

**Ministry of health Republic of Belarus
Establishment of education “Gomel state medical university”**

Department of histology, cytology and embryology

MANUAL
for 1-st year students of faculty of foreign students on gynecology

Topic: 2:
**FUNDAMENTALS OF CELL BIOLOGY. STRUCTURAL AND FUNCTIONAL
ORGANIZATION OF AN ANIMAL CELL**

Duration 4 hours

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THE MOTIVATIONAL CHARACTERISTIC OF THE THEME

Cells and their abilities to live formed as a result not cellular structures are a basis of a structure and functioning of an organism. Internal and external factors (hormones, medical products, etc.) can cause changes structure and function of cells, in turn, entails occurrence morph functional changes in organs and systems. Studying of a microscopic structure of the cells taken during lifetime of or from a corpse helps the doctor to specify the diagnosis. Cytological researches of blood, spleen, liver, and kidneys and other organs are widely widespread in clinic. In this connection for the future doctor are necessary knowledge morphological and cytochemical characteristics of cells. And not cellular substance.

THE PURPOSE

Studying of a microscopic and ultramicroscopic structure and value of the basic structural components of cytoplasm: organelles and inclusions. Studying of structural components of the cell, their role in ability to live of a cell, storage and transfer of the genetic information.

PROBLEMS

The student should know:

- 1) The Structure of a cellular surface and membrane a principle of the organization of cells.
- 2) Morphology of active carry of substances through plasmalemma
- 3) The Microscopic and ultramicroscopic structure organelles membranous and no membranous. A structure and their role in ability to live of a cell.
- 4) Functions and a structure of a nucleus at microscopic and ultramicroscopic levels.
- 5) The Basic phase's mitosis.
- 6) The Functional characteristic of the periods of a cellular cycle.

The student should be able:

- 1) To identify various kinds of inclusions in cytoplasm, lipid droplet carbohydrate, pigment.
- 2) To use concrete data about a structure and a chemical compound organelles and inclusions for the characteristic of a metabolism and a functional condition of cells.
- 3) To use microscopic, ultramicroscopic and histochemical data for the functional characteristic of a nucleus.

REQUIREMENTS TO THE INITIAL LEVEL OF KNOWLEDGE

For full mastering a theme it is necessary for student to repeat from: – medical biology and genetics a general plan of a structure of a cell and its components.

CONTROL QUESTIONS FROM RELATED SUBJECTS

- 1) The general organization of a cell
- 2) The chemical compound and the basic properties of protoplasm
- 3) The basic vital properties of protoplasm
- 4) Levels of the organization chromatin
- 5) Morphology of a chromosome of a nucleus
- 6) Ways of a reproduction of cells

CONTROL QUESTIONS ON THE THEME

1. Structural elements of a cell, their classification.
2. A structure of a biological membrane.
3. The superficial apparatus of a cell (three its elements).
4. Glycocalyx.
5. Classifications of organelles.
6. Endoplasmic reticulum.
7. Golgi complex.
8. Mitochondria. Structure and functions.
9. Lysosome. Mechanisms of endocellular digestion.
10. Ribosome. Structure and functions.
11. The cell center.
12. Cytoskeleton. Structure and functions of its components.
13. Functions of special organelles.
14. Inclusions.
15. Hyaloplasm.
16. Structures and functions of nucleus.
17. A cellular cycle.
18. Mitosis and its biological role.
19. Other ways of a reproduction of cells.
20. Morphological bases of secretion.
21. Endo-, exo- and transcytosis.
22. Cell receptors.

THE PRACTICAL PART

- 1) The scheme of a structure of a cell (exercise № 1 in album)
- 2) The basic components of a cell (exercise №2 in album)
- 3) The structure of a plasmamembrane (exercise №3 in an album)
- 4) Cell receptors – to define « a cellular receptor », «Legend» and to fill the scheme (exercise №4 in album)
- 5) The basic components of membranous receptors – to list components and to specify type of a superficial receptor (exercise №5 in album)
- 6) Mechanisms of transport of substances through plasmalemma – to enter kinds of passive and active transport (exercise № 6 in an album)
- 7) Classification cellular organelles – to list and specify functions (exercise № 7)
- 8) Functional apparatus of cell – to fill the table (exercise №8)
- 9) RER (exercise № 9 in album)
- 10) Golgi complex – to enter designations (exercise № 10 in album)
- 11) Mitochondria (exercise 11 in an album)
- 12) The Scheme of endocellular digestion (exercise № 12 in album)
- 13) The Structure cilia – (exercise № 13 in album)
- 14) Microscopy histological preparations and their sketch in an album (exercise № 14, 15, 16 in album)
- 15) The nucleolus – to sketch the scheme of it and to specify its compound components (exercise № 17 in album)
- 16) Levels of the organization of chromatin (exercise № 18 in album)
- 17) The Complex of a nuclear pores- to sketch (exercise № 19 in album)

