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КАФЕДРА БИОЛОГИИ

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CHAPTER 1
REPRODUCTION AS AN ESSENTIAL PROPERTY OF LIVING MATTER

Reproduction is a universal property of living matter which provides the multiplication of organisms and is based on the transmission of genetic information from generation to generation.

The basis of reproduction at the molecular level is DNA replication, at the subcellular level — duplication of some organelles, at the cellular level — cell division. The division of cells is the basis for the reproduction of living matter.

TYPES OF REPRODUCTION

Reproduction can be sexual or asexual.

Characteristics of asexual reproduction are:

– reproduction occurs via somatic cells;
– genotypes of offspring are the same as parentaonene;
– there is always only one parent;
– the number of individuals increases quickly;
– optimal for living in constant environmental conditions.

Asexual reproduction of unicellular organisms (Fig. 1):

1. *Binary fission:* longitudinal (Euglena), transverse (*Paramecium caudatum*).

2. *Schizogony* — multiple division: nucleus divides into several parts, then cytoplasm divides (malaria parasite).

3. *Budding* — a bud forms on the mother cell; it grows and ultimately separates from the mother individual (yeast).

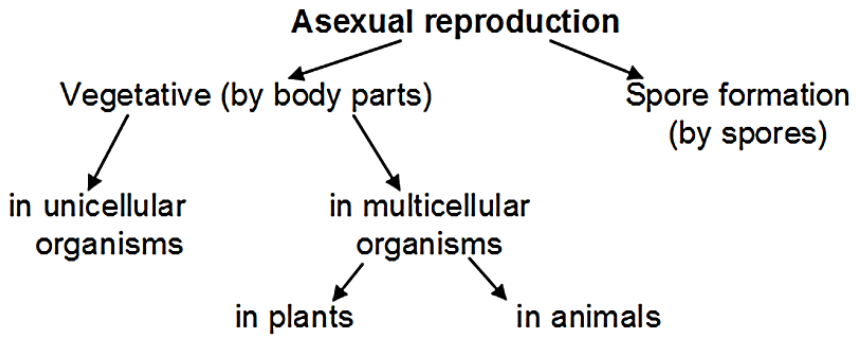


Figure 1. Asexual reproduction

Asexual reproduction of multicellular organisms:

A. Plants — vegetative reproduction (by vegetative organ: roots, stems, leaves).

B. Animals:

1. *Budding* (hydra).

2. *Fragmentation* division of the body into several parts (annelids).

3. *Polyembryony* — the division of a zygote or embryo into parts that form separate organisms (flukes).

4. *Sporogenesis*: special organs (sporogonia) form spores that give rise to a new organism (water plants, mushrooms, mosses, lycopodia, horsetails, and ferns).

Characteristics of sexual reproduction (Fig. 2):

– reproduction via *gametes* — haploid sex cells (egg and sperm) which commonly fuse and form a zygote (this process is called fertilization). The zygote develops into a new organism;

– genotypes of descendants differ from the parental ones due to combinative variation;

– two individuals take part in reproduction (except self-fertilization);

– provides the adaptability of organisms to changing environmental conditions.

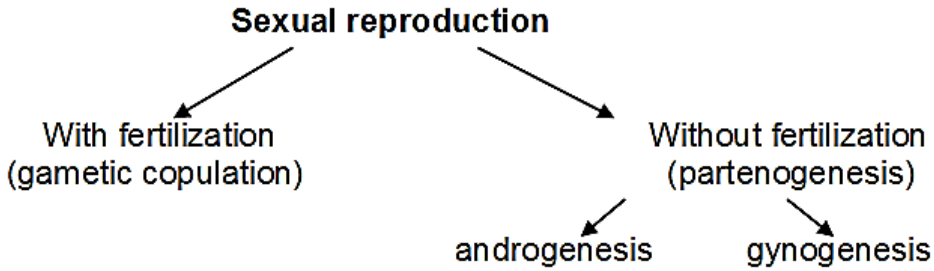


Figure 2. Sexual reproduction

Species that have sexual reproduction can be *dioecious* (with separate males and females) or *hermaphrodites* (have both male and female reproductive organs.

Hermaphrodites have both types of sex glands producing spermatozoa and ova. Such hermaphroditism occurs in flatworms and ringworms.

Dioecious species have only female or only male gonads.

Males and females are characterized by **sexual dimorphism**: differences in body sizes, coloration, structure, voice specificities, behavior, and other characteristics.

In humans, such differences include peculiarities of the musculoskeletal system, distribution of subcutaneous adipose tissue, degree of hair covering, voice quality, peculiarities of behavior, etc.

Sexual reproduction randomly recombines alleles of different genes in a population. This process separates beneficial alleles from deleterious ones and unites different beneficial alleles in one genotype.

Sexual reproduction occurs only in eukaryotes, though prokaryotes also "exchange" their genes via *lateral gene transfer*. Lateral gene transfer is the acquisition of genetic material from another organism without being its offspring. In bacteria, it includes:

– **Conjugation** — the process by which one bacterium transfers a specific plasmid to another through sex pilus.

– **Transduction** — the process by which a bacteriophage transfers genetic material from one bacterium to another.

– **Transformation** — the process by which some bacteria take up foreign DNA from the environment.

GAMETOGENESIS (OOGENESIS AND SPERMATOGENESIS)

Gametogenesis is a process of gamete formation: diploid somatic cells transform into haploid sex cells. The formation of spermatozoa is *spermatogenesis*; the formation of ova is *oogenesis* or *ovogenesis* (Fig. 3).

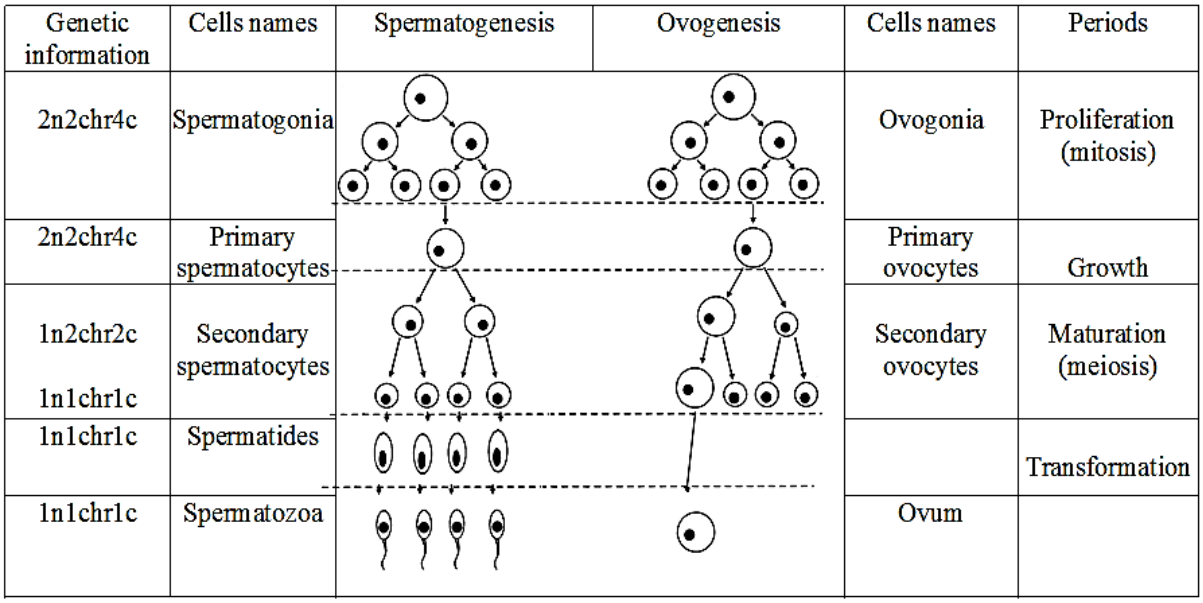


Figure 3. Gametogenesis

Ovogenesis. Ovogenesis begins in the **ovaries** before birth. Formation of a secondary ovocyte takes place approximately every 28 days from puberty (12–13 years) and up to 45–50 years old. The formation of an egg occurs in a **follicle** — a group of cells that enclose a cavity in the ovary.

Ovogenesis consists of the following periods:

1. During the period of **proliferation,** diploid *ovogonia* (set of chromosomes is 2n2chr) divide by mitosis to multiply. This occurs before birth.

2. During the period of **growth**, ovogonia accumulate nutrients, grow, and transform into *primary ovocytes* (set of chromosomes is 2n2chr).

3. During the period of **maturation** primary ovocytes begin *meiosis*. Meiosis I begins during embryonic development but halts in the diplotene stage of prophase I until puberty. Primary oocytes continue to develop only in each menstrual cycle. After the first meiotic division, the primary ovocyte divides into two haploid cells (set of chromosomes is 1n2chr) a large *secondary ovocyte* and a small *polar body*.

After meiosis I, meiosis II starts, but it is also halted at the metaphase II stage until fertilization. If fertilization occurs, the secondary ovocyte forms one *ovum* (1n1chr) and a new *polar body*.

The **ovum** of a human has a spherical shape, its size is about 0.13 mm (Fig. 4). It contains a nucleus with a haploid set of chromosomes, a cytoplasm with organelles (there is a large number of mitochondria), and nutrients. The egg is immobile. There are small vesicles in the outer layer of the cytoplasm near the plasma membrane. They are called **cortical granules**.

The ovum is covered with zona pellucida (glycoprotein layer) on the outside of the plasma membrane. The outermost covering is **corona radiata** which consists of follicular cells.

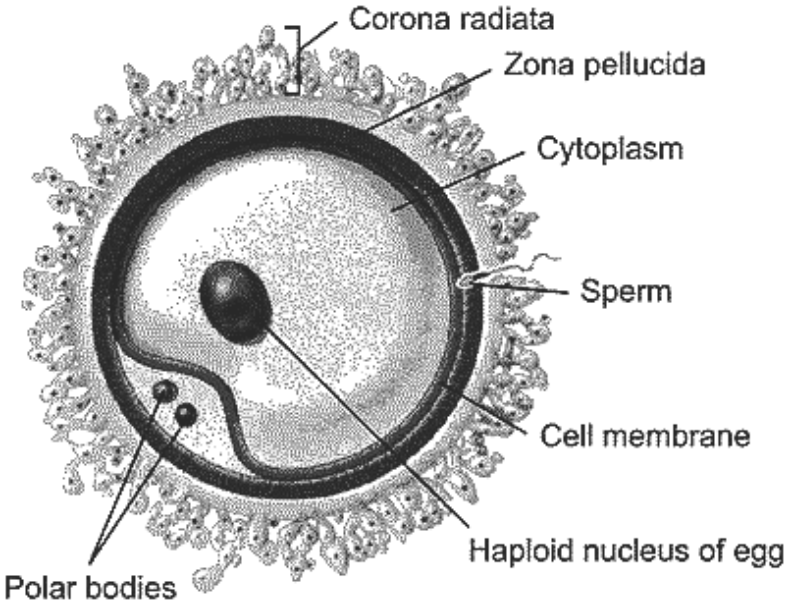


Figure 4. The structure of an ovum

Spermatogenesis. Spermatogenesis occurs from puberty to old age in the **seminiferous tubules** of the **testis**. The formation of sperm from a spermatogonium takes near 70–75 days.

Spermatogenesis includes the following periods:

1. During the period of **proliferation,** diploid ***spermatogonia*** multiply by mitosis. The chromosome set doesn't change (2n2chr).

2. During the period of **growth** spermatogonia transform into ***primary spermatocytes*** (2n2chr).

3. During the period of **maturation,** the primary spermatocytes divide by meiosis. After the first meiotic division each primary spermatocyte forms 2 haploid ***secondary spermatocytes*** (1n2chr).

After the second meiotic division, each secondary spermatocytes divide into 2 spermatids (1n1chr). Consequently, each primary spermatocyte forms four ***spermatids***.

4. During the period of **transformation** (formation) the spermatocytes transform into ***spermatozoa*** (sperms). The chromosome set does not change and is 1n1chr.

A **sperm** consists of a **head**, **midpiece,** and **tail** (Fig. 5). The head contains the haploid *nucleus* and an **acrosome** — the organelle which contains hydrolytic enzymes that help the sperm to penetrate through the zona pellucida of the ovum. It originates from the Golgi apparatus of the cell.

The midpiece contains *centrioles* and *mitochondria*.

Sperms are much smaller than egg cells — 55 micrometers in length (head is about 5 micrometers in length).

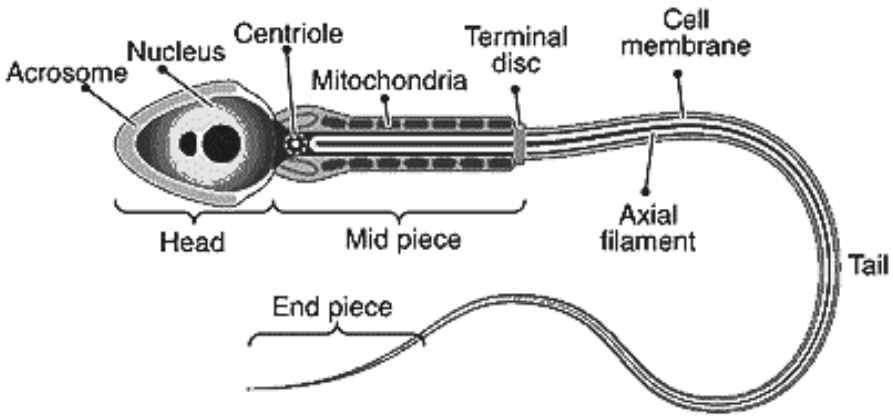


Figure 5. The structure of spermatozoon

Peculiarities of gametogenesis in humans:

1. The mitotic division of ovogonia is finished before the birth of a girl. Mitosis of spermatogonia starts with puberty.

2. The growth period in ovogenesis is very long and overlaps with the period of maturation (meiosis).

3. In oogenesis, the 1st meiotic division stops at prophase I and resumes periodically in a few ovocytes per month. The 2nd division of meiosis stops at the metaphase and resumes after fertilization.

4. Period of transformation is absent in oogenesis and present only in spermatogenesis.

5. A newborn girl has about 30 000 primary oocytes in both ovaries; only 300- 600 of them will become secondary ovocytes (about 13 cells a year).

6. The testes of a male produce up to 300 billion spermatozoa during the period of sexual life.

Regulation of gametogenesis. In females, the hypothalamus–pituitary–ovarian regulatory system starts to function at puberty. The **ovarian cycle** is regulated by hormones of the anterior pituitary lobe:

- **Follicle–stimulating hormone** (**FSH**) produced by the pituitary gland stimulates follicle growth and **estrogens** (female sex hormones) production by the follicle.

• **Luteinizing hormone** (**LH**) produced by the pituitary gland ensures ovulation and development of the *corpus luteum* (a temporary gland formed instead of a follicle that releases an ovocyte; produces progesterone — "the hormone of pregnancy").

• The secretion of LH and FSH by the pituitary gland is regulated by the *releasing hormones* of the *hypothalamus*, which is in turn influenced by the level of ovarian hormones — estrogens. The estrogens influence the development of secondary sexual characteristics, metabolism (increase protein dissimilation), and thermoregulation.

The process of spermatogenesis is also governed by the hypothalamic-pituitary-testicular regulatory system. Gonadotropic hormones of the pituitary gland (FSH and LH) stimulate *Leydig cells* of the testes to produce *testosterone*, (male sex hormone) which influences spermatogenesis.

INSEMINATION AND ITS TYPES. FERTILIZATION AND ITS STAGES

Processes providing contact of female and male gametes are called **insemination**. The insemination is followed by **fertilization** — the fusion of gametes into a zygote. Insemination of aquatic animals occurs in water: gametes are excreted and fused there (consequently *external fertilization* occurs). Insemination of terrestrial animals is associated with the delivery of male gametes into the reproductive system of females. Fertilization of such animals is *internal fertilization*.

The development of any animal, including human development, begins with divisions of a zygote.

• *Zygote* is a diploid cell formed when a sperm and egg merge in the process called *fertilization*.

• Fertilization not only unites the genetic materials from two parents, but *activates the egg*, so it starts to develop.

• Fertilization includes the following stages: *acrosomal reaction, cortical reaction*, and *egg activation*.

1. The **acrosomal reaction** is the release of hydrolytic enzymes from the acrosome of a sperm. The enzymes digest the components of *zona pellucida* and help the sperm to reach the membrane of the egg.

2. The **cortical reaction** is a process in which intracellular signals cause cortical granules to release their content from the egg cell.

Cortical granules are the membrane vesicles situated in the outer layer of the egg's cytoplasm adjacent to the plasma membrane. This process modifies the egg's membrane and *prevents fusion with additional sperms*.

3. **Activation of the egg** occurs when a sperm enters the egg. Protein synthesis and ATP production rates increase. The nucleus of the sperm (which is now in the egg) swells and fuses with the nucleus of the egg. The zygote starts to replicate its DNA and begins the first division.

Fertilization in mammals. In general, the process of fertilization in sea urchins and mammals is, though some differences are present.

- Terrestrial animals, including humans, generally have internal fertilization.
- The secretion in the female's.
- reproductive tract enhances sperm function. This process is called *capacitation*.
- The secondary oocyte (egg) released at ovulation is surrounded by the layer of follicle cells (it is called *corona radiata*) and the sperm must migrate through this layer.
- The egg cell itself is covered with a network of cross-linked glycoprotein filaments. This covering is called *zona pellucida*.
- One of the glycoproteins in the zona pellucida can be recognized by receptors on the sperm's surface.

This process stimulates an *acrosomal reaction*: hydrolytic enzymes are released from the acrosome.

They locally digest the material of the zona pellucida so the sperm can reach the plasma membrane of the egg.

- The membranes of the sperm and egg cell fuse, and the depolarization of the egg's plasma membrane occurs (prevents fusion with other sperms).
- A *cortical reaction occurs*. The contents of the cortical granules are released via exocytosis.

This stimulates the hardening of the zona pellucida and other sperms cannot penetrate through it.

- The whole sperm is pulled into the egg cell.
- The basal body from the sperm's flagellum divides and forms the centrosomes of the zygote.

PARTHENOGENESIS

Parthenogenesis is the development of an organism from an unfertilized egg. *Natural parthenogenesis* occurs in lower cancroides, bees (Fig. 6), butterflies, and rock lizards.

The nuclei of somatic cells in such individuals can be haploid. A diploid chromosome set can be restored by the fusion of the ovum's nucleus with the nucleus of a directing body.

Gynogenesis is a process in which the embryo genome originates exclusively from a female origin, following embryogenesis stimulation by a male gamete.

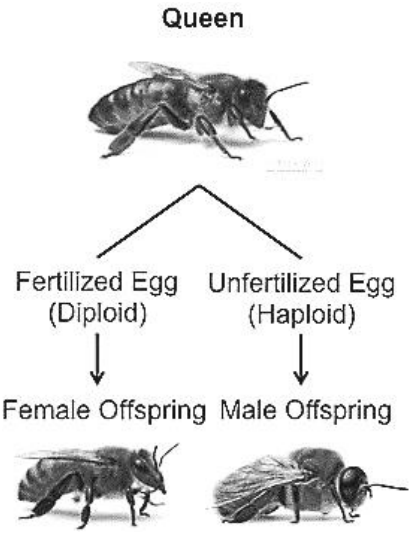


Figure 6. Parthenogenesis in bees

Androgenesis is a process in which the egg nucleus is lost from a zygote, and an individual develops with nuclear material derived solely from one or more sperm nuclei.

Biological peculiarities of human reproduction:

1. In humans, of the 200–300 million sperm that normally enter the female genital tract, only 300–500 reach the fertilization site. Only one of these fertilizes the egg. The others are thought to help the fertilizing sperm penetrate the barriers that protect the female gamete.

2. The ability for reproduction is acquired with puberty (on average 12–15 years in girls and 13–16 years in boys).

3. The reproductive period in women commonly lasts till 40–45 years, and in men — till old age (gamete production by the testes occurs throughout life).

4. Fertilization occurs in the upper parts of a fallopian tube, usually within 12 hours after ovulation.

5. Spermatozoa are able for fertilization during 1–2 days after getting into the female reproductive tract.

Infertility is one of the most serious social problems today. In Belarus, about 14 % of families cannot conceive on their own and in half of the cases, male reproductive function is impaired.

Assisted Reproductive Technologies (ART) in overcoming human infertility:

- *In Vitro Fertilization* — a procedure in which eggs are removed from a woman's ovary and combined with sperm outside the body to form embryos.
- *Intracytoplasmic sperm injection* (*ICSI*) involves injecting a single live sperm directly into the center of a human egg.
- *Artificial insemination* with the sperm of the husband (partner) or donor — the deliberate introduction of sperm into a female's cervix or uterine cavity for the purpose of achieving a pregnancy.
- The use of *donor oocytes*.
- The use of *donor sperm*.
- The use of *donor embryos*.
- *Surrogacy* — an arrangement in which a woman (the surrogate) agrees to carry and give birth to a child on behalf of another person or couple.
- *Cryopreservation* of germ cells, tissues of reproductive organs, and embryos, transportation of germ cells and/or tissues of reproductive organs.

IN VITRO FERTILIZATION

In vitro fertilization (IVF) is a form of assisted reproductive technology in which egg cells are taken from a woman, and fertilized with male sperm outside the body in a laboratory dish.

There are five basic steps to IVF (Fig. 7):

1. *Stimulation* (superovulation). Medicines that boost egg production are given to the woman. The ovaries produce several eggs instead of one.

2. *Egg retrieval*. Eggs are removed from the follicles of ovaries by a thin needle (follicular aspiration). Depending on the number of follicles, the puncture procedure takes 15–30 minutes.

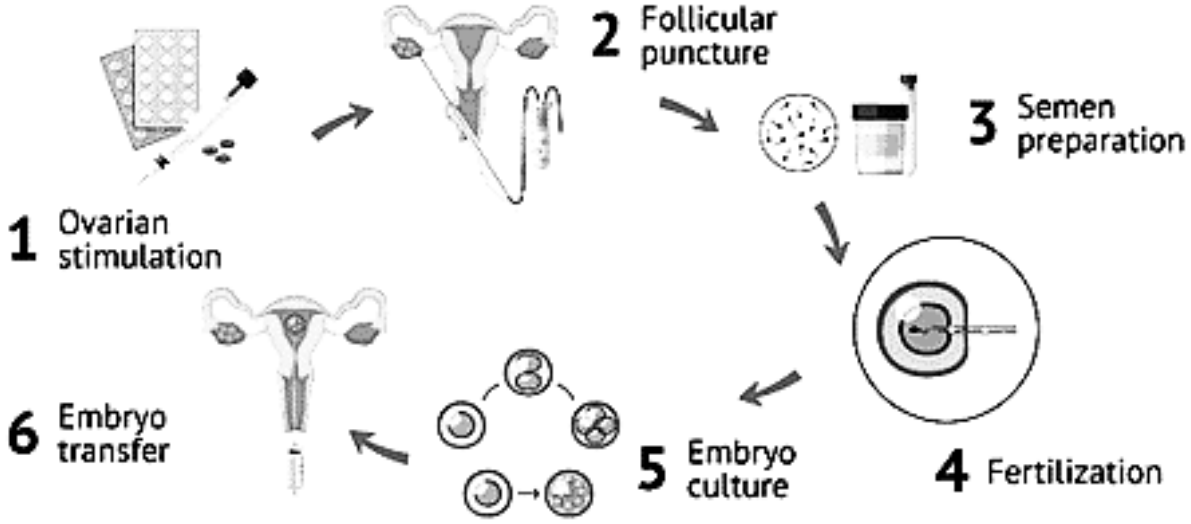


Figure 7. In vitro fertilization

Insemination and fertilization. The best-quality egg cells are placed together with the partner's semen (the spermatozoa are separated from the seminal fluid).

Usually, fertilization occurs a few hours after insemination. Usually, more than 50 % of the eggs are fertilized and transferred to an incubator for 5–6 days.

If the chance of fertilization is low, the sperm may be directly injected into the egg *(intracytoplasmic sperm injection, ICSI).*

3. *Embryo culture*. Zygote divides and becomes an embryo. Within about 5 days, a normal embryo has several cells actively dividing.

Couples with a high risk of passing a genetic (hereditary) disorder to a child may consider **pre-implantation genetic diagnosis (PGD)**.

The procedure is most often done 3 to 5 days after fertilization. A single cell is taken from each embryo and screened for specific genetic disorders.

4. *Embryo transfer*. Embryos are placed into the uterus with a thin tube 3 to 5 days after fertilization. An embryo implants in the lining of the uterus.

More than one embryo may be placed into the womb at the same time, which can lead to twins, triplets, or more. Unused embryos may be frozen and implanted or donated at a later date.

CHAPTER 2
FUNDAMENTALS OF PRENATAL ONTOGENESIS

ONTOGENESIS, ITS TYPES AND PERIODS

Ontogenesis is the individual development of an organism from the formation of a zygote to death.

Division of ontogenesis into periods (Fig. 8).

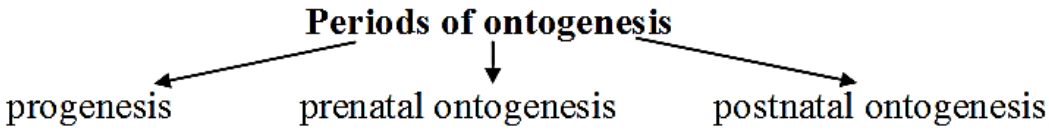


Figure 8. Periods of ontogenesis

Progenesis (prezygotic period) is a period of formation and maturation of those parental gametes that formed a zygote.

Prenatal ontogenesis starts at the moment of a zygote formation and ends with the birth of a new organism or when it leaves the egg.

Postnatal ontogenesis — the period that begins at the moment of birth or hatching from an egg and ends with death.

There are several types of organism development (Table 1).

Table 1

Types of organism development

Direct development (without metamorphosis)	Indirect development (with metamorphosis)
Laying eggs with a lot of yolks (birds)	Stages of incomplete metamorphosis: egg – larva – mature individual (intestinal helminths)
Intrauterine development (mammals)	Stages of complete metamorphosis: egg – larva – pupa – mature individual (butterflies, dipterans)

Types of development. Human prenatal development includes:

– *Germinative* or *initial period* is the 1st week after fertilization when cleavage of a zygote takes place;

– *Embryonic period* — the 2nd–3rd weeks after fertilization when a blastula and gastrula are formed; formation of germ layers and anlagen of axial organs takes place;

– *Prefetal period* — the 4th–8th weeks, when the formation of organ systems and placenta takes place;

– *Fetal period* — since the 9th week the embryo is called a *fetus*; growth of the fetus and formation of organs and organ systems take place.

Characteristic of progenesis. Progenesis is a prezygotic maturation of a female gamete that is the basis for a zygote. It starts in the embryonic period of the mother's organism and is finished when a sperm delivers its genetic material to the cell. That is why the older is the woman, the longer is this period.

Usually, its length coincides with the mother's age. Progenesis of a spermatozoon lasts about 70 days. The quality of gametes and possible mutations of their genes have a considerable effect on the health of future children.

STAGES OF EMBRYOGENESIS

Embryonic development starts from fertilization which was described in the previous chapter. This process includes the fusion of female and male **gametes** (egg and sperm) into a cell called a **zygote**.

When this happens, the haploid nuclei of the two cells form a single diploid nucleus. Activation of the egg occurs, zygote starts to replicate its DNA and begins its first division.

The process in which a zygote divides into multiple cells of smaller size is called **cleavage**. These cells are called **blastomeres**.

- The G_1 and G_2 phases in dividing blastomeres are very short.
- Very little gene transcription occurs during cleavage. In vertebrates, the first generations of blastomeres use mainly the maternal mRNA accumulated in the ovocyte before fertilization.
- The zygote's cytoplasm is *heterogeneous*. The blastomeres which inherited different pieces of the zygote's cytoplasm contain different cytoplasmic components.
- The *polarity* is observed in the eggs of most animals. It results from concentration gradients in the egg of such cellular components as mRNA, proteins, and **yolk**.
- One side of the eggs has the highest concentration of yolk (**vegetal pole**) while the opposite one has the lowest concentration — **animal pole**.
- The division of the zygote follows a specific pattern based on the location of the poles. The cleavage in the *animal hemisphere is more rapid* than in the vegetal hemisphere.
- A zygote of a ***frog*** has an apparent yolk gradient. This causes different rates of cleavage on the poles, so the cells in the different hemispheres of the embryo have different sizes (smaller on the animal hemisphere as cells there divide more rapidly).
- ***Sea urchins*** and many other animals have small amounts of yolk in their eggs. Their blastomeres are about equal in size. Though animal and vegetal poles are present but determined by the concentration gradients of other cytoplasmic components (Fig. 9).
- The complete division in eggs with little yolk or moderate amounts of yolk (e.g. sea urchins, frogs), is called holoblastic cleavage.
- In eggs that contain very large amounts of yolk (e.g. birds, and other reptiles), cleavage occurs only in a small disc of yolk-free cytoplasm at the animal pole of the egg. Such incomplete division of the zygote is called meroblastic cleavage.

• Cleavage produces a solid ball of cells called a **morula**.

• Then a fluid–filled cavity called **blastocoel** develops within the embryo. With this cavity, the embryo is called a **blastula**. The blastula of mammals is called a **blastocyst**.

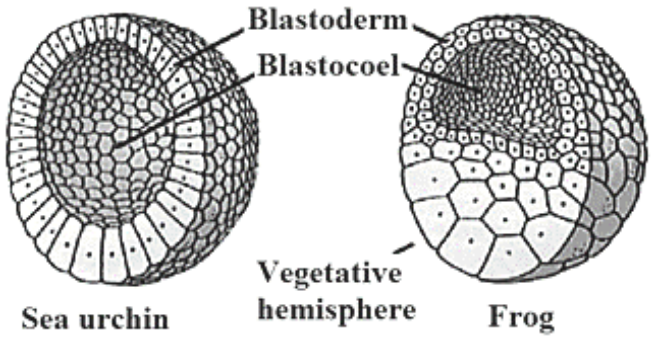


Figure 9. Diagrams of blastula of sea urchin (left) and frog (right)

• *In sea urchins*, the blastocoel is in the center of the blastula due to equal cell divisions. The wall of its blastula has one layer of cells.

• *In frogs*, the blastocoel is in the animal hemisphere because of unequal cell divisions (caused by yolk gradient).

GASTRULATION

The process in an animal's embryonic development when the blastula is rearranged to form an embryo with a **primitive gut** and **germinal layers** is called **gastrulation**. Such an embryo is called a **gastrula**. The three layers produced by gastrulation are embryonic tissues called **embryonic germ layers**: the **ectoderm** (outer), **mesoderm** (middle), and **endoderm** (inner). The germ layers eventually develop into all organs and tissues of the adult animal. Specific details of gastrulation may vary in different animal groups.

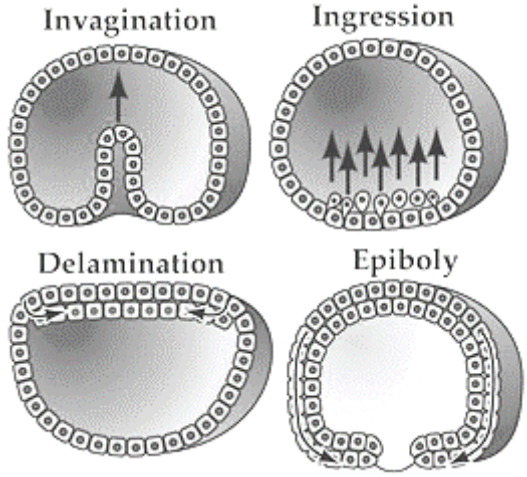


Figure 10. Types of gastrulation

There are several types of cell movements in gastrulation (Fig. 10):

1. **Invagination**. The vegetal pole of the blastula draws inside the blastula. This layer of cells which are now inside the embryo is called an *endoderm.* The cells on the outside are *ectoderm*. The cavity of the gastrula lined with endoderm is called an *archenteron* (primary intestine). It opens to the outside with a primary mouth or *blastopore* (Fig. 11). Its edges form the *upper and lower lips of the blastopore*. In the secondary-mouthed (deuterostomes) such as chordates it transforms into an anus and the mouth is formed at the opposite side of the embryo.

2. **Ingression** — a movement of some blastomeres into the blastocoel. They form endoderm. This way is characteristic of coelenterates.

3. **Epiboly** is typical for telolecithal ova having much yolk on the vegetal pole. Cells of the animal pole divide faster than cells of the vegetal pole, which form an endoderm.

4. **Delamination**. All cells of in a cell layer divide parallelly to its surface and form two germ layers: ectoderm and endoderm.

Usually, gastrulation occurs via a combination of several types of cell movements rather than one of them.

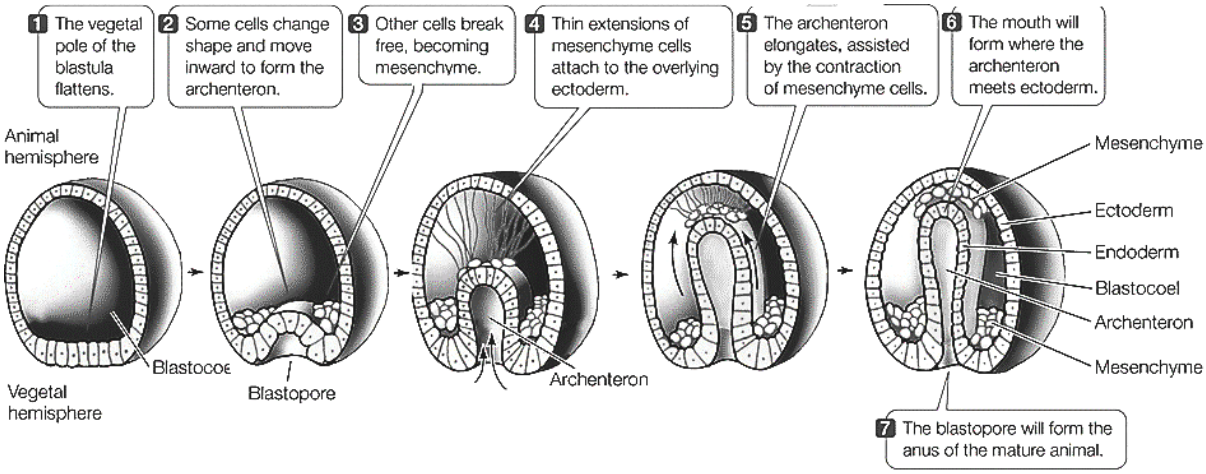


Figure 11. Gastrulation in sea urchin

All animals except sponges and radiates have three germ layers. The secondary body cavity of many animals (it is called **coelom**) can be formed in two ways:

– **Schizocoelous** — a descriptive term for development during which, as the archenteron forms, the coelom begins as splits within the solid mesodermal mass; coelom formation is found in *protostomes*.

– **Enterocoelous** — coelom development during which the mesoderm arises as lateral outpocketings of the archenteron (primitive digestive tube) with hollows that become the coelom.

PECULIARITIES OF EMBRYONIC DEVELOPMENT OF HUMANS

During cleavage, the zygote forms a 16–celled ball or **morula**.

The morula then undergoes cavitation and transforms into the **blastocyst**.

Within the blastocyst, two tissue layers differentiate: an outer shell, known as the **trophoblast**, and an inner collection of cells termed the **inner cell mass** (**ICM**), or **embryoblast** situated on one side of the blastocyst's cavity (Fig. 12). The outer trophoblast will develop into structures that provide nutrients, help the growing embryo implant in the uterine lining, and become part of the placenta. The ICM cells will give rise to the distinctive formation of the fetus.

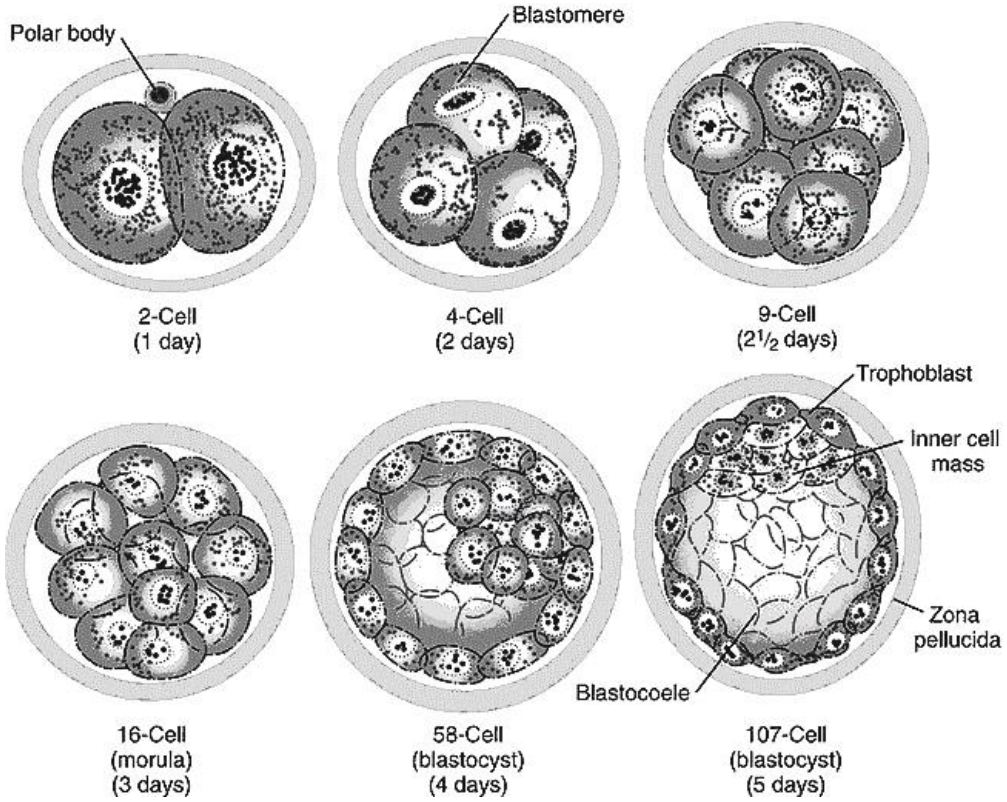


Figure 12. Blastocyst formation

From zygote to blastocyst formation, the organism has been surrounded by the zona pellucida, which plays a role in the protection and prevention of implantation into the uterine tubes. During blastocyst formation, the zona pellucida begins to disappear from the blastocyst, allowing the ball of cells to proliferate, differentiate, change shape, and eventually implant into the uterine wall.

During **implantation**, the outer trophoblast releases digestive enzymes to assist with implantation to the **endometrium** (innermost lining layer of the uterus). This layer also releases human chorionic gonadotropin (hCG, necessary in regulating progesterone secretion), the protein used in many pregnancy tests.

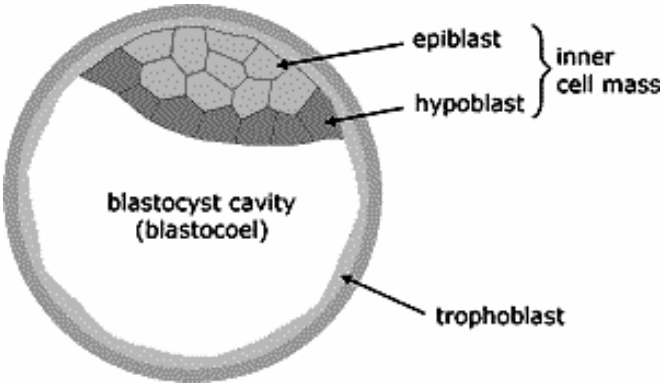


Figure 13. Structure of blastocyst

During the second week of human development, the ICM cells spread into a flattened tissue layer and differentiate into a two-layered tissue containing **epiblast** (columnar epithelial cells) and the **hypoblast** (cuboidal epithelial cells), which are together known as the **bilaminar disc** (Fig. 13). The formation of

the bilaminar disc sets the dorsal/ventral axis as the epiblast cell layer is positioned dorsal to the hypoblast. This is the first stage of gastrulation.

The anatomical location of the bilaminar disc is found between the **amniotic cavity** and the **primitive yolk sac** (Fig. 14).

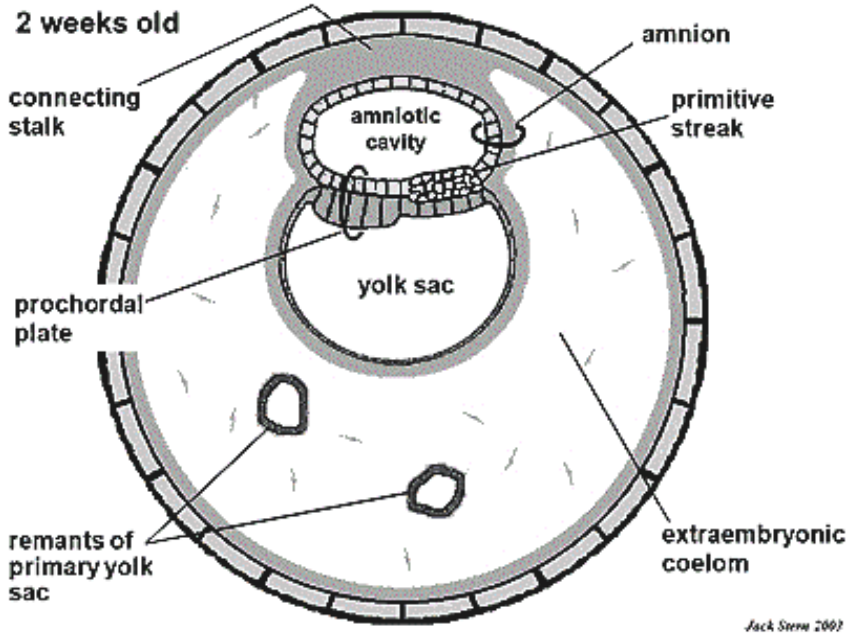


Figure 14. Human embryo 2 weeks after fertilization

The cells of the epiblast stretch to form a semi-sphere known as the amniotic cavity, while the cells of the hypoblast extend to surround the yolk sack. In the 3rd week, a groove called **primitive streak** appears in the midline of the epiblast. Its cranial end is bound with primitive node, which has a primitive pit. Then the 3 germ layers are formed: many cells of the epiblast move to the primitive pit, detach and migrate deeper. By replacing the cells in hypoblast, they form endoderm. The cells that stay in the epiblast become ectoderm. The cells between them form mesoderm. This is the second stage of gaastrulation (according to some textbooks - this is the gastrulation itself).

After the formation of germinal layers **histogenesis** (formation of tissues) and **organogenesis** (formation of organs) occur, anlagen of axial organs are formed.

Ectoderm *gives rise to* the epidermis of the skin and its derivatives (including sweat glands, hair follicles, nervous and sensory systems, pituitary gland, adrenal medulla, jaws, and enamel of teeth.

Mesoderm *gives rise to* skeletal and muscular systems, circulatory and lymphatic systems, excretory and reproductive systems (except germ cells), the dermis of the skin, adrenal cortex.

Endoderm *gives rise to* the epithelial lining of the digestive tract and associated organs, the epithelial lining of respiratory, excretory, and reproductive tracts and ducts, thymus, thyroid, and parathyroid glands.

There are tissues, derived from the fertilized egg, that enclose or otherwise contribute to the support of the developing embryo. These tissues are called extraembryonic membranes. They include:

– **Amnion** is a sac with fluid that forms an aquatic environment for the embryo and fetus and protects it from drying out and injury.

– **Chorion** is the external covering contacting with the shell of an egg or mother's tissues. It provides exchange with the environment and participates in the formation of the placenta.

– **Yolk sac** participates in the feeding of the embryo and is the first hematopoietic (blood-creating) organ.

– **Allantois** is an outgrowth of the posterior region of the gut. It is a reservoir for urea and uric acid. It participates in the formation of the placenta in mammals.

REALIZATION OF GENETIC INFORMATION DURING PRENATAL ONTOGENESIS

Mechanisms of embryogenesis and morphogenesis. The zygote and first blastomeres are **totipotent**. This means that they can give rise to an entirely new organism. Later cells become **determined** — they can develop into only specific cell types.

The zygote and new cells should follow a "developmental program" to develop into a new organism. It is reasonable to expect that they have a plan for the body, but there is no such plan. Cells have only instructions determining their behavior in different conditions.

Cell behavior becomes different soon after cleavage (when they begin to differentiate into various cell types) and depends on signals received by the cell. The signals can be of chemical nature: cells may secrete signaling molecules that influence neighboring cells.

The signals can also be of physical nature: cells can determine if other cells are present when in contact with them. The behavior of cells becomes different in embryogenesis because they are in different conditions: some cells are inside the embryo and others are outside; some cells are exposed to the high concentration of a signaling molecule, others — to its low concentration; some cells have a large amount of certain mRNA inherited from the zygote because the distribution of this mRNA there was not equal. The sum of all the signals acts as a set of "rules" which determine the cell's behavior.

The differentiation of cells into specialized tissues and organs is called *histogenesis* and *organogenesis*.

The developmental process by which tissues and organs acquire the shape that is critical to their function is called **morphogenesis**.

The key concepts of morphogenesis include:

– **Differentiation** — the process by which a cell or group of cells becomes specialized in structure and function.

– **Induction** — the embryonic process in which one group of cells, the inducing tissue, directs the development of another group of cells. Induction occurs mainly due to *morphogens*.

A **morphogen** is a signaling molecule that acts over long distances to induce cell responses based on the concentration of these molecules. Morphogen concentration can gradually change from one part of the embryo to the opposite.

