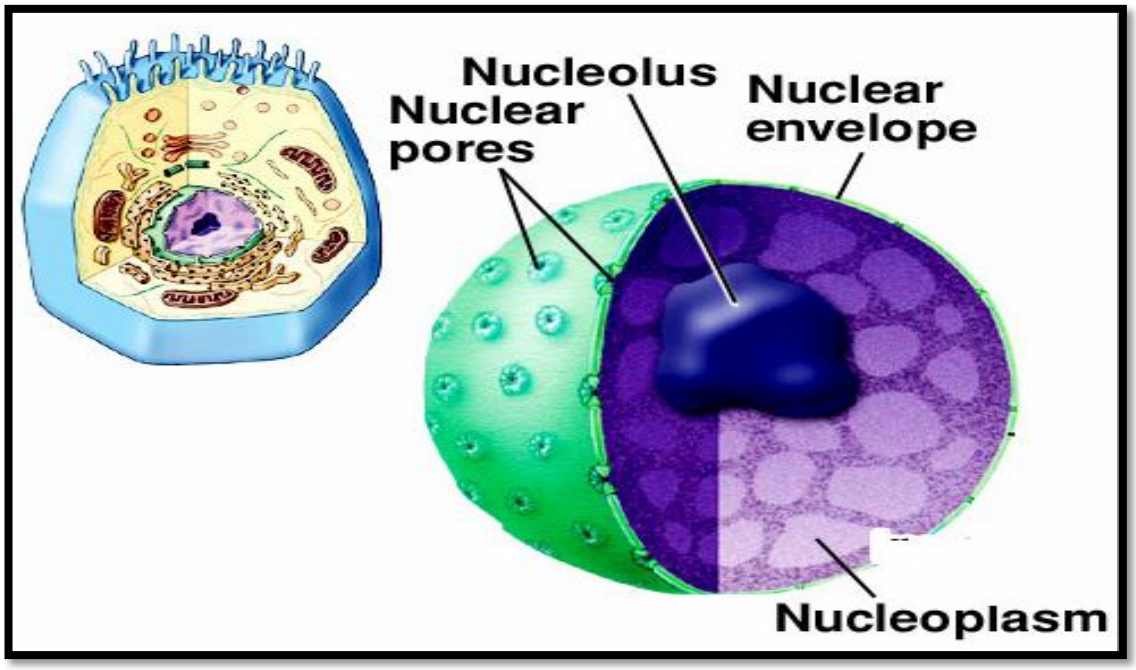
The shape of nucleus are differ with the cell shape , frequently appears as rounded or oval structure taking about 10 percent % of cells ,volume usually in the middle of the cells cytoplasm , they differ in diameter between (5-10 mm) and some cells have nucleus could be reach more than (25 mm) in diameter like ovum.

The function of nucleus

As the nucleus directs all of the cell's functionality, its central location is the key to passing information to the other components of the cell. It present in all cells except the RBC where lose their nuclei when they mature. Most cells have one nucleus but others may have binucleate like cardiac muscle cells or multi nucleated like skeletal muscle cells.

The nucleus stain blue when using basophilic dye such as hematoxylin, where the nucleus is basophilic in nature due to its content of nucleic acid (DNA) and basic protein called histone. Its main components are nuclear envelope which is membrane separating the nucleus from surrounding cytoplasm in the cell, chromatin consisting of DNA, associated proteins and a specialized region of chromatin called nucleolus .

The Structure of nucleus



The double- layered membrane that envelopes the nucleus of a eukaryotic cell, separating the contents of the nucleus from the cytoplasm and serving as a barrier to prevent macromolecules from diffusing freely between the nucleoplasm and the cytoplasm.

It is made up of two layers, each composed of a lipid bilayer, in between these two membranes is a narrow space (40-70 nm) called perinuclear space. The outer membrane is continuous with the endoplasmic reticulum; this structure acts as a conveyor belt to transport amino acids along as they are assembled into proteins. The structure of the nuclear membrane suggests that molecular transport across its barrier is important to the early stages of protein synthesis .