18) To study diagrams

SLIDES

1. Inclusions of lipid droplet in cells
2. Inclusions of glycogen in cells
3. Inclusions of pigment droplet in cells

QUESTIONS FOR SELF-CHECKING KNOWLEDGE

- 1) Write down in copybook structural features plasmalemma. Layers of plasmalemma. Chemical substances
- 2) Think over and write down ways of an exchange of a cell with the extra cellular environment

FUNDAMENTALS OF CELL BIOLOGY. STRUCTURAL AND FUNCTIONAL ORGANIZATION OF AN ANIMAL CELL

According to modern **cell theory**:

1. All living things are made up one or more cells
2. Cells are the basic units of organism, within which the life processes of metabolism and heredity occur.
3. All cells arise by division of preexisting cell.
4. Cells of multicellular organisms are specialized in function and form tissues and organs.

So the cell is the smallest structural and functional unit of the human organism. A more detailed definition is:

The cell is a self-governing, self-regulating and self-regenerating biological system, which possesses all features of the whole organism, such as metabolism, growth, irritability, movement, and others.

The structural and functional component of the cell is the **biological membrane**.

They are lipoprotein structures, which separate cell from outside and form organelles and nuclear envelope.

The current interpretation of membrane organization is known as *the modified fluid-mosaic model*.

The biomembrane consists of two layers of phospholipid molecules. Each phospholipid molecule has a head, which possesses hydrophilic properties, and a thin tail, which possesses hydrophobic properties. The lipids are of following types: phospholipids, sphingolipids and cholesterol.

The proteins are embedded within the thickness of the lipid bilayer. According to their localization there are 3 groups of proteins: superficial, integral and semi-integral.

Protein molecules are situated by the mosaic principle and do not create entire layer.

Functionally, the proteins can be structural proteins, transport proteins, enzymes, receptors and adhesion proteins. Transport proteins are pumps and ion channels. *Pumps* serve to transport certain ions (such as Na⁺ (sodium)) and metabolic precursors of macromolecules (such as amino acids and sugar) across membranes. Ions get attached to the protein on one surface and move with the protein to the other surface. It is active and selected transport. *Channels* allow for the passage of small ions and molecules across the cell membrane in either direction, that is passive diffusion.

Outer membrane is called cell membrane or plasma membrane. Intracellular membranes are called cytomembranes.

Biomembranes provide many different functions. For example:

- Regulate transport of the substances. The polarity of phospholipids determines the **selectively permeability** – most important property of the biological membranes. The non-polar substances can easily pass through membrane, whereas polar substances can enter a cell only with help of transmitter or active transport.
- They form separate compartments within the cell, which have different biochemical composition and different functions (organelles, nuclei) etc.

The human body has about 10^{20} cells, which are subdivided into 200 types. But all cells have similar organization.

The cell consist of three **main components**:

1. Cell coat (cellular surface apparatus).
2. Cytoplasm.
3. Nucleus.

Cell coat is separates a cell from external environment and is made of three parts:

- outmost layer is presented by glycocalyx,
- plasma membrane
- innermost layer is submembrane layer of supportive and contractive elements of cytoskeleton.

Glycocalyx is presented by carbohydrate ends of complex proteins (glycoproteins) and of complex lipids (glycolipids). Glycocalyx includes superficial proteins and semi-integral proteins as well. Their functional regions are located in glycocalyx. There are receptors of tissues compartibility, for immunoglobulines, for hormones and places for enzymes absorption.

Main functions of the glycocalyx :

1. Reception and recognition of cells and intercellular substance.
2. Intercellular contacts.
3. Transport of the substances.