– A **morphogen gradient** is a concentration gradient of morphogen in a developing embryo. Different concentration of morphogens is one of the mechanisms determining positional information of cells.

– **Positional information of cells** means that the differentiation patterns of the cell depend on its position in the developing embryo. The presence of multiple concentration gradients of signaling molecules acts as a "coordinate system" for the cells so they follow the program necessary for their specific position in the embryo.

The processes by which cells produce new structures in an embryo include:

– Cell migration.

– Programmed cell death (apoptosis, Fig. 15).

– Cell shape changes.

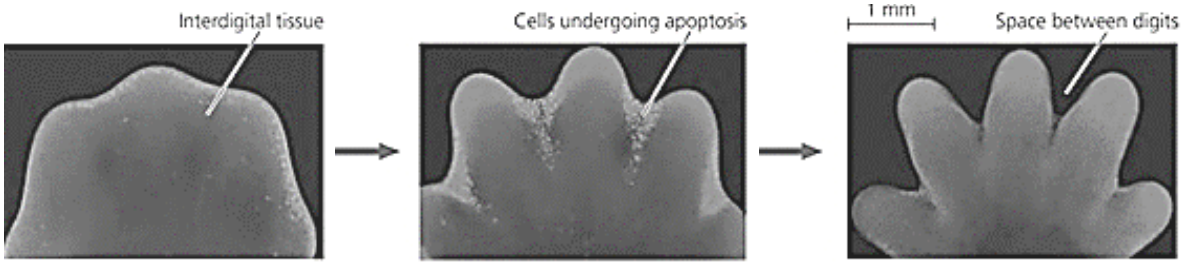


Figure 15. Apoptosis in the developing mouse paw eliminates the cells in the interdigital regions

The concepts described above can be illustrated by the process of *neurulation* (Fig. 16). *Neurulation* is the process in which ectodermal cells on the future dorsal side of the embryo form a nerve tube — the structure that differentiates into the brain and spinal cord.

There is a morphogen called **bone morphogenetic protein 4** (**BMP4**). Under the action of BMP4, the cells of the ectoderm differentiate into *epithelial cells of the skin*. Without BMP4 the ectoderm cells would develop into *neural cells*.

Embryos of all chordates (all animals with backbone and several groups of others) have **notochord** — a rod extending along the dorsal side. It originates from mesoderm.

In humans, notochord appears in the 3rd week of development. These mesodermal cells and other tissues under the ectoderm secrete signaling molecules such as chordin, noggin, and follistatin.

These secreted signaling molecules prevent neighboring ectodermal cells from receiving BMP4 signals so they develop into the **neural plate**.

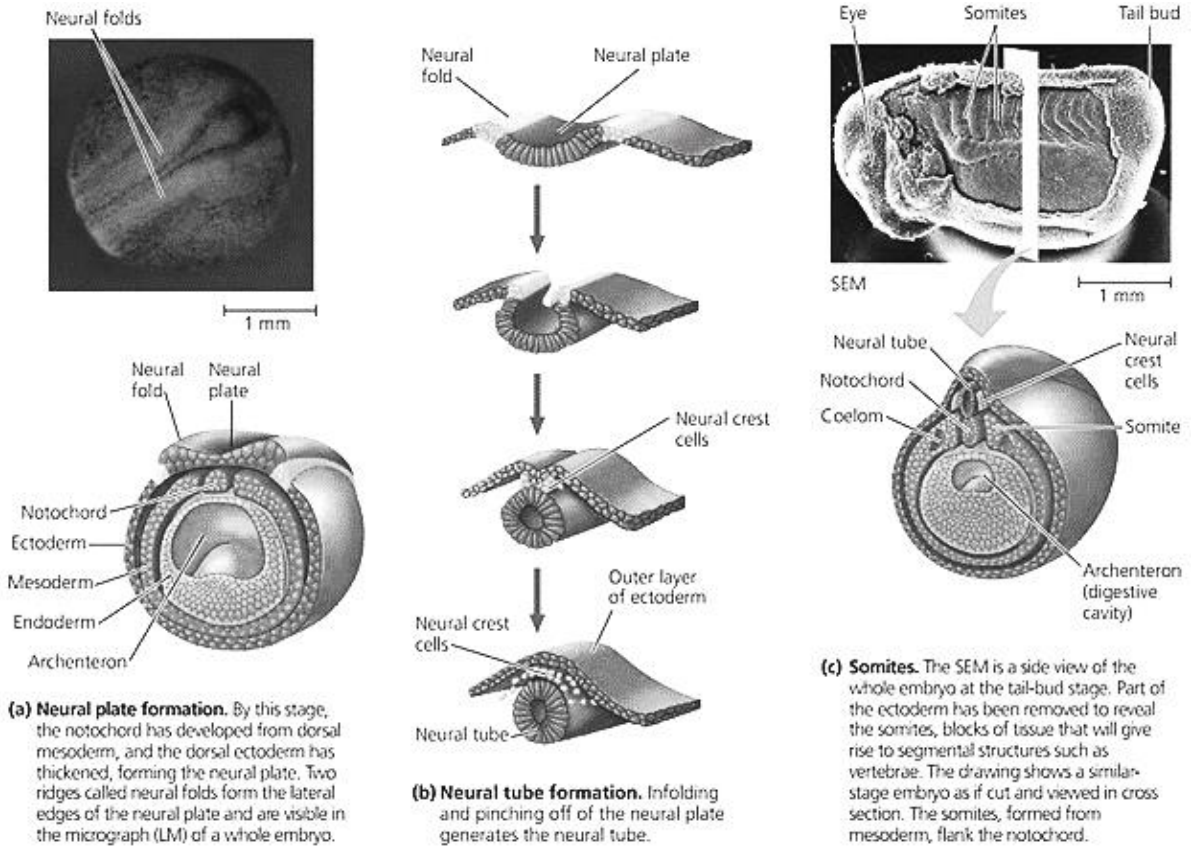


Figure 16. Neurulation

Formation of the neural plate is thus an example of **induction**. As BMP is inhibited in one side of the embryo, its activity is observed in a gradient that is required for dorsal — ventral patterning (Fig. 17).

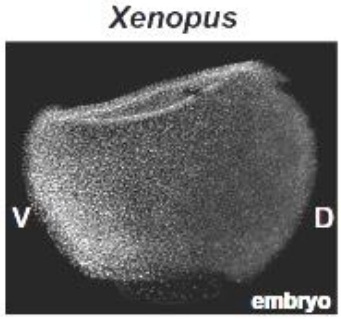


Figure 17. In a frog (Xenopus) gastrula immunostaining reveals the BMP activity gradient that is required for dorsal–ventral patterning

After the neural plate is formed, its cells change shape, curving the structure inward. In this way, the neural plate rolls itself into the **neural tube**, which runs along the anterior — posterior axis of the embryo. Later on, the neural tube differentiates into the brain and the spinal cord.

Neurulation, like other stages of development, is sometimes imperfect. For example, spina bifida occurs when a portion of the neural tube fails to develop or close properly. The opening in the spinal column that remains causes nerve damage, resulting in varying degrees of leg paralysis. Although the opening can be surgically repaired shortly after birth, the nerve damage is permanent.

During neurulation, some embryonic cells pinch off from the ectoderm during the formation of the neural tube. This group of cells is called the neural crest. These cells migrate to many parts of the embryo, forming a variety of tissues that include peripheral nerves, components of teeth, and skull bones.

SPEMANN–MANGOLD ORGANIZER

In 1921 German zoologist Hans Spemann and his student Hilde Mangold transplanted a piece of the dorsal lip from a newt's gastrula to the ventral side of another newt's gastrula.

When an experimental gastrula received the transplant of a dorsal lip from a donor, the recipient embryo formed a second notochord and neural tube in the region of the transplant. Eventually, most of a second embryo developed, producing a twinned tadpole (Fig. 18).

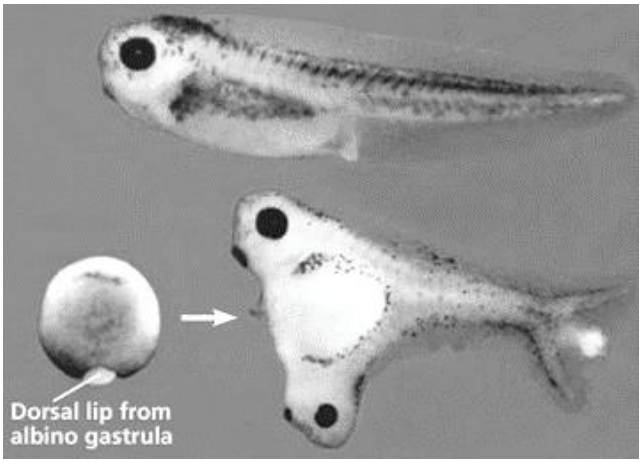


Figure 18. Spemann–Mangold experiment repeated on a frog (Xenopus laevis)

Spemann and Mangold concluded that the dorsal lip of the blastopore in the early gastrula functions as an "**organizer**" of the embryo's body plan, inducing changes in surrounding tissue that direct the formation of the notochord, the neural tube, and other organs.

CRITICAL PERIODS OF ONTOGENESIS. TERATOGENS

Periods of the maximal sensitivity of the embryo or fetus to environmental factors are called **critical periods**.

The human has 3 main critical periods in embryogenesis:

1. *Implantation* of an embryo in the mucous membrane of the uterus (6^{th}–7^{th} day after fertilization);

2. *Placentation* — beginning of the placenta formation (14^{th}–15^{th} day after fertilization);

3. *Delivery* — at this period reconfiguration of all organ systems occurs (39^{th}–40^{th} weeks).

In critical periods organism undergoes crucial functional changes and readjusts to new conditions of existence.

The impairment of the course of embryogenesis caused by environmental factors is called **teratogenesis** (Greek *teras* — monster).

Factors causing teratogenesis are *teratogens*.

They are medicines (antibiotics, quinine, chloride, antidepressants, etc.), alcohol, nicotine, waste products of parasites, and ionizing radiation.

Causes and development mechanisms of malformations are studied by teratology.

The incidence frequency of malformations in human populations is 1–2 %.

Variants of congenital development defects:

– *aplasia* — organ is not laid down;

– *hypoplasia* — underdevelopment of a tissue or organ;

– *hypotrophy* — degeneration of an organ or tissue caused by loss of cells;

– *hypertrophy* — increase in the volume of a tissue or organ produced entirely by enlargement of existing cells;

– *heterotopy* — normal tissue is misplaced;

– *atresia* — the absence or closure of a normal body orifice or tubular passage;

– *stenosis* — constriction or narrowing of a duct or passage.

GENOMIC IMPRINTING

Genomic imprinting is an epigenetic phenomenon resulting in the monoallelic expression of a gene depending on its parental origin (Fig. 19).

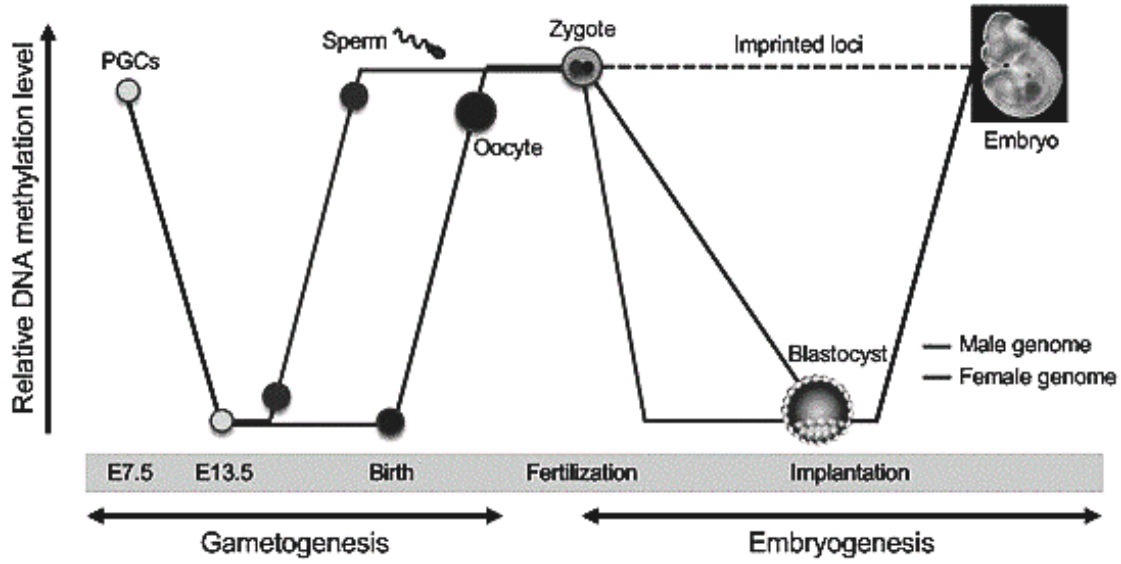


Figure 19. Genomic imprinting

It plays an important role in embryonic, fetal, and placental growth as well as in neurodevelopment and postnatal development.

The parental allele-specific expression is because of differential epigenetic marking on the parental allele during gametogenesis.

The imprint marks are established during gametogenesis, maintained, and read during embryogenesis. Genomic imprinting is susceptible to genetic and environmental influences.

Aberrant imprinting and expression of these genes through genetic or epigenetic alterations can lead to various conditions such as *Prade–Willi* and *Angelman* syndromes.

If chromosome 15 with some defect in the long arm is inherited from the father, the child develops Prader–Willi syndrome, and if from the mother, Angelman syndrome.

There are different hypotheses explaining the differences in gene methylation in female and male germ cells.

The first one explains it by the difference in biological interests of the sexes: the sperm methylation pattern favors the embryo to receive as many resources as possible from the mother, while the oocyte methylation pattern favors the embryo to limit this influence.

This is supported by the fact that most mammalian genes that undergo parental imprinting are in one way or another related to intrauterine development.

Another hypothesis explains the imprinting by improving maternal — fetal compatibility: when some of the paternal genes are turned off, only maternal alleles will be expressed in the embryo, and the embryo will become biologically and physiologically more similar to the mother’s body.

This may be supported by the fact that the number of “switched off” paternal genes is higher than the number of maternal genes, which finds confirmation.

Dynamic changes in DNA methylation during mammalian development. Schematically shown are the two waves of global DNA demethylation and remethylation in the life cycle. Primordial germ cells (PGCs) initially have high levels of DNA methylation.

Global demethylation occurs during PGC expansion and migration. At later stages of germ cell development (before birth in males and after birth in females), de novo methylation results in the establishment of sex-specific germ cell methylation patterns, including methylation marks at imprinted loci.

Shortly after fertilization, the methylation marks inherited from the gametes are erased again (except those at imprinted loci and some retrotransposons), with the paternal genome undergoing active demethylation and the maternal genome undergoing passive demethylation. Upon implantation, a wave of de novo methylation establishes the initial embryonic methylation pattern.

CHAPTER 3
FUNDAMENTALS OF POSTNATAL ONTOGENESIS

Periods of postnatal ontogenesis are:

1. *Neonatal period* (birth — < 28 days of life). The neonate adapts to extra-uterine existence.

During the first 4 or more days the infant commonly loses weight; the birth weight is usually regained by the 10^{th} day.

2. *Infancy, or breastfeeding period* (28 days – 12 months). This period is marked by rapid growth; the birth weight often doubled by the age of 6 months.

First teeth erupt, and the diet is gradually enlarged by the addition of solids from one almost exclusively of milk.

3. *Early childhood* (1–3 years). Children start to walk, learn to speak, and get acquainted with the world around them.

4. *The 1^{st} period of childhood* (4–6 years). The child is interested in everything and tries to understand everything and get the hang of basic game skills.

5. *The* 2^{nd} *period of childhood* (7–11 years in girls, 7–12 years in boys). The growth slows, and intensive development of the muscular system occurs. In this period children go to school.

6. *Puberty, or adolescence* (12–15 years in girls, 13–16 years in boys) Sexual maturation starts, and growth speed intensity increases.

7. *Youths* (16–20 years in girls, 17–21 years in young men) Sexual maturation, growth, and physical development have been completed.

8. *1^{st} period of adulthood* (21–35 years in women, 22–35 years in men) is an optimal period for childbirth; mastering professional skills.

9. 2^{nd} *period of adulthood* (36–55 years in women, 36–60 years in men) is the period of the most active professional activity. The first signs of aging appear after 35 years).

10. *Advanced age* (56–75 years in women, 61–75 years in men). The processes of aging are going on; this is the age of retirement.

11. *Senile age* (76–90 years). Senile changes are marked; some people still can work creatively at this age.

12. *Longevity* (over 90 years).

Critical periods of postnatal ontogenesis. There are 3 *critical periods* in postnatal human ontogenesis:

1. *Neonatal period* (the first days after birth) — reconfiguration of all organ systems for a new environment.

2. *Puberty period* (12–16 years) — a hormonal readjustment, formation of secondary sex characters.

3. *Period of sexual involution* (about 50 years in women, 60–70 years in men) — reproductive function fades functional depression of gonads and endocrine glands occur.

GROWTH. GROWTH TYPES OF HUMAN TISSUES AND ORGANS. ACCELERATION

Growth is the process that provides an enlargement of the size and mass of the body. The growth can be *unlimited* and *limited*.

Unlimited growth lasts all life (crawfishes, fishes, and reptiles) while limited one stops at a certain age (insects, birds, mammals) (Fig. 20).

Regulation of growth

Somatotropin (hypophysis); thyroxin (thyroid); sex hormones	Environmental factors: light, food, vitamins (A, B, D), microelements, social and economic factors

Figure 20. Regulation of tissue growth

The speed of body growth is not uniform. Periods of the most intensive body growth are the first year of life: body length increases by 25 cm. In the 2nd year, it increases approximately by 10–11 cm, in the 3rd by 8 cm, from 4 to 7 years by 5–7 cm per year, during 2nd period of childhood it increases by 4–5 cm per year.

The second period of intensive growth is puberty. During this period the growth speed increases to 7–8 cm a year and then slows down and is 1–2 cm per year till 20–25 years.

The speed of growth is not the same for different tissues and body parts.

Basic growth types for tissues and organs are:

– *General type* of growth. The whole body, muscles, skeleton, respiratory organs, and liver grow intensively during the 1st year of life puberty;

– *Lymphoid type* of growth. The thymus, lymph nodes, and the lymphoid tissue of the intestine, spleen, and tonsils reach their maximal size by 11–12 years, and then their volume decrease;

– *Cerebral type* of growth. The brain, spinal cord, eyes, and head develop earlier than other parts of the body and reach sizes characteristic of adults by 10–12 years;

– *Reproductive type* of growth. Organs of the reproductive system grow rapidly during puberty.

Somatotropic hormone (growth hormone) is produced by hypophysis. Its intensive production occurs from birth to 13–16 years. Hypofunction of hypophysis causes, *pituitary dwarfism*, hyperfunction causes *giantism* and human height can surpass 2 m.

Production of hormones in adult age causes *acromegalia* — enlargement of bones of palms, feet, and face.

Thyroxin enhances energy exchange in the body. Hypofunction of the thyroid gland causes delayed growth, delayed puberty, impairment of body proportions, and mental disturbance.

Sex hormones have an effect on metabolic processes as well.

Environmental factors also have a considerable effect on growth. Normal growth of a child requires a balanced meal with vitamins and microelements. The synthesis of vitamin D is influenced by sunlight.

In recent decades, the **acceleration** of the physical and mental development of children and adolescents is observed. It is marked even at the stage of intrauterine development — the body length of newborns increased by 0.5–1.0 cm, body mass — 50–100 g, and the terms of teeth cutting out changed.

The human height has increased on average by 8 cm over the recent 100 years. The numerous factors were supposed to cause acceleration: better nutrition, and increase heterozygosity due to mixed marriages.

Human age:

1. *Biological age* — correspondence of body functional capacities to a certain age or the age that person looks.

2. *Chronological age* — the number of years a person has lived or passport age.

Criteria for determination of biological age:

– skeletal maturity: ossification of cartilaginous regions and growth zones;

– teeth maturity: the appearance of milk teeth and their replacement with permanent ones;

– the time when secondary sex characters appear and their development degree.

HUMAN CONSTITUTION AND HABITUS

The constitution of humans is genetically conditioned peculiarities of human morphology, physiology, and behavior.

In 1927 M.V. Chernorutsky proposed the classification including three types of the constitution:

Ectomorphic type (asthenics): a narrow chest, low position of the diaphragm, elongated lungs, short intestine that provides lower absorption, thin bones, long extremities, and a thin layer of subcutaneous fat. Statistically, asthenics are characterized by high excitability.

They more often have neuroses, hypotonia, ulcers, and tuberculosis.

Mesomorphic type (sthenics): balanced constitution, moderate development of the subcutaneous fat tissue.

They are usually people of action; more often have neuralgias, atherosclerosis, and diseases of the upper airways.

Endomorphic type (hypersthenics): a broad chest, large stomach, long intestine, and considerable fat tissue. The amounts of cholesterol, uric acid, erythrocytes, and hemoglobin in the blood are higher than in other constitution types. Assimilation processes predominate.

Hyperstenics have tendencies to obesity, diabetes mellitus, hypertension, and diseases of the kidneys and gallbladder.

Habitus includes peculiarities of morphology, physiology, and behavior in a definite period.

Habitus shows the overall condition of a person and his health at a given moment. It includes: peculiarities of the constitution, pose, bearing, gait, skin color, facial expression, and concordance of biological and chronological age.

AGING. BASIC THEORIES OF AGING

Aging is a common biological regularity characteristic of all living organisms. Old age is the final stage of ontogenesis.

The science of aging and old age is called **Gerontology**. It studies the regularities of aging of various organ systems and tissues.

Geriatrics is a science about diseases of old people. It studies the peculiarities of their development, course, treatment, and prophylaxis.

The following phenomena are known to be associated with aging (López–Otín et al., 2013):

1. *Genomic Instability*. It is known that aging is associated with the accumulation of genetic damage (point mutations, translocations, chromosomal gains and losses, telomere shortening, and disruption of genes by viruses or transposons) throughout life. Artificial genomic damage can provoke aspects of accelerated aging.

2. *Telomere Attrition*. The DNA polymerases cannot completely replicate the terminal ends of linear DNA molecules (telomeres). This explains the limited division number of some types of cells in culture (Hayflick limit). Normal aging in mammals is accompanied by telomere attrition. Moreover, pathological telomere dysfunction accelerates aging in mice and humans, while "repair" of telomeres in experiments can delay aging in mice.

3. *Epigenetic Alterations*. Aging is accompanied by epigenetic changes. Epigenetics is the study of heritable phenotype changes that do not involve alterations in the DNA sequence.

4. *Loss of Proteostasis*. There is evidence that aging is associated with changes in biogenesis, folding, trafficking, and degradation of proteins. There are also examples of genetic manipulations that improve proteostasis and delay aging in mammals.

5. *Deregulated Nutrient-sensing*. There is evidence that anabolic signaling accelerates aging, and decreased nutrient signaling extends longevity. Some

manipulations that imitate a state of limited nutrient availability can extend longevity in mice.

6. *Mitochondrial Dysfunction*. It is known that mitochondrial dysfunction can accelerate aging in mammals, though it is not yet clear if the improvement of mitochondrial function can prolong lifespan in mammals.

7. *Cellular Senescence*. Cellular senescence is a phenomenon characterized by the cessation of cell division.

8. *Stem Cell Exhaustion*. Stem cells are cells without specialization, so they can differentiate into other types of cells, and also divide to produce more of the same type of stem cells. Some studies show that stem cell rejuvenation may reverse the aging phenotype at the organismal level.

9. *Altered Intercellular Communication*. Aging is associated with general alteration in intercellular communication

The science that studies a healthy lifestyle and conditions increasing human life span is called **Valeology**.

The theoretically possible human age is 150–200 years; the maximum registered one is 115–120 years. The average life span of men in Belarus is 62–70 years, and that of women is 72–79 years.

CLINICAL AND BIOLOGICAL DEATH. RESUSCITATION. EUTHANASIA

The aging of the organism is terminated by **death**. Death provides alternation of generations. The causes of death can be different.

Physiological death, or natural death, occurs due to aging.

Pathological death, or untimely death, is the result of a disease or an accident.

Clinical death occurs as a result of the termination of vital functions (heart or respiration failure), but processes of substances exchange in the cells and organs are retained.

Biological death is the termination of processes of self-renewal in cells and tissues, impairment of chemical processes, autolysis, and decay of cells. In the most sensitive cells of the cerebral cortex, necrotic changes are revealed already in 5–6 minutes after clinical death.

Prolongation of the period of clinical death is possible by using general hypothermia of the organism that slows down metabolic processes and increases the resistance to anoxia.

Resuscitation is a complex of actions performed to return a person to life from the state of clinical death (when vital organs are not impaired) within 5–6 minutes while cells of the brain are still alive. Resuscitation methods are used in medicine in any threatening conditions.

Euthanasia is medical assistance to pass from life for a terminally ill patient at his will or request of his relatives. Euthanasia is allowed by law only in some countries.

CHAPTER 4
BIOLOGICAL ASPECTS OF REGENERATION AND TRANSPLANTATION

STEM CELLS

Human body consists of more than 200 different types of cells. Cells of these types are different to perform particular work, i.e. they are specialized for performing certain functions.

The process in which a cell acquires specialty is called **differentiation**.

All the cells in the human body arise from a single cell (**zygote**) which is not specialized. As cell divide, they become differentiated.

Stem cell is an unspecialized cell that can differentiate into specialized cells.

It is known that the differentiation of cells does not change their genes. This was confirmed by the transfer of the nucleus from an epithelial cell of the frog to a denucleated egg. The egg containing the nucleus of a differentiated cell developed into a normal tadpole (John Gurdon, 1962).

Though, a differentiated cell *cannot become undifferentiated* again or change its cell type. Once the differentiation pathway of a cell has been chosen, it can no longer become another type of cell.

However, differentiated cells were turned back into stem cells by methods of biotechnology. Several genes expressed in stem cells were inserted into mice fibroblasts by retroviruses (Shinya Yamanaka, 2006). Later on, human stem cells were successfully produced by this method. Such stem cells are called **induced pluripotent stem cells** (**iPSC**). Stem cells can be obtained from embryonic or fetal tissues, cord blood, or tissues of adults (Fig. 21).

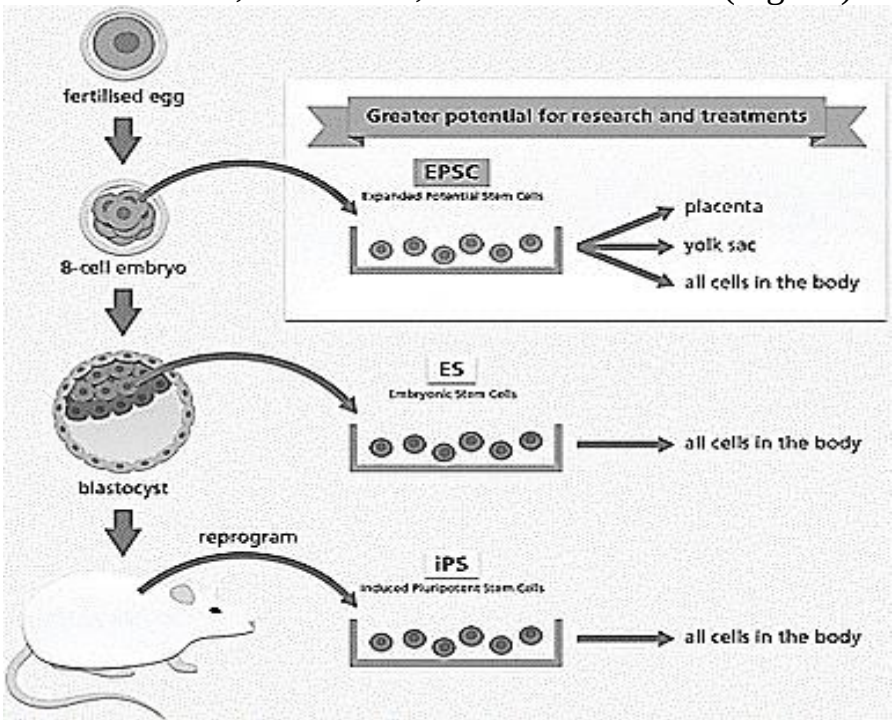


Figure 21. Origin of stem cells

Though these cells have different potencies (i.e. the «choice» for differentiation is different). The potency of stem cells restricts with development of the embryo (Fig. 22).

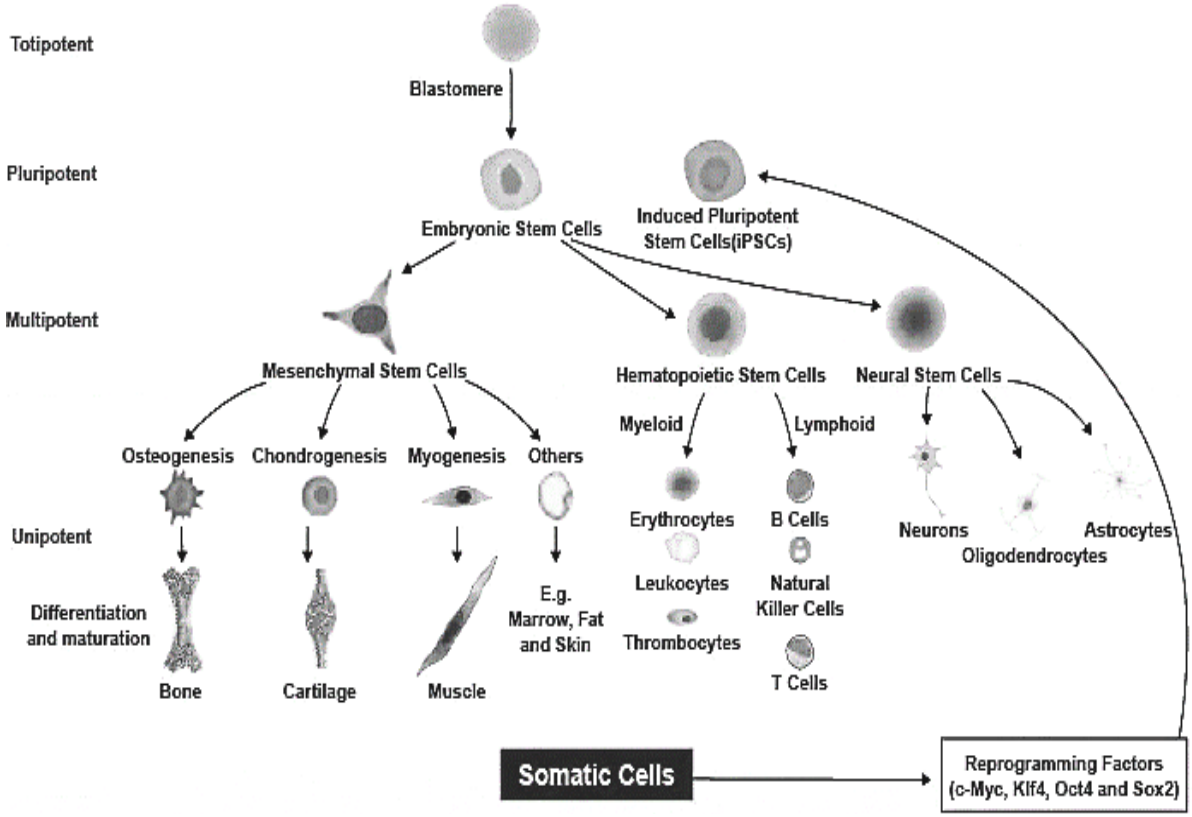


Figure 22. Main types of stem cells

Totipotent stem cells retain the zygote's potential to form a new organism. For example, if the first two blastomeres after the frog's zygote division are separated, each will develop into a normal tadpole.

Pluripotent stem cells can differentiate into the cells of any germ layer. An example of such cells is the inner cell mass of the blastocyst. These stem cells can be obtained from in vitro fertilization clinics (as the number of produced zygotes exceeds the required number). This is associated with some moral and ethical questions, but 5-day old embryo has no even tissues developing into the nervous system. It is a mass of cells that cannot have personhood.

Multipotent stem cells are cells that have the capacity to self-renew by dividing and developing into multiple specialized cell types present in a specific tissue or organ. Such cells are present in adults.

Some important properties of stem cells:

– Undifferentiated state.

– Capability to divide and renew themselves. This is not possible for many specialized cell types (e.g. nervous system).

– Asymmetric division means that one daughter cell stays a stem cell, and the other one differentiates. The fate of cells becomes programmed not after division, but before it is done. The state of stem cells is inherited epigenetically i.e. the properties of the cell are defined not by the specific genes it has, but by specific patterns of the gene expression.

– Capability to migrate in tissues.

The usages of stem cells include:

– Fundamental scientific research (understanding of the mechanisms of cell differentiation, embryonic development, signaling cascades, and gene expression).

– Test of drugs on cultures of stem cells programmed into particular cell types.

– Regenerative medicine — stem cell therapy for the repair of damaged tissues or organs (myocardial infarction, ischemic disease, stroke, diabetes, Alzheimer's disease, wounds, and burns, etc.)

REGENERATION

Regeneration is the renewal or restoration of body parts (or tissues) after injury or as a normal process.

Regeneration occurs at different levels:

– Cellular regeneration (e.g. nerve cells can grow new processes when they are lost);

– Tissue regeneration (e.g. wound healing);

– Organ regeneration (the liver can grow bigger if its fragment was removed);

– Body part regeneration (axolotls can regenerate limbs);

– Whole organism regeneration (both fragments of a planarian cut into two regenerate and become independent organisms).

Regeneration can be physiological and reparative.

Physiological regeneration is the replacement of cells that are lost during the day-to-day activities. Categories of cells:

– *Labile* (or renewing) — regenerate regularly (epidermis — 10–12 days, Epithelium of the gastrointestinal tract — 7 days, RBC — 120 days).

– *Stabile* (or expanding) — regenerate slowly (liver, kidneys, exo and endocrine glands — 300–400 days).

– *Static* (or permanent) — no effective regeneration (neurons, myocardiocytes are unable to divide).

Reparative regeneration is the replacement of lost body parts. Types:

– *Morphollaxis.*

– *Epimorphosis.*

– *Compensatory growth.*

Morphollaxis is the regeneration of a part or organism from a fragment by its reorganization. In other words, a new smaller organism develops from each remaining part. Majority of regenerated tissue comes from already — present cells of the organism.

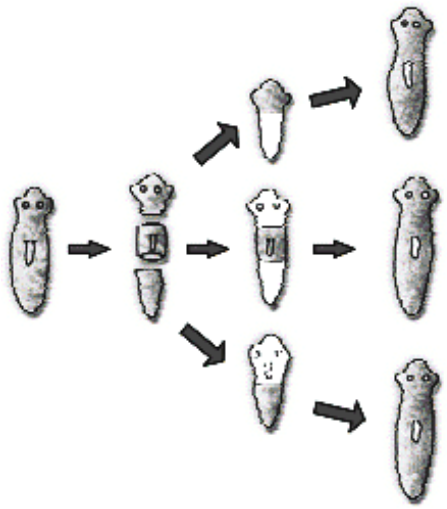


Figure 23. Regeneration in planaria

An example of morphollaxis of the regeneration of planarian. Planarian is a flatworm of the class *Turbellaria*. When it is cut into pieces, each piece can regenerate into a complete organism. Even $1/279^{th}$ of a planarian can regenerate (Fig. 23).

After a planarian has been transected, the wounded area is rapidly covered by a thin layer of epidermal cells.

Undifferentiated cells then accumulate beneath the wound epithelium giving rise to an unpigmented structure referred to as the regeneration *blastema*.

As regeneration proceeds, more of these undifferentiated cells continue to accumulate within the blastema, causing it to grow exponentially.

Within one week of the transection, differentiation of the missing structures occurs.

Regeneration occurs due to pluripotent stem cells *neoblasts* which contribute nearly 20 % of all worm cells.

Epimorphosis (epimorphic regeneration) or — regeneration of a part or organism involving extensive cell proliferation followed by differentiation, e.g. a new limb of axolotl grows from the wound surface to replace the lost one).

Axolotl is the larval stage of the salamander *Ambystoma* which reaches sexual maturity without undergoing metamorphosis.

Within 1 day after limb amputation, the amputated surface is rapidly covered with epithelial cells. (dermis — free epithelial structure *wound epidermis*).

After that, tissues beneath the wound epidermis undergo histolysis generating a population of undifferentiated cells (including proliferative and multipotent mesenchymal cells). Then the mesenchymal cells build up a blastema — a cone-shaped mass of cells that is a structure comparable to the limb bud in limb development (Fig. 24).

Until the process of limb regeneration is completed, the blastema continues to grow distally by the active proliferation of blastemal mesenchymal cells.

Simultaneously with blastema elongation, redifferentiation and repatterning begins, and a complete limb structure is finally re-established.

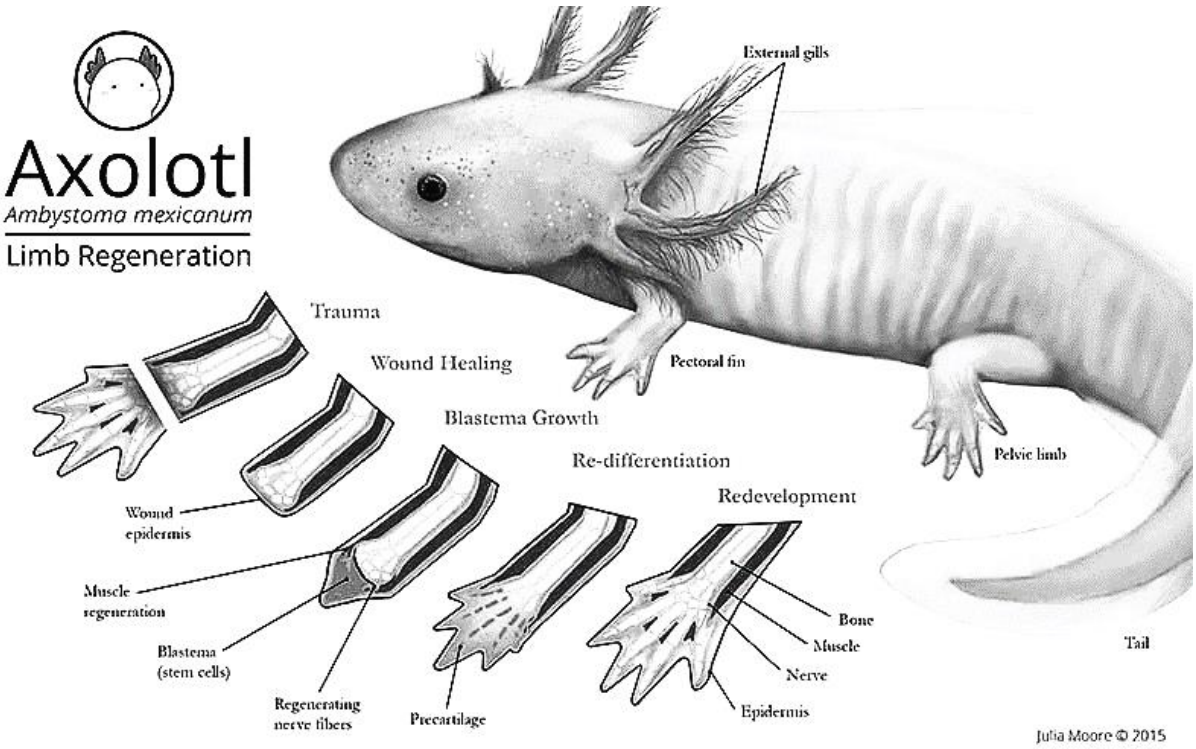


Figure 24. Regeneration in Axolotl

Regeneration does not occur if the limb is denervated (Schwann cells of the nerve produce a signaling molecule necessary to induce regeneration).

Inactivation of macrophages also disturbs regeneration.

Regeneration by epimorphosis is similar to the embryonic development of limbs. Many signaling pathways participate both in the embryonic development and regeneration. Activation of some of those causes some regenerative processes in the animals which are unable to regenerate, e.g. β-catenin activation caused partial wing regeneration in the chicken embryo (Yasuhiko Kawakami et al., 2006).

Compensatory growth or endomorphosis — the part of an organ left after amputation enlarges as a result of cell enlargement and division. For example, if one kidney is missing, the other one becomes bigger to perform the functions of two kidneys (Fig. 25).

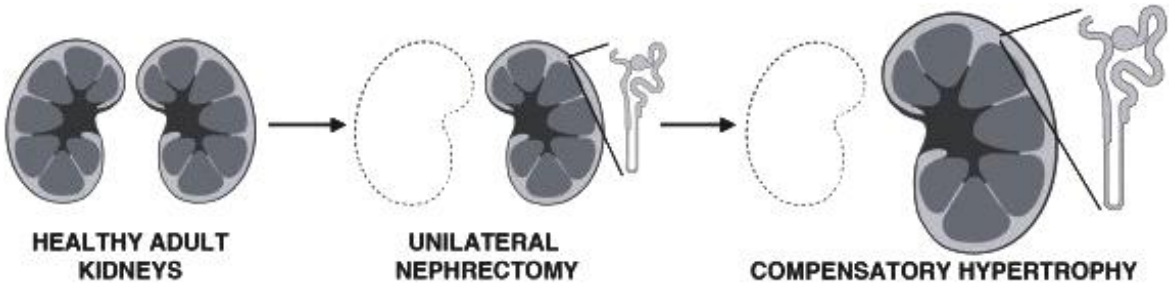


Figure 25. Compensatory hypertrophy

Such enlargement of organs is based on two processes:

– **Hypertrophy** — increase in the volume of an organ or tissue due to the enlargement of its cells.

– **Hyperplasia** — increase in the volume of an organ or tissue due to the cell proliferation.

Reparative regeneration of various organs and tissues in humans and mammals is manifested differently.

When skin, connective tissue, or mucosa are damaged, the regenerated tissue is similar to the lost one. When skin is damaged, both the dermis and the epidermis regenerate.

However, the rate of regeneration of connective tissue is faster than that of the epidermis, so after large skin lesions, scar connective tissue is formed in the center of the damage.

When striated muscle tissue and cardiomyocytes are damaged, connective tissue develops in their place, but the neighboring cardiomyocytes increase in volume, which leads to partial restoration of myocardial function.

TRANSPLANTATION

Organ transplantation is a medical procedure in which an organ or tissue (it is called *graft* or *transplant*) is removed from one body (from a *donor*) and placed in the other body (to a *recipient*), in order to replace a damaged or missing organ.

Important points in the history of transplantation were:

• Development of the technique of vascular suture and the transplantation of blood vessels (Alexis Carrel, The Nobel Prize 1912), Vladimir Demikhov's work with animals that included: first artificial heart, heart transplant, lung transplant, heart-lung transplant, liver transplant, mammary — coronary anastomosis, head transplant.

• The discovery of the ABO blood group system by Karl Landsteiner, the discovery rhesus factor discovered. This led to the discovery of HLA (human leukocyte antigens) and the role of the immune system in transplant rejection is revealed (Peter Medawar, The Nobel Prize 1960).

• First successful kidney transplant was done by Joseph Murray in 1954.

The first successful heart transplant in humans was done in South Africa by Christiaan Barnard in 1967.

Types of transplantation:

1. Based on the genetic relation of donor and recipient (Fig. 26):

– **Autotransplantation** is the transplantation within the same organism.

– **Isotransplantation** is the transplantation from a genetically identical donor (i.e. from a twin).

– **Allotransplantation** is the transplantation from a genetically non-identical donor of the same species.

– **Xenotransplantation** is the transplantation in which the donor and recipient belong to different genera, families.

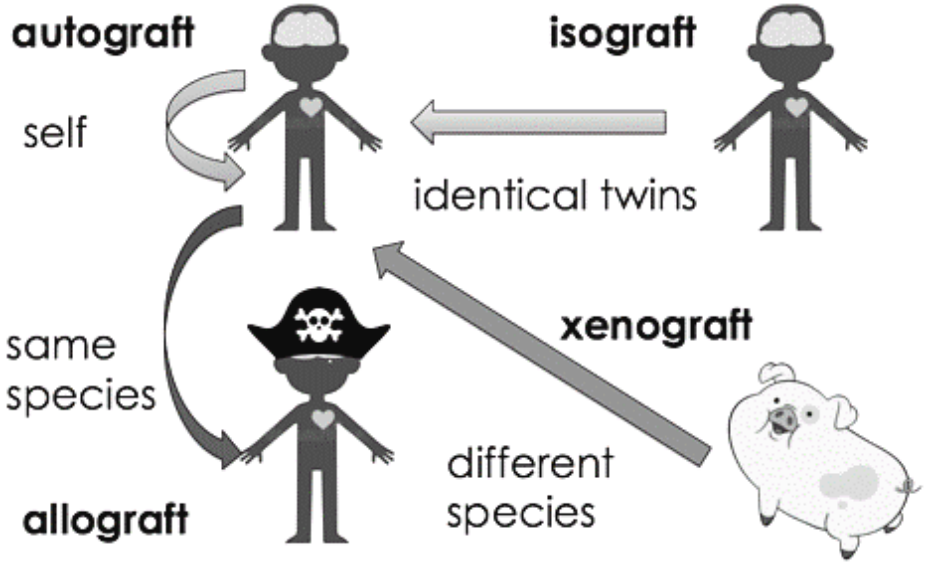


Figure 26. Types of transplant

2. Based on the location of the graft in the recipient:

– **Orthotopic transplantation** is the transplantation of the donor's organ to its native place;

– **Heterotopic transplantation** is the transplantation of the donor's organ to a place that not the normal organ location.