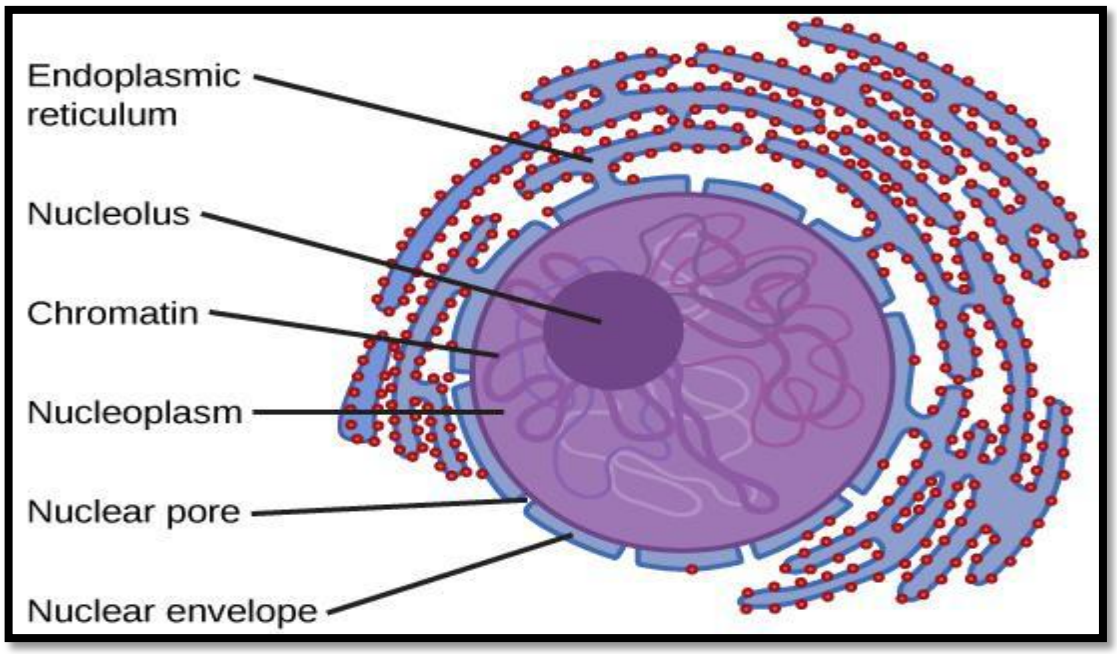
The inner membrane is associated with a network of intermediate filaments called nuclear lamina, which is made of poly peptides called lamina. The nuclear lamina is composed mostly of lamin proteins. Like all proteins, lamins are synthesized in the cytoplasm and later transported to the nucleus interior, where they are assembled before being incorporated into the existing network of nuclear lamina.

Lamins found on the cytosolic face of the membrane, which bind to the cytoskeleton to provide structural support, also lamins are found inside the nucleoplasm where they form another regular structure, known as the nucleoplasmic. The lamina acts as a site of attachment for chromosomes, maintains the shape of nucleus and adds mechanical support; much like the cytoskeleton supports the cell as a whole.

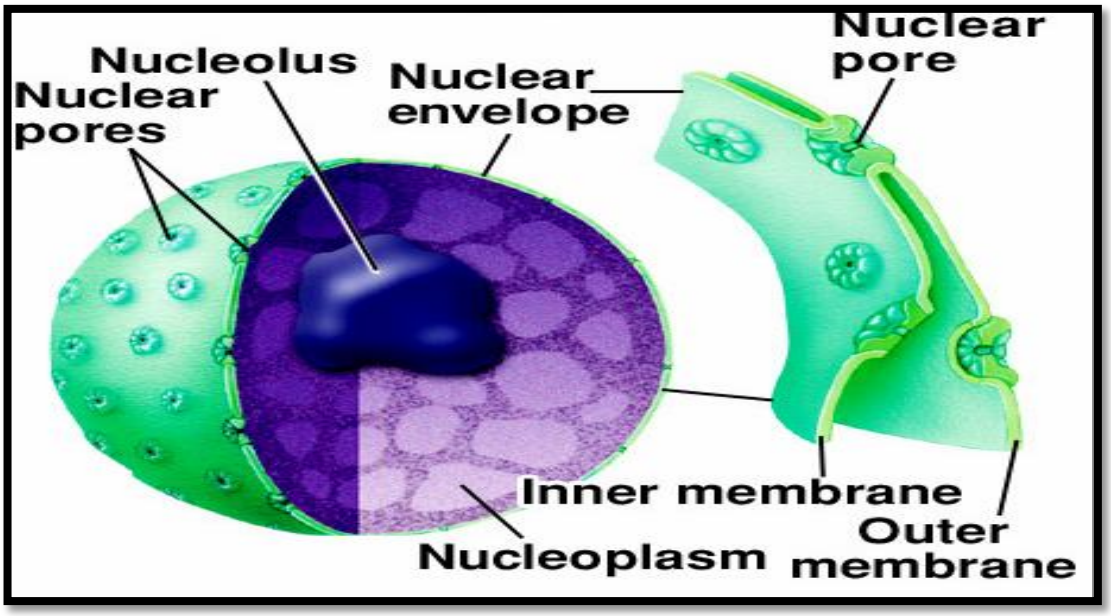
At sites where the inner and outer membranes of nuclear envelope fuse, the resulting lipid free space contain circular gaps about (70nm) in diameter called nuclear pore complex(NPC), these pores consist of cylindrical annulus, each annula composed of ring of eight granules that made of several proteins arranged in octagonal pattern.