Functions of the submembrane layer:

1. Maintaining of cellular shape
2. Changing of cellular surface, which provide transport processes and cell movement.
3. It connects cellular surface with components of cytoplasm and maintain the pattern of their orientation.

So main functions of the cell coat are:

1. It separates a cell from external environment, maintaining cell homeostasis. .
2. Barrier-defense function (protection from harmful factors).
3. Transport of *the substance into or out of the cell*..
4. Formation of intercellular junctions.
5. Formation of various projections of the cell surface.
6. Reception. The surface of the cell membrane bears receptor that may be specific for particular signals (e.g. for molecules of hormone, neurotransmitters, cytokines). Stimulation of the receptors can produce profound effects on cell activity.

The **surface membrane receptors** are usually integral glycoproteins, which can link with ligand's molecule or other cells. Membrane receptor consist of submembrane part, which link with ligand, transmembrane part and cytoplasm part.

They exist for polar substances, which can not pass lipid membrane without assistance, so they act through the system of external receptors and secondary messengers. (циклическая АМФ или фосфоинозитол, calcium ions)

They are classified:

- catalytic receptors (enzymes receptors). Their cytoplasm parts present enzyme.(insulin, growth factor)
- receptors connected with ion channels. They include membrane channel, which open after linking with ligand (neurotransmitter receptors).

G-protein receptors. They are integral proteins, containing subunits of G-protein, which can be connected with either ion channel or enzyme. They use secondary messengers. G-protein receptors mediate the action of majority of hormone and neurotransmitters.

– Molecules of cell **adhesion**.

Adhesion – is specific interaction between two contacting cells or between cells and extracellular matrix. All molecules of cell adhesion are subdivided into 4 classes:

1. Cadherines. It is transmembrane proteins which use calcium ions for adhesion. They are responsible for cytoskeleton organization and intercellular connection.
2. Integrines. It is membrane receptors for extracellular matrix proteins such as fibronectine and laminin. They connect extracellular matrix with cytoskeleton through intracellular proteins talline, vinkuline and a-activin. They participate in the cell movement, exocytosis, endocytosis and etc.
3. Selectines. They provide leukocyte adhesion to endothelium of vessels and by this provide leukocyte-endothelial interaction, leukocyte migration through vessels wall to a tissue.
4. Immunoglobuline family. They play very important role in immune response.

Intracellular receptors exist for non-polar hormones which can pass lipid membrane without assistance. They are hyaloplasm receptors, cytoplasmatic receptors (e.g. mitochondrial membrane have receptors for thyroid hormones) and nuclear receptors (for steroid and thyroid hormones. They are transcription factors)

Cytoplasm

Cytoplasm consist of the hyaloplasm, organelles and inclusions.

Inclusions – are temporary components of a cell.

Classification of Inclusions:

1. Trophic (glycogen, lipid droplets)
2. Pigmennt (melanin, hemoglobin, in erythrocytes, lipofuscin – aging pigment)
3. Secretory inclusions are revealed in secretory cells.
4. Excretory inclusions contain substances, which are needed to be evacuated from cell. (urea inclusions in kidney cells).

HYALOPLASM (cellular juice, or cellular matrix, or cytosol). It *is* comprise about 55% of cell volume. The main cellular metabolic processes take place here. The hyaloplasm is complex colloid system, which may change aggregative state: from liquid sol to more viscous gel. While this, the shape, metabolism and motility of a cell may be

significantly changed. It contains water, proteins, nucleic acids, polysaccharides, lipids and inorganic substances. It is cell internal environment.

Important part of the hyaloplasm is cytoskeleton. It is network of protein threads within the cell. There are 3 components of the cytoskeleton: microtubules, microfilaments and intermediate filaments.

Microtubules are straight, hollow cylinders, made of globular protein tubulin. Microtubules are very dynamic structures, their polymerization and depolymerization occur very quickly and their length change. Microtubule Associated Proteins (MAP) stabilize microtubules and facilitate their attachment to other cell components. The kinesin protein also connects microtubules with ATP and the cell organelles.

Microtubules participate in organelles and substances transport, form centrioles, flagella, cilia and division spindle.

Microfilaments thin threads made up actin protein. They form the network or bundles.