Obtaining the organs for transplantation. Organs for transplantation can be taken from:

– Donation from a living donor. Living donors may donate a kidney, part of the liver, part of the lungs, stem cells, and bone marrow.

– Donation from a dead donor. The organs and tissues which can be used as grafts are kidneys, heart, lungs, liver, pancreas, small intestine, corneas, skin, bone, tendons, cartilage, and heart valves. Donation from a dead donor occurs after brain death.

Brain death is irreversible brain damage and loss of brain function, but other organs can still work and are kept functioning by life support. It should be distinguished from *biological death* (permanent cellular damage, resulting from lack of oxygen, that is not reversible) and *clinical death* (reversible cessation of blood circulation and breathing).

– Donation from genetically engineered animals. This practice is under investigation. The domestic pig is the optimum donor for such transplants.

However, xenogeneic transplantation from pigs to humans involves high immune incompatibility and a complex rejection process.

The rapid development of genetic engineering techniques enables genome modifications in pigs that reduce the cross-species immune barrier.

In 2022, a heart from a genetically modified pig was transplanted to 57-year-old patient. The patient lived with the heart for almost 2 months.

In 1984, a heart from a baboon was transplanted to a newborn girl who was born with heart malformations. Though she died 21 days after the procedure, she lived weeks longer than any previous recipient of a non-human heart.

Growing organs in the laboratory is still under research. So far only organoids were obtained from stem cells.

Organoids are tiny, self-organized three-dimensional tissue cultures that are derived from stem cells. They do not have the architecture of the original organ.

Organoids can be used for fundamental medical researches, but are not yet applicable in practical medicine. However, these studies may lead to growing artificial organs in the future.

3D-bioprinting is the utilization of 3D printing-like techniques to combine cells, growth factors, and biomaterials to fabricate biomedical parts that maximally imitate natural tissue characteristics. This practice is under investigation. In 2017, 3D-bio printed ears were transplanted to children with congenital ear defects in China.

TISSUE INCOMPATIBILITY

Tissue incompatibility is the complex immune response to foreign cells, tissues, or organs. The immune system of the recipient strives to damage the foreign cells of the transplant. This is the cause of transplant (graft) rejection.

– Major histocompatibility complex (MHC) is a group of protein markers that aid in the ability of the immune system to recognize its own cells and distinguish them from foreign pathogens.

– Human MHC genes are situated in the p arm of the 6th chromosome.

– Human MHC are highly polymorphic due to numerous alleles of these genes.

Measures to overcome tissue incompatibility:

1. Selection of donor. The choose of the donor having matching antigens (primarily for the locus D) allows to increase successful graft retention. Complete retention is possible only in monozygotic twins.

2. Suppression of the immune response. Therapy with immunosuppressive drugs, corticosteroids anti-lymphocyte serum, X- and gamma-rays.

CHAPTER 5
INTRODUCTION TO PARASITOLOGY

ORIGIN AND AGE OF PARASITISM. CRITERIA OF PARASITISM

According to the study of Yevgeny Pavlovsky, "parasites are animals that live at the expense of individuals of other species; they are closely associated with these species biologically and ecologically during a long or short period of their life cycle."

Criteria of parasitism:

1. Spacial relations with the host.
2. Feeding at the expense of the host.
3. Pathogenic action on the host.

The **host of a parasite** is an organism that provides the parasite with inhabitation and food and is harmed by it. A specific habitation is characteristic of the parasite. Primary habitation is the host's organism. It actively reacts to the presence of a parasite. The secondary habitation is the external environment. The host is a link between the parasite and the environment.

Parasitism is the most common form of *symbiosis*: all viruses, many bacteria, some kinds of fungi, and higher plants are parasites. Parasites are 10 000 species of protozoans, 7000 species of arthropods, 20 000 species of helminths. Some classes include only parasites — Sporozoa, Flukes, and Tapeworms.

Diseases caused by various parasites have different names:

– those caused by viruses and bacteria are called *infections* (flue, hepatitis, tuberculosis, etc.);

– by protozoans and helminths are *invasions* (ascariasis, taeniasis, enterobiasis, etc.);

– diseases caused by arthropods (ticks, insects) are *infestations* (pediculosis, myiasis, scabies, etc.).

There are various biological interactions between species in the nature:

– *Competition* is the interaction of organisms that require the same conditions or resources of existence.

– *Predation* — interactions of organisms of different species in which one predator organism kills the other one — prey — and uses it for feeding.

– *Antibiosis* (Greek anti — against, bios — life) — interactions of organisms of different species in which metabolites of one of them suppress the development of another.

An example is the production of antibiotics by mildew fungi, and secretion of phytoncides (Greek phyton — plant, caedo — kill) by some higher plants (pine, cedar, onion, garlic). Antibiotics and phytoncides are used in medicine to treat various diseases.

Symbiosis is any form of interaction between different species. The term was introduced into biology by de Barry in 1879 (Greek sym — near, bios — life).

The following forms of symbiosis are distinguished:

– *synoikia* or *hosting* (Greek syn — together, oikos — house) — one species uses the other one as habitation without causing any harm or benefit (cancroid sea acorns on a mollusks' shells);

– *commensalism* (French commensal-co — eater) — permanent or temporary co-habitation of individuals of different species in which one of them eats food remains or excretion products of the other one without any harm (shark and sticking fish);

– *mutualism* (French mutuus — mutually beneficial) — mutually beneficial co-habitation of organisms of different species;

– *parasitism* (para — near; sitos — feeding) is antagonistic symbiosis.

The most common form of symbiosis is one variety of interspecies relations.

Age of parasitism. Theoretically, parasites presumably could appear together with protists as parasitic bacteria were found in the amoebae. Multicellular parasites existed in the Paleozoic era: ichnolites of the stems of sea lilies (Echinodermata) had gall-like growths caused by nematodes.

Origin of parasitism:

1. *Predator → ectoparasite*. Medicinal leeches are temporary ectoparasites for human; the leech can be predators for small animals as it sucks a great amount of blood and the animal dies.

2. *Free-living organism → attached mode of life → ectoparasitism*. Free-living cirripedia may pass to an attached mode of life. They attach to underwater parts of wooden buildings or the bottoms of ships. They pass to ectoparasitism if they attach to living objects — shells of mollusks or fish bodies.

3. *Commensalism → ectoparasitism*. *Commensalism → endoparasitism*. If a commensal settles on the body coverings of the animal, it may become an ectoparasite. It becomes an endoparasite when it gets inside the organism (in body cavities connected with the environment). Entamoeba coli is an endocommensal in the human organism.

4. *Transit through the digestive tract → endoparasitism* (larvae of domestic fly).

CLASSIFICATION OF PARASITES AND THEIR HOSTS

Classification of parasites:

1. According to interaction with the host:

– *obligate* parasites — parasitism is the only possible way of living for such species (Ascaris, lice);

– *facultative* parasites are free-living organisms that can get into a living organism and behave as parasites (larvae of the domestic fly);

– *hyperparasites* or superparasites are parasites of parasites (bacteria in parasitizing protozoans).

2. According to the location in the host:

– ectoparasites inhabit body coverings of the host (lice, fleas);

– endoparasites live inside the host's organism:

a) intracellular parasites (toxoplasma);

b) cavity parasites (Ascaris);

c) tissue parasites (liver fluke);

d) intradermal parasites (itch mite).

3. According to the duration of the interaction with the host:

– permanent parasites spend their entire life cycle (or most stages of development) in a host, using it as a source of food and habitat (e.g. Ascaris); they may have one or several hosts;

– temporary parasite they live on the host and feed at its expense at a certain stage of the life cycle, or attack it only for feeding (e.g. larval parasitism of a botfly larva, imago parasitism of mosquitoes and fleas).

Classification of hosts:

1. According to the parasite's life stage:

– *principal* (definitive) host — a host where a parasite maturates and reproduces sexually (human for *Taenia solium*);

– *intermediate* host — a host where a parasite lives for a period and reproduces asexually (human for malaria parasite);

– *supplementary* or *accessory* host — additional intermediate host (fish for a cat liver fluke).

– *reservoir* host — in this host invasive stage of the parasite accumulates (predatory fish for larvae of *Diphyllobothrium latum*).

2. According to conditions of the parasite's development:

– *obligate* (or natural) host provides optimal conditions for the parasite's development and there is biocenotic contact (natural ways of invasion) — the human for the *Ascaris lumbricoides*;

– *optional* (or permissive, accidental) host: there is biocenotic contact, but no normal biochemical conditions for the parasite's development (the human for the *Ascaris suum* — affects pigs);

– *potential* host can provide normal biochemical conditions for the development of the parasite, but there is no biocenotic contact — no ways for invasion (Guiney pig for trichinella).

The parasite-host system. Parasitism is an ecological phenomenon. Ecological Parasitology studies the interrelations of parasites and their populations with each other, the host's organism, and the environment. The parasite-host system includes one host individual and a parasite (or an entire group of parasites) of the same species.

Conditions necessary for the formation of this system:

1. Contact between the parasite and the host.

2. The host must provide proper conditions for the development of the parasite.

3. The parasite must resist the host's protective reactions.

The system's evolution tends to improve its stability, reach equilibrium, and diminish antagonism between the parasite and the host. The antagonism is lessened due to co-adaptation:

– in the parasite — morphologic and biologic adaptations;

– in the host — a complication of defense mechanisms.

Directions of evolution are also different (co-evolution):

– in the parasite — a complication of adaptation mechanisms to the host;

– in the host — improving all defensive reactions (to destroy the parasite).

TRANSMISSION ROUTES OF PARASITES

Pathogens of diseases have four basic ways of entering the body. They can be **engulfed**:

1. *Alimentary* (fecal-oral) route — orally with food and water (eggs of helminths, cysts of protists).

2. Infecting stages of parasites can be *inhaled*: *respiratory* (droplet) — through the respiratory tract (cysts of some Amoebae, some viruses, and bacteria).

3. Infecting stages of parasites can enter the body *across the skin* or mucous membranes during *contacts*: indirect and direct contact — contact with a sick one through household goods (itch mite) or with his body surface.

4. *Sexual* — in sexual contact (Trichomonas vaginalis).

5. Other ways are more diverse. As a rule, they are associated with direct or indirect contact with **blood** or with uncommon transmitting factors.

6. *Vertical* (*transplacental*) — from mother to fetus (toxoplasma, malaria parasite).

7. *Iatrogenic* — due to medical procedures, for example, transfusion of infected blood or usage of unsterile surgical instrument (trypanosomes, malaria parasite).

8. *Vector-borne* — carriage of a pathogen by an arthropod (trypanosomes, malaria parasite). **Vector** is an arthropod that carries a pathogen causing a disease of a host.

– *Biological vector* is an arthropod in which a parasite multiplies or develops to become infective (malaria pathogen developing in the mosquito).

– *Mechanical vector* is an organism where the pathogen of a disease does not multiply or develop, but is only carried on the body surface or appendages.

ADAPTATIONS TO PARASITISM

Parasites are highly specialized organisms, maximally adapted to their inhabitation and way of living.

Morphological and physiological adaptations of parasites:

a) progressive adaptations:

– enlargement of the body (up to 20 m in tapeworms);

– high development of the reproductive system;

– hermaphroditism;

– fixation organs (adhesive discs of Giardia lamblia, suckers of flukes, bothria or hooks of tapeworms, claws of lice, etc.);

– integument that protects the parasite from host's defense;

– molecular mimicry — similarity of proteins of the parasite and the host;

– excretion of anti-enzymes.

b) regressive adaptations:

– simplification of sense organs — endoparasites have only tactile and chemical sense organs;

– simplification of the organ systems — the absence of alimentary tract in tapeworms.

Biological adaptations are associated with structural peculiarities of the reproductive system, reproduction, and life cycles of parasites:

– high fertility (Taenia solium excretes 100 thousand eggs with every mature segment, an Ascaris — 250 thousand eggs per day);

– diversity of asexual reproduction (schizogony in malaria parasite, polyembryony in flukes);

– migrations within the host's organism (larvae of Taenia solium and Ascaris lumbricoides);

– complex life cycles with alternation of hosts.

The results of interactions of the parasite and the host on the level of the organism may be different: death of the parasite, death of the host, and carriage of the parasite.

PATHOGENIC ACTION AND SPECIFICITY OF PARASITES

Pathogenicity is the ability to cause disease. It depends on:

– genotype of the parasite, its species;

– host's age (children and old people are more susceptible to invasion);

– diet regimen (improper diet weakens the organism and contributes to increasing the number of parasites in the organism and their sizes, reduces the terms of their development);

– dose and degree of invasion (the more eggs or larvae get to the host's organism, the more severe the course of the disease is);

– resistance of the host;

– presence of other parasites and diseases.

The *specificity* of the parasite is the degree of a historically formed adaptation to certain hosts. Its types are:

– *hostal specificity*: monohostal parasites have one species of the host (Ascaris lumbricoides), polyhostal parasites have hosts of several species (trichinella);

– *topical specificity* (a site of parasitizing): Ascaris lumbricoides live in the intestine, head louse — on the hairy region of the head and etc.;

– *age specificity*: enterobiasis is more common for children;

– *seasonal specificity*: outbreaks of amebic dysentery are more typical for the end of spring and summer).

Pathogenic action of parasites:

1. *Mechanic*: parasites harm tissues by their body mass (ball of Ascaris lumbricoides in the intestine, a cyst of echinococcus in the brain), by fixation organs (injury of the intestinal mucous membrane by suckers), impairment of skin, etc. This action is revealed due to a pain syndrome.

2. *Toxicoallergic* action is produced by metabolites of parasites that are antigens; histolysis and decay products of dead parasites. Manifestations of this action: skin eruptions, dermatitis, eosinophilia, allergic reactions.

3. *Absorption of nutrients* and vitamins results in avitaminosis (mainly A and C), loss of weight, and exhaustion.

4. Impairment of the metabolic processes reduces the host's resistance and *increases sensitivity to pathogens of other diseases*.

5. Biologically active substances of some parasites have *immune-depressive effect* on the host.

6. Some parasites stimulate *oncogenesis*: schistosomes may cause cancer of the bladder and rectum.

7. Parasites produce an unfavorable *effect on the course of pregnancy* and the development of a fetus (malaria parasite, toxoplasma, cat liver fluke, etc.).

Response of the host to parasitic invasion. The basis of all reactions is the host's immune response. Allergy is a kind of immune reactivity. The first reaction to a parasite is an attempt to kill it with enzymes, then — to neutralize factors of its "aggression" by proteases, inhibitors of enzymes.

Reactions at the cellular level show as hypertrophy and modification of the shape of affected cells (erythrocytes in malaria).

At tissue level: isolation of the parasite from healthy tissue (formation of a capsule in trichinellosis, formation of pseudocysts in toxoplasmas).

At the organism level: humoral reactions (production of anti-bodies) and various forms of immunity: complete – relative, active – passive, inborn – acquired.

BIOLOGICAL BASIS OF PROPHYLAXIS OF PARASITIC DISEASES

K. I. Skriabin elaborated biological basis of prophylaxis to control parasitic diseases. It is a complex of prophylactic measures based on detailed studying of the pathogen's biology, migration ways, life cycle, and biology of intermediate hosts. It is possible to interrupt any link in the parasite life cycle. Parasitology's final practical aim is protecting humans, animals, and plants from parasitic action and eliminating parasitic diseases.

Diagnosis of parasitic diseases. Accurate diagnosis of parasitic diseases is can be made due to the following methods:

1. Microscopy — detection of different forms of parasites in biological specimens of a patient.
2. Immunological methods — identification of diseases using laboratory techniques involving the interaction of antigens with specific antibodies.
3. PCR — the presence or absence of particular DNA can be confirmed by polymerase chain reaction.

CHAPTER 6
GENERAL CHARACTERISTICS OF THE KINGDOM PROTISTA. PHYLUM APICOMPLEXA, CLASS SPOROZOA

The kingdom Protista, includes eukaryotic, primarily unicellular organisms with animal-like (*Protozoa*), plantlike (*Algae*), or funguslike (slime molds) modes of nutrition.

Inhabitance: almost any environment that contains water (water pond, damp soil, plants, animals including humans). More than 10 000 of 65 000 species are parasites.

The cell of a unicellular protozoan performs the functions of an entire organism. The cell envelope consists of a plasma membrane with an elastic pellicle or denser cuticle. The structure of pellicle varies in different species (for example thickenings and ridges of plasma membrane and other structures). The shape of protozoans can be constant (*Zoomasticota* and *Infusoria*) or changeable (*Sarcodina*). Sizes of cells are from 3 to 150 μm (Fig. 27).

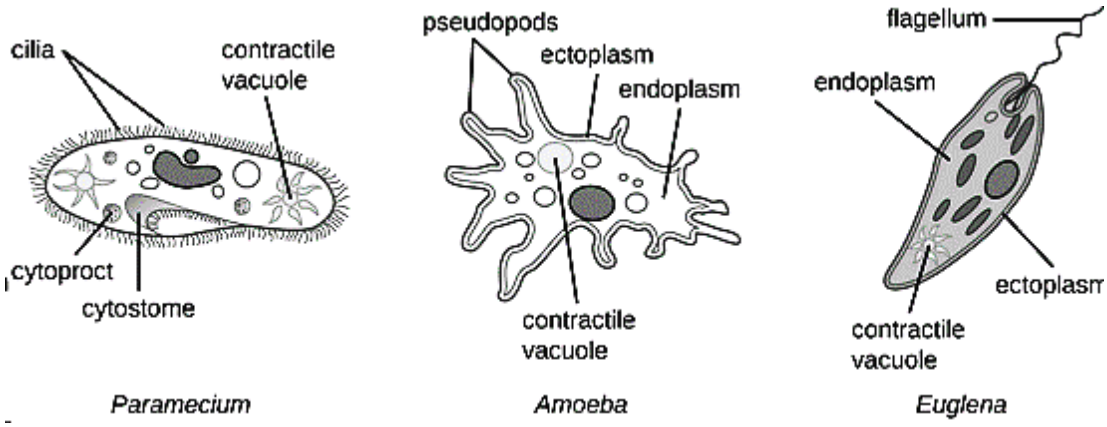


Figure 27. Cytoplasm and locomotory organelles of some free-living protists

There are 2 layers in the cytoplasm:

– *endoplasm* — the dense and usually granulated cytoplasm in the center of the cell;

– *ectoplasm* — liquid and agranular layer of the cytoplasm adjacent to plasma membrane; it contains actin filaments that support the plasma membrane.

There are organelles typical for all cells (mitochondria, ER, ribosomes, Golgi complex, etc.) and those characteristics of only such protists (contractile vacuoles, conoid of toxoplasma and etc.). Organelles of movement are pseudopodia, flagella and cilia.

The majority of protists are heterotrophs. They feed by means of endocytosis, active transport, osmotically, or through the cell mouth (cytostome). The engulfed food particles are enclosed in food vacuoles that merge with lysosomes. The undigested remains of food are removed from the cell by

exocytosis (through any region of the plasma membrane or through the anal pore). Protozoans have contractile vacuoles performing osmoregulation: they remove a surplus of water that flows to the cell by osmosis.

Cells of protozoans contain one or several nuclei. Reproduction is asexual: binary fission or multiple fission (schizogony), though many species have various forms of the sexual process (conjugation or gametic copulation). Conjugation is the temporary pairing of two individuals for the exchange of pronuclei. Gametic copulation is the phenomenon when two individuals transform into haploid gametes and merge into a zygote.

The active motile and feeding stage of protozoans is called a *trophozoite*. In unfavorable environmental conditions, many protozoans can transform into an inactive form called a *cyst*. When cysts are in favorable conditions again, excystation occurs: vegetative form (*trophozoite*) comes out from the *cyst*.

Taxonomy: protists considered in this book belong to the phylum *Sarcomastigophora* (classes *Sarcodina* and *Zoomastigota*), phylum *Apicomplexa* (class *Sporozoa*), and phylum *Infusoria* (class *Ciliata*).

CHARACTERISTICS OF THE CLASS SPOROZOA

All the species of the class Sporozoa are parasites. They do not have locomotory organelles, digestive and contractile vacuoles. The life cycles of sporozoans are complicated and require an alternation of hosts where sexual and asexual reproduction occurs.

Plasmodium spp. Pathogens of human malaria refer to the order Haemosporidia, genus Plasmodium.

There are 5 species of plasmodia causing malaria in humans:

– *Plasmodium vivax* (causes benign tertian malaria).

– *Plasmodium ovale* (causes benign tertian malaria).

– *Plasmodium malariae* (causes quartan malaria).

– *Plasmodium falciparum* (causes malignant tertian malaria).

Plasmodium knowlesi (causes quotidian malaria).

Malaria is common mostly in countries with subtropical and tropical climates.

Life cycle. The human is the intermediate host for the plasmodium while female mosquitoes are principal hosts and biological vectors (Fig. 28).

The parasite undergores asexual phases (*exoerythrocytic* and *erythrocytic cycles*) in humans (intermediate host) and sexual phase *gamogony* with another asexual reproductive phase *sporogony* in mosquito (definitive host).

1. Exoerythrocytic cycle:

• Female mosquitoes of the genus Anopheles transmit the disease. The mosquito injects *sporozoites* into the host while taking a blood meal.

• These parasites are taken by the bloodstream to the liver, where they invade liver cells (hepatocytes) and transform into *trophozoites*.

• The trophozoites grow and in 5–16 days develop into *schizonts which* reproduce asexually by *schizogony* (multiple fission) producing numerous *merozoites*. The invaded cells rupture and the *merozoites* are released to the bloodstream.

• There are no clinical signs and symptoms at this stage.

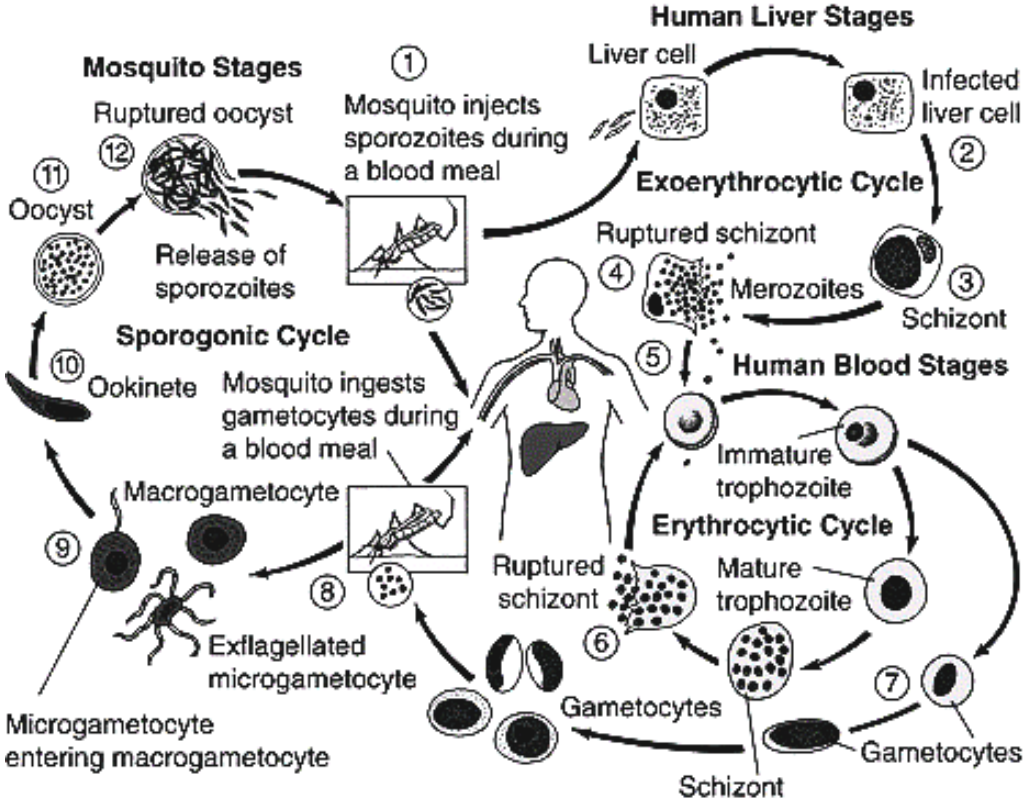


Figure 28. Life cycle of malaria pathogens

2. Erythrocytic cycle:

• The merozoites invade erythrocytes. Within the erythrocyte, a merozoite develops into an *early trophozoite (ring-form trophozoite)*, which then develops into a *mature trophozoite (ameboid-form trophozoite)*.

• The mature trophozoite undergoes schizogony forming a schizont which then produces numerous merozoites.

• The invaded erythrocyte containing merozoites ruptures, releasing them into the bloodstream (this process is *merulation*, at this moment attack of malaria starts).

• Most of these merozoites invade erythrocytes again to repeat the cycle.

3. Gamogony:

• Some of the merozoites develop within the erythrocytes into *microgametocytes* and *macrogametocytes* (male and female gametocytes).

• The sexual phase occurs in the female Anopheles and begins when the mosquito takes a blood meal that contains macrogametocytes and microgametocytes.

• The erythrocytic material surrounding gametocytes ruptures and releases gametocytes into the lumen of the stomach.

• There, a microgametocyte produces microgametes, macrogametocyte maturates into macrogametes.

• Fertilization occurs, zygotes turn into motile and elongated *ookinetes*. The ookinetes invade the midgut wall and develop into *oocysts*.

4. Sporogony:

• Multiple sporozoites develop inside the oocyst. The oocyst grows, ruptures, and releases the sporozoites into the body cavity of the mosquito. The sporozoites are carried to the salivary glands. Such a mosquito becomes able to infect humans.

Routes of transmission. As noted above, infection of human occurs through a bite of a *female Anopheles* mosquito that injects sporozoites with saliva (vector-borne route of transmission).

Infection is also possible in *blood transfusion* (transfusion-transmitted malaria) and *transplacentally* (congenital malaria). In this case, the infecting stage for humans is not sporozoite, but erythrocytic schizont.

Clinical presentation. The incubation period depends on the species of the parasite and may vary from 9 to 40 days.

In the case of *P. vivax* and *P. ovale* infection, exoerythrocytic cycle of some parasites can be delayed (due to hypnozoites — dormant forms of the parasite) and this may prolongate the incubation or cause relapses of the disease many months after recovery.

Classically, malaria causes attacks with periodicity that repeats the durations of the erythrocytic cycles of the parasites:

– every 48 hours (P. vivax, P. ovale, P. falciparum);

– every 72 hours (P. malariae);

– every 24 hours (P. knowlesi).

Though, such strict periodicity is not always observed. When parasites develop in the erythrocytes, numerous toxins accumulate there, and when the erythrocytes rupture these toxins are released to the bloodstream. These toxins cause the symptoms of malaria attack.

The attack usually lasts 6–12 hours and consists of 3 stages:

1. *Cold stage* lasts 1–2 hours, and temperature elevates. Symptoms are shivering and the sensation of cold.

2. *Hot stage* lasts 5–8 hours; symptoms — fever of 40–41 °C, aches of head and lumbar area, sometimes vomiting.

3. *Sweating stage* is the end of the attack when the patient returns to normal temperature. This stage is characterized by profuse sweating.

Malaria may complicate with anemia, jaundice, and renal failure. One of the severe complications is cerebral malaria (commonly caused by

P. falciparum) characterized by impaired consciousness, delirium, and focal and generalized convulsions.

As falciparum malaria causes severest complications, it is referred to as malignant tertian malaria.

Laboratory diagnosis is usually based on finding parasites in blood (thick blood smear).

It is necessary to take blood during the attack or immediately after. Species of plasmodia causing malaria in human have morphological differences that may help to identify them (Fig. 29):

– *Plasmodium vivax* has amoeboid-shaped trophozoite.

– *Plasmodium ovale* is similar to *P. vivax*, but affected erythrocytes have distorted elongated shape.

– *Plasmodium falciparum* has gametocytes of crescent or semi-lunar shape.

– Schizont of *Plasmodium malariae* band-shaped trophozoites.

Other methods used for diagnosis are based on antigen detection or PCR.

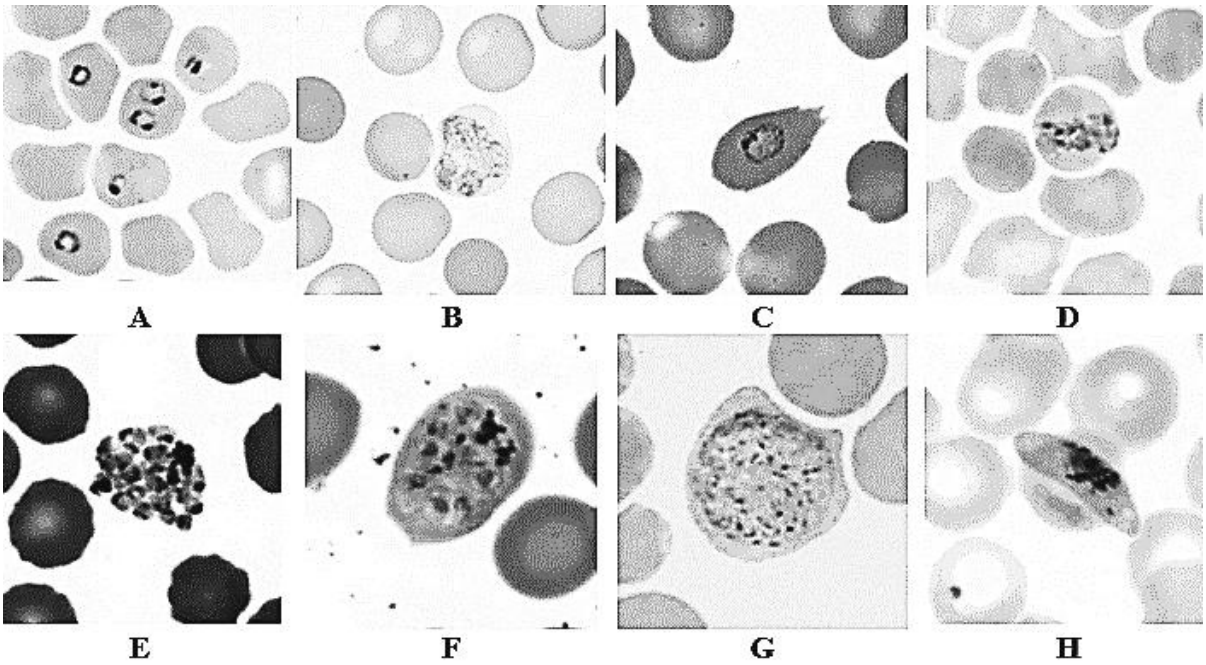


Figure 29. Morphology of malaria parasites in thin blood smear:
A — ring — form trophozoites of P. falciparum; *B* — amoeboid — form trophozoites of P. vivax; *C* — trophozoite of P. ovale; *D* — band — form trophozoite of P. malariae; *E* — schizont (morula) of P. vivax; *F* — schizont of P. ovale; G — macrogametocyte of P. vivax; *H* — gametocyte of P. falciparum

Personal prophylaxis: prevention of mosquito bites (using repellents) and chemical prophylaxis.

Social prophylaxis: revealing and treating sick people and carriers, hygiene education, elimination of mosquitoes of g. Anopheles.

Fighting mosquitoes includes the following directions:

1. Protection from bites — wearing covering — up clothes, usage of repellents, nets on windows; zooprophylaxis — making biological barriers (cattle — breeding farms) between places of mosquitoes' reproduction and dwelling houses, etc.).

2. Elimination of adult mosquitoes — dispersion of insecticides in places of wintering of mosquitoes (basements, garrets, cattle yards).

3. Elimination of larvae:

– drainage of small water ponds having no economic significance;

– using insecticides;

– shading water reservoirs with trees;

– drainage of mashes, deepening of reservoirs, straightening of a river — beds;

– dispersion of mineral oils over the surface of water reservoirs (they block spiracles of larvae)

– raising gambusia fish which feeds on the larvae.

TOXOPLASMA GONDII

Toxoplasma gondii is the pathogen of *toxoplasmosis*. It belongs to the class *Sporozoa*, order *Coccidia*. According to World Health Organization reports toxoplasmosis is present in every country and rates of people having antibodies to the parasite range from less than 10 % to over 90 %.

Morphology (Fig. 30): tachyzoites have a crescent shape, sizes 4–7 × 2–4 μm. Toxoplasma is an intracellular parasite (i.e. exists inside the host's cells).

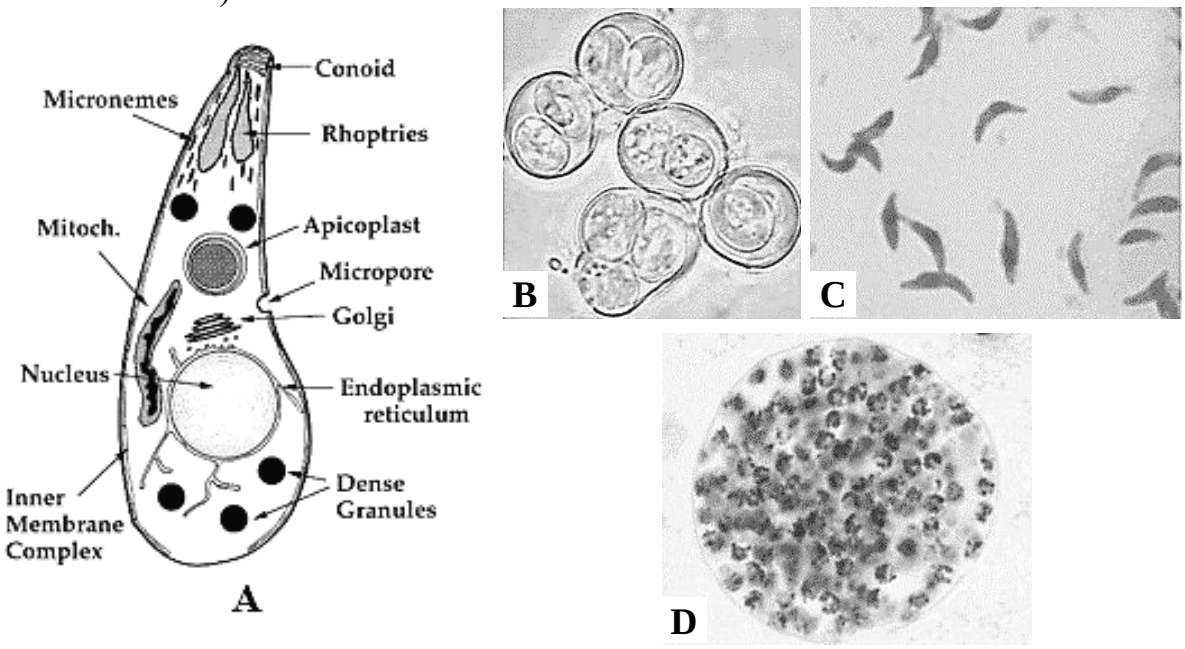


Figure 30. Morphology of T. gondii:
A — diagram; *B* — oocysts; *C* — tachyzoites; *D* — tissue cyst

One end of the cell is sharpened and has a conoid which provides entrance of the parasite to the host cell, and the other end is rounded. The membrane is double, the nucleus is large.

Life cycle. The only known definitive hosts of toxoplasma are representatives of the family Felidae (cats, lynx, etc.). Intermediate hosts are probably all warm-blooded animals including humans (Fig. 31).

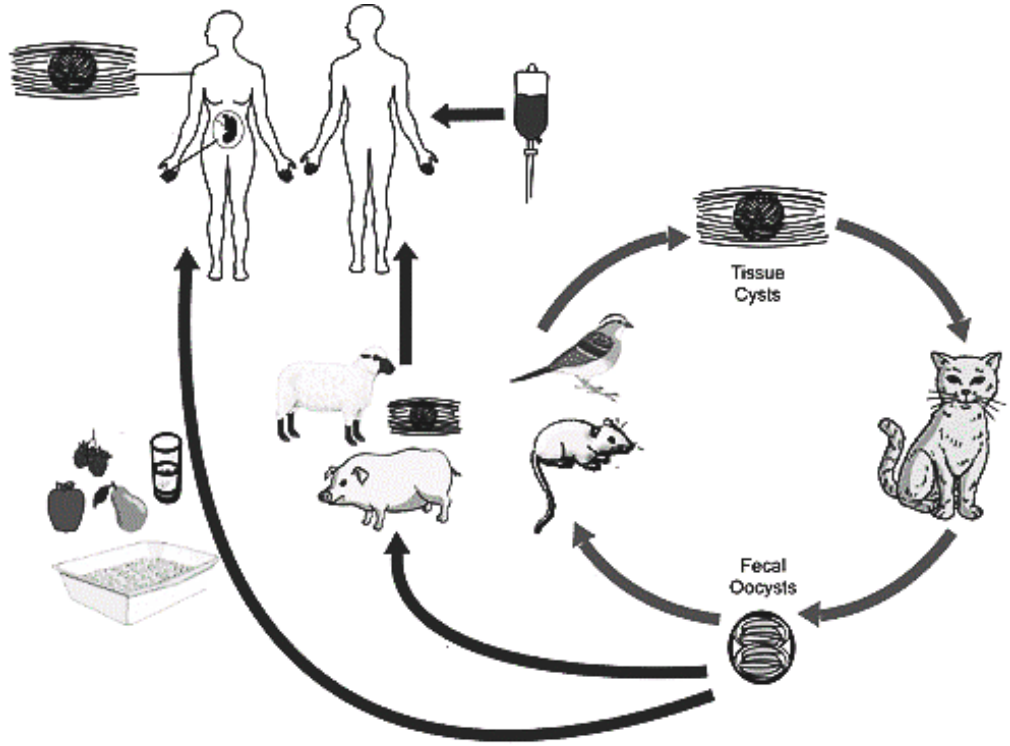


Figure 31. Life cycle of T. gondii

In a definitive host, *T. gondii* multiplies in epithelial cells of the small intestine.

1. At first they multiply asexually and then start sexual reproduction.

The sexual reproduction leads to formation of oocysts which are then released into the intestinal lumen and passed into the environment with the feces.

In the environment the fecal oocysts continue their development.

Each infectious oocyst contains two sporocysts, each containing four sporozoites.

In an intermediate host, the parasites undergo two phases of asexual development.

2. The first phase is the rapid multiplication of tachyzoites inside many different types of host cells.

3. The second phase is the formation of tissue cysts containing bradyzoites which multiply slowly (it is the terminal developmental stage in the intermediate host).

4. Most of the tissue cysts affect the central nervous system, skeletal and cardiac muscles and eyes, though they can be formed in visceral organs.

T. gondii has 3 infectious stages in the life cycle:

– Tachyzoites (contained in tissues of the intermediate hosts);

– Bradyzoites (contained in tissue cysts);

– Sporozoites (contained in fecal oocysts).

All these stages are infectious for both definitive and intermediate hosts.

Routes of transmission:

– Ingestion of oocysts from the environment;

– Ingestion of tissue cysts contained in raw or undercooked meat;

– Vertically from mother to fetus;

– By blood transfusions or organ transplantation.

Clinical presentation. Acquired toxoplasmosis is usually asymptomatic. Some patients may have flu-like symptoms. Symptoms usually resolve within a few weeks to months. Immunodeficient patients (for example those with AIDS) have a severer course of disease.

Primary infection in a pregnant woman can cause severe and disabling disease in the developing fetus (congenital toxoplasmosis) or miscarriage. Symptoms are chorioretinitis, blindness, hydrocephaly, encephalitis, mental retardation, and enlarged liver, and spleen.

Laboratory diagnosis. Serological analysis (measurement of antibodies in the blood of sick people). Other methods that can be used are microscopy of tissue samples, and PCR.

Personal prophylaxis: observing rules of hygiene after contact with cats, non-eating of raw and undercooked meat, boiling milk, observing rules of working with animal carcasses.

Social prophylaxis: prevention of contamination of the environment and water sources with cat feces, hygiene education. Examination of pregnant women is necessary for prophylaxis of congenital toxoplasmosis.

CRYPTOSPORIDIUM PARVUM

Cryptosporidium parvum is the pathogen of *cryptosporidiosis*.

The organisms live in the brush border underneath the cell membrane of the small intestine and respiratory epithelium of a number of mammals, including humans. Acquisition is by ingestion of the oocyst usually in contaminated drinking water.

Epidemiology. Cryptosporidium is cosmopolitan in distribution, occurring in a wide variety of hosts such as primates (including humans), cattle, sheep, rodents, and birds.

Several distinct species of Cryptosporidium have been described. Cryptosporidium parvum is the most dominant species in nature.

Therefore, a large number of hosts can act as reservoirs. None of the purification chemicals used in municipal water treatment plants is effective against the oocysts.

Filtration is the best means of reducing the number of oocysts in public drinking water.

Morphology. The morphological characteristics of Cryptosporidium vary between the different stages of the parasite (Fig. 32).

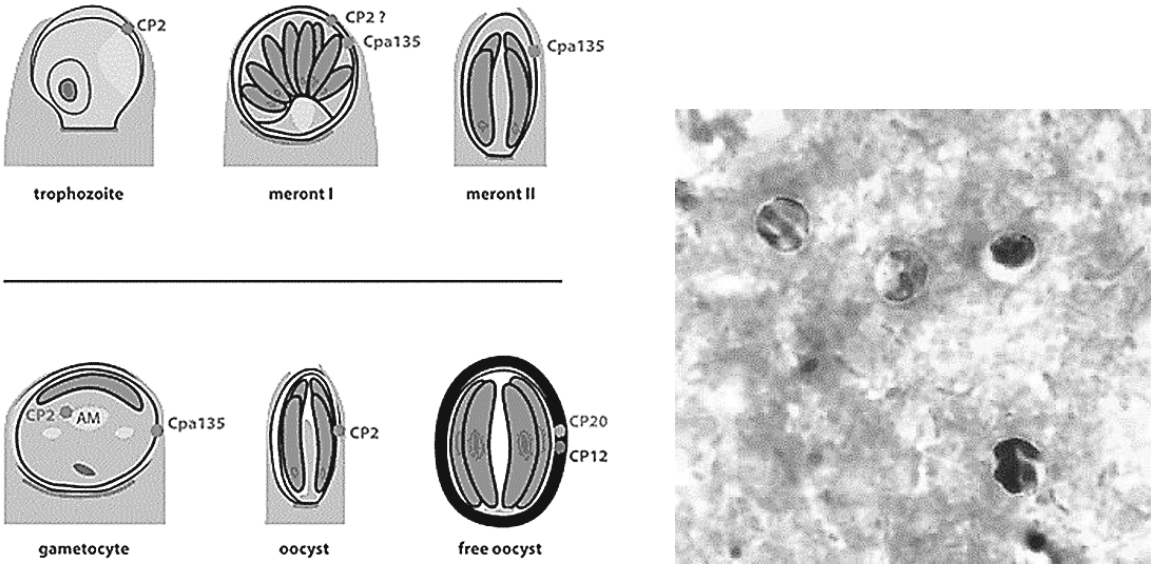


Figure 32. Cryptosporidium sp.:
A — morphology of stages; *B* — oocysts stained with modified acid-fast

The oocysts released into the environment are ovular in shape with a smooth surface. Although it has a thick wall that makes it resistant, it also has a cleft on one side that allows for sporozoites to be released during excystation.

These oocysts measure about 4.2 × 5.4 μm. Sporozoites, on the other hand, measure about 5 × 0.5 μm and are characterized by a rough surface and a pointed apical region as well as a rounded posterior.

Trophozoites, on the other hand, measure between 1 and 2.5 μm in length and are characterized by a smooth surface and hood-like shape.**Life Cycle**. The infective oocysts contain four sporozoites (Fig. 33).

Oocysts are expelled with the feces of a number of infected mammals and, when ingested, sporozoites excyst in the small intestine and attach to the epithelial surfaces of the intestine.

Once enclosed in a parasitophorous vacuole formed from the convergence of microvilli of infected cells, each sporozoite becomes a trophozoite, which, in turn, undergoes merogony (type I meront) to produce several first-generation merozoites.

These erupt from the infected cells into the intestinal lumen.

Each released first-generation merozoite attaches to an uninfected epithelial cell surface where it is enveloped by microvilli and transforms to trophozoite to form additional type I meronts or to form type II meronts.