The nuclear pore provide pathway to facilitate and regulate the exchange of materials (for example, proteins and RNA) between the nucleus and the cytoplasm. The number of nuclear pore varies from cell to cell, increasing in cell activities involved in protein synthesis. The nucleus of typical mammalian cell contains 3000-4000 such pore complexes. These pores are permeable to some molecules like mRNA and ribosomes units that formed in the nucleus and then exported to the cytoplasm, and cytoplasmic proteins that moving into the nucleus where it is essential for DNA replication.

Although the interior of the nucleus does not contain any membrane-bound sub compartments, its contents are not uniform, and



a number of subnuclear bodies exist, made up of unique proteins, RNA molecules, and particular parts of the chromosomes. The best known of these is the nucleolus.



Medical application

1- Neoplastic proliferation

-Cell populations can become transformed to grow of a higher rate and in an uncoordinated manner.

- Typically allows damages to the DNA of proto-oncogenes and failure of the cells to be eliminated.

2- Laminopathy

- Certain mutations in the gene coding for lamin are associated with a subtype at the disorder ***progeria*** .

- In this and other rare laminopathies the nuclear envelope is abnormal.

Nucleolus

Dr.Emad Al-Radhi

Ph.D. Molecular cytology

Definition *Lec.2*

The nucleolus is the largest round granular structure in the nucleus of eukaryotic cells, it takes about 25% of the volume of the nucleus.

- The nucleolus composed of protein and rRNA and small amount of DNA, they don't have membranes, so they can disassemble when the cell divides during mitosis.

●Nucleolus is involved with ribosomal RNA synthesis and formation of ribosomes in eukaryotes .It appears to form a part of the Linin network, but has usually also a strong affinity for nuclear stains.

●The nucleolus is generally spherical (1-3mm) in diameter, highly basophilic structure due to presence of densely concentrated rRNA. It present in the nuclei of cells active in protein synthesis for growth and secretion.

●The molecules of rRNA synthesis and modified in the nucleolus very quickly associate with the many ribosomal proteins which are imported from the cytoplasm through the nuclear pore.

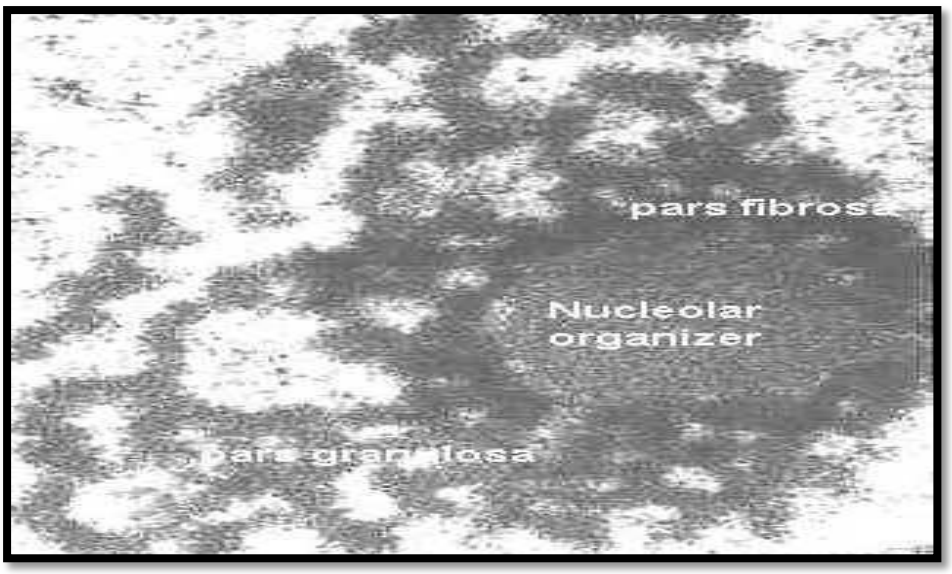
●The nucleus contain one nucleolus but in some cases contain two or multi nucleoli usually in metabolically active cells for protein synthesis. The size of nucleoli are vary, the large nucleoli are encountered in cells that actively synthesizing proteins and in cells of rapidly growing malignant tumors.