Intermediate filaments have larger diameter than microfilaments. They are most stable filaments of cells. They perform supportive function. The cells of different type have the different intermediate filaments, which may be used as markers of cell origin.

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Organelles

The organelles are constant cell structures.

Functionally all organelles are divided into 2 groups:

1. Special organelles presenting in the cells which perform some particular function. They are myofibrils, neurofibrils, flagella, cilia, acrosome.
2. General organelles, which are in all cells. Structurally they are divided into:
 - a) membranous organelles (mitochondria, EPR, Golgi complex, lysosomes and peroxysomes).
 - b) non – membranous organelles (centrioles, ribosomes)

There are some functional apparatus: cell synthetic apparatus, cell digestive apparatus, energy apparatus of the cell, genetic apparatus.

Cell synthetic apparatus includes EPR, Golgi complex, ribosomes.

Ribosomes are small beadlike clusters. They are made up of two different-sized subunits.

Each subunit consist of r- RNA and proteins. Single ribosomes are inactive. They form polysomes – groups of several ribosomes helded together by messenger RNA. Most of ribosomes are attached to membranes of the endoplasmic reticuium.

They are organelles of protein biosynthesis. Free polysomes produce the proteins for cells own use.

Endoplasmic reticulum

EPR is a system of connected canals, vacuoles and sacs, which make a continuous network in the cell. The EPR membrane is thinner than plasma membrane and contain more proteins as different enzyme systems. There are two types of EPR: granular (rough) and agranular (smooth).

Rough RER are covered by ribosomes and takes part in synthesis of proteins.

Ribosomes on rough EPR produce the proteins which are segregated into the cisternae of the reticulum. These proteins can be secreted (for out-cellular usage), or stored in the cell (enzymes of lysosomes), or can be membrane proteins.

Synthesis of their polypeptide chain begins from special signal peptide. It provides the attachment ribosome to a receptor of RER – "docking protein" and integral membrane protein – ribophorin. Ribophorin binds to large subunit and forms transmembranous channels, thus allowing passage of newly proteins into the lumen of RER. Inside signal peptide is removed by specific enzyme, signal peptidase. Translation continues, accompanied by secondary and structural changes as well as certain posttranslational modifications (mainly glycosylation, but also hydroxylation, sulphatation, phosphorylation and ets).

Specific start and stop transfer peptide participate in the synthesis of membrane proteins.

So, function of granular EPR are:

- Synthesis
- Modification
- Storage
- Transport of extracellular, lysosomal and membrane proteins.

Smooth endoplasmic reticulum (SER) arise from RER. Both types take part in transportation of substances inside the cell. The place of transformation is called transitional zone.

However, it differs from RER. It lacks ribosomes, its membrane cisternae more tubular and it contains another enzymes.

Functions of smooth EPR:

2. Biosynthesis of lipids and carbohydrates.
3. Peroxisomes formation.
4. Biosynthesis of steroid hormones.
5. Detoxification of exo- and endogenous toxins, hormones, biogenic amines, drugs due to activity of special enzymes.
6. Calcium ions storage.
7. The source of membranes for nuclear envelope repair after mitosis.

GOLGI COMPLEX. Golgi complex consists of flat membranous cisterns with dilatations of the ends, which are continuous with vesicles and vacuoles. The cisterns are stacked over one another, forming the dictyosome. One dictyosome includes 5-10 ampullar cisterns. There are several tens dictiosomes in a cell. Each dictiosome has proximal, immature, CIS-zone (toward the nucleus) and distal, TRANS-zone (toward cell coat). CIS-zone is the place of accepting of transport vesicles derived from EPR. Transport

vesicles serve to shuttle newly synthesized substances to the Golgi for further processing. Transport vesicles merge with CIS-zone.

The secretory vesicles and lysosomes are segregated from TRANS-zone.

Thus, we may conclude that there is constant flow and maturation of membranes in Golgi complex.

Functions of Golgi complex:

1. Accumulation, sorting, parking and transport of synthesized products.
2. Synthesis of polysaccharides and conversion of simple proteins to glycoprotein.
3. Formation of lipoproteins.
4. Formation of secretory inclusions and excretion them from the cell.
5. Formation of primary lysosomes.
6. Formation of cellular membranes.
7. Formation of acrosome.