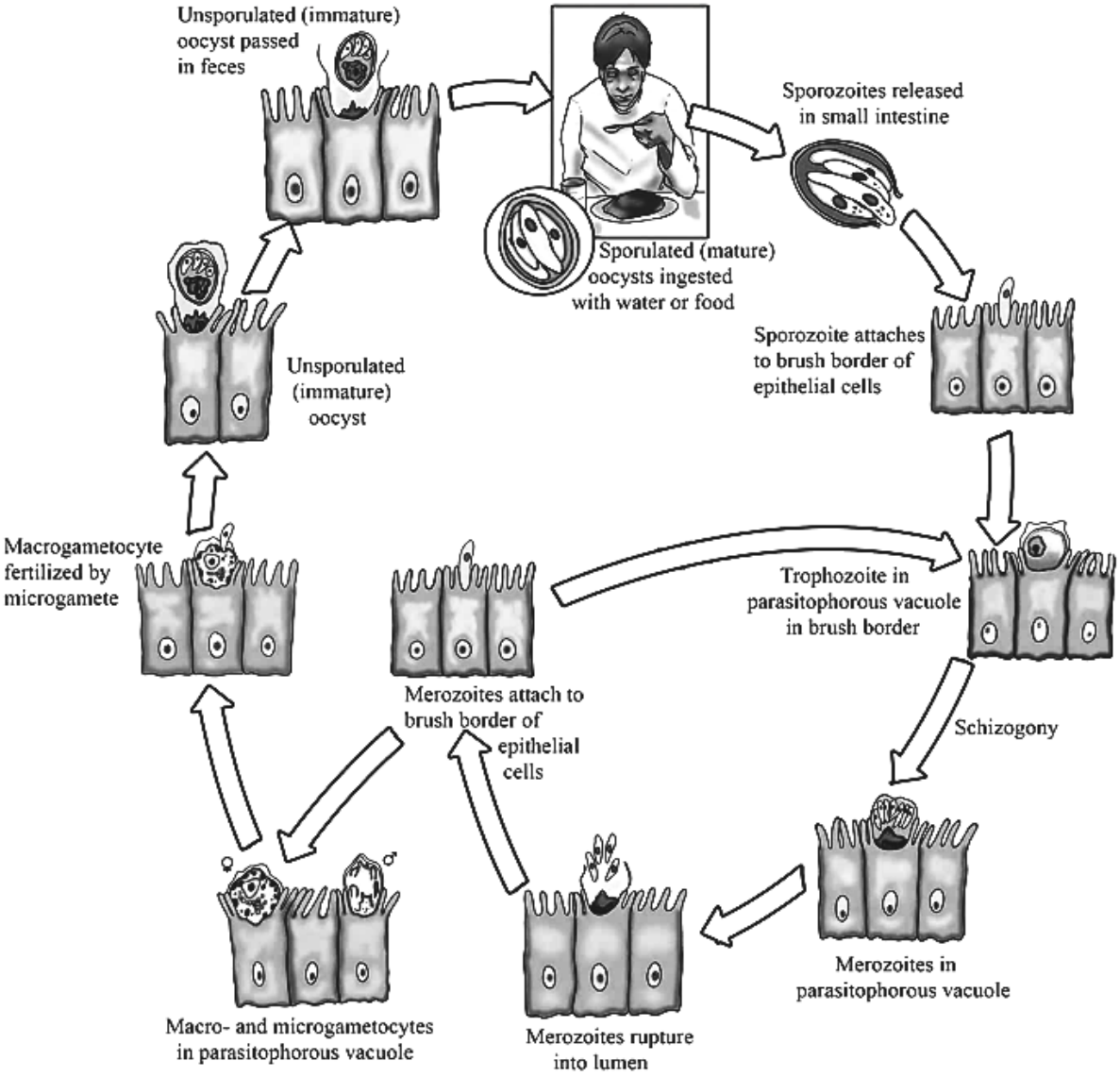


Figure 33. Life cycle of Cryptosporidium

After merogony, the second generation of merozoites are formed, they erupt from the infected cell, and incorporate to the surface of other uninfected epithelial cells. The second-generation merozoites differentiate into microgametocytes and macrogametocytes.

The microgametocytes undergo several divisions producing numerous microgametes, the macrogametocytes transform to macrogametes.

The microgametes burst from the infected cell and enter cells containing macrogametes. Following fertilization, the resulting zygote differentiates into an oocyst, which is then shed with the feces of the host.

The oocyst is infectious upon shedding.

Clinical features. The incubation period is an average of 7 days (range: 2–10 days). Morphological alteration in the intestinal epithelium of infected individuals includes villous atrophy, mitochondrial changes, and increased lysosomal activity in infected cells.

Symptoms vary from none to mild diarrhea to diarrhea with severe cramping, anorexia, nausea, and vomiting. In immunologically competent individuals, the infection is self-limiting, lasting from several days in most patients to several weeks.

In immunologically compromised individuals, however, cryptosporidiosis is a chronic disease lasting months or even years. In extreme cases (e.g., AIDS patients) the disease can be extremely severe with patients losing as much as three liters of fluid daily.

Mortality in such instances may reach 50 %, and secondary extraintestinal complications are common, such as biliary disease and, possibly, pneumonitis from respiratory tree infection.

Diagnosis depends upon the identification of oocysts in the stool. The oocysts are rounded or oval and measure 4.2 to 5.4 μm in diameter. Sporozoites are sometimes visible inside the oocysts, indicating that sporulation has occurred. Other diagnostic methods are immunoassays and molecular methods (PCR).

CHAPTER 7
PHYLUM INFUSORIA AND CLASS CILIATA. PHYLUM SARCOMASTIGOPHORA, CLASSES SARCODINA, ZOOMASTIGOTA

BALANTIDIUM COLI

Balantidium coli is a human parasite of the phylum *Infusoria* and class *Ciliata*. It causes balantidiasis (balantidial dysentery). The disease is common worldwide.

Morphology (Fig. 34): *Balantidium coli* is known for being the largest protozoan parasite of humans (trophozoite — 30–150 × 40–70 μm, cysts — 40–60 μm).

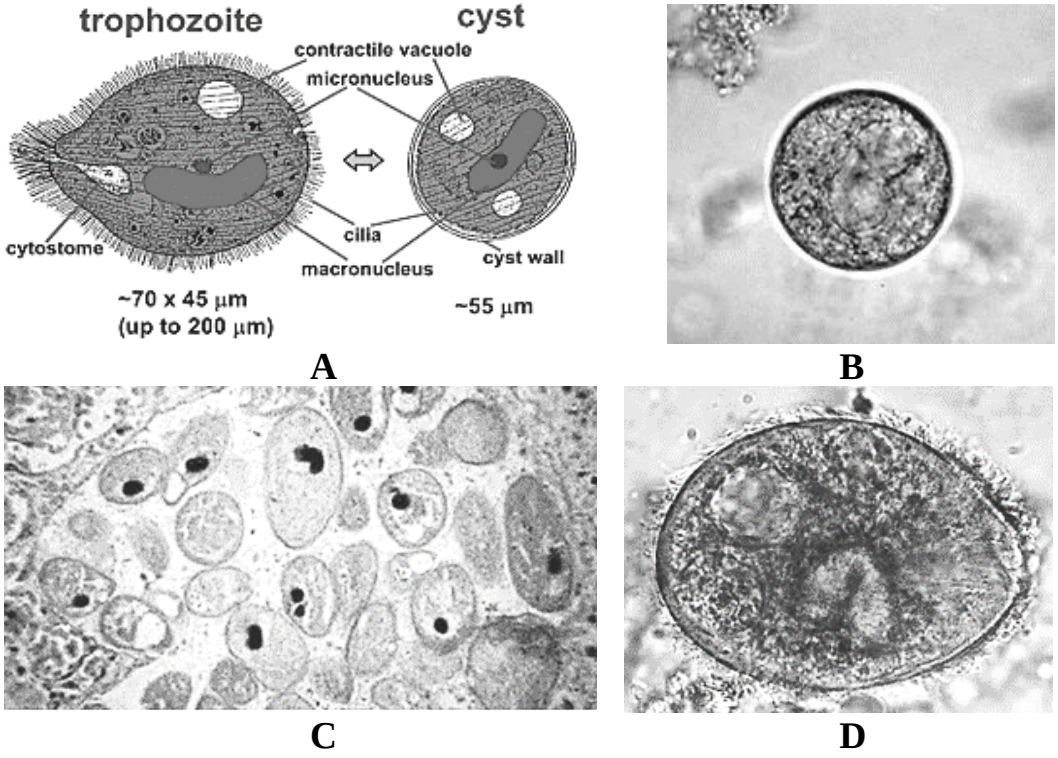


Figure 34. Morphology of Balantidium coli:
A — diagram; *B* — cyst; *C* — parasites in tissues; *D* — trophozoite

There is a peristome at the anterior end, which leads to the cytostome. At the posterior side of the cell is the anal pore (cytoproct).

The elongated macronucleus usually has the shape of a bean or rod, the micronucleus is spherical and is situated near the concave side of the macronucleus. *B. coli* has 2 contractile vacuoles. In the rectum of the host as feces are dehydrated or soon after the feces have been excreted *B. coli* forms cyst (i.e. encystation occurs).

Life cycle. The infective stage of the parasite is a cyst. The host usually becomes infected through ingestion of contaminated food or water (fecal-oral

route). Workers of pig farms are affected more commonly because pigs are natural the source of infection. After the cyst has been ingested, excystation occurs: each cyst produces a trophozoite. This takes place in the intestine of the host. The trophozoites in the lumen of the large intestine multiply by binary fission. Some trophozoites invade the wall of the colon.

Clinical presentation. Many cases are asymptomatic. When symptoms develop, diarrhea with blood, pains in the abdomen, vomiting, and malaise are observed.

Laboratory diagnosis. Microscopic examination of feces to find trophozoites and cysts is commonly used.

Prophylaxis: observing rules of personal hygiene, revealing and treating sick people; protection of the environment from contamination by feces of pigs and sick people, hygiene education.

PARASITIC SARCODINAE (PHYLUM SARCOMASTIGOPHORA, CLASS SARCODINA)

The class Sarcodina includes about 10 000 species. They are the most primitive representatives of the phylum Sarcomastigophora. They have a single nucleus. The body shape of these protists is irregular and changeable as they have no pellicle. Organelles of movement are pseudopodia — temporary projections of the cytoplasm. In unfavorable conditions the protists of the class *Sarcodinae* can form cysts.

Organelles of parasitic *Sarcodinae* are not highly specialized. Feeding occurs by means of endocytosis (engulfment of bacteria, organic substances, erythrocytes, and other cells).

ENTAMOEBA HISTOLYTICA

Entamoeba histolytica (Dysenteric amoeba) is a pathogen of amoebiasis (amoebic dysentery). Cases of the disease are reported everywhere, more commonly in countries with warm climates.

Morphology. *Entamoeba histolytica* exists in two forms: trophozoite and cyst. Cysts (8–16 μm) contain 4 nuclei (Fig. 35).

There are 3 forms of trophozoites of Entamoeba histolytica: minor vegetative form (lat. forma minuta), major vegetative form (lat. forma magna) and tissue form. Forma minuta is capable of movement and feeds on bacteria. It is not pathogenic. Forma magna and tissue form are pathogenic. The forma magna engulfs erythrocytes. Tissue trophozoites are very motile (Table 2).

Life cycle. Amoebiasis is transmitted via the fecal-oral route. Infection occurs by ingestion of cysts. Transmitting factors are contaminated vegetables, fruit, and water. Mechanical vectors of cysts are flies and cockroaches.

Four trophozoites (forma minuta) come out from each cyst in the small intestine and immediately divide forming eight cells. They migrate to the large

intestine. As forma minuta is not pathogenic, the trophozoites can live in the host for a long time (feed, multiply) and transform into cysts. Such a host is a cyst carrier.

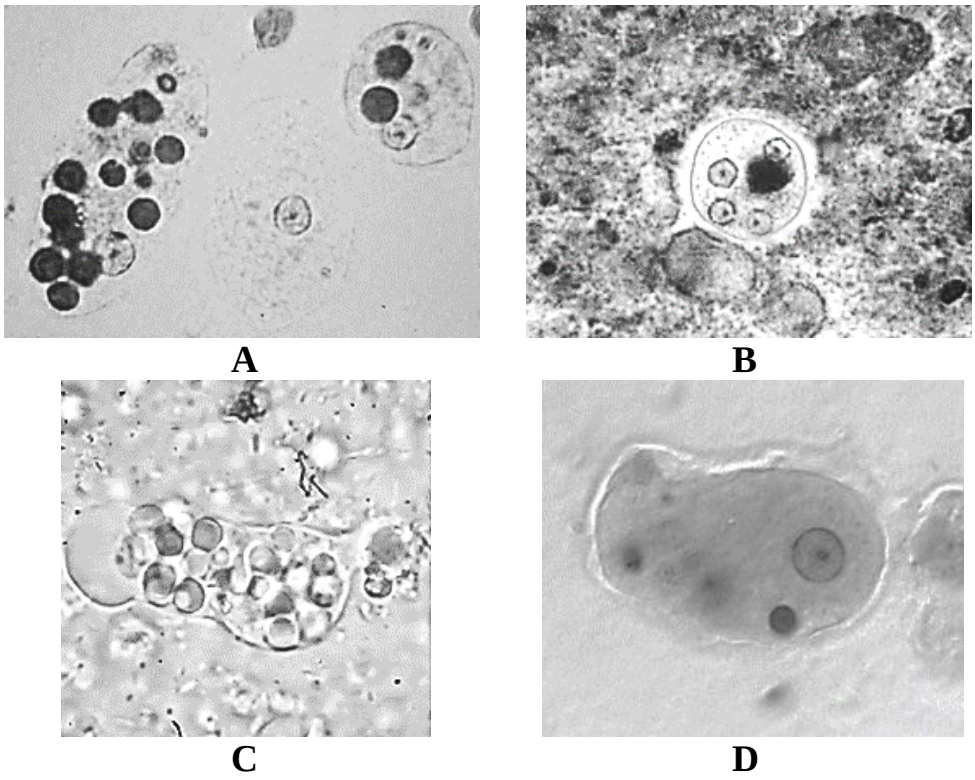


Figure 35. Morphology of trophozoites and cysts of E. histolytica: *A, C, D* — trophozoites; *B* — cysts with four nuclei

Table 2

Trophozoites of E. histolytica

	Forma minuta	**Forma magna**	**Tissue form**
Pathogenic	No	Yes	Yes
Size	12–20 μm	30–40 μm	20–25 μm
Location	Intestinal lumen	Intestinal lumen	Intestinal wall, affected organs
Confirms that person is sick	No, can be found in stool samples of carriers and after recovery	Yes, can be found in stool samples at the acute stage of the disease	Seldom found in stool specimens

When the host's organism is weakened, forma minuta can transform into forma magna and invade the mucous membrane of the large intestine. In the intestinal wall, it transforms into tissue form. Entamoeba causes lysis of epithelial cells causing the formation of ulcers. When reach blood vessels, trophozoites can be carried into the liver, brain, and other organs where an abscess may develop. In remission, the pathogenic trophozoites in the intestinal lumen transform into forma minuta and cysts.

Symptoms can vary from asymptomatic form or mild diarrhea to severe form with bloody diarrhea up to 10 times a day and more, intoxication, and ache on the lower right side of the abdomen.

Complications are amoebic abscess in the liver or sometimes in the lungs, brain, and skin; perforation of the intestine, and purulent peritonitis.

Laboratory diagnosis is made by microscopy of stool in order to find forma magna (or cysts may confirm only the asymptomatic form of the disease), and antigen detection.

Personal prophylaxis: observing hygiene rules (washing hands, washing vegetables and fruits with hot water, protection of food from flies and cockroaches).

Social prophylaxis: finding and treatment of sick individuals and carriers; control over sanitary condition of water ponds, food manufacturers, shops and markets; prophylactic examination of workers of food manufacturers; elimination of flies and cockroaches; hygiene education.

PARASITIC FLAGELLATES (PHYLUM SARCOMASTIGOPHORA, CLASS ZOOMASTIGOTA)

There are more than 8 000 species of *Zoomastigota*. Many representatives of the class are parasites of animals and human. Such protists have one or several flagella (that is why the other name of the class is Flagellata), constant body shape (due to pellicle), and a single nucleus.

Locomotion organelles are flagella and undulating membrane (the fold of cytoplasm). Parasitic species are heterotrophs, their feeding is osmotic. They multiply by longitudinal binary fission. Some species are capable of sexual process copulation.

GENUS LEISHMANIA

The species of the genus cause leishmaniasis. It is a natural-focal disease.

Morphology. Leishmania has 2 forms: promastigote (elongated cell 10–20 μm, has a flagellum) and amastigote (round or oval cell 3–5 μm without flagellum, exists inside cells of the host, Fig. 36).

Pathogens of leishmaniasis are morphologically similar but have biochemical and antigenic differences.

Life cycle. Infection occurs via the bite of an infected sand fly of the genus Phlebotomus (vector-borne route of disease transmission) i.e. the sandflies are biological vectors transmitting the disease. They inject promastigotes during a blood meal (Fig. 37).

In the wound, promastigotes are engulfed by phagocytic cells (macrophages). Promastigotes transform in these cells into amastigotes (an intracellular form of the parasite without flagellum). The amastigotes multiply and proceed to infect other phagocytic cells. Sandflies become infected by

ingesting infected cells during blood meals. In sandflies, amastigotes transform into promastigotes, develop in the gut and migrate to the proboscis.

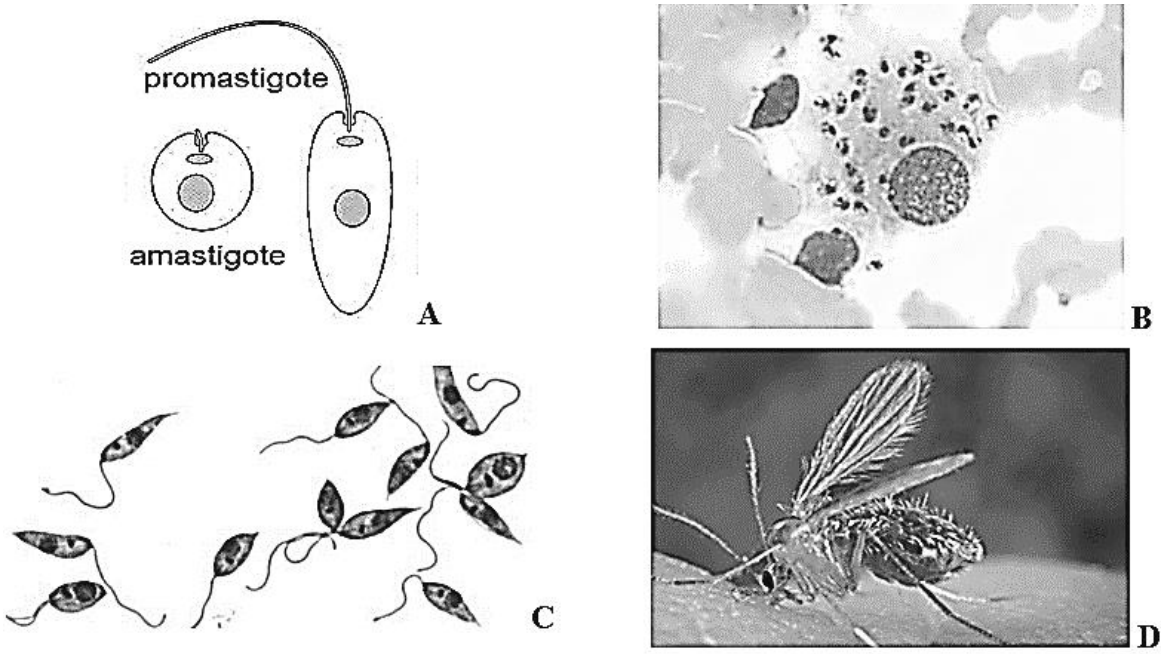


Figure 36. Morphology of leishmania and its vector:
A — diagram of amastigote and promastigote; *B* — aflagellate form of L. infantum in a macrophage; *C* — flagellate form of L. donovani; *D* — the vector of leishmania — sand fly

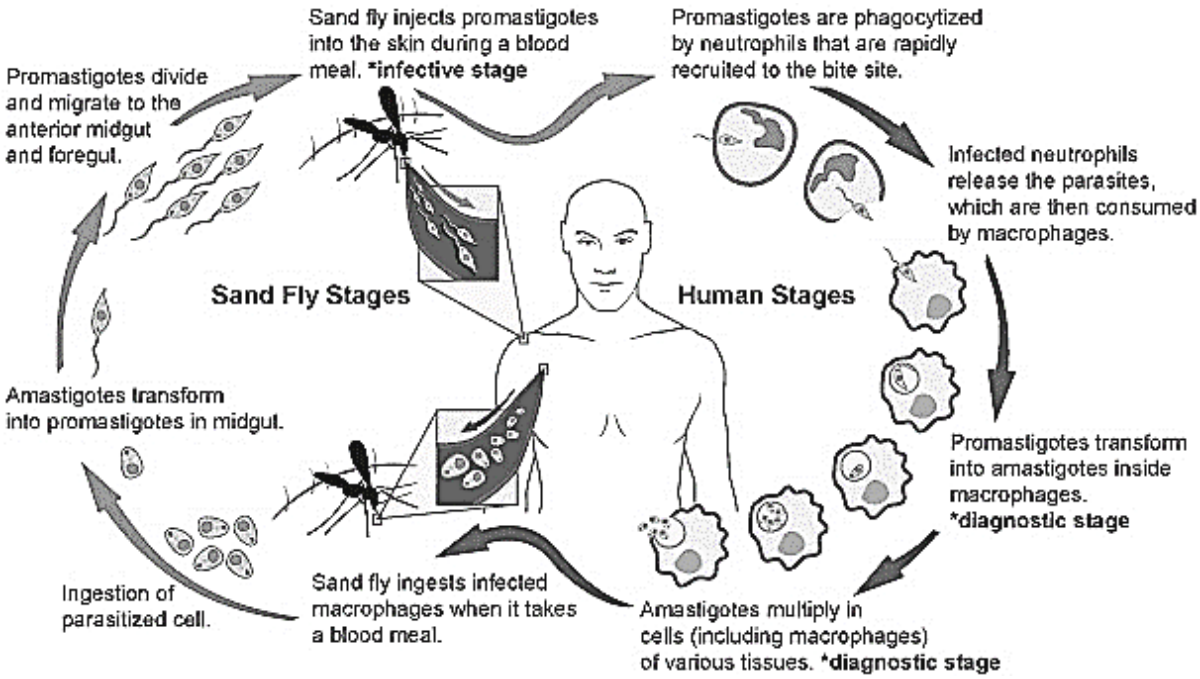


Figure 37. Life cycle of leishmania

Forms of leishmaniasis are (Table 3):

– Visceral leishmaniasis (black disease, dumdum fever, kala-azar, infantile leishmaniasis).

– Cutaneous leishmaniasis (oriental sore).

– Mucocutaneous leishmaniasis (espundia).

Natural reservoirs of *L. donovani* are coyotes, dogs, rodents; those of *L. tropica* are rodents, those of *L. braziliensis* are rodents, primates and sloths.

Prophylaxis: protection from sand fly bites (repellents, insect nets), finding and treatment of sick people, elimination of sandflies and animals-reservoirs of the disease, hygiene education.

Table 3

Forms of leishmaniasis

Form	***Visceral leishmaniasis***	***Cutaneous leishmaniasis***	***Mucocutaneous leishmaniasis***
Pathogen	*L. donovani* *L. infantum*	*L. tropica major* *L. tropica minor*	*L. braziliensis* *L. Mexicana* *L. peruviana*
Affected organs	Visceral organs	Skin	Skin and mucous membranes of the nose and buccal cavity
Clinical manifestation	Sevearest form of the disease. The incubation period is commonly from 2 to 6 months. Symptoms include fever, weight loss, edema, and abdominal swelling, hepatosplenomegaly (enlarged spleen and liver), low count of all blood cells, darkened or gray skin color. Many cases are asymptomatic	Most common form of the disease. It starts as a papule (commonly 2–6 weeks after bite) that transforms into an ulcer with elevated edges and surrounding zone of inflammation; it usually resolves in two months to a year leaving a depressed unpigmented scar	The incubation period lasts 2–3 weeks to 1–3 months. Lesion involves the nasal and buccal mucosa causing destruction and malformations of the cartilage and soft tissues. The ulcerations can involve the nose, pharynx, palate, and lips
Laboratory diagnosis	Microscopy of tissue samples (e.g. bone marrow) allows to find amastigotes in macrophages; PCR	Skin biopsy with the following finding of amastigotes in macrophages; PCR	Skin biopsy with the following finding of amastigotes in macrophages; PCR
Location of foci	Area of the Mediterranean Sea, Middle and South Asia, Africa and South America	South Europe, North and West Africa, Near East, Central, and South Asia	South and Central America

GENUS TRYPANOSOMA

Trypanosoma brucei gambiense (West Africa) and *Trypanosoma brucei rhodesiense* (East Africa) are pathogens of *African trypanosomiasis* (sleeping sickness).

Trypanosoma cruzi (South America) is a pathogen of American trypanosomiasis (Chagas disease). Both diseases are natural-focal and vector-borne. The cell of trypanosoma is elongated (13–40 μm) and curved, flagellum extends along the edge of the undulating membrane (Fig. 38). Feeding is osmotic (i.e. nutrition is transported to the cell across the membrane). Trypanosomes multiply by binary fission.

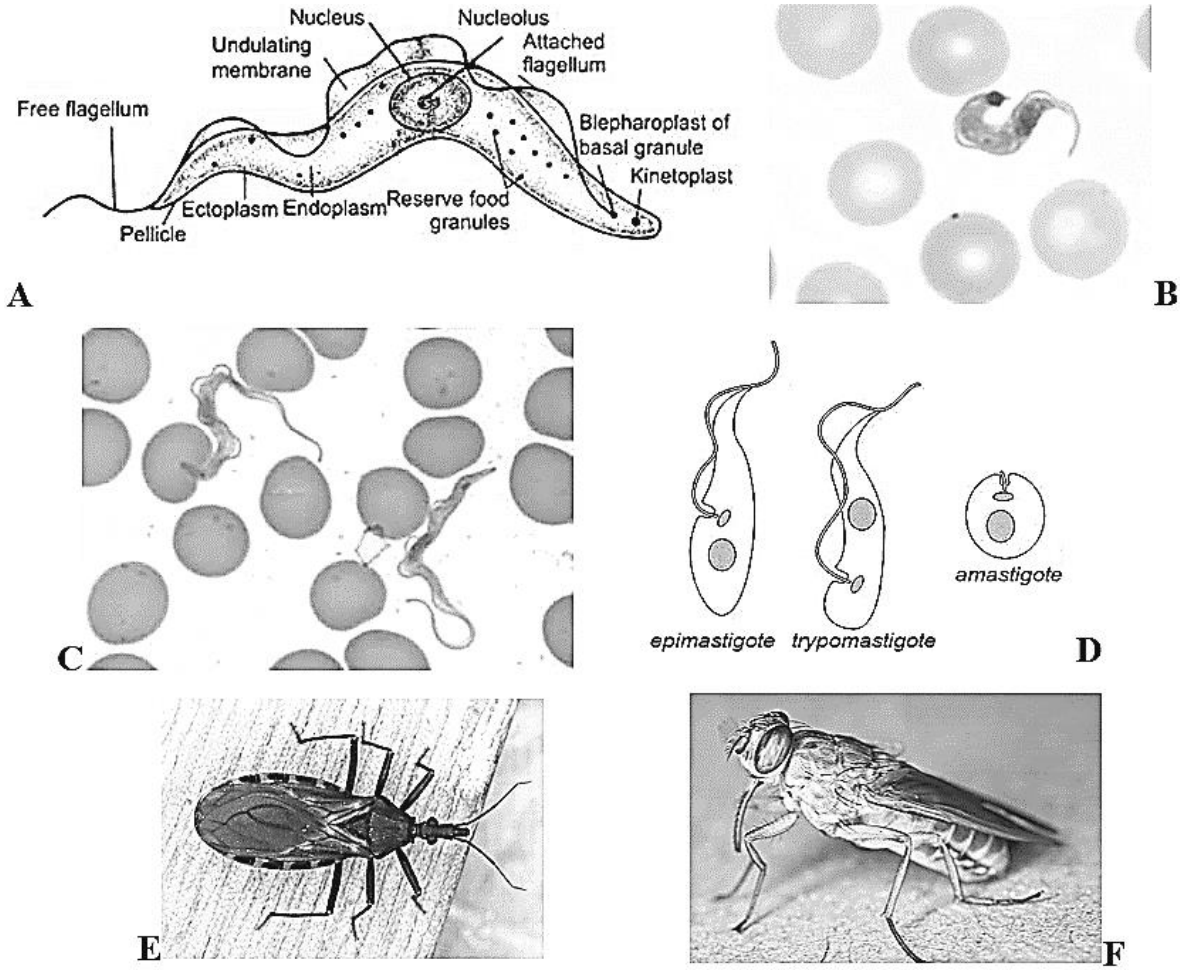


Figure 38. Morphological peculiarities of pathogens of trypanosomiasis:
A — diagram; *B* — T. cruzi; *C* — T. brucei spp; *D* — diagram of trypomastigote, epimastigote and amastigote; *E* — Triatoma infestans; *F* — Glossina palpalis

Life cycle of trypanosomes includes several stages:

– trypomastigote is an elongated cell with long flagellum and undulating membrane. It affects vertebrate hosts and is the infecting stage for them;

– epimastigote is similar to trypomastigote, but its flagellum is shorter and the undulating membrane is smaller. It exists only in the organism of the vector and can transform into a trypomastigote;

– amastigote is an immobile intracellular parasite. It affects vertebrate hosts and can transform into trypomastigote.

TRYPANOSOMA BRUCEI

Life cycle (Fig. 39). The life cycle of *Trypanosoma brucei* includes only extracellular stages. Tsetse flies (flies of the genus Glossina) are the biological vectors transmitting the disease.

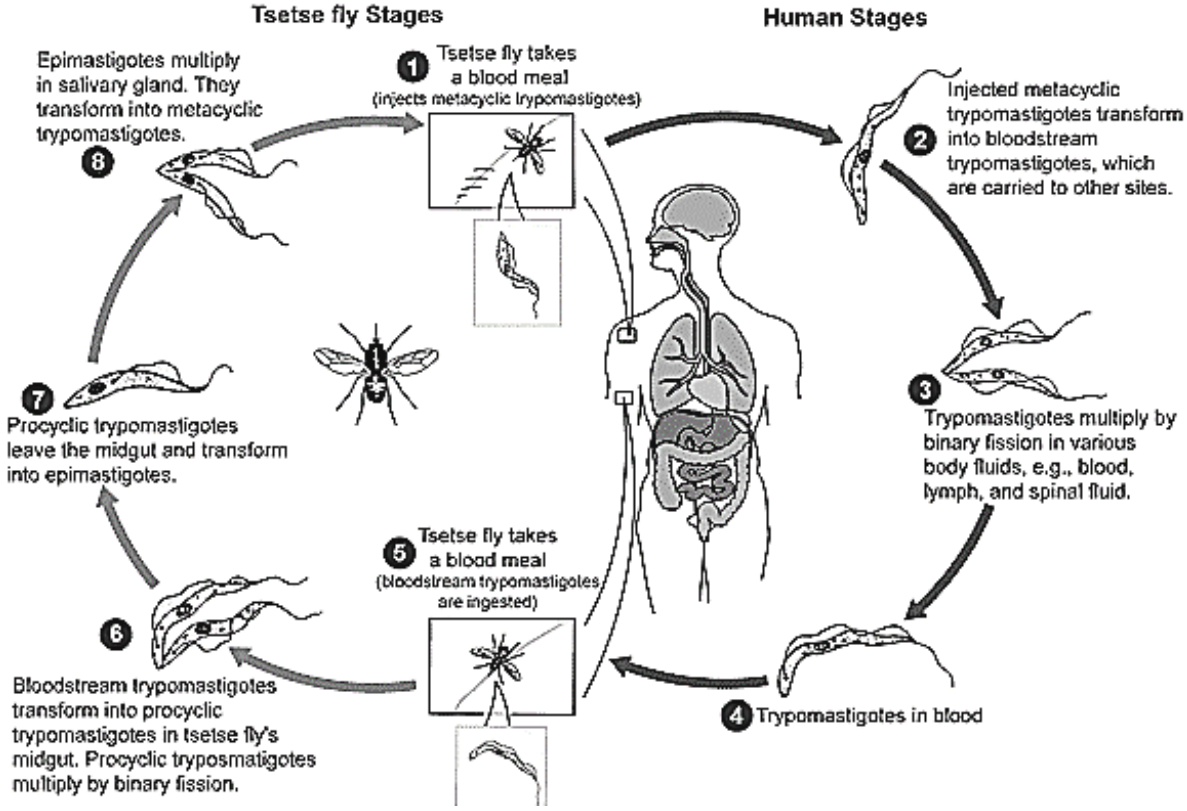


Figure 39. Life cycle of Trypanosoma brucei

An infected fly injects trypomastigotes into the skin during a blood meal on a mammal. Trypanosomes multiply and in 20–25 days pass into the bloodstream. Then the parasites are carried throughout the whole body, and reach lymph and spinal fluid where they continue multiplication by binary fission. The tsetse fly becomes infected when takes a blood meal with trypomastigotes on an infected mammalian host.

The cycle in the fly lasts about 20 days. In the midgut of the tsetse fly, the trypomastigotes multiply by binary fission. Then they leave the midgut, and transform into epimastigotes that reach the fly's salivary glands.

Incubation period is 1–3 weeks to 2 and more years.

Clinical presentation. The course of African trypanosomiasis has two stages:

– The first stage when the parasite is in the peripheral circulation.

– The second one when the parasite invaded the central nervous system.

The disease caused by *Trypanosoma brucei rhodesiense* develops rapidly causing death in several months. Common symptoms: red painful nodular

swelling 2–5 cm in size that develops at the bite site within 2 weeks of the bite, fever, malaise, weight loss, aches in muscles and joints, headache, enlarged lymph nodes in the posterior triangle of the neck. In a few weeks of infection, the parasite invades the central nervous system and causes neurologic symptoms.

The disease caused by *Trypanosoma brucei gambiense* develops slower. At first, there may be only mild symptoms. After 1–2 years, affection of the central nervous system becomes evident. It includes progressive confusion, personality changes, daytime sleepiness (sleeping sickness) with nighttime sleep disturbance, and lack of coordination of voluntary movements. The untreated disease causes death in several years.

Laboratory diagnosis is based on finding trypanosomes in blood smears, lymph node aspirate, and cerebrospinal fluid. Immunological rests (detection of antibodies in the blood serum) can also be used.

Prophylaxis: prevention of tsetse flies' bites, treatment of sick people and carriers, reducing the disease reservoir, hygiene education.

TRYPANOSOMA CRUZI

Morphology of *T. cruzi* is similar to that of *T. brucei*, but it is slightly shorter and shows a characteristic "U" or "C" shape in stained blood preparations.

Life cycle (Fig. 40): *Trypanosoma cruzi* affects humans and animals (armadillos, ant — bears, etc.) that are natural reservoirs the disease. Biological vectors are kissing bugs (genus Triatoma).

When an infected kissing bug takes a blood meal, it releases trypomastigotes in its feces near the site of the bite wound. Trypomastigotes commonly enter the host through the wound. In the wound, the parasites invade the cells nearby, where they differentiate into amastigotes. The intracellular amastigotes multiply by binary fission. They differentiate into trypomastigotes, then are released into the circulation and infect cells of different tissues where they transform into amastigotes. Bugs become infected when take a blood meal with parasites. The ingested trypomastigotes transform into epimastigotes in the midgut.

Incubation period lasts 4–14 days.

Clinical presentation. Infection may be mild or asymptomatic. At the site of the bite, chagoma appears (inflammatory tumor of skin with hyperemia and edema). Fever or swelling around the site of inoculation may develop. Rarely, an acute infection may result in myocarditis (inflammation of the heart muscle) or meningoencephalitis (inflammation of the brain and its lining). The mortality rate is up to 14 %.

Laboratory diagnosis: in acute phase — detection of trypanosomes in blood smears, cerebrospinal fluid, and puncture samples of lymphatic nodes.

Other methods include immunoassay (revealing antibodies in the blood serum), and PCR.

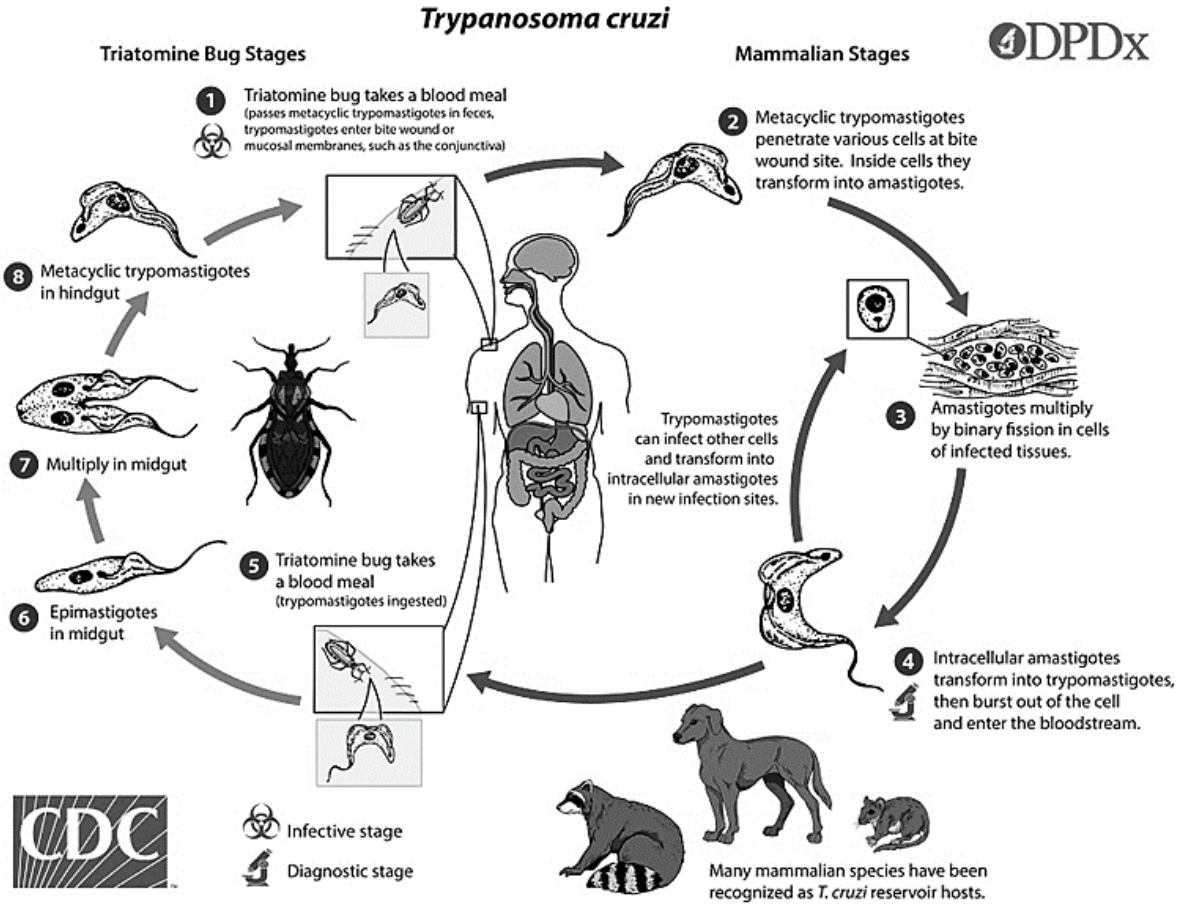


Figure 40. Life cycle of Trypanosoma cruzi

Prophylaxis: identification and treatment of sick people, elimination of vectors and protection from their bites (repellents, etc.), health education.

GENUS GIARDIA

Lamblia intestinalis (or *Giardia lamblia*) affects humans and causes lambliasis (giardiasis). The disease is spread worldwide, more prevalent in warm climates.

Morphology (Fig. 41). The trophozoite is pear-shaped and 10–18 μm long. It is bilaterally symmetrical i.e. has symmetrical halves: 2 nuclei, two axostyles, and 4 pairs of flagella. The dorsal side of the cell is convex and the ventral side is flat. There are sucking disks on the ventral side which serves as the parasite's method of attachment to the mucosa of the host. Cysts have an oval shape, each cyst contains four nuclei and eight pairs of flagella. Upon excystation, each cyst produces two trophozoites.

Life cycle. The infecting form of the parasite is a cyst. Infection occurs alimentary when cysts are ingested with contaminated vegetables, fruit, or water. Excystation occurs in the duodenum. In the small intestine, the trophozoites

float free or are attached to the mucosa of the lumen with ventral sucking discs. They reproduce asexually (longitudinal binary fission). Some trophozoites then encyst. They can survive outside the body for several months.

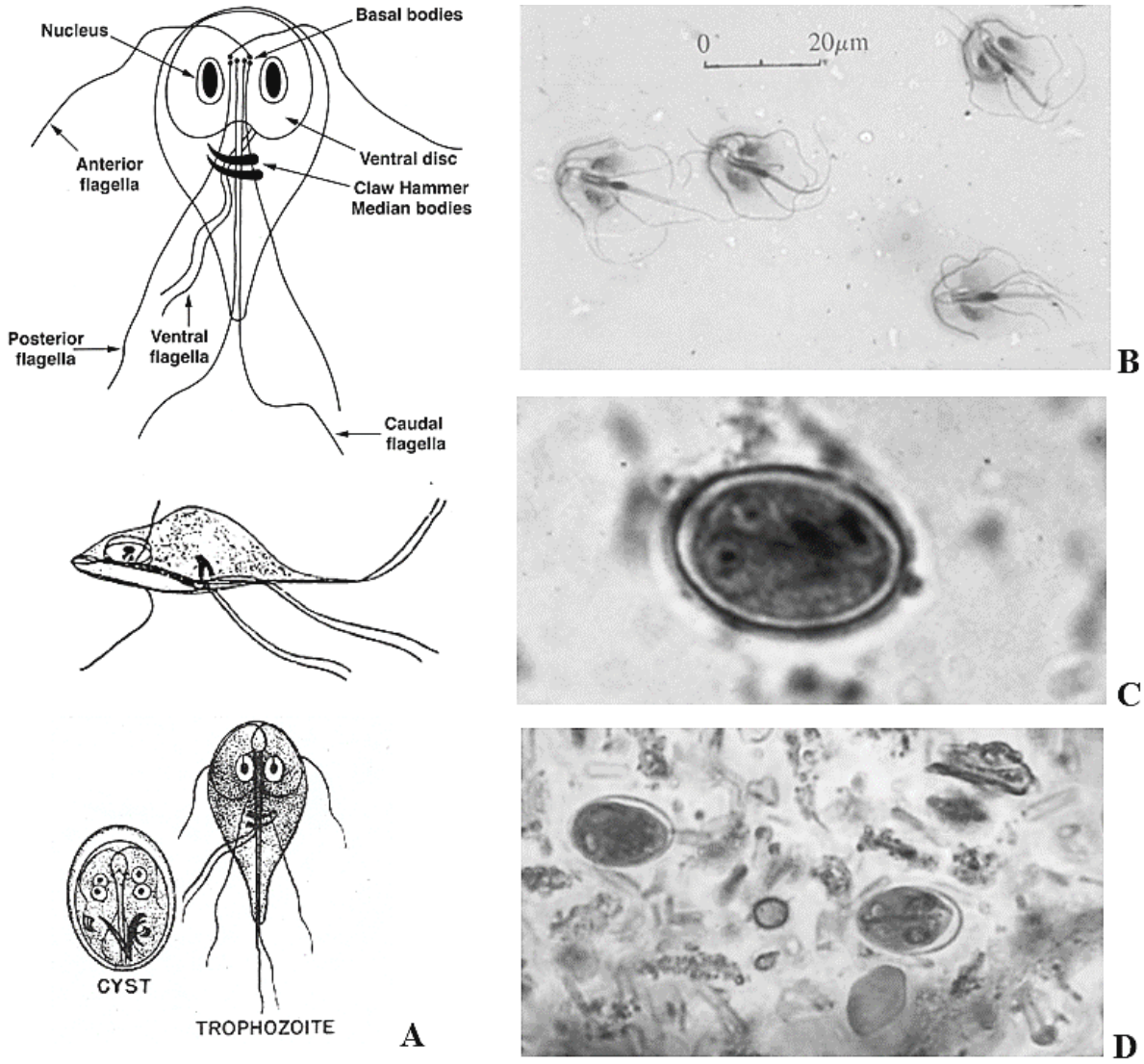


Figure 41. Morphology of Lamblia intestinalis:
A — diagrams of trophozoites and cyst; *B* — trophozoites; *C*, *D* — cysts

Clinical presentation varies from severe diarrhea with malabsorption (impaired absorption of nutrients from the gastrointestinal tract) to asymptomatic carriage. The incubation period of acute giardiasis lasts from 1 to 14 days. Symptoms include diarrhea, abdominal pain, bloating, nausea, and vomiting.

Laboratory diagnosis: finding cysts or trophozoites in the feces. Immunological methods can be used.

Prophylaxis: observing rules of personal hygiene such as drinking only purified water, washing uncooked food; treatment of sick people and carriers, and hygiene education.

TRICHOMONAS VAGINALIS

Trichomonas vaginalis is a pathogen of *trichomoniasis*. The disease is common worldwide.

Morphology. The cell is oval, up to 30 μm long, and has 5 flagella — 4 directed anteriorly and one directed posteriorly along the edge of the undulating membrane (Fig. 42). There is an axostyle in the middle, it forms a sharpened long spike at the end of the cell. There are a single nucleus and digestive vacuoles in the cytoplasm.