The regions within nucleolus

1- The major parts of the nucleolus are one or more pale staining **nucleolar organizer DNA –sequences** of bases coding for rRNA.
2- **Pars fibrosa (PF)** which consist of primary transcripts rRNA genes, this region composed of ribonucleoprotein fibers (5-10 nm) and closely associated with nucleolar organizer.
3- **Parsgranulosa (PG)** consist of 15-20nm granules that represent maturing ribosomal subunits.

- The network formed by pars granulosa and pars fibrosa is called nucleonema, and the DNA that is responsible for the synthesis of the ribosomal subunits is localized in the interstices of that network. The function of the nucleolus is to transcripts DNA into ribosomal RNA and assembles rRNA into ribosomal subunits. The creation of rRNA is important because rRNA makes up ribosomes which are responsible for protein synthesis in the cell

- When DNA is transcribed into rRNA in the nucleolus, three or four (depending on the organism) distinct rRNAs are produced. These rRNAs are combined with proteins in order to assemble a large ribosomal subunit and a small ribosomal subunit. The subunits are then exported from the nucleolus and nucleus to the endoplasmic reticulum and the cell's cytosol in order to carry out the process of translation, or protein synthesis.



Nuclear matrix

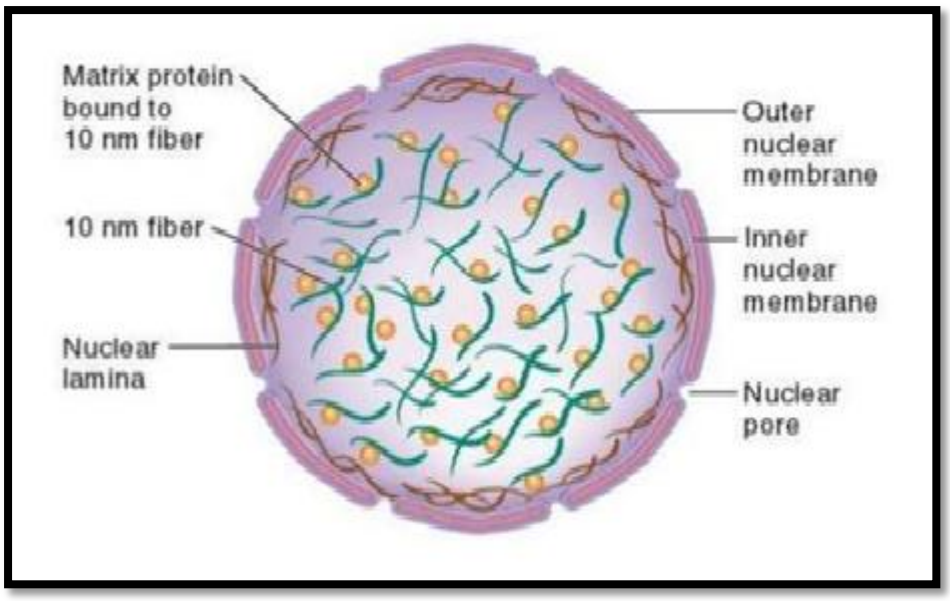
Definition

It is semi –fluid matrix that fill the space between the chromatin and nucleolus, composed mainly of proteins (some of which have enzymatic activity), metabolites, ions and fibrous lamina of the nuclear envelope.

●When the nuclei acids and other soluble components are removed, a continuous fibrillar structure remains, forming the nucleoskeleton. This structure probably contributes to the formation of a protein base to which DNA loops are bound, and it regulated the assemble and disassemble of the nuclear membrane during cell division.

●The function of nuclear matrix is still being studied; in fact it binds to hormone receptors and serves as medium for diffusion of metabolites larger molecules.

●The nuclear matrix composed of two parts (Figure 1-35):
a-Nuclear-lamina.
b- Internal matrix proteins.



Chromatin

Definition

Chromatin is a complex of nucleic acids(DNA) and proteins (histones) and some RNA, which condenses to form chromosomes during cell division.

●It's found within the nucleus of eukaryotic cells whereas prokaryotic cells have different organization of their DNA which is called **genophore** (not chromatin) which found within the nucleoid.