Cell digestive apparatus includes endosomes and lysosomes.

Lysosomes

Cell digestion begins from formation primary lysosomes or hydrolase vesicles. Hydrolytic enzymes synthesized in ER reach the GK where they packed into membrane-limited vesicle containing more than 50 hydrolytic enzymes: acid phosphatase, lipase, proteases, nucleases and other. Primary lysosomes just have been segregated from Golgi complex. Their enzymes are inactive because of the lack an acid medium.

Endosomes are membrane vesicles, containing ingested material, which form during process phagocytosis.

Hydrolase vesicle fuses with endosome, which poses the membrane proteins necessary for production an acid medium. After fusion *secondary* lysosome or *endolysosome forms*.

H⁺ ions are pumped into the vesicle to create an acid environment. This activates the enzymes.

Undigested waste material get out of the cell by exocytosis. However, some of material may remain within the cell in the form of membrane bound residual bodies. The

Example is lipofuscin inclusion, which are accumulated with aging.

Autophagosomes appear when primary lysosomes fuse with aged organelles and destroy them.

There *is* group of diseases, which is called diseases of accumulation. The cause of them is insufficiency of one or another lysosome enzyme. The cell accumulates undigested products, which leads to gradual cell death [3 – 6].

Functions of lysosomes:

1. Intracellular digestion.
2. Participation in phagocytosis.
3. Participation in mitosis – degradation of nuclear envelope.
4. Participation in intracellular regeneration.

PEROXISOMES like lysosomes, but contain oxidative enzymes. These enzymes protect the cell from endogenic peroxides, breaking down hydrogen peroxide (H₂O₂). They

detoxify various substances by oxidizing them. Peroxisomes participate in metabolism of fatty acids and amino acids.

Function of peroxisomes:

1. Utilization of the oxygen. The product is H_2O_2 .
2. Degradation of peroxides excess – protection of cells.
3. Detoxification.
4. Participation in metabolism of fatty acids and amino acids.

Energy apparatus of the cell include mitochondria.

Mitochondria consist of a smooth outer membrane and plicated inner membrane. The folds of the inner membrane are called *cristae*. The inner compartment of the mitochondria is called *matrix*. Mitochondrial DNA, RNA, ribosomes are located in the matrix.

Mitochondria contain the enzyme system that generates ATP by means of Krebs' cycle and oxidative phosphorylation. APT-synthetase complexes are called oxysomes and locate at the cristae.

ATP is united source of energy in the cell. So, mitochondria provide energy for various cellular functions.

There are mitochondria with tubular cristae. They participation in steroid hormone biosynthesis.

Functions.

1. Providing energy for the cell in form of ATP.
2. Participation in steroid hormone biosynthesis.
3. Calcium storage.
4. Participation in nucleic acid synthesis.

New mitochondria appear by division.

Mutations of mitochondrial DNA results in mitochondrial diseases with very wide range of symptoms [1– 4].

Stucture and functions of cell nucleus

Nucleus is the major cell component. It provides the storage, realization and transmitting of hereditary information.

Majority cells have one nucleus. Its shape and size depend on cell type and functional state of a cell. Nucleus present only during interphase. It composed of nuclear envelope, nucleolus, chromatin (chromosomes), nuclear juice.

The nuclear envelope consists of two membranes. External membrane is continuous with RER. Internal membrane is smooth. It is closely connected with nuclear lamina – a condensing of intermediate filaments. There is perynuclear space between two membranes (20-40 nm in width).

At several points the membranes fused, forming *nuclear pores*. Each pore contain *pore complex* – complex of fibrillar and granular structures, which regulate substances flow [1 – 3, 5].

Chromatin is a complex of DNA and proteins – histones and non-histones. It is interphase decoiled form of chromosome being.

There are two types of chromatin. The regions of DNA with decoiled DNA are called euchromatin. Highly condensed or tightly packed chromatin is called

heterochromatin. Euchromatin predominates in metabolically active nuclei, that are called *open-faced nuclei*.

The basic structural unit of chromatin is *nucleosomes*. This consists of a histone core, around which are wrapped DNA molecules. The DNA regions, which connect two neighboring nucleosomes, are named linker DNA. The next level of organization is nucleomere or chromatin fibril. One nucleomere contains 8 nucleosomes. Before mitosis the chromatin fibrils are folded in the shape of loops and become chromomere. Each loop domain corresponds to one or several genes.