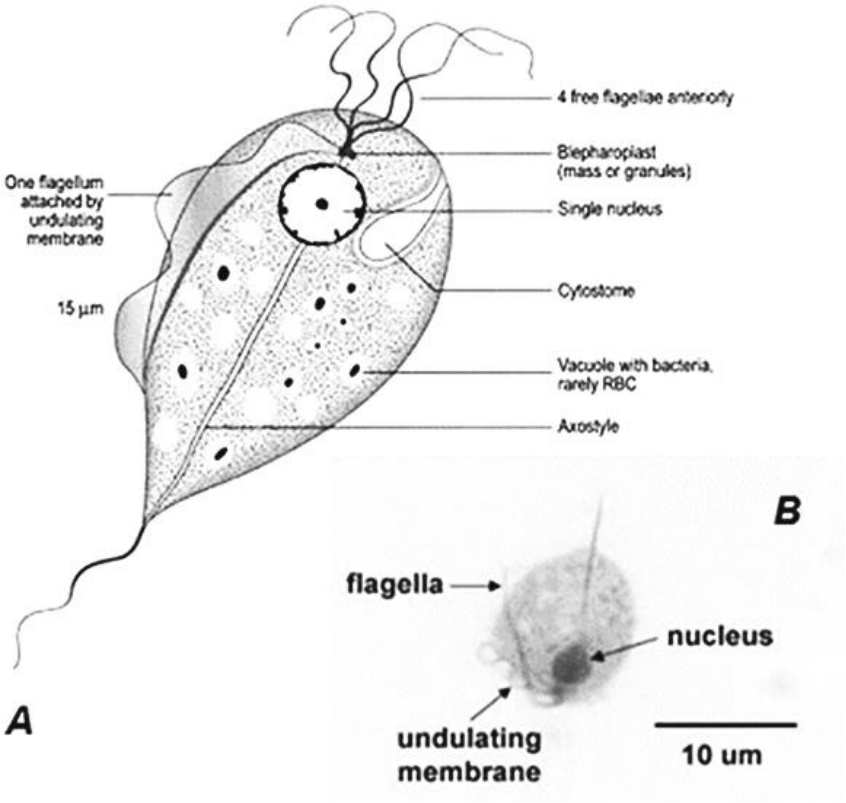


Figure 42. Morphology of Trichomonas vaginalis:
A — diagram; *B* — photograph

Life cycle. The only known host of *Trichomonas vaginalis* is human. Trophozoites are transmitted by means of sexual intercourse (the parasite does not form cysts). Trichomonas affects the female lower genital tract and the male urethra and prostate where they cause inflammatory processes.

Clinical presentation. Most of the infected people do not have any symptoms. When symptoms are present, they can vary from mild irritation to severe inflammation. Infected people may notice burning after urination, irritation and itching in genitals, and vaginal discharges.

Laboratory diagnosis: microscopy for revealing trophozoites in smears from genitourinary tracts.

Prophylaxis: monogamous sexual relationship, revealing and treating sick people, sterility of gynecological tools, hygiene education.

CHAPTER 8
PHYLUM PLATHELMINTHES, CLASS TREMATODA

GENERAL CHARACTERISTICS AND CLASSIFICATION OF THE PHYLUM

The phylum Platyhelminthes is the taxonomic group of flatworms. It includes more than 15 000 species. Some groups of flatworms include free-living species (class *Turbellaria)*, others — only parasites (the class *Trematoda* or flukes and the class *Cestoidea* or tapeworms). Features of the phylum:

1. Development from *3 germ layers*.

2. *Bilateral symmetry* (i.e. bodies consist of two symmetrical halves — left and right).

3. Elongated and flattened body.

4. The integument is the *dermo-muscular body wall*. It consists of an outer *tegument* (syncytial epithelium) and 3 layers of smooth muscles (circular, longitudinal, and diagonal).

5. There is no body cavity — the space between organs is filled with connective tissue.

6. There are no respiratory and circulatory systems.

The digestive system of flukes has 2 regions: foregut (mouth, pharynx) and blind-end midgut. Tapeworms have no digestive system. The excretory organs of flatworms are protonephridia. Their nervous system includes circumpharyngeal nerve ring, suprapharyngeal and subpharyngeal ganglions, and nerve chords. The lateral cords are the most developed. The sensory systems include tactile organs and organs of chemical senses. The majority of species are hermaphrodites.

Characteristics of flukes (class *Trematoda*): adaptations to parasitism, life cycles. Flukes are usually leaf-shaped, 2 to 80 mm long. Their fixation organs are oral and ventral suckers located on the abdominal side of the body. The tegument protects the parasites from the digestive enzymes of the host's organism. The majority of flukes are hermaphrodites.

Male reproductive system: testes, vasa defferentia, ejaculatory duct, cirrus.

Female reproductive system: single ovary, uterus, vitelline gland, ootype, Mehlis gland. Flukes have complex life cycles and produce thousands or tens of thousands of eggs per day.

Life cycle (Fig. 43). Definitive hosts are vertebrates including humans, the first intermediate hosts are fresh-water snails. Many species have second intermediate hosts such as fish, crawfish, and crabs.

Life cycles of flukes includes adult worms and many larval forms.

1. The form of adult fluke is called ***marita***. It multiplies sexually in the definitive host and lays eggs.

2. The eggs are released from the host and continue their development in water where the first intermediate hosts live.

3. Each egg hatches to produce a ***miracidium*** — a free-swimming ciliated larva that seeks out and penetrates a snail. Eggs of some trematode species produce miracidia only when eaten by the snail.

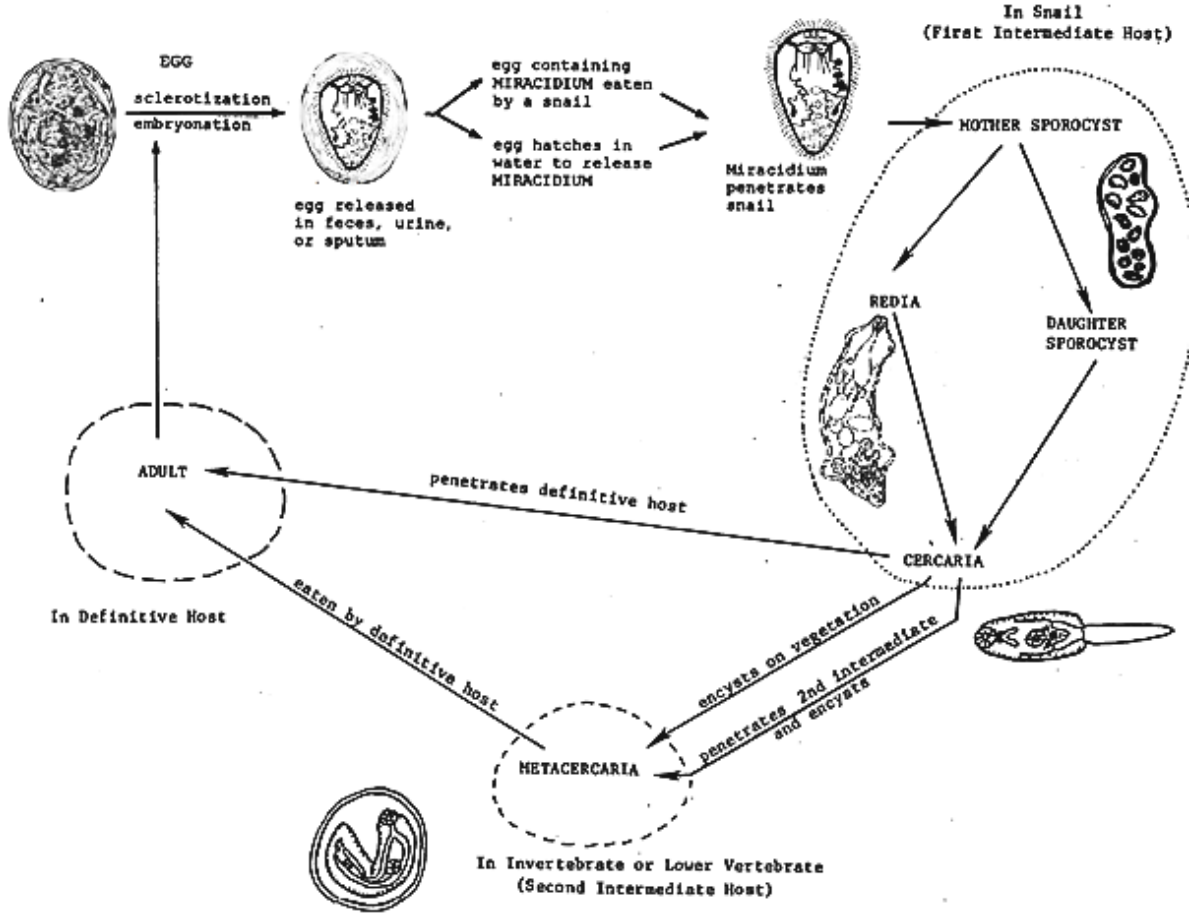


Figure 43. Life cycle of trematodes

4. When the miracidium finds and penetrates the snail, it loses its cilia and transforms into sac — like ***sporocyst*** that develops at the site of penetration.

5. The sporocyst produces a number of ***rediae*** that burst out of the sporocyst. Each redia is motile and migrates to the liver of the snail. In some species, the stage of redia is missing and another generation of sporocysts develops instead (*daughter sporocysts* develop from the *mother sporocyst*).

6. Redia feeds on snail tissue and produces a generation of ***cercariae*** (in species that have no redia stage they are produced by daughter sporocysts). Cercaria has anatomical structures of adult flukes (oral and ventral suckers, bifurcated intestine) and a long tail.

7. As cercariae are movable, they escape from the rediae and migrate out of the snail. Cercaria of different species have different ways to continue their life cycle:

– find a grass stalk or aquatic plant, lose the tail, cover with a cyst, and transform into immovable ***adolescaria*** that develops into adult worm when ingested by a definitive host;

– invade the second intermediate host (fishes, crawfishes, crabs) lose the tali, cover with cyst and transform into immovable ***metacercaria*** that develops into adult worm when the intermediate host eaten by a definitive host;

– invade the definitive host and develop into an adult.

Diseases caused by flukes are called *trematodoses*.

COMMON LIVER FLUKE (FASCIOLA HEPATICA)

Fasciola hepatica is a biohelminth (i.e. its larval stages develop in intermediate hosts), a pathogen of *fascioliasis*. According to WHO, cases of fascioliasis have been reported from more than 75 countries worldwide. No country can be considered free from the risk of fascioliasis.

Morphology (Fig. 44). *F. hepatica* is leaf-shaped, 3–5 cm in length, and has oral and ventral suckers. The intestine branches to form the ceca that extend through the body. There is a uterus and branching ovary behind the abdominal sucker, brunching testes are in the posterior portion of the body. Multiple yolk glands (vitellaria) on the lateral sides extend through the body.

Eggs are 135 × 80 μm, oval, yellowish-brown, and have a lid on one of the poles. The lid opens when miracidium is released (Fig. 44).

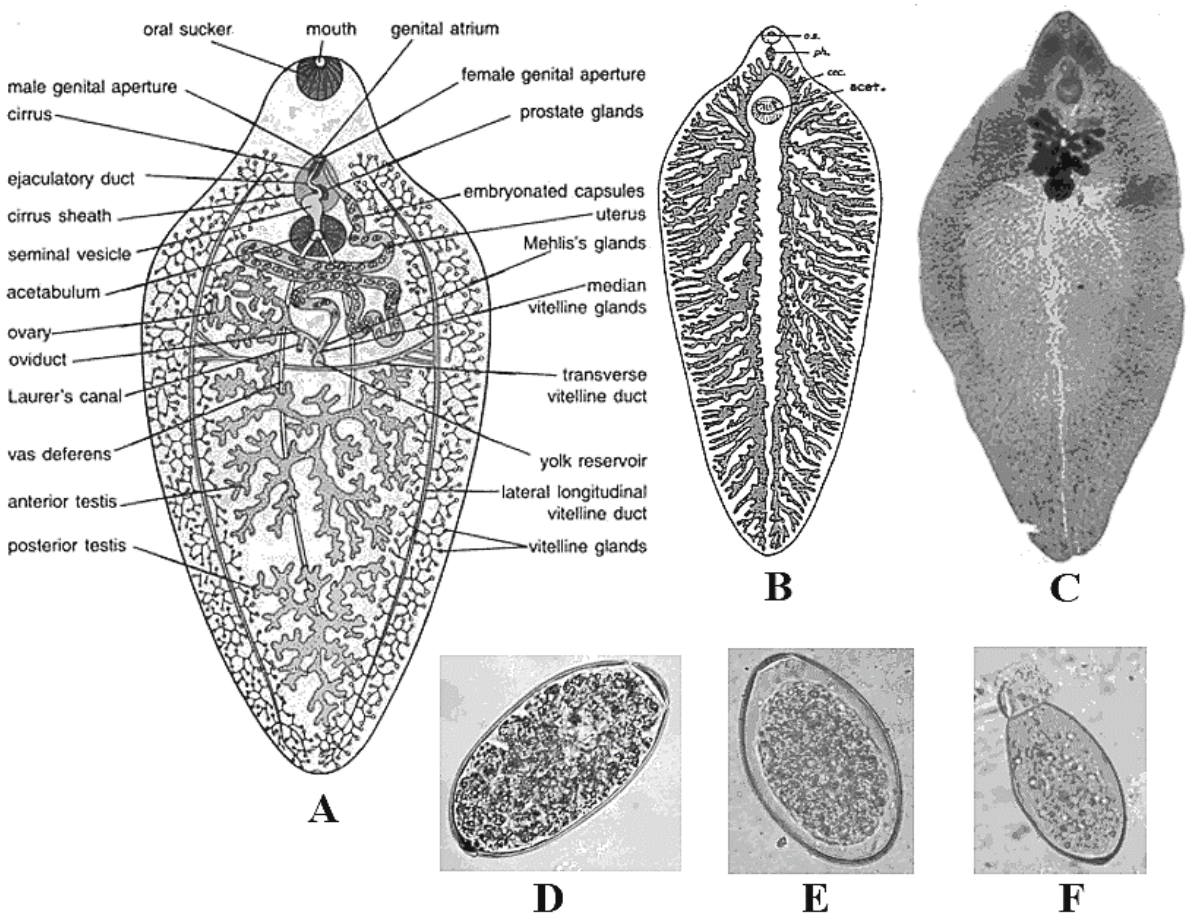


Figure 44. Morphology of F. hepatica:
A — reproductive system; *B* — digestive system; *C* — photograph; *D*, *E* — eggs; *F* — miracidium hatching from the egg

Life cycle. The definitive hosts are plant-eating mammals and sometimes humans. The intermediate hosts are freshwater snails such as *Limnea truncatula*.

Stages of the life cycle: ***marita — egg — miracidium — sporocyst — redia — cercaria — adolescaria***.

The miracidium develops in the egg within several weeks. Miracidium hatches and swims to find an intermediate host. It dies within a few hours if a suitable host is not found.

Having invaded the snail, the miracidium transforms into a sporocyst, in several weeks it gives rise to 6–8 rediae, each redia feeds in the tissues of the snail and ultimately produces 15–20 cercariae. The cercariae leave the host, find aquatic plants, and transform into adolescariae.

The human becomes infected when ingests adolescaria with freshwater plants or water.

The adolescaria excyst in the duodenum and migrate through the intestinal wall, the peritoneal cavity, and the liver parenchyma into the biliary ducts, where they develop into adults.

Clinical presentation. The course of the disease includes two phases.

The *acute phase* lasting 2–4 months is the period when the parasite migrates from the intestine through tissues to the bile ducts and feeds on the tissues. Typical symptoms are fever, nausea, vomiting, severe abdominal pain, and rashes.

The *chronic phase* starts when the parasite settles in the bile ducts, maturates, and starts laying eggs.

The symptoms are intermittent aches in the right hypochondrium, jaundice, anemia, and biliary obstruction. The liver enlarges and becomes dense and painful when palpated.

Laboratory diagnosis. Microscopy of stool specimens (or duodenal content when available) is used to find eggs of the parasite. Eggs are large (135 × 80 μm), oval, yellowish–brown, and have a lid on one of the poles.

Sometimes transit eggs are revealed in healthy people after eating the liver of animals sick with fascioliasis. Immunological methods can also be used.

Prophylaxis requires non–use of water from open ponds for drinking and watering vegetable gardens, a thorough wash of water plants and vegetables, treatment of sick persons, hygiene education, and sanitation of animals.

CAT LIVER FLUKE (OPISTHORCHIS FELINEUS)

Opisthorchis felineus is a biohelminth, pathogen of opisthorchiasis. The disease is common in Siberia along large rivers, though cases of opisthorchiasis were reported in other countries. Similar species cause infections in other regions of the world.

Morphology (Fig. 45). Adult worms are approximately 10 mm long. There are 2 testes lying one behind the other in the posterior portion of the body, and the S-shaped excretory canal is between them.

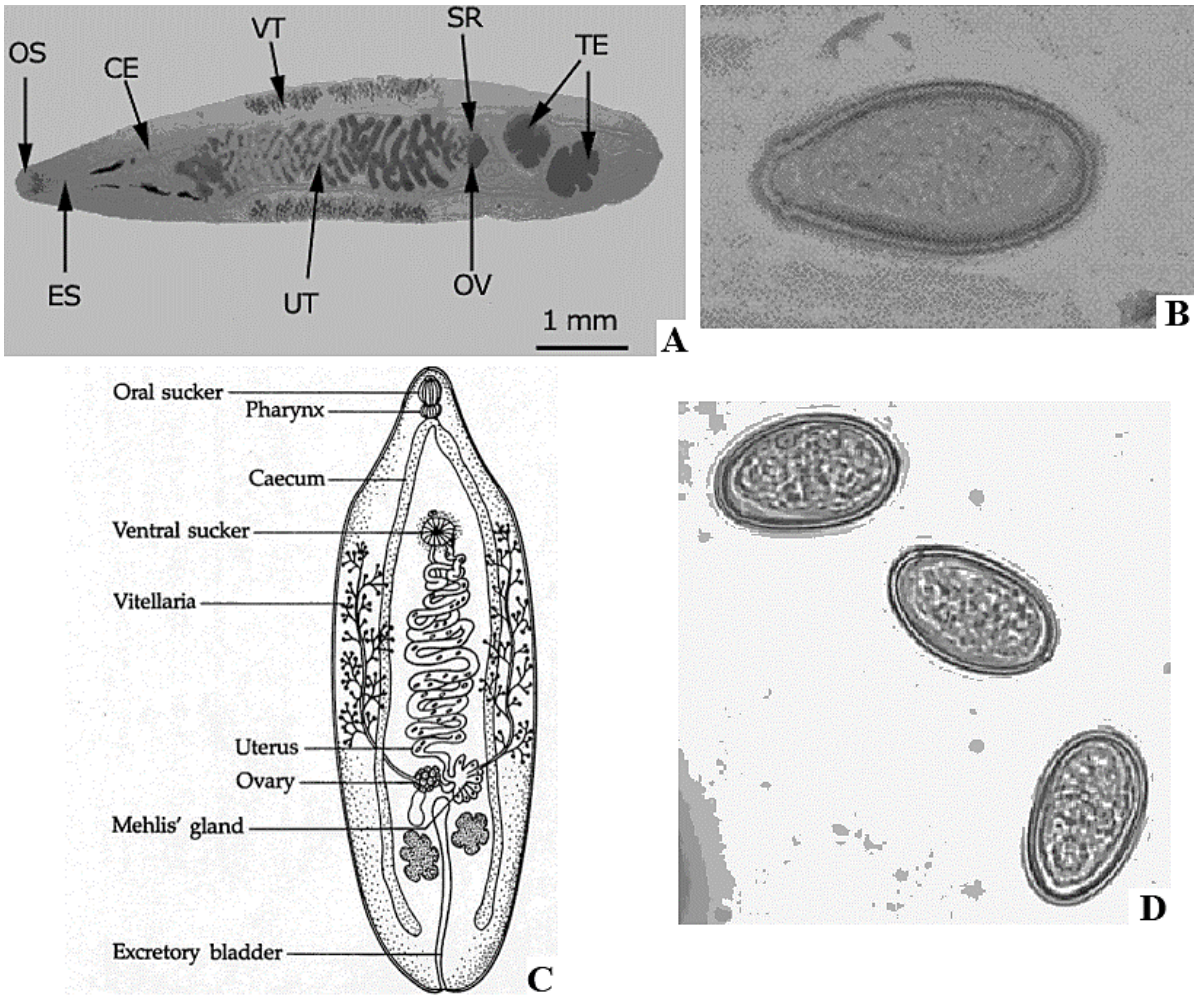


Figure 45. Morphology of O. felineus:
A — photograph; *C* — diagram; *B, D* — eggs

The ovary is anterior to the testes and a uterus is between the ovary and ventral sucker. The yolk glands (vitellaria) are situated on the lateral sides in the middle of the body. The two canals of the gut do not form lateral branches and lay between the vitellaria and other reproductive organs.

Eggs are 26–30 × 10–15 μm in size, and have a lid that opens to release miracidium on the narrow pole.

Life cycle (Fig. 46). Life cycle: *marita — egg — miracidium — sporocyst — redia — cercaria — metacercaria*.

The definitive hosts are humans, cats, dogs, and other fish-eating animals.

The 1st intermediate host is a freshwater snail (*Bithynia leachi*).

The 2nd intermediate host is freshwater fish.

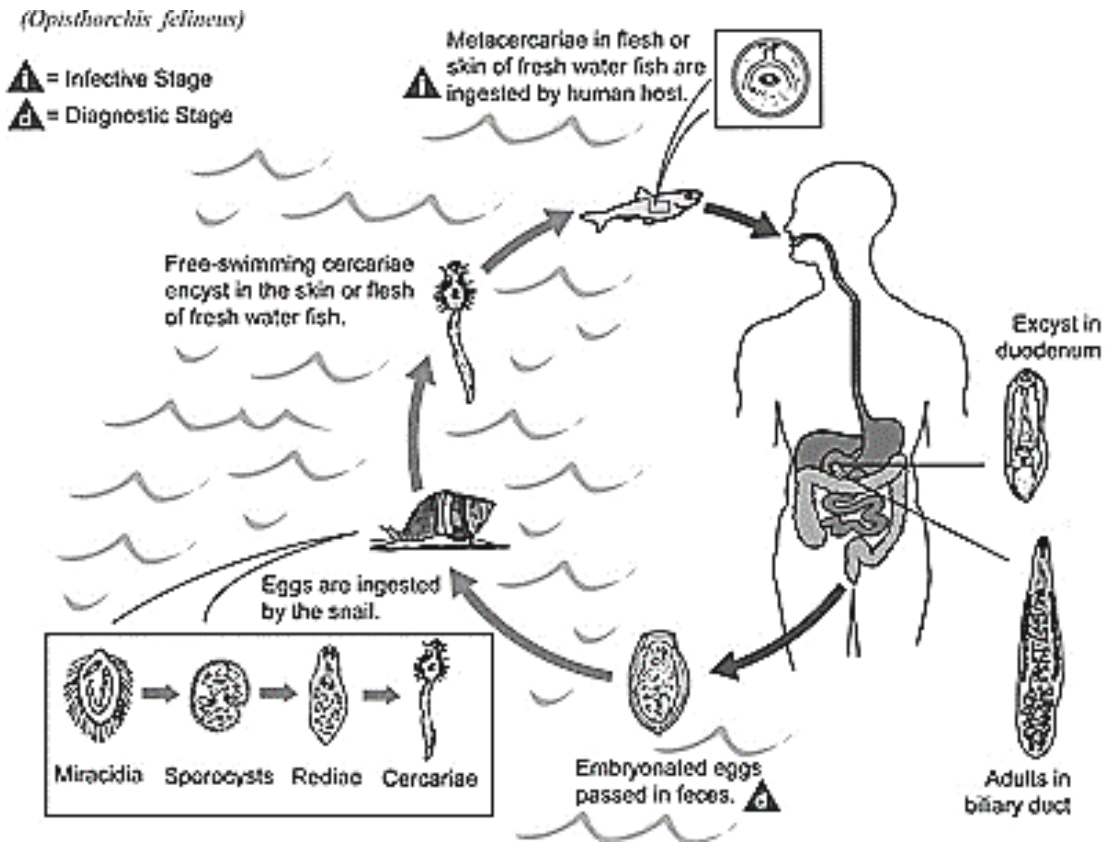


Figure 46. Life cycle of O. felineus

The adult flukes live in bile ducts and lay eggs that are released to the environment with feces. After ingestion by a suitable snail, the eggs release miracidia. Their development is similar to those of other flukes (sporocysts → rediae → cercariae). The cercariae escape from the snail to penetrate a freshwater fish which is the second intermediate host. In the fish, they encyst and transform into metacercariae. Infection of humans occurs when they ingest undercooked fish containing metacercariae. Metacercariae excyst in the duodenum and ascend into the biliary ducts, where they maturate into adults and start laying eggs in several weeks.

Clinical presentation. Symptoms depend on the number of flukes that invaded the person. Most of the cases are asymptomatic.

When symptoms develop, there can be diarrhea, abdominal pain, and enlargement of the liver and spleen. Severe cases can lead to fever, acute pain, significant enlargement of the liver, and jaundice. There is insufficient evidence of a causal link between opisthorchiasis and liver cancer.

Laboratory diagnosis is based on the detection of eggs in stool specimens. Immunological methods can also be used.

Prophylaxis. The disease can be prevented by proper cooking and salting fish; freezing the fish also kills the parasites. Other measures are the treatment of sick people; prevention of water contamination with feces; hygiene education.

ORIENTAL LUNG FLUKE (PARAGONIMUS WESTERMANI)

Paragonimus westermani is a biohelminth, a pathogen of *paragonimiasis*. The disease caused by *P. westermani* and similar species is common in the South-Eastern Asia and South Asia, Central Africa, and South America.

Morphology. The adult parasites are egg-shaped, slightly flattened, 7.5–12 mm in length (Fig. 47).

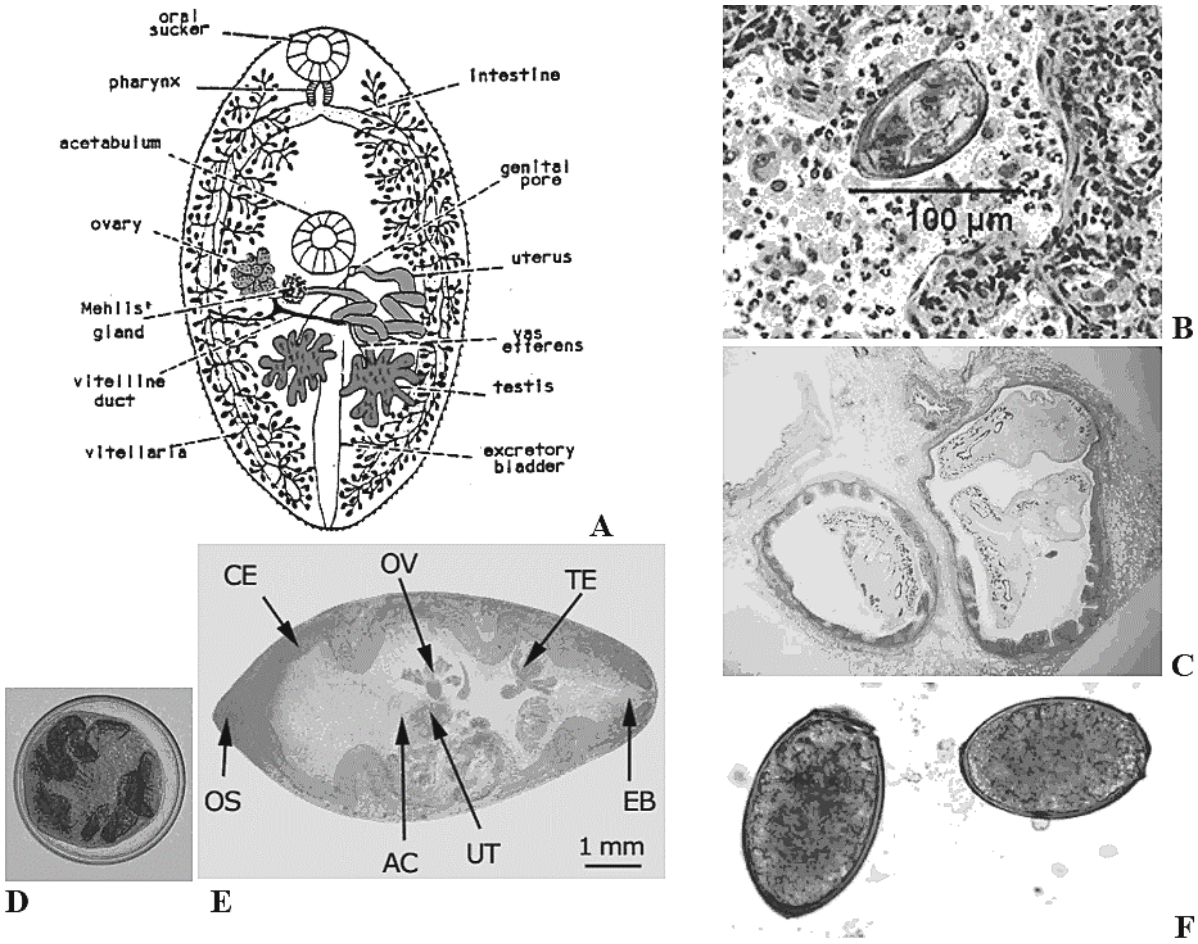


Figure 47. Morphology of P. westermani:
A — diagram; *B* — egg in lung tissue; *C* — section of cat's lung with parasites; *D* — metacercaria; *E* — photograph; *F* — eggs

The ventral sucker is in the middle of the body. There lobular ovary and uterus are on the left and right in the middle of the body, two testes are posterior to them. Vitelline glands extend along the two branches of the intestine on the left and right sides of the body.

Eggs are large (up to 100 μm), oval, of yellowing color, and have thick membrane and a lid on the pole.

Life cycle: the definitive hosts are humans, dogs, cats, pigs, and other mammals. The 1st intermediate hosts are freshwater snails of the genus *Melania*, the 2nd intermediate hosts are crawfish and crabs. Stages of the life cycle: *marita — egg — miracidium — sporocyst — redia — cercaria — metacercaria*.

Eggs are excreted with sputum and feces and mature to miracidia in freshwater. Miracidia hatch and infect the first intermediate hosts (snails) where they undergo asexual reproduction (sporocysts → rediae → cercariae).

The cercariae leave the host and infect the second intermediate host (crabs and crayfish), encyst, and become metacercariae which are infective to definitive hosts.

Infection of human occurs through ingestion of crawfish and crabs containing metacercariae.

They excyst in the duodenum, and penetrate through the intestinal wall and diaphragm into the lungs. They maturate and become adults approximately 8–10 weeks after infection.

Clinical presentation. The earliest stages of paragonimiasis may be asymptomatic or scarcely symptomatic. When worms reach the lungs, symptoms may be significant.

They typically include chronic cough with blood-stained sputum, chest pain, and fever. The disease can be misdiagnosed with tuberculosis. Complications: pleural effusion, pneumothorax.

Laboratory diagnosis. Microscopic detection of eggs in sputum or feces, immunological analysis to detect worm specific antibodies or antigens.

Prophylaxis. The main measure to prevent the disease is not-eating raw or undercooked crawfish and crabs. Travelers should avoid traditional meals containing undercooked freshwater crustaceans.

BLOOD FLUKES

Schistosomes are prevalent in tropical and subtropical areas, especially in poor communities without access to safe drinking water and adequate sanitation. Several species of schistosomes can affect humans. The most common species:

– *S. haematobium* causes genitourinary schistosomiasis;

– *S. mansoni* causes intestinal schistosomiasis;

– *S. japonicum* causes intestinal schistosomiasis (Katayama fever).

Morphology. Schistosomes are dioecious (have separate sexes). Males are short and broad (10–15 mm), and females are up to 20 mm long (Fig. 48).

The male fluke encloses the female with *gynecophoral canal* for the entire adult lives of the worms. Males have a strong abdominal sucker, which ensures a reliable fixation to the walls of blood vessels.

Life cycle. Principal hosts of schistosomes are human and other mammals, intermediate hosts are freshwater snails. Stages of the life cycle: ***marita — egg — miracidium — mother sporocyst — daughter sporocyst — cercaria.***

The adult flukes settle veins of the abdominal cavity and urogenital system. Females lay eggs in the vascular lumen in the walls of such organs as the urinary bladder or intestine.

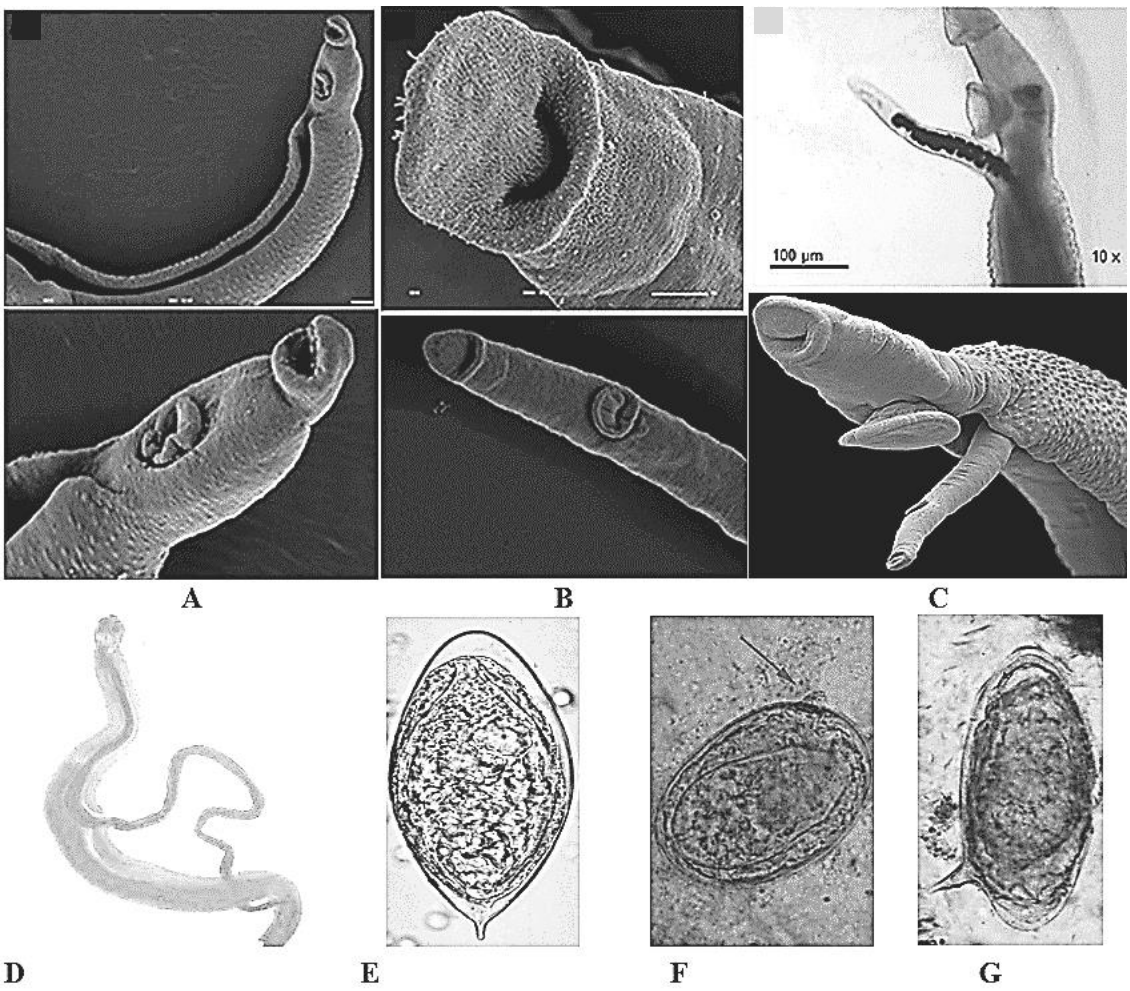


Figure 48. Morphology of schistosomes and their eggs:
A — male S. mansoni; *B* — female S. mansoni; *C, D* — a thin female S. mansoni resides in the gynecophoral canal of the thicker male; *E* — egg of S. haematobium; *F* — egg of S. japonicum; *G* — egg of S. Mansoni

The eggs move toward the lumen of the intestine (*S. mansoni* and *S. japonicum*) and of the bladder and ureters (*S. haematobium*). Eggs are eliminated from the host with feces or urine, hatch, and release miracidia, which find a suitable snail and penetrate it.

The development in the snail includes 2 generations of sporocysts. Ultimately cercariae are produced. The cercariae swim and penetrate the skin of the human host. People are infected during routine activities, which expose them to infested water.

In the host, the parasites shed their forked tail and migrate to the *mesenteric venules* which are specific for each species: *S. haematobium* is most often found in the venous plexus of the urinary bladder, *S. japonicum* and *S. mansoni* are more common in the superior mesenteric veins draining the small and the large intestine respectively. The location of parasites defines the clinical forms of schistosomiasis (Table 4).

Table 4

Clinical forms of schistosomiasis

Parasite	***S. mansoni***	***S. japonicum***	***S. haematobium***
Form of the disease	Intestinal schistosomiasis	Intestinal schistosomiasis	Urogenital schistosomiasis
Affected blood vessels	Mostly superior mesenteric veins	Mostly superior mesenteric veins	Mostly venous plexus of the urinary bladder
Elimination of eggs to the environment	Eliminated with feces	Eliminated with feces	Eliminated with urine
Common symptoms	Abdominal pain, diarrhea, blood in the stool. In advanced cases — liver and spleen enlargement, accumulation of fluid in the peritoneal cavity, and hypertension of the abdominal blood vessels.		Haematuria (blood in urine), fibrosis of the bladder and ureter. In women — genital lesions, vaginal bleeding, pain during sexual intercourse. In men — pathology of the seminal vesicles, prostate, and other organs.
Geographical distribution	Africa, the Middle East, the Caribbean, Brazil, Venezuela and Suriname	China, Indonesia, the Philippines	Africa, the Middle East, Corsica (France)

Clinical presentation. In the spots of where cercariae penetrate the skin, rash elements develop.

Schistosomes lay eggs in small venules, the presence of eggs is associated with the granulomatous inflammatory response.

The disease is often asymptomatic, acute symptoms may develop weeks after the initial infection.

Manifestations include fever, cough, abdominal pain, diarrhea, and enlargement of the liver and spleen.

Laboratory diagnosis is based on the detection of parasite's eggs in stool or urine specimens; immunological methods can be used (detection of antibodies or antigens detected in blood or urine samples).

– Schistosoma mansoni: eggs (114–180 μm long) have a prominent lateral spine.

– Schistosoma haematobium: eggs (110–170 μm long) have a prominent terminal spine.

– Schistosoma japonicum: eggs (70–100 μm long) have a miniscule lateral spine.

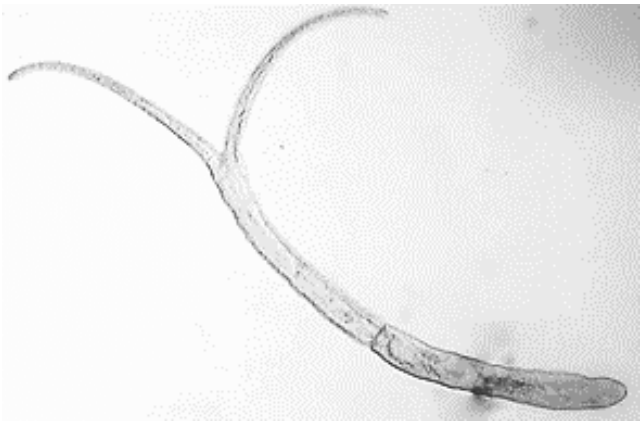
Prophylaxis. The disease can be prevented by avoiding contact with freshwater in disease-endemic countries; large — scale treatment of at-risk population groups, access to safe water, improved sanitation, hygiene education, and snail control.

CERCARIAL DERMATITIS (SWIMMER'S ITCH)

Cercarial dermatitis is dermatitis caused by the cercariae of certain species of schistosomes (family *Schistosomatidae*). Although the cercaria can penetrate human skin, their natural hosts are birds or some mammals and the cercariae do not mature into adults in the human body.

The species causing cercarial dermatitis in Belarus is *Trichobilharzia ocellata.*

Morphology of cercariae. The larva is motile, transparent, 0.2–0.4 long, and has a forked tail (Fig. 49).



Figurq 49. Cercaria of Trichobilharzia ocellata

The **life cycle** of such schistosomes is similar to that of other flukes. The definitive hosts are birds (such as ducks, and geese), and the intermediate hosts are snails.

Stages of the life cycle are: *marita — egg —miracidium — sporocyst — redia — cercaria.*

Clinical presentation. The penetration causes a red papular rash within hours or days. A repeat of invasion is severer and usually accompanied by intense itching and reddening. The symptoms usually resolve within 1–2 weeks.

Laboratory diagnosis is usually not required.

Prophylaxis. The syndrome can be prevented by avoiding contact with freshwater in endemic areas, control of definitive and intermediate hosts, and hygiene education.

DIAGNOSIS AND BIOLOGICAL BASICS OF PROPHYLAXIS OF TREMATODOSIS

Most helminths reside in the intestine or organs connected with the intestine. For this reason, most diagnostic techniques are based on microscopy of stool specimens.

Macroscopic and microscopic methods are used to detect parasites and their parts (*helminthoscopy*) or their eggs (*helminthoovoscopy*).

Such tests are cheap and easy to perform. This work requires strict adherence to Hygiene rules, sterilization of inoculation loops and glass sticks in flame, sterilization of laboratory dishes, glasses, and tools, and cleanliness of the workplace.

Immunological techniques are still at an experimental stage. These techniques are usually sensitive as they allow to detect worm — specific antibodies in blood serum or worm–specific antigens in serum or stool samples.

Molecular techniques such as the polymerase chain reaction are also at an experimental stage.

The biological basics of prophylaxis of trematodosis is a complex of measures that are based on studying the biology of the pathogen, its migration ways, life stages, the biology of intermediate hosts. That gives the possibility to interrupt some links of the parasite life cycle.

The prophylaxis measures carried out in endemic regions include:

– Community diagnosis carried out at the district level;

– Preventive chemotherapy (single administrations of antihelmintic medicines);

– Information and education on safe food practices (avoiding food that may contain parasites, proper cooking);

– Improved sanitation (prevents transmission of eggs and miracidia to the water pools where intermediate hosts live);

– Intermediate host control.

CHAPTER 9
PHYLUM PLATHELMINTHES, CLASS CESTODA

CHARACTERISTIC OF TAPEWORMS, THEIR ADAPTATIONS TO PARASITISM

The class *Cestoda* (*Cestoidea*) or tapeworms includes 1800 species. All these species are endoparasites. Cestodes are hermaphrodites, they have long (1 mm to 10–18 m) flattened bodies that resemble tapes.

Body parts of tapeworms:

1. *Scolex* is the «head» of tapeworms which bears the organs of attachment. Such organs of different species are *suckers*, rostellum with *hooks*, *bothria* (sucking grooves).

2. *Neck* that is the region of segment proliferation (i.e. new body segments are created here).

3. *Strobila* (body) which is a chain of *proglottids* (segments). The number of segments in different species varies from 3 to several thousand.

- The proglottids nearest the neck are *immature* (sex organs not fully developed).
- Those more posterior are *mature* (contain male and female reproductive systems).
- The terminal proglottids are *gravid*, with the egg-filled uterus.

The gravid proglottids containing eggs separate from the body and are passed to the environment with feces.

Eggs of Diphyllobothria exit through a uterine pore in the center of the ventral surface. In other tapeworms (Taenia, Echinococcus, Hymenolepis), the uterus has no pore. Thus, the eggs are released only when the tapeworms shed gravid proglottids into the intestine.

As well as all other flatworms, cestodes do not have circulatory and respiratory systems. A characteristic feature of tapeworms is the absence of a digestive system, as they inhabit the small intestine.

The tegument (syncytial epithelium of the dermo-muscular wall) has hair-like projections *microthriches*.

The microthriches resemble the microvilli of the mammalian intestine and perform the same function — absorption of nutrients in the host's intestine.

The excretory organs of cestodes are protonephridia. The nervous system and sense organs are poorly developed.

Life cycles of tapeworms. The life cycles of *Taenia*, *Hymenolepis*, and *Echinococcus* are similar but different from that of *Diphyllobothrium*. They include stages: *adult worm → egg → oncosphere → measle* (Fig. 50).

The *adult worm* lives in the definitive host and multiplies sexually (produces eggs). The *eggs* are released to the environment (in some species it is not required) where they can be ingested by the intermediate hosts.