●It is usually arranged in repeating units of small particles called **nucleosomes,** which consist of core of protein histones (two copies of H2A, H2B, H3, and H4) surround by double stranded of helical DNA with about 150 base pairs .

●Each nucleosome has larger linker histone (H1) that binds both wrapped of DNA and the surface of the core.

●The series on nucleosomes in chromatin is also associated with many diverse non histones proteins with a wide variety of enzymatic functions. These nucleosomes are arranged into helix (become coiled around an axis) to form chromatin fiber which then more condenses to form chromosome.

●There are two types of chromatin can be distinguished under electron microscope:

1-Euchromatin

●It is visible under electron microscope less coiled portion of chromosomes visible as finely dispersed granular material and lightly stained basophilic area under light microscope .

●The euchromatin is metabolically active, which play an important role in transmission of genetic information and in protein synthesis.

●The standard structure of euchromatin is unfolded, elongated, and only about the size of a 10 nanometer microfibril. This minute chromatin functions in the transcription of DNA to mRNA products; helps produce proteins for the production of energy.

2-Heterochromatin

●The chromatin can fold upon itself to compact the nucleosomes, forming a highly condensed structure called heterochromatin.

●It is commonly found on the peripheral areas of the nucleus, and it's is metabolically inert , it could be responsible for gene regulation and protection of chromosomal integrity and involve in cytoskeletal function .

The distribution of this condensed chromatin includes three locations:

1-Marginal chromatin: It is forming a thin peripheral layer which lines the inner nuclear envelope.

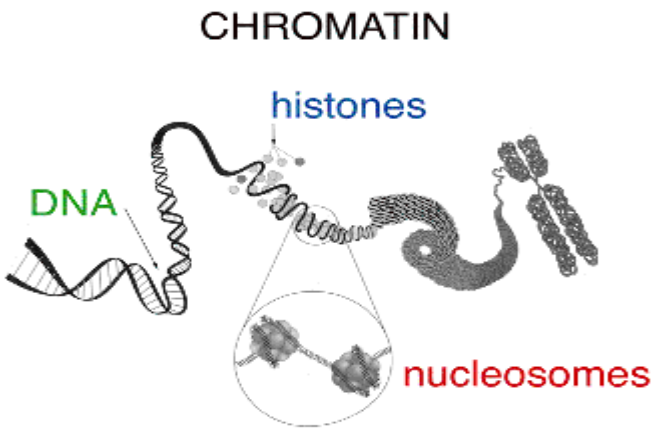
2-Karyosome: It form patches scatter in the nucleoplasm.

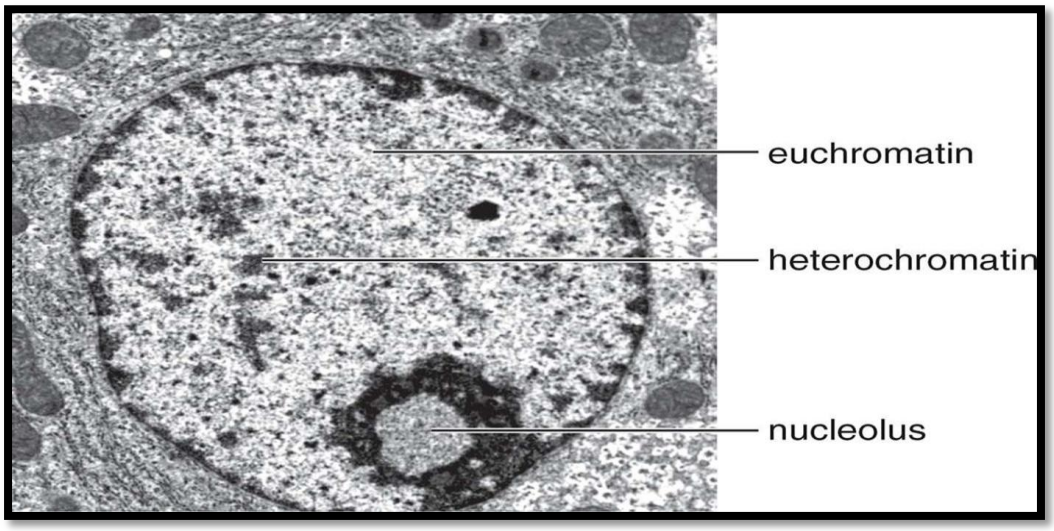
3-Nucleolar associated chromatin: It is found as a rim condensed chromatin in association with nucleolus.