The last step of chromosome packing is spirilized chromosomes, which are visible in mitosis.

The nucleus contains one or several nucleoli. It is regions of chromosome, which are called nucleolar organizing centers. They contain multiply copies of rRNA genes. It is the site of active synthesis of ribosomal RNA. Then RNA binds with protein and forms ribosomal subunits, which leave the nucleus via nuclear pores to be assembled into functional ribosomes in the cytoplasm.

NUCLEAR JUICE – it is a fluid component of nucleus. It is colloid solution of proteins, carbohydrates, nucleotides and different salts.

The ratio between nucleus volume and cytoplasm volume is called nucleocytoplasmic ratio (NCR), The NCR shows the functional state of a cell [5].

Cell cycle is the time from one cell division to another or to the cell death. The time from one division to another also is referred as **mitotic cycle**.

Cell cycle of a somatic cell is divided into two periods: *mitosis* and *interphase*. They are called as *cell cycles*.

Interphase is a period between two divisions. Just after mitosis follows the G_1 phase. It is a period in which the cell grows, performs its routine functions.

Most of the cells complete G_1 period by growing old and death of the cell. It's typically for nondividing cells. Part of the cells transfer in S period by the influence of special inductors.

DNA molecules are duplicated during the S period that is why this phase is called synthesis phase.

During **G_2 -period** synthesis of different molecules, which are required for cell division, takes place. After phase G_2 mitosis always begins.

Sometimes the cells which have reached the point of transmission from phase S to phase G_2 come back again to phase S. The result is the additional synthesis of DNA. Such cells are called polyploids. They provide more high level functional activity.

The cell can leave the cycle in any phase, except G_2 , and enter to so-called G_0 phase (outside the cycle). The cell that leaves the cycle is considered as reserve *stem cell*.

There are three cell types with different cell cycle:

1) **Stem cells**. These cells are capable for permanent cell division. They provide the new cells formation on a place of died cells. The cycle of these cells corresponds with mitotic cycle, but the stem cells divide very rare. After division they stay in elongated G_1 -period. Some stem cells can become semi-stem cells after division. The semi-stem cells divide very actively.

2) **Differentiated cells**.

– *Irreversible differentiated cell*. Such cells are capable for division only during embryonic period. The examples of such cells are neurons and cardiac myocytes. Their

cell cycle has the following periods: mitotic cycle —» determination (choosing of differentiation way) —«

differentiation (forming the particular features of cell for performing the function) —» specialization • —» • period of active functioning —» • aging —> death.

- *Reversible differentiated cells*. Such cells (like liver cells) can leave mitotic cycle and enter Go-period or resting state. From this point they have two ways to go. One is mitotic cycle and another is way of differentiation. The preference is given according to tissue needs [3].

According to these classifications there are some types of a cellular population

1. Static (stationary) cell populations. There are only irreversibly differentiated cells in mature state of tissue. The stem cells are absent. The examples of such populations are nervous and cardiac muscular tissues.

2. Growing cell populations. Such populations contain: 1) very few stem cells, 2) differentiated cells, 3) resting cells.

There are groups with small proliferative index in normal state, but after injury the multiplication of resting cells may recover cell loss.

3. Renewing cell populations. The intensive multiplication of cells in the populations of this type is balanced by intensive cells lost by apoptosis. Such populations have: 1) few stem cells 2) irreversibly differentiated cells.

Regeneration – is ability of a cell or tissue to repair damaged or lost parts.

Regeneration can be physiological and reparative. Physiological regeneration is renewing of old cell parts or whole cells. Reparative regeneration is the cell repair after injury. After injury, there are compensative and adaptive changes in a cell together with reparation. They are directed on smoothing injury consequences.

Reactive properties of cells – are changing in structure and functions of cells in response on external factors influence. If external factor is a moderate one, the cell doesn't die, but it is subject to compensative and adaptive changes. Such changes may be as following:

1. **Hyperplasia** is an increase in cell number by mitosis.
2. **Hypertrophy** is an increase in cell size.
3. Formation of diploid and polyploid cells. Such cells are functionally more active and resistant.
4. Rising of metabolism rate [2].

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