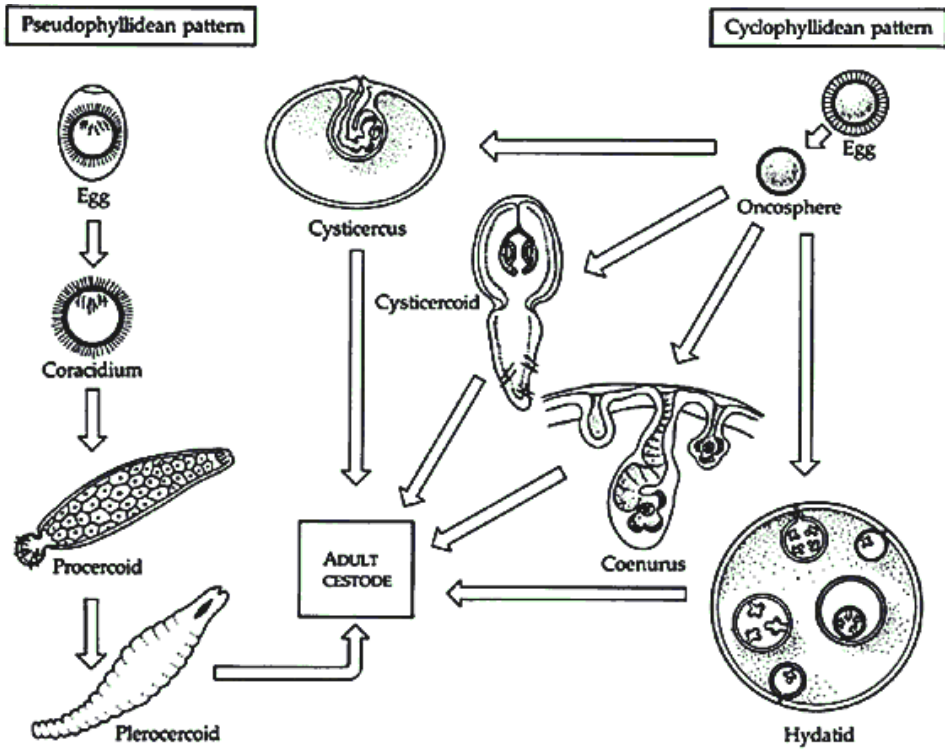


Figure 50. Life cycles of cestodes

In the intermediate host, each egg hatches, releasing the larva called *oncosphere*. The oncospheres migrate to the tissues of the host and transform into larval cestodes (sometimes referred to as *measle*). The definitive hosts become infected when eat the contaminated tissues of the intermediate hosts. Types of larval cestodes are (Fig. 51):

– *Cysticercus* — bladder containing invaginated scolex of a tapeworm (*T. solium*, *T. saginatus*);

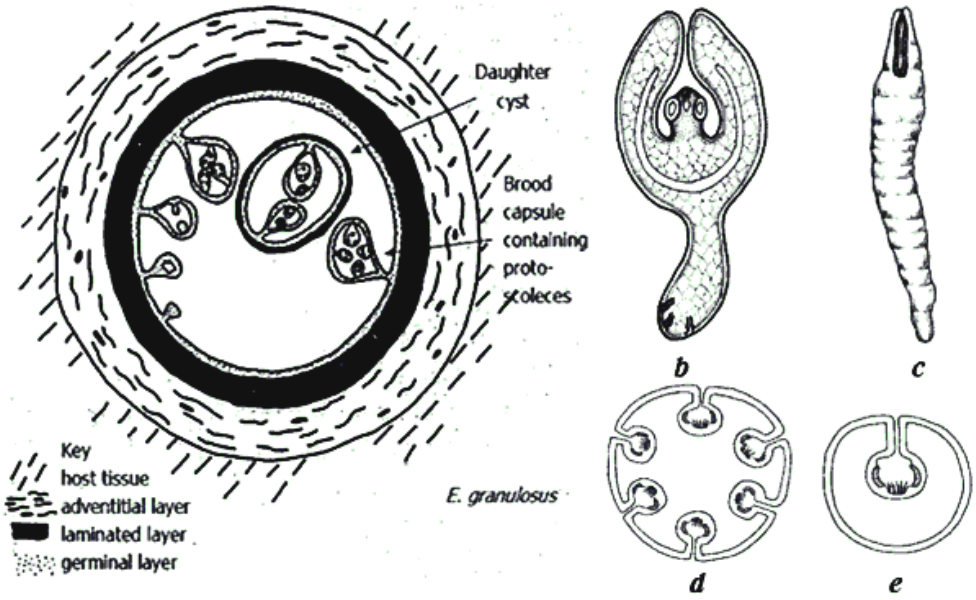


Figure 51. Larval forms (measles) of tapeworms:
a — hydatid cyst; *b* — cysticercoid; *c* — plerocercoid; *d* — coenurus; *e* — cysticercus

– *Cysticercoid* — smaller bladder containing invaginated scolex completely filling the enclosing cyst and solid elongated portion (*H. nana*);

– *Coenurus* — bladder containing many invaginated scolices (*Taenia multiceps*);

– *Hydatid cyst* — bladder containing daughter cysts, each of which, if fertile, will have many protoscolices. (*E. granulosus*, *E. multilocularis*).

TAENIA SOLIUM AND TAENIA SAGINATA (TAENIARHYNCHUS SAGINATUS)

Taenia saginata (or *Taeniarhynchus saginatus*) is a biohelminth adult worm of which causes *taeniasis* (*taeniarhynchiasis)*.

The adult *Taenia solium* causes *taeniasis*, and its larvae may cause *cysticercosis* in human. These helminthes and diseases they cause are similar and reported worldwide.

Morphology (Fig. 52, 53, Table 5). The tapeworms have scolex with attachment organs, neck, and strobila consisting of proglottids. The mature proglottids (in the middle of the body) contain male and female reproductive organs (uterus, vitellaria, ovaries, ootype, testes). The gravid proglottids contain uterus with tens of thousands of eggs. The gravid proglottids will be casted off out of the human body.

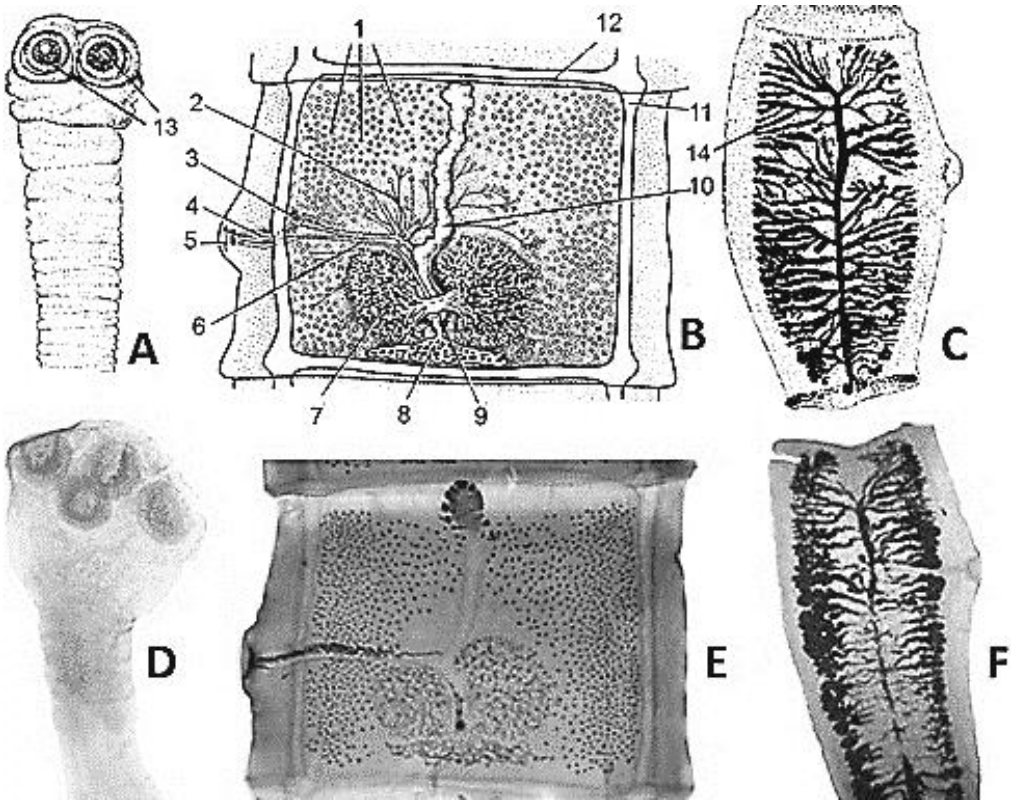


Figure 52. Morphology of Taenia saginata:
A–C — diagrams, *D–F* — microphotographs: *A*, *D* — scolex, *B*, *E* — mature proglottid, *C*, *F* — gravid proglottid: *1* — testes; *2*, *3* — seminal ducts; *4* — cirrus; *5* — genital atrium; *6* — vagina; *7* — ovary; *8* — vitelline gland; *9* — ootype; *10*, *14* — uterus; *11*, *12* — canals of excretory system; *13* — suckers

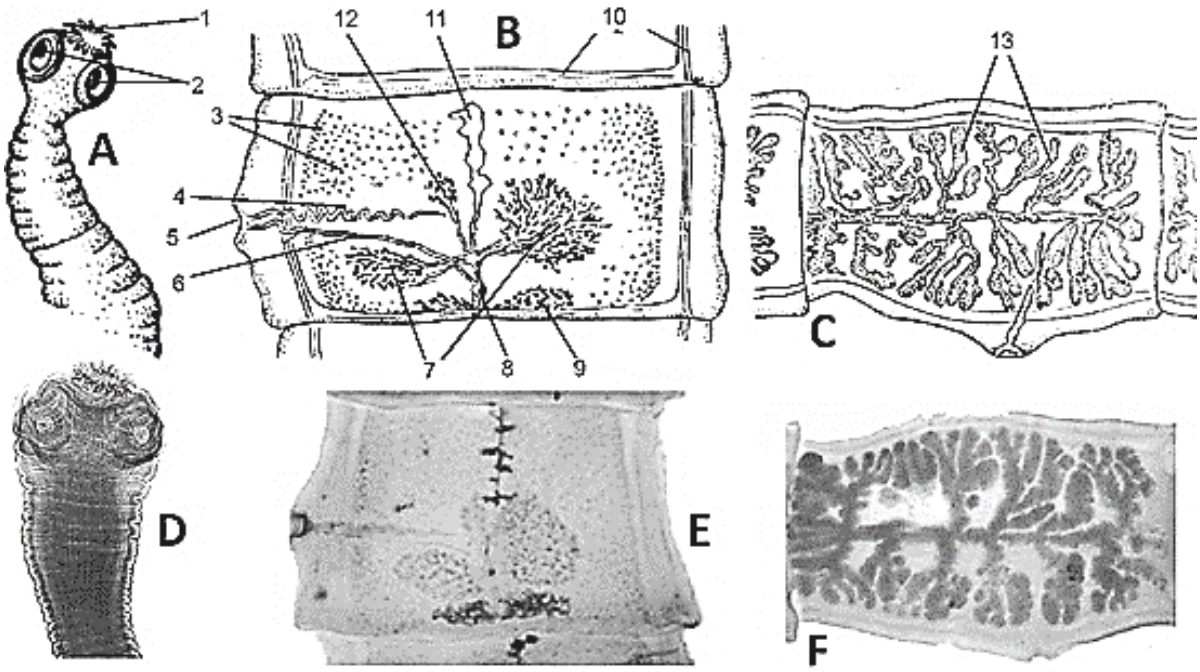


Figure 53. Morphology peculiarities of Taenia solium:
A–C — diagrams; *D–F* — microphotographs: *A, D* — scolex; *B, E* — mature proglottid; *C, G* — gravid proglottid; *1* — hooks; *2* — suckers; *3* — testes; *4* — seminal duct; *5* — genital atrium; *6* — vagina; *7* — ovary; *8* — ootype; *9* — vitelline gland; *10* — excretory canals; *11*, *13* — uterus; *12* — the 3rd lobe of the ovary

Table 5

Morphology of T. saginata, T. solium

	T. saginatus	***T. solium***
Common length	4–10 m	2–3 m
Attachment organs on the scolex	4 suckers	4 suckers + rostellum with 2 rows of hooks
Approximate number of proglottids	~1000	~800
Mature proglottids can be recognized by	Bilobed ovaries	Trilobed ovaries
Gravid proglottids can be recognized by	17–35 lateral branches on each side of the uterus	7–12 lateral branches on each side of the uterus
Motile gravid proglottids	Yes	No

Life cycle (Fig. 54). The only definitive host of *T. solium* and *T. saginata* is human, the intermediate hosts are *pigs* and *cattle* respectively. They become infected by ingesting vegetation contaminated with eggs or gravid proglottids. In the intestine of the intermediate host, the oncospheres hatch from the eggs, invade the intestinal wall, migrate to the striated muscles, and transform into *cysticerci*. Cysticerci can survive for several years in the animal.

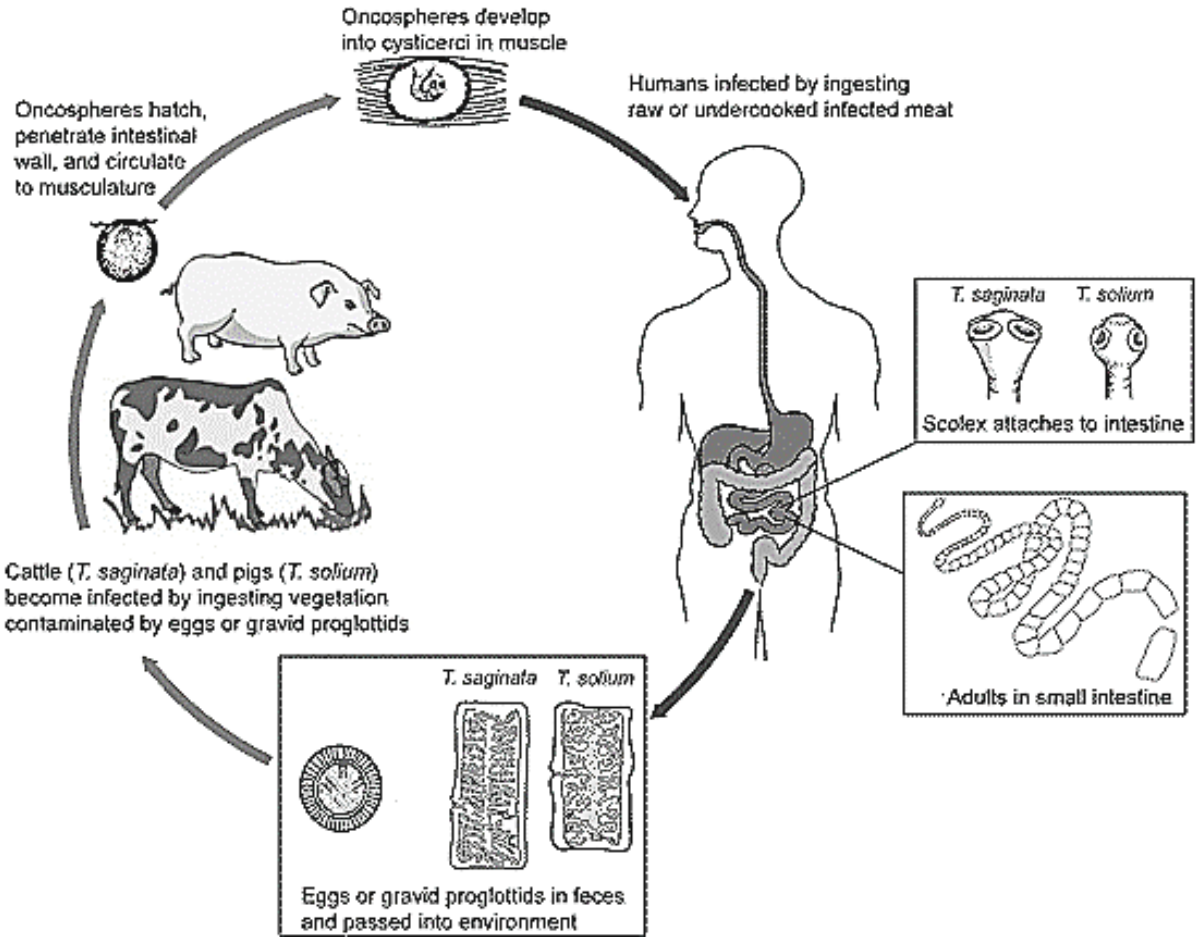


Figure 54. Life cycle of T. Solium and T. saginatus

Humans become infected with taeniasis by ingesting raw or undercooked meat of infected animals. In the human intestine, each cysticercus develops over 2 months into an adult tapeworm, which attaches to the wall of the small intestine. The life span of adult worms in the human body is up to 25 years.

If a human ingests eggs of *T. solium* (but not *T. saginatus*) cysticerci invade its tissues and *cysticercosis* develops.

Clinical presentation. Taeniasis is usually characterized by mild and non-specific symptoms. Abdominal pain, nausea, diarrhea, or constipation may arise when the tapeworms become fully developed in the intestine, approximately 8 weeks after ingestion of meat containing cysticerci.

Human *cysticercosis* is caused by the cysticerci of *T. solium* developing in the tissues of humans. The most dangerous location in the body is the CNS. Symptoms depend on the location of parasites. In the case of CNS affection, they are epileptiform attacks, headaches, learning difficulties, and convulsions.

Laboratory diagnosis: the examination of stool samples to find proglottids or eggs. Eggs (Fig. 55) of *T. solium* and *T. saginata* are indistinguishable. They are round, 30–40 × 20–30 μm, have a thick striated covering, and six-hooked oncosphere inside.

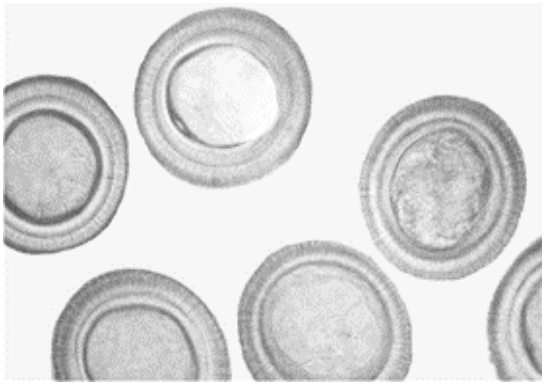


Figure 55. Eggs of T. solium and T. saginata

Prophylaxis. Personal prophylaxis requires non-eating raw and undercooked beef and pork, and cooking meat to safe temperatures. Social prophylaxis according to WHO includes:

– mass drug administration for the diseases;
– identification and treatment of disease cases;
– health education, including hygiene and food safety;
– improved sanitation;
– improved pig husbandry;
– anthelmintic treatment and vaccination of pigs;
– improved meat inspection and processing of meat products.

HYMENOLEPIS NANA

Hymenolepis nana is a contact helminth (i.e. host-to-host transmission is possible), causing *hymenolepiasis*. The disease is encountered worldwide. Its incidence in children is higher.

Morphology (Fig. 56). The length of the *H. nana* is 1–5 cm. The body of the parasite contains about 200 proglottids. The scolex has 4 suckers and a rostellum with a double circlet of hooks.

Life cycle (Fig. 57) includes stages: adult worm → egg → oncosphere → cysticercoid.

Adult worms live in the intestine and multiply sexually. Eggs can pass to the environment with feces and have 3 ways to continue the life cycle:

1. If an *egg* remains in the intestinal lumen of the same definitive host, an *oncosphere* hatches, invades a villum of the small intestine, and develops into *cysticercoid*. When the villus ruptures, the cysticercoid returns to the intestinal lumen, attaches to the intestinal mucosa and develops into a sexually mature *adult* in 1–2 weeks.

2. If an egg passes to the environment with feces, it can be ingested by another definitive host. The oncosphere hatches, develops in a villus, and produces new adult worms.

3. The egg can be ingested by an intermediate host (various species of beetles and fleas) where cysticercoids develop. The cysticercoids can infect humans or rodents upon ingestion and transform into adults in the small intestine.

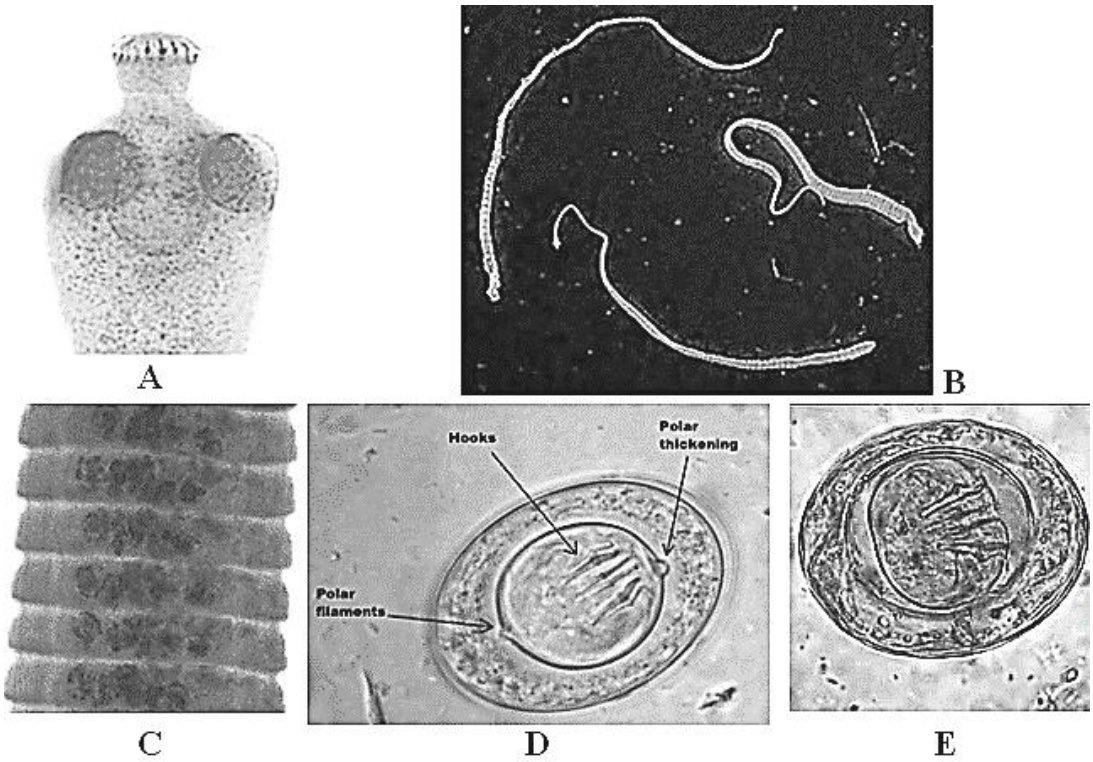


Figure 56. Morphology of Hymenolepis nana:
A — scolex; *B* — three adult worms; *C* — proglottids; *D*, *E* — eggs

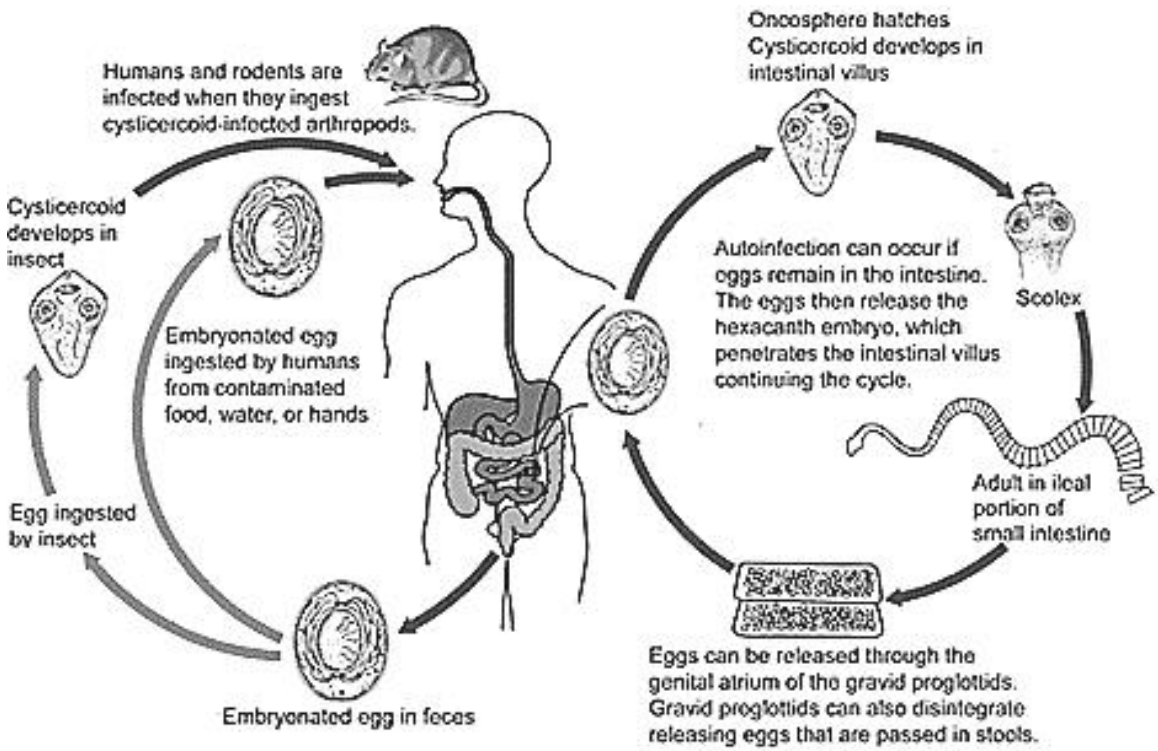


Figure 57. The life cycle of Hymenolepis nana

The life span of the parasite is 1–2 months, but autoinfection allows the disease to persist for longer periods.

Clinical presentation. As a rule, hymenolepiasis causes no symptoms or slight symptoms. Some patients complain of headache, dizziness, loss of appetite, nausea, indigestion, anorexia, abdominal pain, and diarrhea.

Laboratory diagnosis is based on the detection of eggs in stool specimens. Eggs are round 30 to 47 μm in diameter. The oncosphere has two polar thickenings (the shape of a "lemon") and polar filaments that lie between the oncosphere and the shell.

Personal prophylaxis. As *H. nana* is transmitted from person to person, observing personal hygiene rules is the main preventive measure.

Social prophylaxis: hygiene education of children, isolation, and treatment of sick people, thorough moist mopping of children's rooms, and sanitary treatment of toys.

ECHINOCOCCUS GRANULOSUS

Echinococcus granulosus is a biohelminth whose larval stage cause *cystic echinococcosis* in human. There is another similar parasite causing the disease — *Echinococcus multilocularis*.

Morphology (Fig. 58). The length of the adult worm is 3–5 mm. The scolex has suckers and a rostellum with hooks. The strobila of echinococcus consists of 3–4 proglottids. The anterior proglottid is immature, the middle one is mature with functional testes and ovaries, and the posterior one is gravid with the uterus filled with eggs.

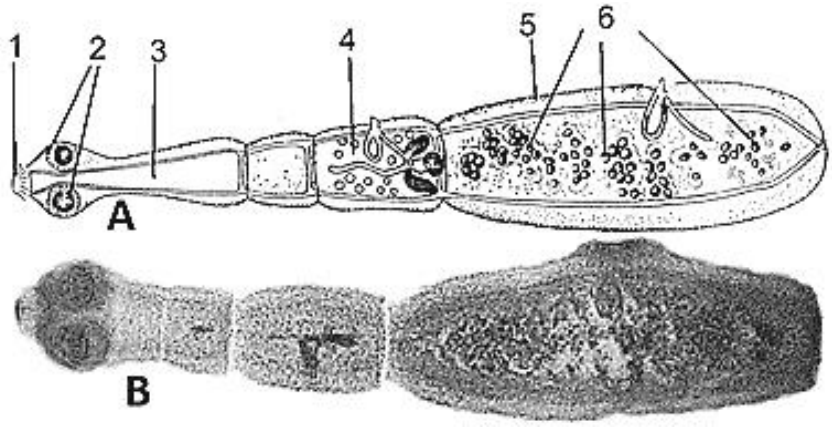


Figure 58. Morphology of Echinococcus granulosus:
A — diagrams; *B* — microphotograph; *1* — a rostellum with two circlets of hooks; *2* — sucker; *3* — neck; *4* — mature proglottid; *5* — gravid proglottid; *6* — uterus

Life cycle. The definitive hosts of the *E. granulosus* are carnivorous animals (dogs, wolfs, coyotes), the intermediate hosts are herbivorous and omnivorous animals (large and small cattle, pigs, camels, deer, etc.) and human. Stages of the life cycle: *adult worm → egg → oncosphere → hydatid cyst.*

The *adult worms* reside in the small intestine of the definitive hosts and multiply sexually. Gravid proglottids release *eggs* that are eliminated from the environment with feces. An egg is ingested by a suitable intermediate host and releases an oncosphere in the small intestine. The *oncosphere* penetrates the intestinal wall and migrates through the circulatory system into various organs (especially the liver and lungs) where it develops into a *hydatid cyst.* Such cyst gradually grows, producing daughter cysts inside of itself (in *E. multilocularis* — outside).

The definitive hosts become infected when ingest contaminated tissues of infected animals.

A human usually becomes infected by sick dogs when ingesting eggs. In humans' hydatid cysts affect the liver, lungs, brain, muscles, and bones.

Clinical presentation. The cystic echinococcosis caused by *E. granulosus* is characterized by an asymptomatic incubation period that can last many years until the parasite cysts evolve and trigger clinical signs, depending on the location and size of the cysts and the pressure exerted on the surrounding tissues. The larval stages of the parasite develop mainly in the liver and lungs, and less frequently in the bones, kidneys, spleen, muscles, central nervous system, and eyes. Abdominal pain, nausea, and vomiting commonly occur when cysts invade the liver. If the lung is affected, clinical signs include chronic cough, chest pain, and shortness of breath.

Laboratory diagnosis. Human cystic echinococcosis is diagnosed with imaging tools such as ultrasound or computed tomography, and its laboratory confirmation relies on serological tests.

Prophylaxis. The disease can be prevented by periodic deworming of dogs, improved hygiene, and health education.

DIPHYLLOBOTHRIUM LATUM

Diphyllobothrium latum is a biohelminth causing diphyllobothriasis.

Morphology (Fig. 59). The adult worm reaches up to 10–18 m and has thousands of proglottids. The scolex is elongated and spoon-shaped with two long bothria (sucking grooves) which serve as suckers. The mature and gravid proglottids are broader than long, with the typical rosette-shaped uterus.

Life cycle (Fig. 60). Definitive hosts are human and fish-eating mammals (cats, dogs, polar foxes, bears). The 1st intermediate hosts are small crustaceans (Cyclops, Daphnia), and the 2nd ones are fishes. Predator fishes are reservoir hosts. Stages of the life cycle: *adult worm → egg → coracidium → procercoid → plerocercoid.*

Adult worms multiply sexually in the definitive hosts and lay up to million *eggs* per day. The eggs are passed to the environment in feces. Under appropriate conditions, the eggs mature in 18–20 days. The ciliated larva *coracidium* escapes from the egg and swims in the water. It is ingested by

cyclops and transforms into *procercoid* larva. When the infected cyclops are ingested by a small fish, procercoid develops into *plerocercoid* larva. The plerocercoid larvae are the infective stage for humans.

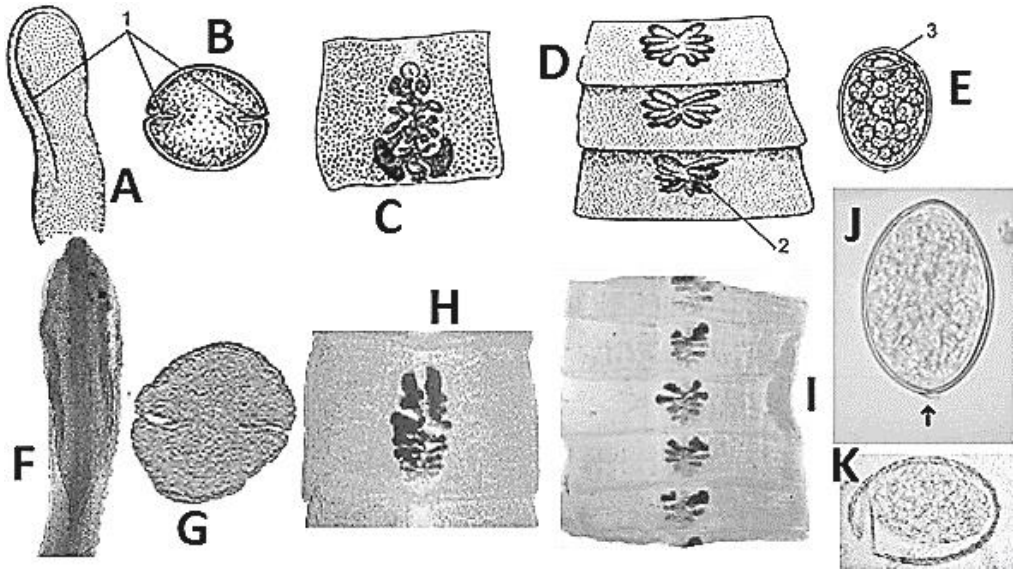


Figure 59. Morphology of Diphyllobothrium latum:
A–E — diagrams; *F–K* — photographs; *A*, *F* — scolex, *B*, *G* — transverse section of the scolex; *C*, *H* — mature proglottid; *D*, *I* — mature proglottid; *E*, *J*, *K* — egg; *1* — bothria; *2* — uterus; *3* — lid on the egg

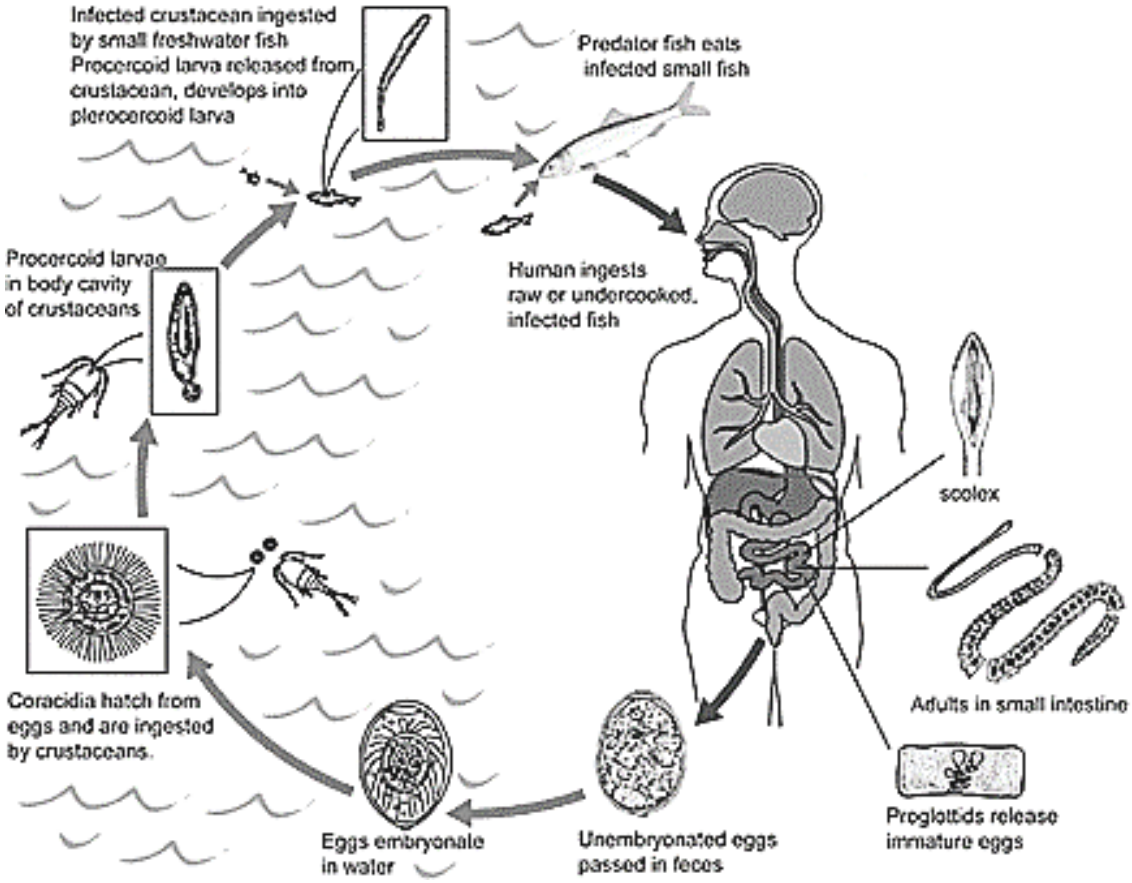


Figure 60. Life cycle of Diphyllobothrium latum

As humans do not generally eat small freshwater fish, these do not represent an important source of infection. Nevertheless, these small second intermediate hosts can be eaten by larger predator fish. In this case, humans can ingest plerocercoid when eating raw or undercooked predator fish. The plerocercoid develops into adults residing in the small intestine.

The life span of adult *D. latum* is up to 25 years.

Clinical presentation. The presence of the adult worm in the intestinal tract causes mild and non-specific abdominal symptoms (diarrhea or constipation, abdominal pain, vomiting, and weight loss).

The characteristic feature of the *D. latum* is the absorption of vitamin B_{12}. The deficiency of this vitamin leads to the development of anemia.

Laboratory diagnosis. Diagnosis is made by finding eggs or proglottids in a stool. Eggs are oval, there is a lid on one pole, and a prominence on the other one. They measure 70 by 50μm.

Prophylaxis. The disease can be prevented by non-eating raw and undercooked fish and caviar.

TECHNIQUES USED FOR LABORATORY DIAGNOSIS OF CESTODOSES

Visual examination of feces. Small portions of feces are mixed with water in a flat bath or a Petrie dish.

They are examined in good illumination against a dark background with a magnifying glass if needed. This allows to reveal helminths, their scolexes, portions of strobila, and proglottids.

Sedimentation techniques: if the specific weight of eggs exceeds the specific weight of the fluid, then the eggs concentrate in the sediment, which is studied under the microscope. It is used for the detection of trematode eggs.

Krasilnikov technique. Under the action of detergents of washing materials eggs of helminths are concentrated in the sediment. The technique allows revealing of eggs of all helminths excreted with feces.

Direct smear. A small part of feces is brought by a stick on the preparation glass into a drop of the 50 % of water — glycerin solution and rubbed until an even smear is obtained, then it is examined under the microscope.

Cellophane thick smear (Kato technique). Eggs of helminths are revealed in a thick smear of feces with glycerin that is stained with malachite green dye. The method reveals eggs of ascaris, whipworms, diphyllobothria, trematodes, and taenia.

Floatation techniques: if the specific weight of eggs is less than the specific weight of the fluid, then eggs float to the surface of the fluid. They are taken to the film which is studied under the microscope. It is used for revealing eggs of ancylostoma, whipworm, and dwarf tapeworm.

Fulleborn technique. A saturated solution of NaCl is used. Eggs of nematodes, dwarf tapeworm, and Diphyllobothrium latum are revealed.

Kalantaryan technique. Excrements are mixed up with a saturated solution of $NaNO_3$ in a ratio of 1 : 20. Eggs of the majority of helminths quickly float up and are revealed in a scum. Oncospheres of taeniae and eggs of trematodes do not float up.

BIOLOGICAL BASIS OF CESTODOSES PROPHYLAXIS

It is a complex of measures that are based on studying the biology of the pathogen, its migration ways, life stages, and the biology of intermediate hosts. That gives the possibility to interrupt a link in the parasite's life cycle. The measures of prophylaxis carried out in endemic regions include:

– Community diagnosis carried out at the district level;

– Preventive chemotherapy (single administrations of antihelmintic medicines);

– Information and education on safe food practices (avoiding food that may contain parasites, proper cooking);

– Improved sanitation (prevents transmission of eggs and larvae to the intermediate hosts);

– Intermediate host control.

CHAPTER 10
PHYLUM NEMATHELMINTHES, CLASS NEMATODA

General Characteristics of the Phylum Nemathelminthes and the Class Nematoda

More than 15 000 species of nematodes are known. There are free-living species that inhabit water, soil, and decaying organic matter; many species are parasites. The phylum Nemathelminthes includes 5 classes. The class Nematoda has a medical significance.

General features of nematodes:

1. Development from 3 germ layers — endoderm, mesoderm and ectoderm.
2. Bilateral symmetry.
3. Unsegmented cylindrical or spindle-like elongated bodies which vary in length from 1 mm to 1.5 m. The cross-section is round.
4. Primary body cavity or *pseudocoelom* (the body cavity which *has no lining* as is not derived from the mesoderm; pseudocoelom originates from blastocoel).
5. The body wall consists of 3 layers: the inner one is a layer of *longitudinal muscles*, *hypodermis* (epidermis), and flexible *cuticle* secreted by the hypodermis.
6. As soon as the cuticle limits the growth, *molting* happens in the juvenile stages.
7. The digestive system consists of 3 regions, the middle one does not have muscles (Fig. 61).

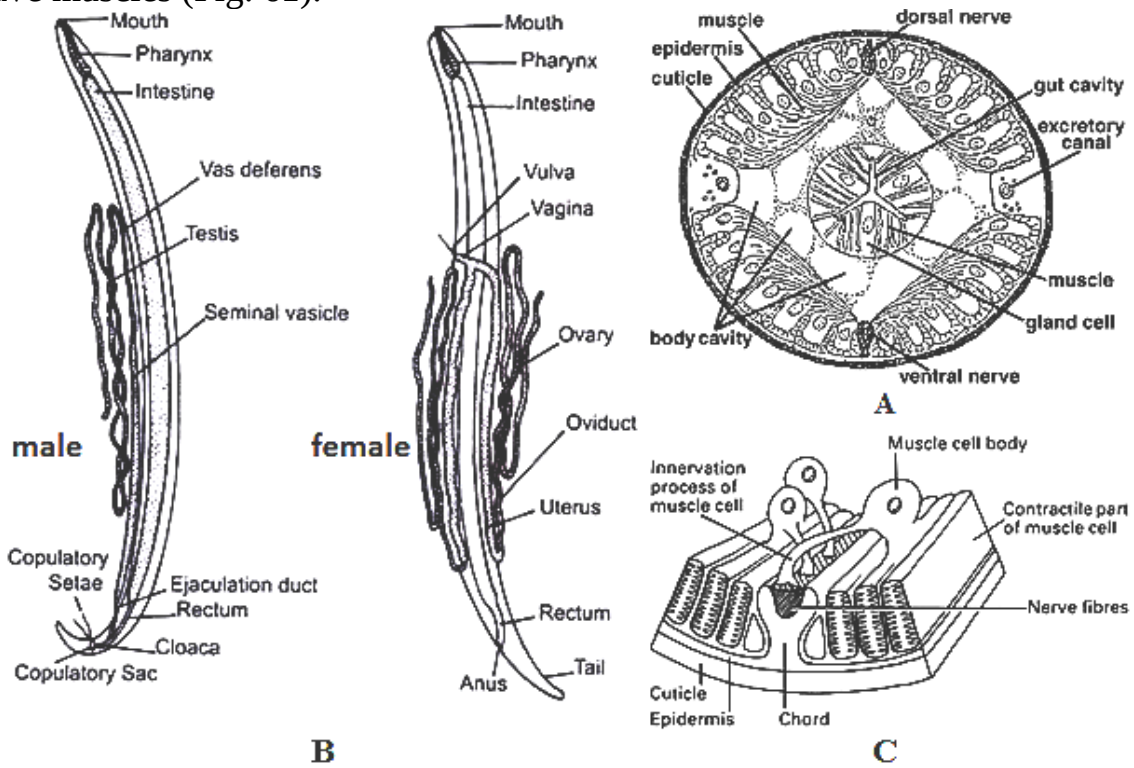


Figure 61. Anatomy of nematodes:
A — cross-section; *B* — dissected male and female ascaris; *C* — fragment of the body wall

8. Waste (such as ammonia) is mostly excreted through the *body's surface*. The excretory system is present. Its ducts are usually H-shaped: two canals are situated in the lateral thickenings of hypodermis, and these canals are joined by a transverse duct. In the region of the junction are 1–2 gland cells. The *excretory pore* is located in the anterior at the ventral side of the body. Removal of wastes from metabolism is also performed by *phagocytic cells* which are situated in the body cavity near the ducts of the excretory system.

9. The nervous system consists of a *nerve ring* surrounding the pharynx and *nerves* (dorsal, ventral, lateral) extending from the ring to the anterior and posterior. Unlike other animals, where the nerves branch out to the muscle cells, a nematode's muscle cells branch toward the nerves. Nematodes have *tactile organs* and *organs of chemical sense*;

10. Nematodes are *dioecious* (i.e. not hermaphrodites; there are males and females) and have noticeable sexual dimorphism: males are smaller than females and their posterior end is spirally curved.

The reproductive system consists of long convoluted tubes. In males, such a tube is single and is differentiated into testes, vas deferens, seminal vesicle, and ejaculatory duct. In females, such tubules can be single or double. They are differentiated into ovaries, oviducts, and uteri which join together to form a vagina. The genital pore is in the middle of the body or near the mouth. Females lay eggs, though some species are viviparous.

The majority of nematodes are *geohelminthes* — they do not require an intermediate host and larval stages develop in the environment. Diseases caused by nematodes are called *nematodoses*.

ASCARIS LUMBRICOIDES

Ascaris lumbricoides is a geohelminth causing *ascariasis* in humans. About a billion people in the world are infected. According to WHO, ascariasis is found worldwide and occurs with greatest frequency in tropical and subtropical regions, and in any areas with inadequate sanitation. Ascaris infections cause approximately 60 000 deaths per year, mainly in children.

Morphology (Fig. 62). The body is cylindrical, sharpened at the ends. The length of an adult female is 15–40 cm, and the length of a male is 15–25 cm. The tail of males is curved, and that of females is straight. There are cuticular lips on the anterior end of the body.

Life cycle. Adult *A. lumbricoides* live and feed in the small intestine. Each female lays up to 240 000 eggs per day, the eggs are passed to the environment with feces. The eggs are unembryonated (larva is not developed yet) and thus non-infective. Eggs develop in soil. This development requires favorable conditions (temperature 20–25 °C, humidity, and oxygen) and lasts 21– 24 days. Humans become infected by ingestion of embryonated eggs with contaminated food or water.