●The chromatin DNA is a major form of DNA in the cell and carrier most of genetic information, within the chromatin there are sites of RNA synthesis where synthesis of precursors of messenger, ribosomal and transfer ribonucleic acid (mRNA, rRNA, tRNA).

●The amount of euchromatin and heterochromatin usually indication of the metabolic activity .The nucleoprotein of chromatin is coiled and the degree of coiling varies during cell activity.

●The cells with light nuclei (with few heterochromatin clumps) are more active where more DNA surface available for the transcription of genetic information. The cells with darkly nucleus (the coiling of DNA makes less surface available) therefore less active.





Sex chromatin

Human male somatic cells have (46) chromosomes arranged in (23) pairs, (22) pairs called autosomes and (1) pair is formed by X and Y or sex chromosomes.

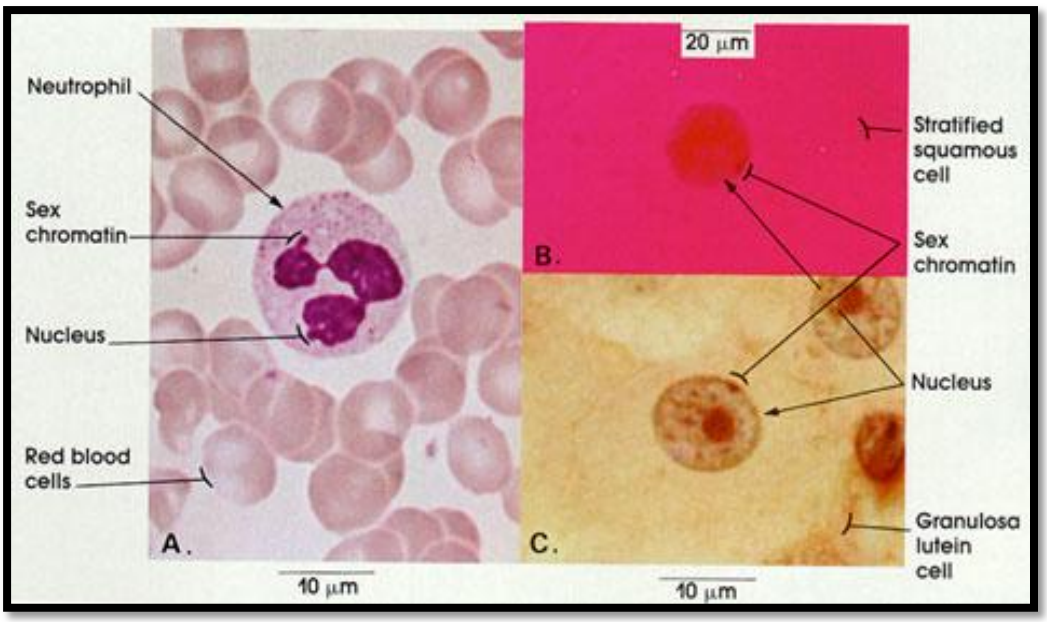
In female , there are (22) pairs of autosomes and two X chromosomes. One of these X chromosome is extremely heterochromatin and forms a visible tightly coiled mass in the interphase nucleus. This small visible mass is called Barr body or sex chromatin, it is about (1µm) in diameter, whereas the other X chromosome is uncoiled and not visible. The coiling of this chromosome explain why it is easily stained and can be observed with light microscope. Evidence suggests that the coiled X chromosome including the sex chromatin is genetically inactive.

In male, there is (22) pairs of autosomes and (1) pair of sex chromosome include X and Y chromosome as sex determinants. The X chromosome is uncoiled, therefore no sex chromatin is visible, so Barr body is not seen in normal male somatic cells.

The Barr body appear clearly in epithelial cells as a small granule attached to the nuclear envelope .It is seen well in nuclei of squamous epithelial cells that lining the internal surface of the check or buccal cavity. Blood smears are also used, in which the sex chromatin appears as drumstick –like appendage attached to the nuclei of the neutrophil leukocytes.

The study of sex chromatin has wide application in medicine, because it permits determination of genetic sex in doubtful cases, such as in patients whose external sex organs do not permit to determine of gender as in hermaphroditism. Sex chromatin is essential for the study of other anomalies involving the sex chromosomes that include:

1- Klinefelter's syndrome XXY chromosomes (male represent female properties).
2- Turner's syndrome XO chromosomes (female represent male properties)**.**


Neutrophil
Sex chromatin
Nucleus
Red blood cells
A.
10 μm
20 μm
B.
Stratified squamous cell
Sex chromatin
Nucleus
C.
Granulosa lutein cell
10 μm