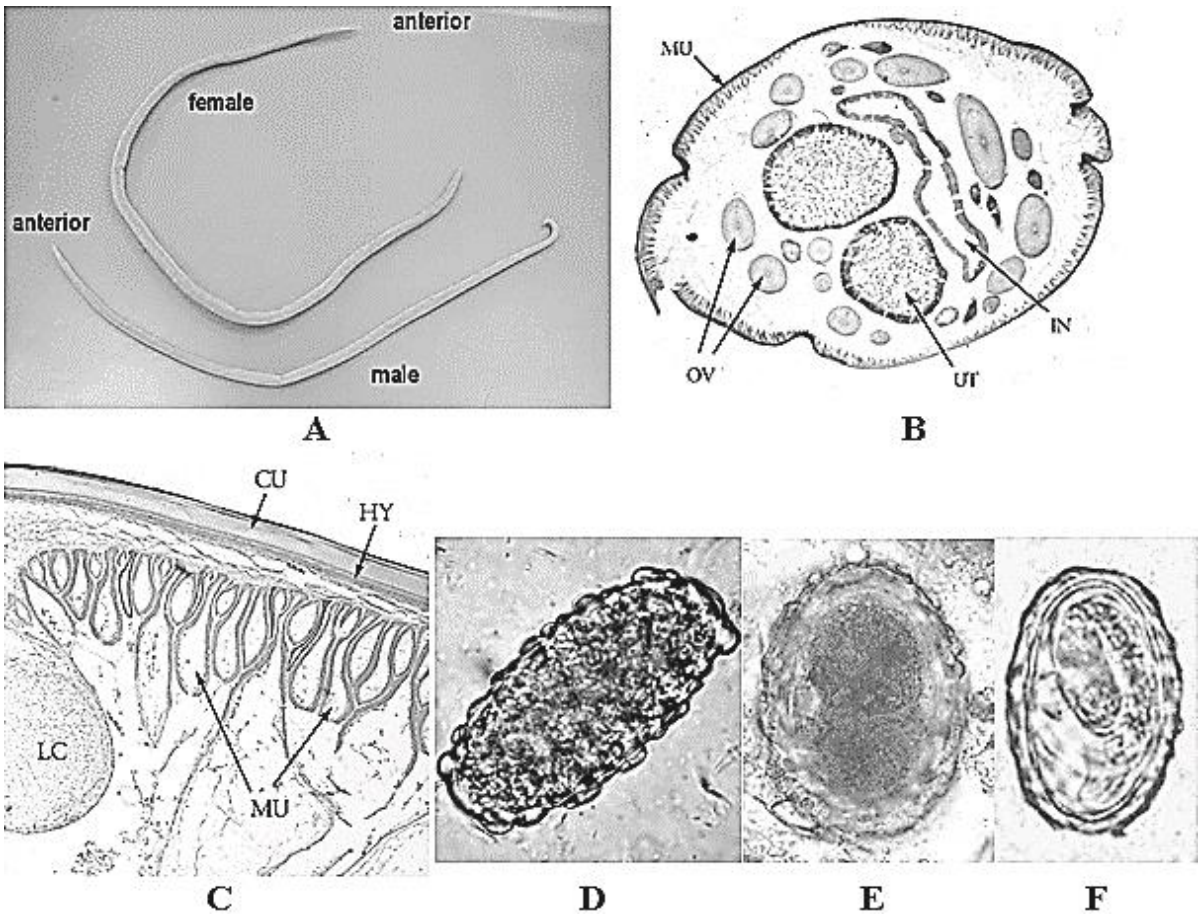


Figure 62. Morphology of Ascaris lumbricoides:
A — adult male and female; *B* — cross-section of a female worm; *C* — cross-section of the cuticle of an adult: MU — muscles; OV — ovaries; UT — uterus; IN — intestine; CU — cuticle; HY — hypodermis; LC — lateral cord; *D*, *E* — unfertilized and fertilized eggs; *F* — larva in an egg (images from CDC)

In the small intestine, larvae hatch out of the eggs, penetrate the intestinal wall, and are carried to the liver through the portal circulation. With blood, the larvae migrate through the heart and reach the alveoli of the lungs. From the alveoli, the larvae then pass through the bronchi and trachea to be swallowed. Larval migration lasts about 2 weeks.

Larvae of other ascaris species (Ascaris of pigs, dogs, etc.) may migrate in the human organism but do not reach maturity. The syndrome they cause is called Larva migrans.

Clinical presentation. Most people infected with ascariasis have no symptoms or have mild symptoms. Infections with a large number of worms may cause severer symptoms.

Clinical presentation of *pulmonary ascariasis* (larval migration): dry cough, difficulty in breathing, wheezing. This is caused by larvae escaping from capillaries in the lungs and causing pneumonitis.

Clinical presentation of *intestinal ascariasis*: abdominal discomfort or pain, nausea, vomiting, diarrhea, weight loss, and growth retardation in children.

Complications of intestinal ascariasis: intestinal obstruction, perforation of the appendix, migration of the parasite to the biliary tree or to the peritoneal cavity. There were cases when parasites were found in the frontal sinuses, cranial cavity, middle ear, and ovaries.

Laboratory diagnosis is based on microscopy of feces in order to find eggs of the parasite. Ascaris egg is round or oval, 60 × 45 μm size, have a thick brown shell with a rough surface. Sometimes larvae can be detected in sputum.

Prophylaxis: to avoid contact with soil that may be contaminated with human feces, to wash hands with soap and water before handling food, wash, peel, or cook all raw vegetables and fruits, protect food from soil, and wash or reheat any food that falls on the floor. Social prophylaxis requires finding and treating sick people, adequate sanitation, and hygiene education.

TRICHURIS TRICHIURA

Human whipworm**,** *Trichuris trichiura* (*Trichocephalus trichiurus*), is a geohelminth causing *trichocephaliasis* (trichuriasis). The disease is common worldwide.

Morphology (Fig. 63). Whipworms have a narrow anterior containing only their gut with a thicker posterior with all organs. The length of an adult female is 3.5–5 cm, males are somewhat shorter (3.0–4.5 cm). The tail of males is coiled, and that of females is straight.

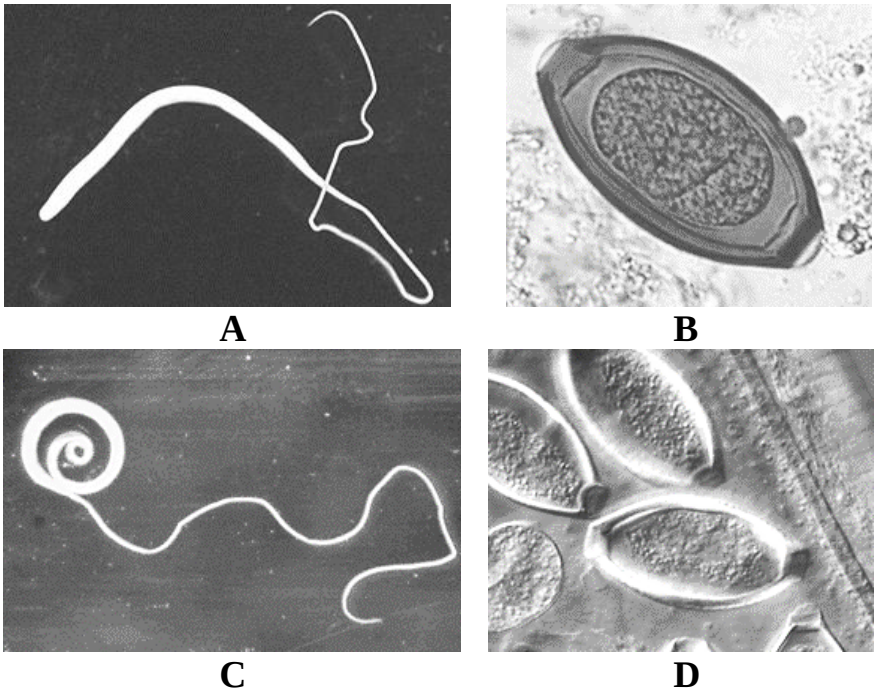


Figure 63. Morphology of Trichocephalus trichiurus:
A — adult female; *B* — egg; *C* — adult male, *D* — eggs

Life cycle. Each female lays up to 60 000 eggs per day. The eggs are passed in feces and develop in soil (temperature 25–30 °C, high humidity, presence of oxygen). The larva develops in the egg in 25–30 days. Ingestion of vegetables, fruit, and water contaminated with eggs causes infection in humans. In the intestine, larvae escape from the eggs and in 1–1.5 months maturate into adults. Larvae do not migrate. The parasites establish themselves in the cecum and ascending colon where they invade mucosa and feed on blood. The life span of whipworms is more than 5 years.

Clinical presentation. In many cases, infected people do not develop symptoms. In other cases, vomiting, diarrhea or constipation, meteorism, and spastic abdominal pains may develop. Consumption of blood by the parasites leads to anemia which causes weakness, dizziness, and paleness. Sometimes appendicitis and rectal prolapse may develop.

Laboratory diagnosis is based on the microscopy of stool specimens for the detection of eggs. Eggs are lemon-shaped, 50–55 × 20–25 μm in size, and have "plugs" on both poles.

Prophylaxis is similar to that of ascariasis.

ENTEROBIUS VERMICULARIS

Enterobius vermicularis **(**seatworm or pinworm**)** is a contact helminth (i.e. human-to-human transmission is possible) causing *enterobiasis*. The disease is common worldwide and is more frequent in children.

Morphology (Fig. 64).

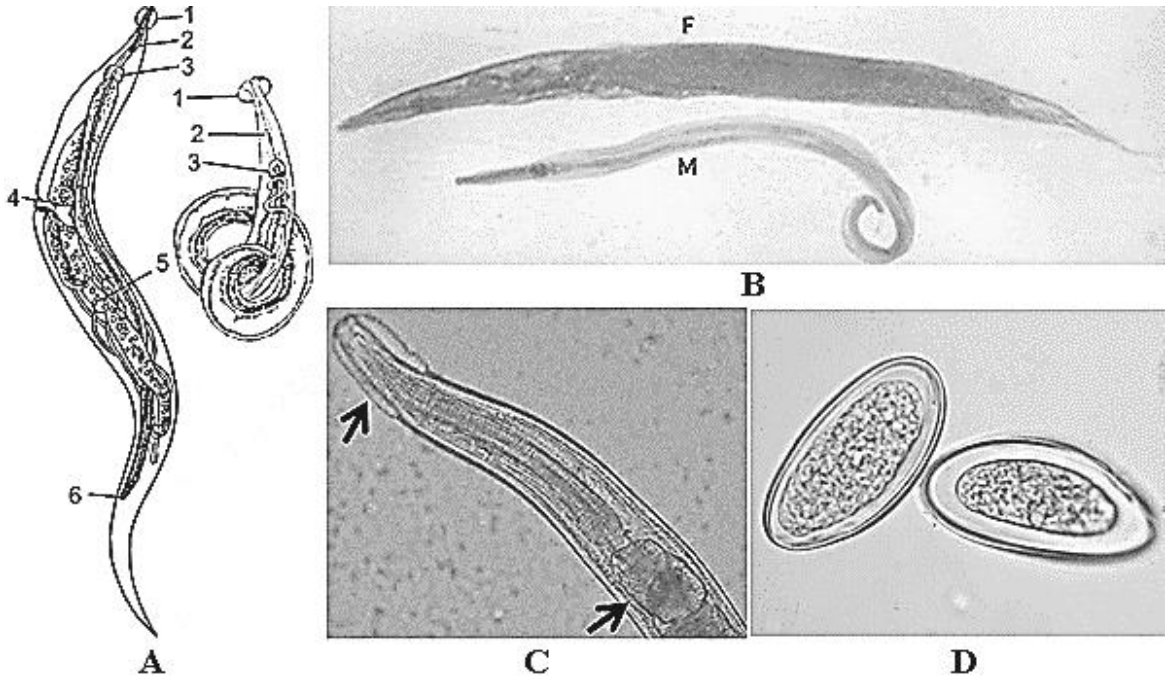


Figure 64. Morphology of Enterobius vermicularis:
A — diagrams of female (left) and male (right); *B* — photograph of female (F) and male (M) whipworms; *C* — anterior end of the parasite; arrows indicate cephalic alae and esophageal bulb; *D* — eggs

Adult parasites look like pins as they have narrow tails, the length of a female is about 10 mm, and that of a male is 2–5 mm. There are cuticular extensions called *cephalic alae* on the anterior end of the body. The esophagus has a prominent swelling called the *esophageal bulb*.

Life cycle. Infection occurs by ingestion of infective eggs, larvae hatch in the small intestine and reach sexual maturity in 2 weeks. Adults colonize the colon. After fertilization males die and gravid females migrate outside the anus (usually at night) and lay eggs on the skin of the perianal area and die. The larvae contained inside the eggs develop in 4 to 6 hours and the eggs become infective. As the secretion produced by a female while laying eggs causes itching in the host, eggs are transferred to the mouth or household goods with hands that have scratched the skin. This provides reinfection and person-to-person transmission.

Clinical presentation. Enterobiasis often does not cause any symptoms except itching and a burning sensation in the perianal area. This may lead to the carrying of infection to the scratched skin. Other symptoms may include sleeplessness, irritability, abdominal pain, and anorexia.

Laboratory diagnosis. A transparent sticky tape is used to touch the perianal area of a patient and collect the eggs. The eggs can be seen under a microscope. As patients scratch the skin, eggs can be found under their fingernails. Eggs are colorless, transparent, oval, and asymmetric as they are slightly flattened on one side, 50–60 × 26–30 μm in size.

Detection of the eggs may be not required as adult female worms can be observed in the perianal area (at night).

Personal prophylaxis. Observing personal hygiene, clean hands, and bed-linen. Prevention of reinfection is dependent upon scrupulous hygiene, including daily washing of the perianal area, regular changes of clothes and nightwear, and strategies to prevent infected children from scratching.

DOG ROUNDWORM (TOXOCARA CANIS)

Toxocara canis (dog roundworm) is a geohelminth that causes *toxocariasis*. The parasite affects dogs, though the larvae may affect humans.

Morphology (Fig. 65). The length of females is 6.5–10 cm, and that of males is 4–6 cm. The posterior end of males is curved ventrally. Both males and females have three prominent cuticularized lips and cervical alae. The life span of the adults is 4–6 months.

Life cycle (Fig. 66). The natural host of *T. canis* is a dog, and humans are accidental hosts. In such hosts its life cycle, in many ways, resembles that of *Ascaris lumbricoides*.

Unembryonated eggs are passed with the feces of the definitive host and develop in the environment to become infective. If such an egg is ingested by a dog, the egg hatches and the larva penetrates the wall of the host's gut.

In younger dogs, the larvae migrate, pass through the lungs and maturate when are in the intestine again.

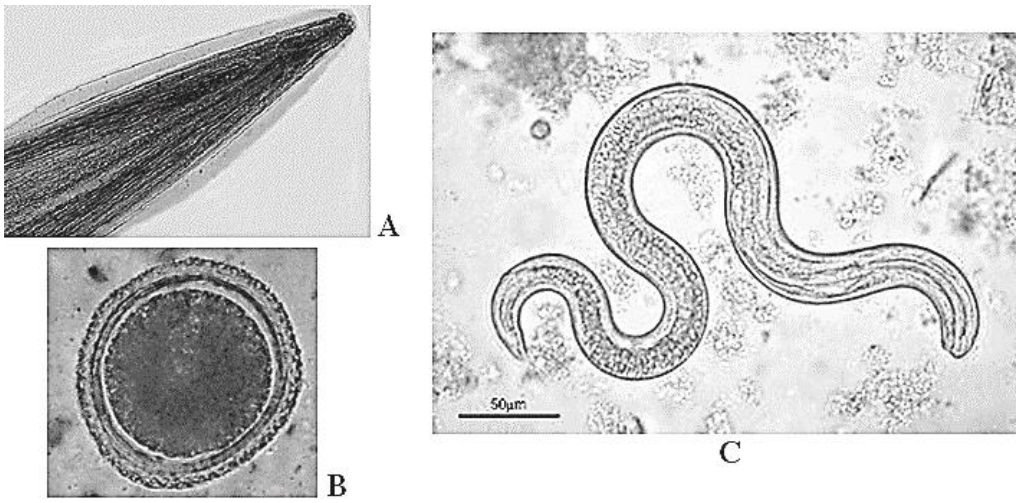


Figure 65. Morphology of Toxocara canis:
A — anterior end of an adult with apparent cervical alae; *B* — egg; *C* — larva

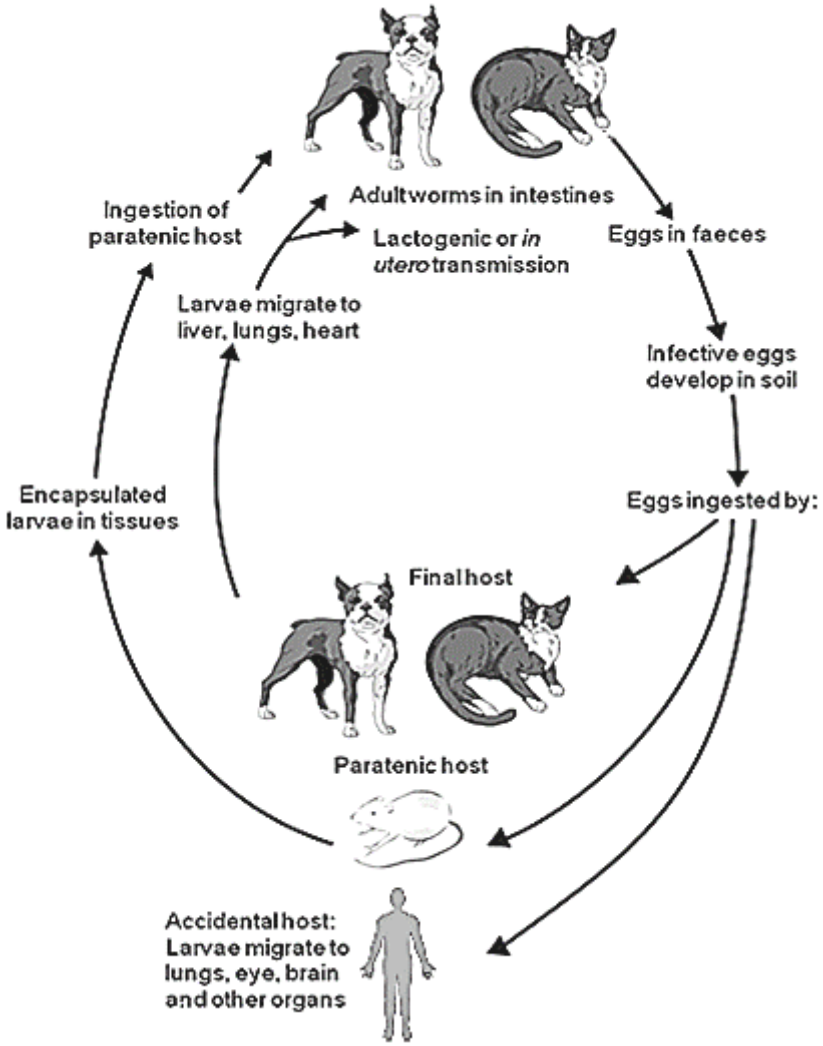


Figure 66. Life cycle of Toxocara canis (affects dogs) and Toxocara catii (affects cats)

In older dogs, the same migration occurs, though larvae can encyst in tissues. In female dogs such encysted larvae reactivate during pregnancy and infect puppies transplacentally.

Toxocara canis can also be transmitted through ingestion of infected hosts having larvae in tissues (small mammals).

Humans are accidental hosts. They become infected when ingest infective eggs with contaminated soil. The eggs hatch, larvae penetrate the intestinal wall and are carried by the circulation to different tissues: heart, liver, brain, lungs, muscle, and eyes.

Larvae do not continue development in these sites but cause severe local inflammatory reactions.

Clinical presentation. The basic mechanism of pathogenesis is antigenic action of larvae and activation of allergic reactions and formation of granulomas in organs. The larvae remain viable for months and years.

Children 1–4 years old fall ill more often. There are several clinical forms of the disease: visceral larva migrans (fever, eosinophilia, enlargement of liver and spleen, rash), ocular larva migrans (affection of an eye, the immunological response is not as strong as in the case of visceral larva migrans), asymptomatic form.

Laboratory diagnosis: detection of larvae in sputum, immunoassay, X-ray, eosinophilia in blood.

Prophylaxis: general sanitary practice for prevention of environmental pollution from dog feces, their treatment, creation of dog-run areas, and obeying hygiene rules.

THREADWORM (STRONGYLOIDES STERCORALIS)

Strongyloides stercoralis is a geohelminth causing *strongyloidiasis*. The disease is common in the South-East Asia, East and South Africa and South America.

Morphology (Fig. 67). *S. stercoralis* may exist as free-living or parasitic worm and these forms have morphological difference. Parasitic females colorless thread-like nematodes about 2.2 mm in size, uteri contain 8–12 thin, shelled, transparent segmented ova. Free-living females are about 1 mm in length. Males are smaller.

Life cycle (Fig. 68). The parasites affect the duodenum, bile, and pancreatic ducts. After mating males die and females lay eggs. *Rhabditiform* (non-infectious) larvae hatch and are passed with feces to the environment. The further development of *rhabditiform larvae* occurs in the soil **in two ways**:

1. If the environmental conditions are unfavorable, they turn into *filariform* (invasive) *larvae* that are able to penetrate human skin. When this happens they migrate to the small intestine (via the bloodstream through lungs like ascaris larvae or directly through tissues) where they maturate into adults.

2. If the conditions are favorable, the rhabditiform larvae transform into free-living males and females who lay eggs. Newly hatched rhabditiform larvae can transform into free-living worms or in filariform larvae.

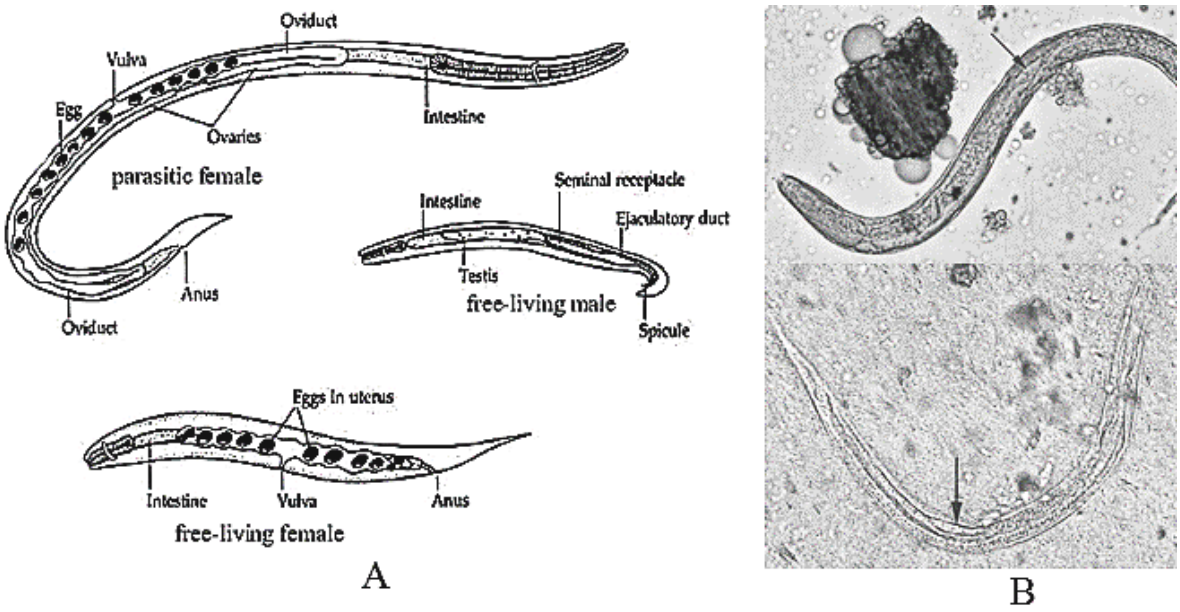


Figure 67. Morphology of Strongyloides stercoralis

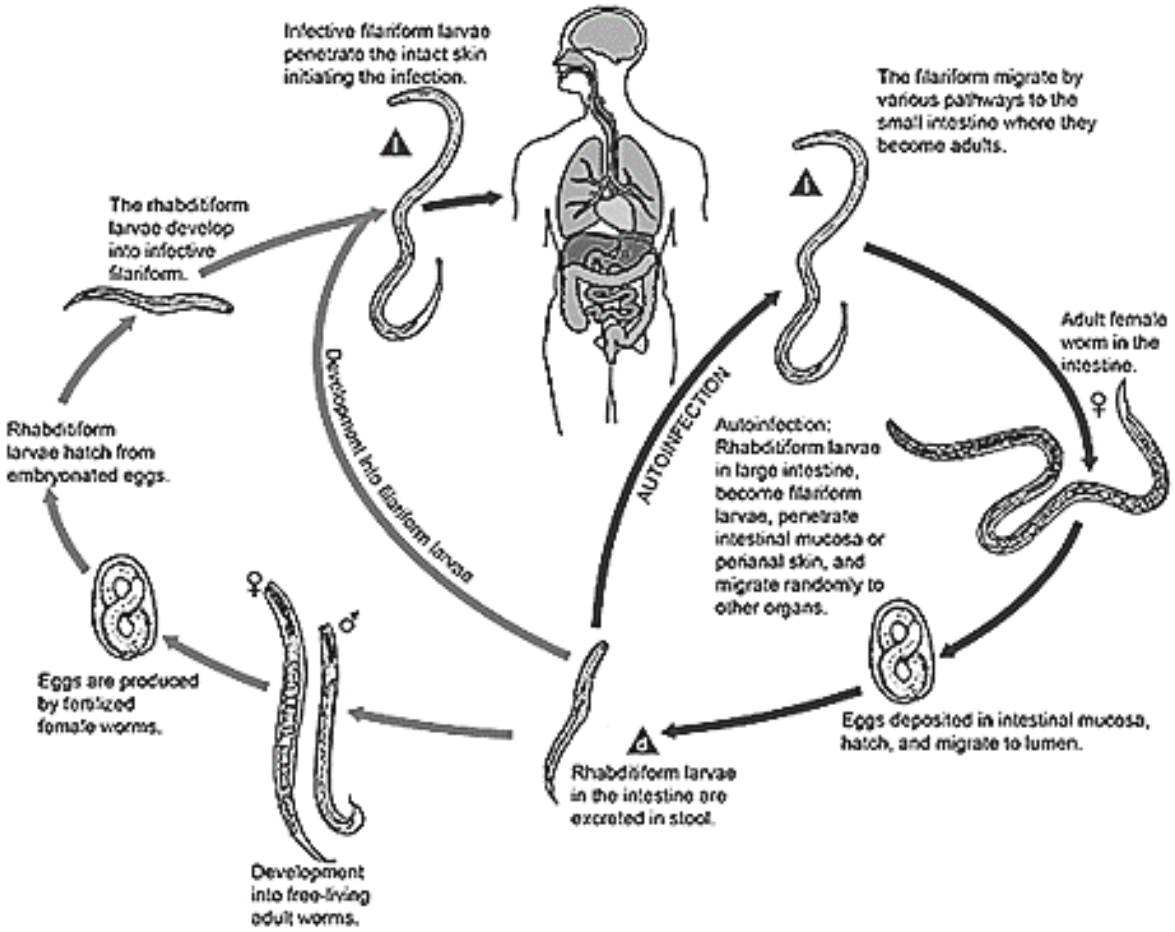


Figure 68. Life cycle of Strongyloides stercoralis

Rhabditiform larvae may not leave the host: they undergo several moltings and transform into filariform larvae in the intestine. The filariform larvae migrate and maturate.

Clinical presentation. Strongyloidiasis may cause intermittent symptoms that mostly affect the intestine (abdominal pain and intermittent or persistent diarrhea), the lungs (cough, wheezing, chronic bronchitis), or the skin (pruritus, urticaria). In asymptomatic cases, the host may stay unaware of the infection for years.

Although strongyloidiasis has usually mild manifestations, the infection may be severe and life-threatening in cases of immunodeficiency (hematological diseases, immunosuppressive therapies). For this reason, it is extremely important to suspect, diagnose and treat the infection.

Laboratory diagnosis is based on the detection of rhabditiform larvae in the stool. This often does not yield positive results even when the disease is present. Serology and polymerase chain reactions are more efficient.

Personal prophylaxis. Avoiding the infection is possible due to observing rules of hygiene, and wear shoes when walking on soil in endemic areas.

ANCYLOSTOMA DUODENALE

Ancylostoma duodenale (Old World hookworm) is a geohelminth, a pathogen of ancylostomiasis. The disease is spread in countries with subtropical and tropical climates.

Morphological peculiarities: length of a female is 10–13 mm, and that of a male is 8–10 mm. There is a funnel-like buccal capsule with 4 cuticular teeth on the head (Fig. 69).

Life cycle: adult worms are located in the duodenum. After fertilization, the female lays eggs that get into the environment with feces.

Under optimal conditions in a day, non-infectious (rhabditiform) larvae come out of eggs in the soil. After several moltings, they transform into infectious (filariform) larvae (Fig. 70).

Humans can be infected by several routes:

1. By active permeation of larvae through the skin.
2. Alimentary by swallowing larvae with contaminated food and water.
3. Vertically (through the placenta).

Having permeated through the skin, larvae migrate: blood carries them through the heart to the lungs where they pass through alveolar walls and get into the respiratory tract, ascend to the pharynx, and are swallowed to reach the duodenum. If a larva gets to the human organism through the mouth migration does not occur. In the intestine larvae of an ancylostoma maturate. The life span of sexually mature parasites reaches 5–6 years.

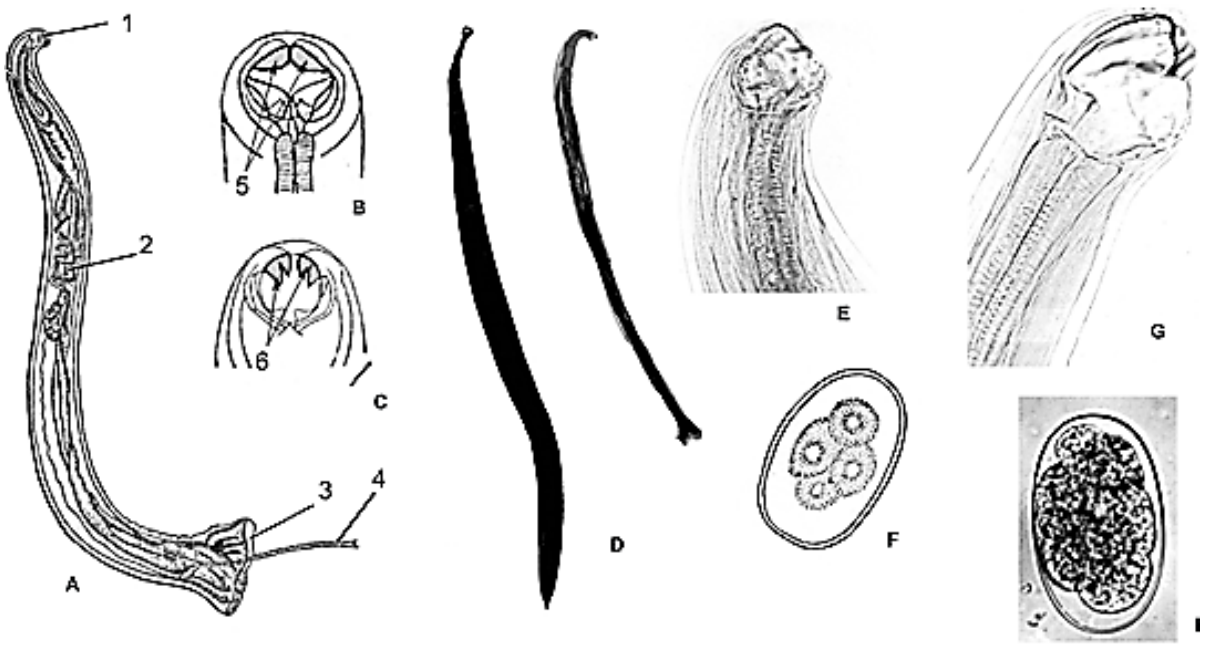


Figure 69. Morphology of hookworms:
A–C, *F* — sketches; *D*, *E*, *G*, *H* — microphotographs; *A*, *D* — sexually mature worms, *B*, *E* — buccal capsule of a necator; C, G — buccal capsule of an ancylostoma: *1* — buccal capsule; *2* — testis; *3* — copulatory bursa; *4* — spicules; *F*, *H* — egg

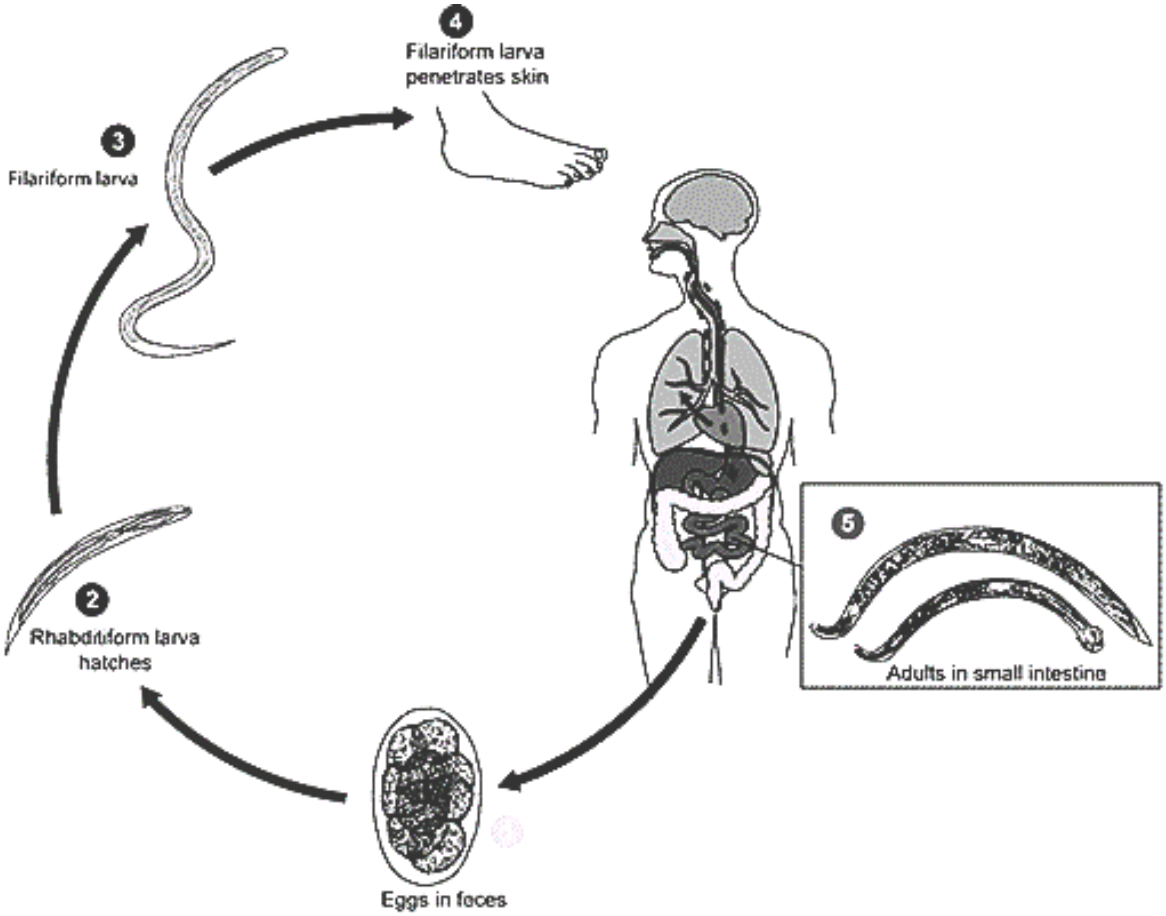


Figure 70. Life cycle of hookworms

Pathogenic action:

1. *Mechanical* (rupture of capillaries, injury of alveoli, harm to the mucous membrane of the intestine by larvae and cuticular teeth of mature parasites).

2. *Toxicoallergic* (poisoning by waste products).

3. *Feeding at the expense of the host's organism* (each hookworm consumes 0.36–0.7 ml of blood per day) *and impairment of metabolic processes*.

Clinical manifestations: in sites of larvae permeation occur painfulness, later itching, and erythema with red papules; pains in the epigastric area, nausea and diarrhea. Children are arrested in physical development. In chronicity of the disease, there are edema, headache, breathlessness, and worsening of memory and workability.

Laboratory diagnostics: revealing eggs or larvae in feces. The eggs are thin–shelled, colorless and measure 60–75 μm by 35–40 μm.

Personal prophylaxis: observing rules of hygiene. It is recommended not to walk barefoot or lie on the ground in foci of ancylostomiasis.

Social prophylaxis: revealing and treating sick people, building sanitary facilities in settlements (water supply, sewage systems), and personal and social health education.

NECATOR AMERICANUS

Necator americanus (New World hookworm) is a geohelminth, a pathogen of necatoriasis. The disease is common in tropical and subtropical regions of Asia and South America.

Morphological peculiarities: in comparison with the ancylostoma, it has 2 sharp plates in the buccal capsule instead of teeth.

The life cycle is same as in ancylostomosis.

Pathogenic action:

1. *Mechanical* (rupture of capillaries and alveoli by larvae, injury of the mucous membrane of a small intestine).

2. *Toxicoallergic* (poisoning by waste products).

3. *Feeding at the expense of the host's organism* (the content of the intestine) *and impairment of metabolic processes.*

Clinical manifestations: skin inflammation, weakness, irritancy, headache, skin itching, symptoms of bronchitis, pneumonia. Then appear signs of enteritis, and gastroenteritis. Complications: perforation of the intestine with peritonitis, pancreatitis.

Laboratory diagnostics: finding rabditform larvae in fresh feces, sometimes in duodenal content, sputum, and vomited matter. A high eosinophilia reaching 70–80 % is noted.

Prophylaxis is the same as in ancylostomiasis.

DIAGNOSTIC TECHNIQUES USED FOR DIAGNOSIS OF NEMATODOSES

The adhesive tape technique is used for the diagnosis of enterobiasis. A sticky side of a piece of transparent tape 4–5 cm long is applied to perineum folds near the anus and is taken off. It is stuck to the prepared glass and studied under the microscope. The examination should be performed in the morning.

Diagnosis of tissue helminthoses. To diagnose tissue helminths (trichinellosis, cysticercosis and etc.) **immunotechniques** are used: immunoprecipitation (IP), complement-fixation test (CFT), indirect hemagglutination test, and others.

Muscular biopsy technique for diagnosis of trichinellosis: a specimen of the gastrocnemius or deltoid muscles is taken. Coiled larvae of trichinella in capsules are well-seen under the microscope.

Muscle digesting technique: artificial gastric juice is added to finely cut muscle specimen and placed into the thermostat at 37 °C for 12–16 hours. Then the sediment is put on the preparation glass with a dropper and examined under the microscope. Trichinella larvae are revealed to be free of capsules.

BIOLOGICAL BASICS OF PROPHYLAXIS OF NEMATODOSES

It is a complex of measures that are based on studying the biology of the pathogen, its migration ways, life stages, and the biology of intermediate hosts. That gives the possibility to interrupt some links of the parasite life cycle.

The prophylaxis measures carried out in endemic regions include:

– community diagnosis carried out at the district level;

– preventive chemotherapy (single administrations of antihelmintic medicines);

– information and education on parasite transmission;

– improved sanitation (prevents transmission of eggs and larvae to soil and other hosts).

CHAPTER 11
PHYLUM NEMATHELMINTHES, CLASS NEMATODA

TRICHINELLA SPIRALIS

Trichinella spiralis is a biohelminth causing *trichinellosis (trichinosis)*.

Morphology (Fig. 71). Females are about 2 mm long, males are smaller (about 1 mm). Female reproductive organs are single.

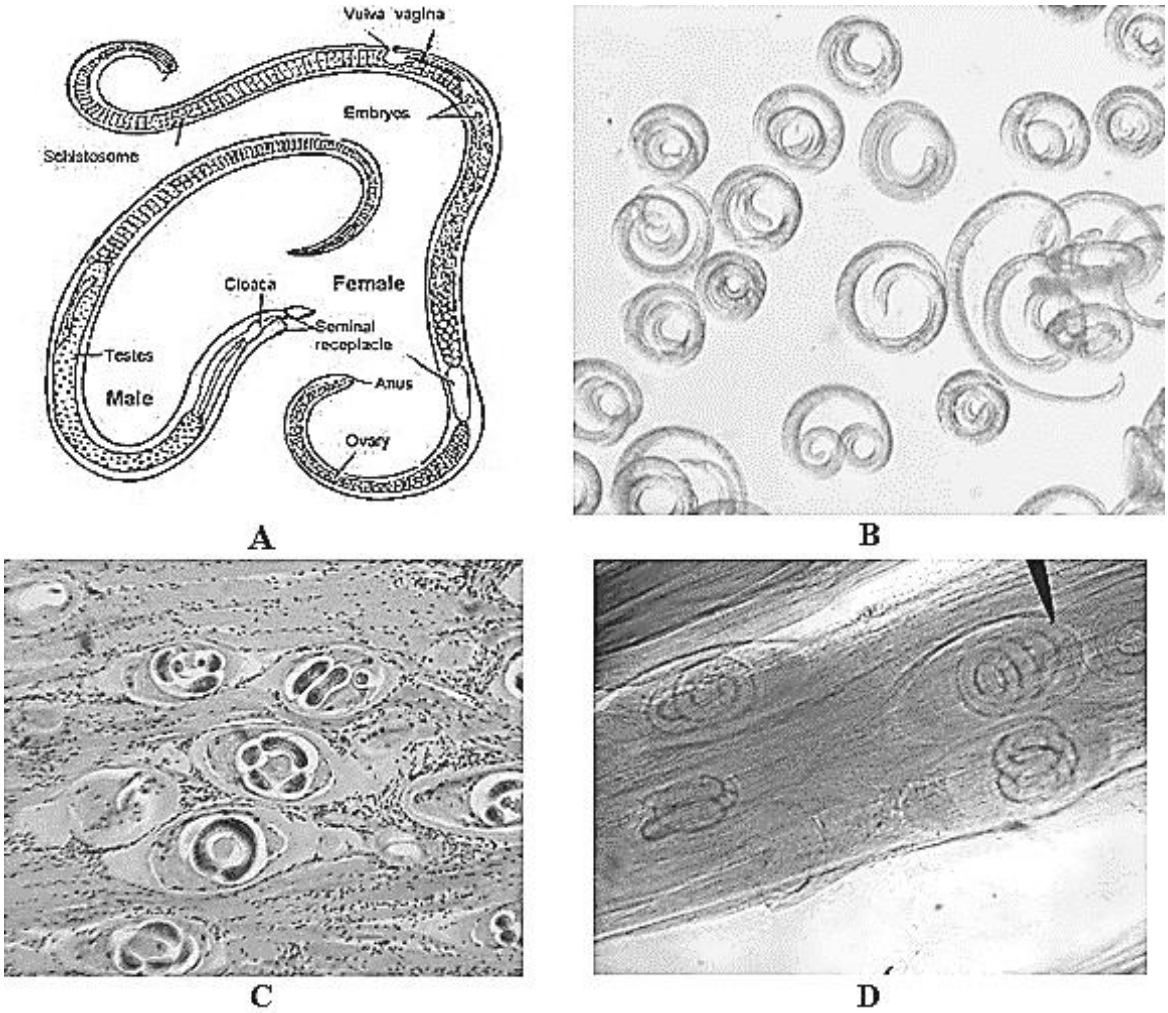


Figure 71. Morphology of Trichinella spiralis:
A — diagram adult worms; *B* — larvae in a sample after digestion of muscle fibers; *C*, *D* — encapsulated larvae in muscles

Life cycle (Fig. 72). Trichinella affects carnivorous and omnivorous animals (pigs, wild boars, cats, dogs, mice, rats, bears, etc.). One and the same organism serves as a definitive and intermediate host (adults live in the intestine, and larvae are in muscles).

Infection occurs by ingestion of meat containing encysted larvae. Gastric enzymes liberate larvae from cysts and they invade the mucosa of the small intestine where they develop into adult worms. The life span of the adults is 4 weeks. The females do not lay eggs, but release larvae which migrate to

the striated muscles and encyst. Such encysted larva may remain viable for several years. Another host becomes infected when ingests encysted larvae.

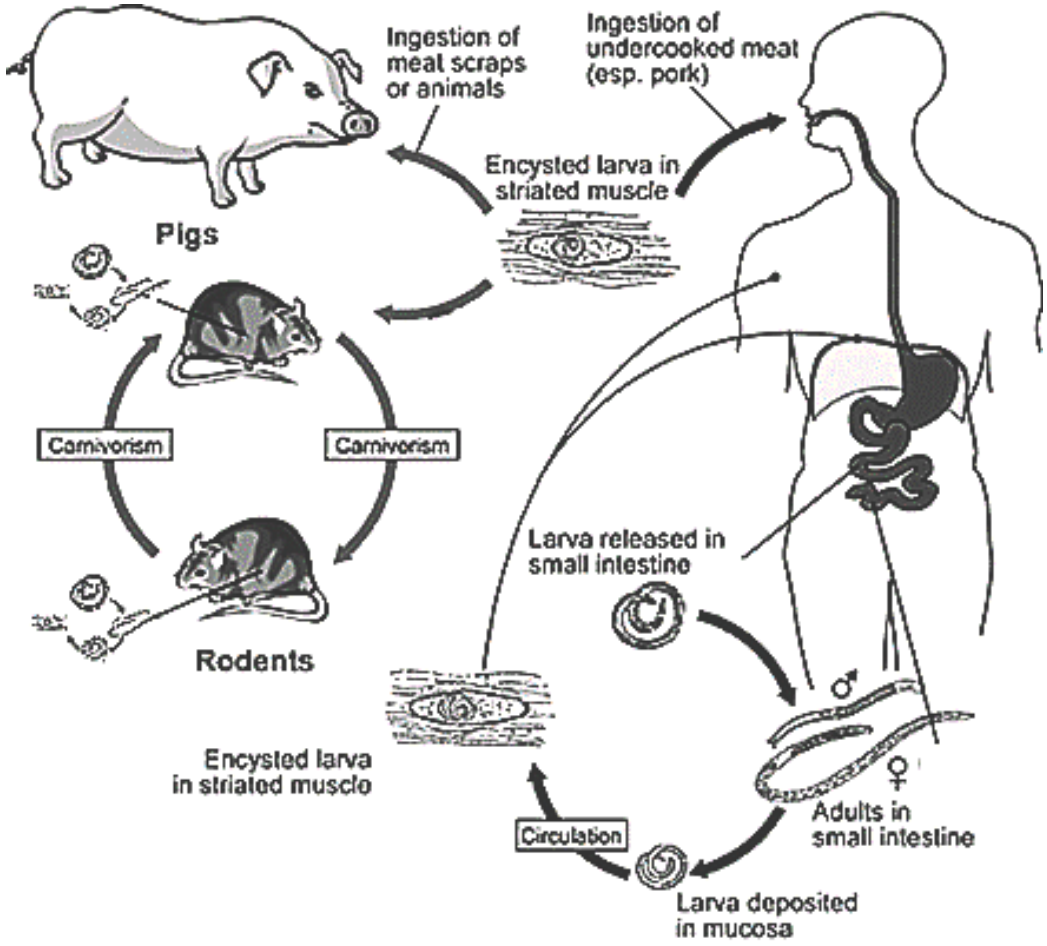


Figure 72. Life cycle of Trichinella spiralis

Rats and rodents are primarily responsible for maintaining the parasite in the nature. Various carnivorous or omnivorous animals become infected when feed on rodents. The common way of human infection is the pork of domestic pigs or wild boars.

Clinical presentation. Gastrointestinal symptoms occur in the first days after infection and may include abdominal pain, nausea, vomiting, and diarrhea. Some facial edema may be present also, accompanied by a slight rash.

Classic symptoms occur about 2 weeks after infection and are associated with the presence of larvae in the body. The symptoms include difficulty in breathing, swelling of facial muscles, heart damage, and nervous disorders.

Death may result from heart failure, respiratory complications, peritonitis, or cerebral involvement.

Laboratory diagnosis. Usual techniques are antibody tests and muscle biopsy for the identification of parasites by microscopy.

Personal prophylaxis: to cook meat to safe temperatures, freeze and salt the pork.

DRACUNCULUS MEDINENSIS

Dracunculus medinensis (Guinea worm) is a biohelminth, a pathogen of dracunculiasis. Foci of the disease are in Africa, the Near East, South-Western Asia, and South America.

Morphological peculiarities: the length of a female is 30–150 cm, and that of a male is 1.2–2.9 cm. Guinea worm is viviparous. The reproductive system has no openings and larvae are liberated through ruptures of the uterus and cuticle on the anterior end of the body.

Life cycle. The definitive hosts of *D. medinensis* are humans, sometimes dogs and monkeys. The intermediate hosts are copepods (genus Cyclops). A sexually mature female worm is located in the subcutaneous tissue of the lower extremities. After fertilization larvae develop in the female. The worm moves its anterior end closer to the host's skin surface and causes the development of a blister (2–7 cm in diameter) filled with fluid. This structure eventually bursts leaving cap-shaped ulcer.

In contact with water, the parasite releases up to 3 million larvae and dies. The larvae are ingested by the intermediate hosts (copepods) and become infective. Infection of human occurs in the case of drinking water with infected copepods. In the intestine, they are digested, and the larvae burrow through the mucosa and migrate to the body cavity and subcutaneous tissue where they maturate in several months. The blister on the skin develops 10–14 months after ingestion of the parasite.

Clinical manifestations: erythema, pains in the extremities, difficulty in movement, skin ulceration, fever, diarrhea, urticaria, and vomiting.

Laboratory diagnostics: not required.

Personal prophylaxis boiling and filtration of water in foci of dracunculiasis. Measures of **social prophylaxis** are revealing and treating sick people, protection of water sources from contamination, and health education.

FILARIAL WORMS

Filarioidea (filarial worms) are biohelminthes, pathogens of filariasis, and is widely spread in countries with tropical and subtropical climates.

The parasites have a threadlike shape, reside in tissues and cavities of the human body, and produce larvae called microfilariae which can be detected in blood or tissues. Filarial worms are viviparous.

The definitive hosts are humans and, for some species, other mammals.

The intermediate hosts and vectors are blood-sucking dipteran insects.

DIROFILARIA REPENS

Nematodes of the genus *Dirofilaria* causes a zoonotic infection called dirofilariasis. Most reported cases involve *Dirofilaria repens*, and *D. immitis* infection has been rarely reported.

Epidemiology. Foci of dirofilariasis are located in the tropical regions of North and South America. Sporadic cases of human infections are registered in European countries and in Belarus.

Morphology. Females are 10–17 cm long and 0.3–0.7 mm wide. Males are somewhat smaller — 5–7 cm long and 0.37–0.45 mm wide.

Life cycle (Fig. 73). *Dirofilaria repens* is a parasite of subcutaneous and intramuscular connective tissues. The definitive hosts of *D. repens* are dogs, cats, wolves, foxes, etc. They, as well as humans, are infected through the bites of infected mosquitoes of genera *Aedes*, *Culex*, *Anopheles*, or *Mansonia*.

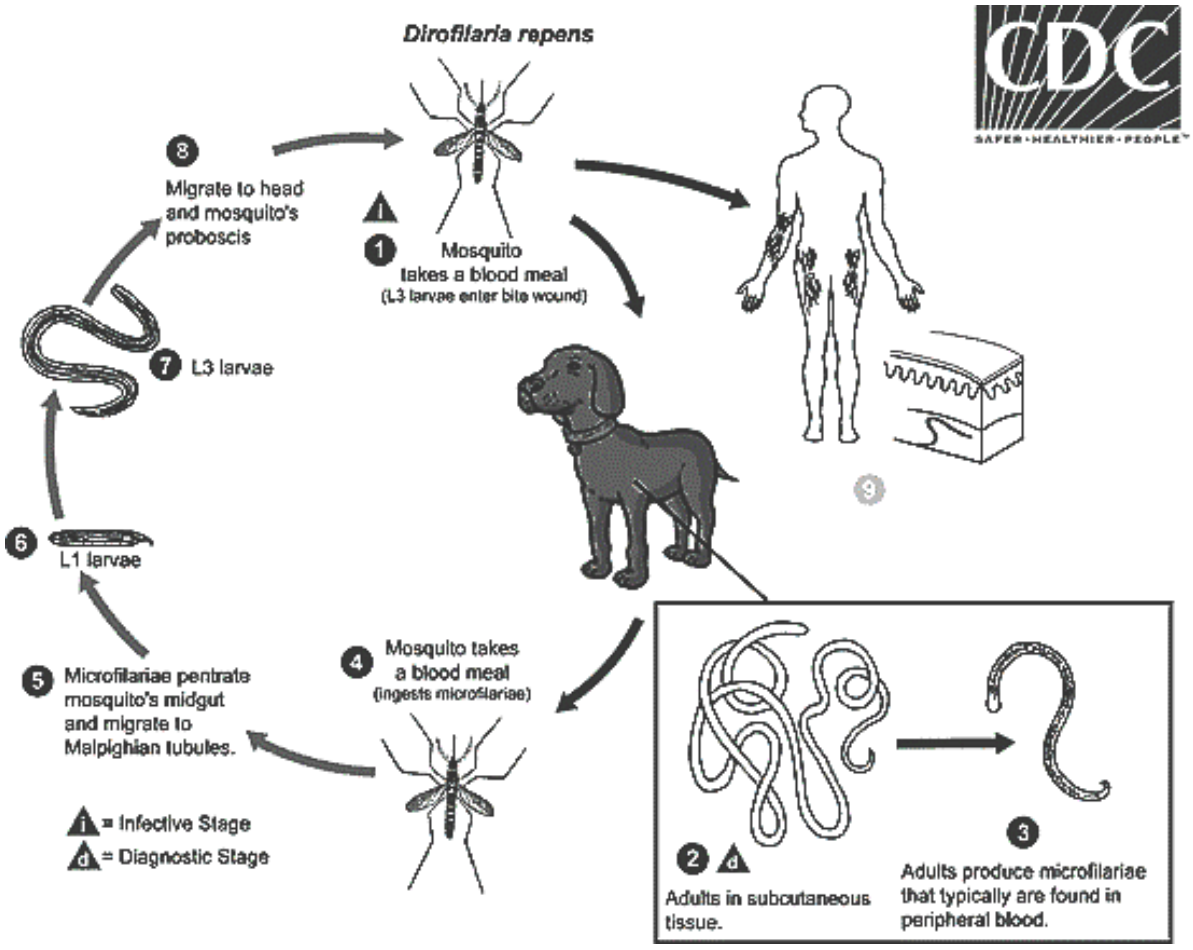


Figure 73. The life cycle of Dirofilaria repens

Mosquitoes are intermediate hosts and vectors of the pathogen. During a blood meal, an infected mosquito introduces third-stage filarial larvae of *Dirofilaria repens* onto the skin of the definitive host.

In the definitive host, the larvae develop into adults which reside in subcutaneous tissues. Adults can live for 5–10 years. In subcutaneous tissue, viviparous females of *D. repens* release microfilariae after mating in the peripheral blood. A mosquito ingests the microfilariae during a blood meal. After ingestion, the microfilariae migrate from the mosquito's midgut through

the hemocoel to the Malpighian tubules in the abdomen. There the microfilariae develop into infective larvae which migrate to the mosquito's proboscis.

Characteristic symptoms. Humans acquire the infection in the same manner as dogs, by the bite of a mosquito. After the bite, a reaction with erythema, swelling, and pruritus lasting 5–8 days is observed. In most cases, a single worm develops, in rare cases the worm may develop into a mature adult and very rarely even release microfilariae. In infected patients, the developing stages of *D. repens* migrate subcutaneously for weeks up to several months, usually with mild and unrecognized symptoms sometimes causing irritation and itching.

During migration *D. repens* may reach the eyes, becoming visible through the subconjunctiva. After weeks to several months from the infection, *D. repens* may stop to migrate and form a nodule of about one centimeter. In most cases, the nodules develop subcutaneously, but have been reported in various human body areas and tissues, mostly in the superficial tissues of the facial regions, skin of the lower leg, soft tissues of the hand, scrotum, the breasts.

Various reasons have been hypothesized for these preferences, such as lower body temperature of these areas, higher awareness of patients for these body parts or a tropism of *D. repens* to higher concentrations of sexual hormones. The nematodes may also reach deeper body areas, such as lymph nodes, the abdominal cavity, lungs, and muscles. If left untreated, *D. repens* may survive for up to 1.5 years. The symptoms caused by *D. repens* nodules usually being limited to local irritation, erythema, and pruritus. Rarely, a strong local immune reaction develops.

Diagnosis: diagnosis in most cases is not made until several weeks or even months after the first signs of the disease as an accidental finding during surgery. Immunological and molecular-genetic methods of dirofilariasis diagnosis are being developed.

Prevention of dirofilariasis in humans can be achieved by protecting people from the bites of mosquitoes through the use of repellents and by reducing the prevalence of *D. repens* in dogs, the principal reservoir of the parasite.

WUCHERERIA BANCROFTI

Wuchereria bancrofti is a pathogen of wuchereriasis.

Morphology: a female has a thread-like body of white color. The length of a female is 8–10 cm and a male is 4 cm.

Life cycle. The definitive hosts are humans, and the intermediate hosts and vectors are the mosquitoes of genera *Culex*, *Anopheles*, *Aedes*, and *Mansonia*. Adult parasites are located in lymphatic vessels and lymph nodes. Female *W. bancrofti* deposit microfilariae that migrate into blood vessels. Mosquitoes can become infected when ingesting microfilaria with blood. Microfilariae develop in the mosquito and become infective larvae. When

the mosquito takes a blood meal from a human, the larvae migrate into the lymphatic system and reach sexual maturity (Fig. 74).

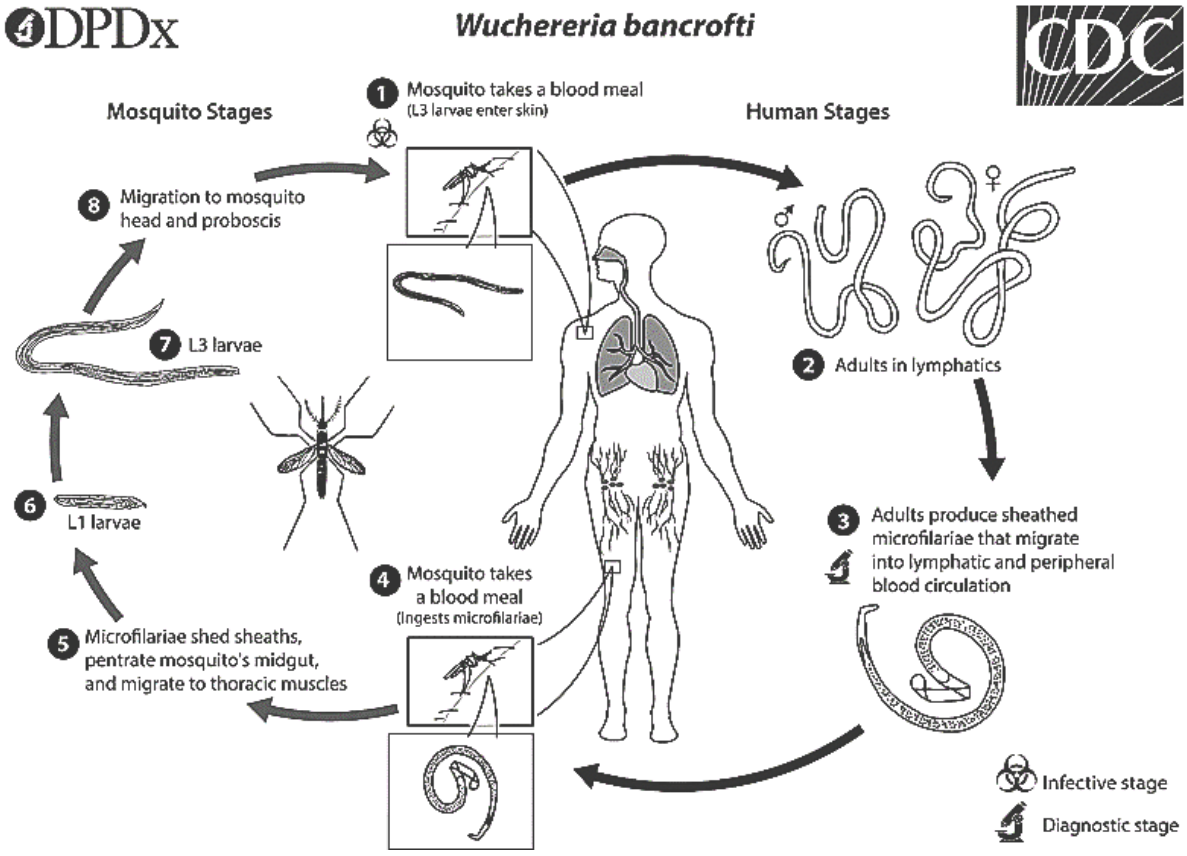


Figure 74. The life cycle of W. bancrofti

Clinical manifestations. Severe manifestations do not develop in the majority of infections. The disease is potentially highly disfiguring and disabling. The most prominent clinical feature is the development of severe lymphedema of the limbs ("elephantiasis") and occasionally genitalia (hydrocele) due to dysfunction of lymphatic vessels. Affected limbs become grossly swollen; the skin may become thick and pitted, and secondary infections are frequent due to lymphatic dysfunction. Scrotal hydrocele is also seen in some infected males. Lymphangitis, lymphadenopathy, and eosinophilia may accompany infection in the early stages.

Diagnosis: detection of microfilaria in blood by microscopy.

Personal prophylaxis: protection from mosquitoes, chemoprophylaxis.

Social prophylaxis: revealing and treating sick people, elimination of the vectors, personal and social health education.

BRUGIA MALAYI

Brugia malayi is a pathogen of *brugiasis*. The morphology and life cycle are similar to those of *W. bancrofti*. *The definitive hosts* are humans, monkeys, cats, and dogs. *The intermediate hosts* and vectors are mosquitoes of the genus

Mansonia. The disease affects mainly the extremities. Pathogenic action, clinical manifestations, and diagnosis are the same as in wuchereriasis.

ONCHOCERCA VOLVULUS

Onchocerca volvulus is a pathogen of onchocerciasis.

Morphology and life cycle: the definitive host is human and the intermediate hosts and vectors are black flies of g. Simulium. Adult parasites reside in the superficial layers of the skin. The subcutaneous nodule that contains encysted parasites is called onchocercoma. After fertilization, females produce microfilariae that permeate into the skin, eyes, and lymphatic nodes. If a sick person is bitten, the microfilariae enter the intermediate host and develop into infective larvae. When the infected black fly bites a healthy person, the larvae enter into the skin, migrate into the subcutaneous tissue, and reach sexual maturity.

Clinical manifestations: onchocerciasis dermatitis (affected areas of the skin become thickened, depigmented, wrinkled, and cracked). Inflammation of sclera and cornea caused by microfilariae may lead to loss of vision ("river blindness").

Laboratory diagnostics: finding microfilariae in section of superficial layers of skin or mature worms in onchocercomata.

Personal prophylaxis: protection from bites of black flies.

Social — treatment of sick people, elimination of black flies, personal and social health education.

LOA LOA

Loa loa is the pathogen of *loaiasis* (*loiasis*).

Morphology: thread-like females are 5 cm long and the males are 3 cm in length.

Life cycle: the definitive hosts are humans, monkeys, and the intermediate hosts are horse-flies. The location of mature parasites is subcutaneous adipose tissue, and eye serous cavities while microfilariae are located in the cardiovascular system. The microfilariae are characterized by a daily periodicity of migrations in the human organism.

Clinical manifestations: pains in the extremities, paresthesia (impairment of sensitivity), edema. If eyes are affected — edema and hyperemia of lids, pains, and decrement in visual acuity. As a result of secondary infection, abscesses may develop in muscles and lymphatic nodes.

Laboratory diagnostics: finding microfilariae in blood smears and in a thick — blood film. Parasites are also seen beneath the conjunctiva.

Personal prophylaxis: protection from horse flies.

Social prophylaxis: revealing and treating sick people, elimination of vectors, personal and social health education.

CHAPTER 12
PHYLUM ARTHROPODA, CLASS ARACHNIDA

GENERAL CHARACTERISTICS AND TAXONOMY OF THE PHYLUM ARTHROPODA

The number of species is over 1.5 million. **Characteristic features:**

1. Development of organ systems from 3 germ layers.
2. Bilateral symmetry.
3. Heteronomous segmentation (body segments are differentiated from one another and perform different functions).
4. Bodies can consist of 2 regions (cephalothorax and abdomen in arachnids and crustaceans) or 3 regions (head, thorax, and abdomen in insects).
5. Jointed appendages.
6. The body is covered with chitinized cuticle (exoskeleton).
7. Presence of striated muscles and separated groups of muscles.
8. The body cavity is mixocoel (or haemocoel). It develops when blastocoel fuses with coelom.
9. The digestive system consists of 3 regions: foregut, midgut, and hindgut. It begins from a mouth with mouthparts and ends with an anal opening. There are digestive glands such as salivary glands and hepatic ceca (which perform some functions analogous to those of the liver in vertebrates).
10. Excretory organs are green, coxal, and other glands or Malpighian tubules.
11. Respiratory organs are: various forms of gills in aquatic arthropods, or book lungs and trachea in terrestrial ones.
12. The circulatory system is open: "blood" is pumped to the haemocoel and then diffuses back to the circulatory system. The "blood" of arthropods is hemolymph. The tube–shaped heart is located on the dorsal side of the body.
13. The nervous system includes a large cerebral ganglion sometimes referred to as the brain, a nerve ring surrounding the pharynx, and a ventral nerve chord.
14. There are sensory organs of sight, smell, tactile sense, taste, hearing, and equilibrium. Arthropods are dioecious (have separate sexes). Males and females differ in size and color (such distinction is sexual dimorphism). Development is direct or indirect (with metamorphosis).

Classes of the phylum *Arthropoda*: *Crustacea*, *Arachnida,* and *Insecta*.

GENERAL CHARACTERISTICS AND CLASSIFICATION OF THE CLASS ARACHNIDA

The number of species is about 40 000. They adapted to living on land. Arachnids have 2 regions of the body: cephalothorax and abdomen, but the bodies of ticks and mites have no regions. The body wall of arachnids is

covered with a cuticle saturated with chitin. The cephalothorax carries 6 pairs of appendages. The first and second pairs (chelicerae and pedipalps) are used to hold and fragmentize food. The other 4 pairs are walking legs. The digestive system is adapted for feeding on semi-liquid food.

Excretory organs of arachnids are coxal glands and Malpighian tubules. Respiratory organs are book lungs and trachea.

The circulatory system is open (blood bathes the organs in the body cavity). There is a tube-shaped heart with openings called ostia on the dorsal side of the abdomen. Ostia (3–7 pairs) act as non-return valves allowing blood to move in only one direction into the heart. There are also 2 short aortae (anterior and posterior ones) and lateral arteries branching from the heart.

The nervous system consists of a cerebral ganglion that performs the functions of the brain, ventral nerve cord, and nerves. Sensory organs are simple eyes, organs of smell and chemical taste. Arachnids are dioecious. Sexual dimorphism is marked. Reproduction is sexual, and development is direct or indirect (with metamorphosis).

Orders: scorpions (*Scorpiones*), spiders (*Araneae*), ticks, and mites (*Acarina*).

ORDER ACARI

Acari (or *Acarina*) is a group of arachnids that contains ticks and mites (mites are considered to be microscopic ticks).

Classification: phylum *Arthropoda*, class *Arachnida*, order *Acari*, families: *Ixodidae, Tyroglyphidae, Sarcoptidae,* and *Demodicidae*.

FAMILY IXODIDAE

Representatives: *Ixodes ricinus* or a castor bean tick, *Ixodes persulcatus* or the taiga tick, *Dermacentor pictus*, *Dermacentor marginatus, Hyalomma anatolicum*.

Morphology (Fig. 75). The ticks are from 5 to 25 mm in size. They inhabit forests and steppe. The bodies of the ticks are dorsoventrally flattened and have no regions. There is 1 pair of eyes and 4 pairs of walking legs.

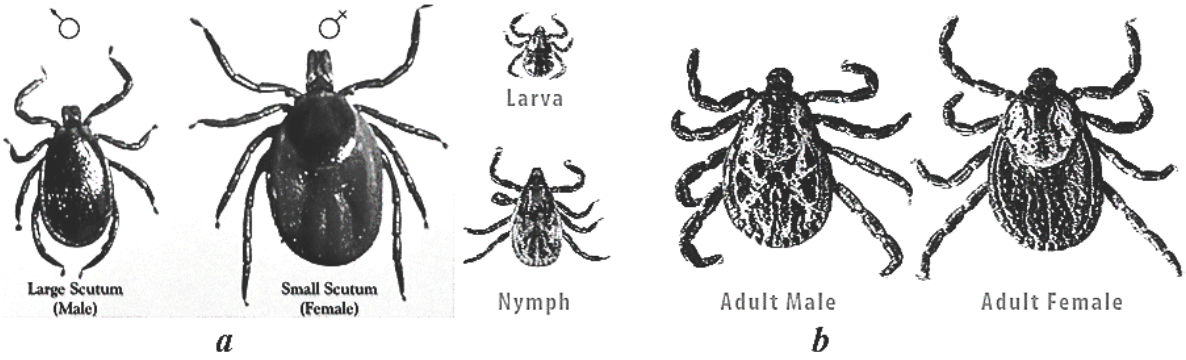


Figure 75. Ticks of the family Ixodidae:
a — genus Ixodes; *b* — genus Dermacentor

The first two pairs of appendages are transformed into mouthparts of piercing and sucking type. The complex of a tick's mouthparts is called the *capitulum*. It is located on the anterior end of the body and can be seen from the dorsal side.

There is a chitin dorsal shield (*scutum*) covering the whole dorsal side in males and only the anterior part of the back in females. This provides greater elasticity of the female's abdomen during a blood meal.

The ticks of the genus *Ixodes* have dark-brown scutum. The ticks of the genus *Dermacentor* have scutum with a marble pattern.

Life cycle (Fig. 76). A female tick lays about 17 000 eggs in the soil or bark of dead trees. Ticks go through four life stages: egg, six-legged larva, eight-legged nymph, and adult (imago). Passing from one stage to the next is marked with moltings. After hatching from the eggs, ticks must feed on blood at every stage. Blood meal lasts up to several days. The ticks can starve for up to 3 years. The bites are painless as their saliva contains anesthetics.

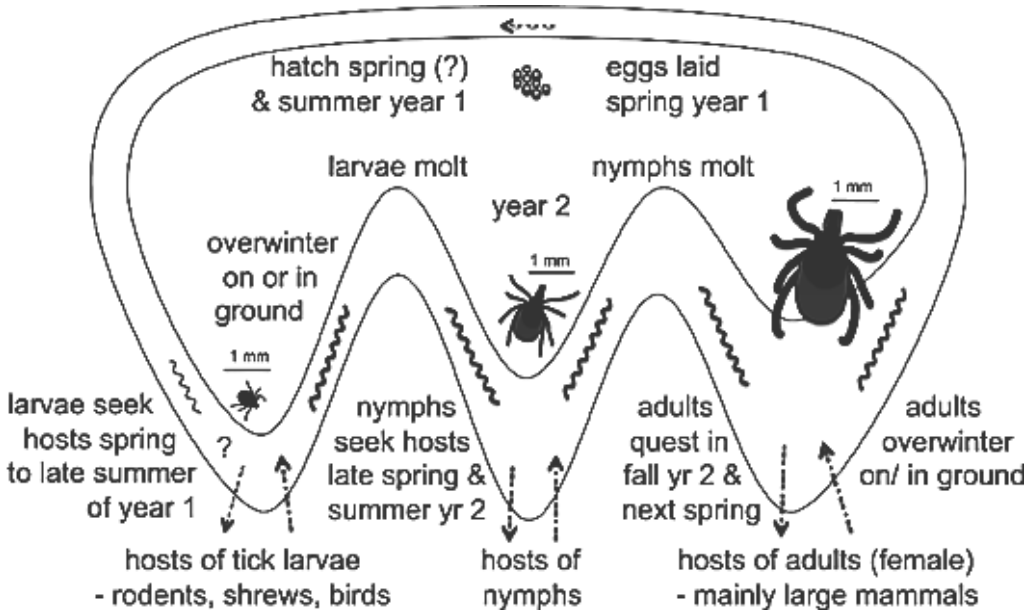


Figure 76. The life cycle of a typical tick of the family Ixodidae (Ixodes scapularis)

Medical significance. Ticks of the family *Ixodidae* are biological vectors of the *tick-borne encephalitis*. The virus of tick–borne encephalitis (family *Flaviviridae*) is present in the salivary glands and gonads of ticks. The disease is transmitted by the bite of a tick (from tick to human) and transovarially (from tick to its larva through the cytoplasm of the egg). The natural reservoirs of the virus are birds and rodents.

Ticks of the genus *Ixodes* also transmit *viral hemorrhagic fevers*, *brucellosis*, *typhus*, *plague*, and *tularemia*. Ticks of the genus *Dermacentor* transmit the virus of *Scotland encephalitis*.

FAMILY ARGASIDAE

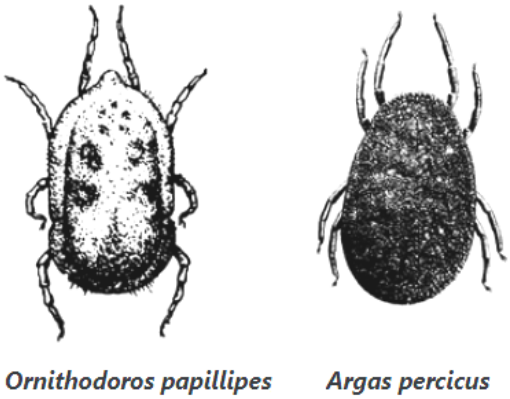


Figure 77. Ticks of the family Argasidae

Family Argasidae includes *Ornithodoros papillipes, Argas persicus*, or the fowl tick.

Morphology: the body sizes are from 2 to 30 mm. A scutum is absent. The capitulum is located on the underside of the body and can not be seen from the dorsal side. There is a marginal welt. Eyes are absent (Fig. 77).

Life cycle. Argasidae ticks inhabit caves, holes of rodents, and abandoned buildings. Blood meal lasts about 50 minutes. Ticks can starve for up to 12–15 years. Females lay 50–200 eggs. There are several stages of nymphs. Transovarial transmission of pathogens is possible.

Medical significance. Argasidae ticks are specific vectors of a *tick-borne relapsing fever* — infection caused by bacteria in the genus *Borrelia*. Natural reservoirs of the pathogen are cats, dogs, and wild rodents. The saliva of Argasidae ticks is toxic, their bites may cause dermatitis.

FAMILY GAMASIDAE

Example: *Dermanyssus gallinae* or the chicken mite.

Morphology: the size of the mite is 0.2–0.3 mm. The body is covered with bristles. Eyes are absent.

Life cycle: Gamasidae ticks inhabit holes of rodents, and nests of birds. Females feed on blood and then hide away from daylight and lay eggs. From nests of pigeons, they can get to human habitation through ventilation pipes.

Medical significance: the mites are permanent or temporary ectoparasites of various animals and birds. Their bites cause dermatitis. Asthmatic symptoms may develop if the mites enter the host's respiratory tract. They transmit pathogens of rat-borne typhus, encephalitis, hemorrhagic fevers, plague, and tularemia.

Protective measures against ticks: while walking in a forest travelers can minimize areas of exposed skin by wearing long-sleeved shirts, long pants, and hats. Tucking shirts, tucking pants into socks, and using repellents may reduce risk. Travelers should examine the clothes and the body to remove ticks after going to the forest.

FAMILY TYROGLYPHIDAE

Tyroglyphus farinae (*Acarus siro*) or flour mite.

Morphology (Fig. 78, *a*). The body of a flour mite is of a slightly — yellow color, sizes are 0.4–0.7 mm and has no eyes.

T. farinae may inhabit granary (flour, groats, corn, cheese, etc.), spoil grain and seeds with their excretions.

Medical significance: eating contaminated food may cause diarrhea. During harvesting, the mites may cause *grain itch.* When inhaled they may cause asthmatic symptoms.

FAMILY SARCOPTIDAE

Sarcoptes scabiei (itch mite) is a permanent parasite of humans and animals that causes *scabies*. According to WHO reports, globally, scabies affects more than 130 million people at any time. The disease can affect people in all countries.

Morphology (Fig. 78, *b*). The mites have a wide, oval, slightly yellowish body. The body length of a female is about 0.3–0.4 mm, males are smaller than females. There are 4 pairs of cone-shaped short legs, and eyes are absent. The mites breathe with the whole body surface.

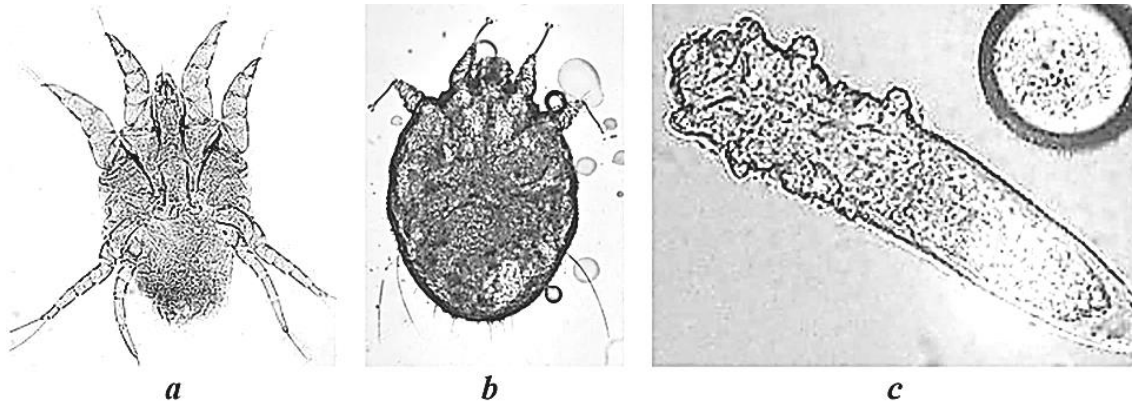


Figure 78. Mites causing human diseases:
a — Tyroglyphus farinae; *b* — Sarcoptes scabiei; *c* — Demodex folliculorum

Life cycle. Mites burrow into the skin and trigger a host immune response that leads to intense itching in response to just a few mites. A fertilized female burrows into the stratum corneum of the skin per 2 mm a day and lays about 1–2 eggs per day in the burrow. Males do not burrow the skin. The mites feed on the host's tissues. The development from an egg to an imago takes about 1–2 weeks. Adult mites live up to 2 months.

Medical significance. The most common symptom of scabies is severe itchiness becoming worse at night. This symptom can be present across most of the body or only some areas such as wrists, areas between fingers, or along the waistline. Scabies is usually transmitted through skin-to-skin contact or through contact with contaminated clothes. Scabies is frequently complicated by bacterial infection, leading to the development of skin sores.

Diagnosis. Generally, the diagnosis of scabies is based on clinical recognition of the typical features. Laboratory diagnosis includes obtaining a skin scraping to examine under a microscope for mites, eggs, or mite fecal matter.

Prophylaxis of scabies: following basic hygiene rules in communicating with animals and sick people; maintaining the purity of the body; treatment of sick persons; sanitary inspection of hostels and bathhouses.

FAMILY DEMODICIDAE

Demodex folliculorum is a mite causing demodicosis.

Morphology (Fig. 78, *c*): the worm-shaped body has a length of about 0.4 mm. The cuticle is thin and transparent. Legs are very short and have per a pair of claws.

Life cycle. The mites affect sebaceous glands and hair follicles on the face, neck, and shoulders (the head of such mites is directed to the depth of the gland). They are often found in healthy people. In people predisposed to allergy, the mites may intensively multiply and obturate ducts of sebaceous glands.

Medical significance: *Demodex folliculorum* causes demodicosis which is characterized by acne of pink color with pus. Infection occurs by means of direct contact with a sick person. Diagnosis is based on microscopy of the content of sebaceous glands or hair bulbs which reveals imago, larvae, nymphs, or eggs of the parasites.

THE STUDY OF YEVGENY PAVLOVSKY ABOUT THE NATURAL FOCI OF VECTOR-BORNE DISEASES. CHARACTERISTICS OF A NATURAL FOCUS

The diseases are called **vector-borne** if their pathogens are transmitted by blood-sucking arthropods. Transmission of a pathogen occurs during blood meal through a proboscis (*inoculation*), through the host's skin by vector's feces containing pathogens (*contamination*). Many blood-sucking arthropods are characterized by the transmission of the pathogen through eggs during sexual reproduction (*transovarially*) from mature arthropods to its larvae.

Pathogens undergo definite development stages in the organism of **biological vector** (malaria parasites develop in Anopheles mosquitoes). **Mechanical vectors** (flies, cockroaches) transmit pathogens on the body surface or mouthparts. *Obligate vector-borne diseases* are transmitted only by a vector (leishmaniasis). *Facultative vector-borne diseases* (plague, tularemia, anthrax) are transmitted by the vector and in other ways (alimentary or respiratory transmission routes).

A vector-borne disease is characterized by 3 components: 1) Pathogen (parasite); 2) Host; 3) Vector (arthropod).

Natural focus and its structure. In 1940 Y. Pavlovsky formulated a study about the natural foci of vector-borne diseases. A natural focus is a definite geographic territory, where the circulation of the pathogen from a donor to a recipient occurs through a vector. *Donors of a pathogen* are sick animals, and *recipients of a pathogen* are healthy animals, which become donors after getting infected.

CHAPTER 13
PHYLUM ARTHROPODA, CLASS INSECTA

GENERAL CHARACTERISTIC AND TAXONOMY OF CLASS INSECTA

The number of species is over 1 million.

Anatomical peculiarities:

• Bodies of insects are segmented; each segment has a pair of appendages (on some segments they are reduced).

• Insects have 3 body regions: head, thorax, and abdomen.

• The head carries one pair of compound eyes (i.e. consisting of numerous little "eyes").

• Appendages of the head are transformed into a pair of antennae (sense organs) and some mouthparts. The mouthparts of insects are the upper and lower lips (labrum and labium), upper and lower jaws (mandible and maxilla), and hypopharynx.

• There are different types of mouthparts in insects. It depends on the common food of the species (piercing-sucking, sponging, chewing, siphoning).

• The thorax consists of three segments. Each segment has a pair of walking legs, thus insects have 3 pairs of legs. Insects may have 1 or 2 pairs of wings which are located on the 2^{nd} and 3^{rd} segments on the dorsal side of the thorax.

• The abdomen consists of 6–12 segments without appendages.

• The layers of the body wall of insects are chitin (the outer one), and hypodermis (the inner one) containing such structures as odoriferous glands, wax glands, and prothoracic glands.

• The muscles of insects are striated, they are differentiated and specialized. The digestive system of insects consists of a foregut, midgut, and hindgut.

• The excretory organs of insects are Malpighian tubules and fat body (the organ which stores nutrition and metabolic wastes removing them from metabolism).

• The respiratory system of insects is consists of multiple branching trachea which open to the environment with spiracles.

• The circulatory system includes tube — like heart on the dorsal side of the body. The heart pumps hemolymph to the aorta which opens on the anterior side of the body and hemolymph passes to the body cavity (hemocoel). Blood is absorbed by the heart through openings which are called *ostia*.

• The nervous system consists of suprapharyngeal ganglion (the brain having 3 regions — anterior, middle, and posterior) and the ventral nerve cord. Tactile organs are sensitive hairs covering the body. Olfactory organs are located on palps, antennae, and mandibles. Taste receptors are located on mouthparts and legs.

• The reproduction of insects is sexual, they are dioecious and have sexual dimorphism. Development is direct or indirect with complete or incomplete metamorphosis).

The following criteria are used for the division of insects into classes: type of mouthparts, presence and the number of wings, and type of development (Table 6).

Table 6

Orders of insects

Order	Examples	Metamorphosis	Structure of wings	Mouthparts
Heteroptera (true bugs)	Bedbug, kissing bug	Incomplete	2 pairs: fore wings are partially membranous, hind wings are membranous	Piercing-sucking
Blattoidea (cockroaches and termites)	Oriental cockroach, German cockroach, American cockroach	Incomplete	2 pairs: fore wings look leathery, hind wings are membranous	Chewing
Anoplura (lice)	Head lice, body lice, pubic lice	Incomplete	Absent	Piercing-sucking
***Aphaniptera* (Siphonaptera)** (fleas)	Human flea, oriental rat flea	Complete	Absent	Piercing-sucking
Diptera (true flies, mosquitoes)	Sandflies, mosquitoes, house fly, tsetse fly, stable fly, spotted flesh fly	Complete	2 pairs: forewings are membranous; the back wings are reduced and transformed into halteres	Piercing-sucking, sponging

Medical significance. Many insect species are vectors or pathogens of diseases (ectoparasites), and bites of many insects may cause allergic reactions.

SUCKING LICE (ORDER ANOPLURA)

Taxonomy. There are two genera in the order *Anoplura*: genus *Pediculus* and genus *Pthirus*. The genus *Pediculus* has only one species — ***Pediculus humanus***, which, in turn, includes 2 subspecies — the *Pediculus humanus capitis* and the *Pediculus humanus humanus*. Both of them can cross and produce fertile offspring, though they have some morphological and biological differences.

THE HEAD LOUSE (PEDICULUS HUMANUS CAPITIS)

Morphology (Fig. 80, *b*). The length of a male is about 2–3 mm, female — 3–4 mm. The posterior end of a male's body is rounded, and that of a female is slightly forked. Mouthparts are piercing-sucking.

Life cycle (Fig. 80, *a*). Lice live in the hairy area of the head. They feed on human blood 2–3 times a day and may starve for several days. The life cycle of the body louse includes stages of egg (nit, Fig. 80, *f*), nymphs, and adult.

Nits are attached to the hair with a sticky secretion and develop for about a week. During the whole life (up to 38 days) a female lays about 300 eggs. A larva comes from an egg and in several days transforms into an imago (mature form).

BODY LOUSE (PEDICULUS HUMANUS HUMANUS)

Morphology (Fig. 79, *b–c*). Body lice are slightly larger than head lice (up to 4.7 mm), less pigmented and the visible fissures between segments are not as deep as those of head lice.

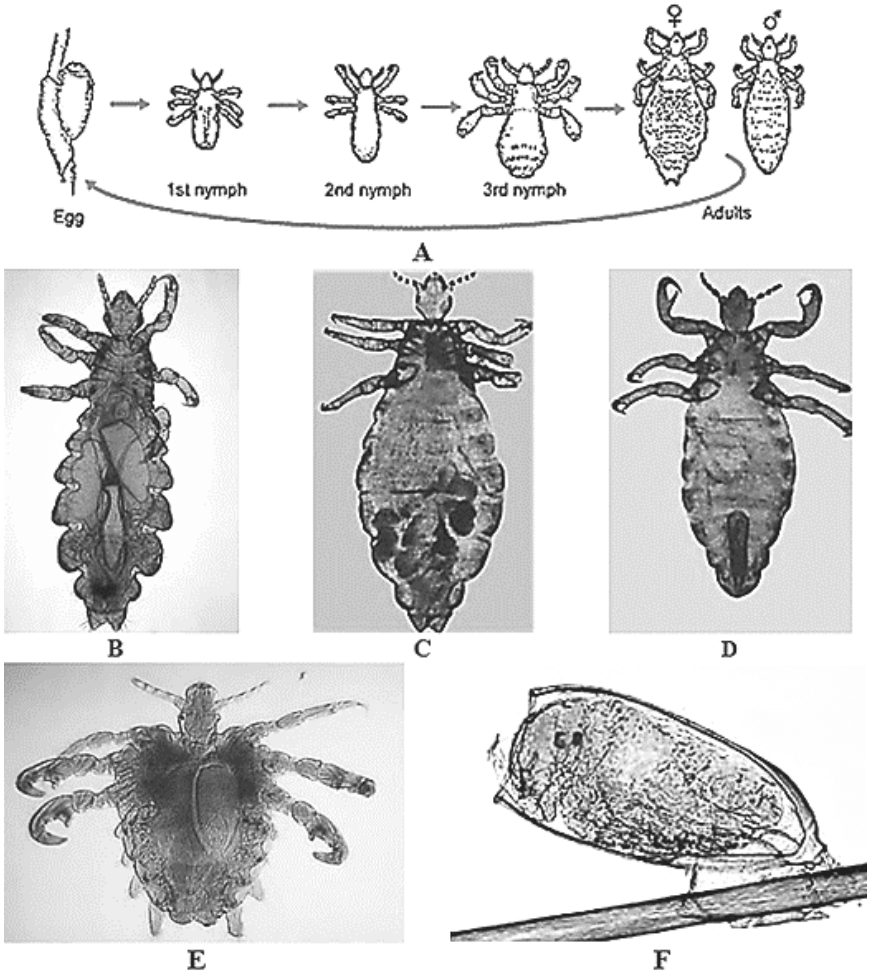


Figure 79. Lice (order Anoplura):
A — life cycle of Pediculus humanus; *B* — female P. humanus capitis; *C* — female P. humanus humanus; *D* — male P. humanus humanus; *E* — Pthirus pubis; *F* — a nit of P. humanus capitis

Life cycle (Fig. 79, *a*). Body lice live in clothing and travel to the skin several times a day to feed on blood. Nits are stuck with secretion to fabric (usually in the seams). The life span is up to 48 days, the development lasts not less than 16 days. By the end of its life female can have about 4000 offspring.

Medical significance. Lice of the genus *Pediculus* cause *pediculosis*. Bites of lice cause itching. Intense itching leads to scratching which can cause sores and secondary bacterial infection of the skin. There may be post-inflammatory pigmentation of the skin. Lice are biological vectors of *epidemic typhus* (caused by bacterium *Rickettsia prowazekii*) and a *louse-borne relapsing fever* (caused by bacterium *Borrelia recurrentis*), tularemia.

Infection of epidemic typhus occurs by specific contamination — rubbing louse feces or hemolymph into damaged skin during scratching.

PUBIC LOUSE (PTHIRUS PUBIS)

Morphology (Fig. 79). Bodies of pubic lice look shorter and wider compared to head or body lice. The length is up to 1.5 mm.

The life cycle is similar to that of other lice. The parasite affects areas with thick hair: pubic area, armpits, eyelashes, and beard. The female lays about 50 eggs during its life. The life cycle from an egg to an adult insect form lasts 22–27 days.

Medical significance. Pubic lice cause *pthiriasis* (severe itching usually in the pubic — hair area). Humans can get pthiriasis through sexual contact, rarely — through underwear and clothes.

Diagnosis of pediculosis and pthiriasis. Lice and nits can be visible to the naked eye. Thus the diagnosis is performed by visual examination of the scalp, hair, seams of clothing.

Prophylaxis of pediculosis and pthiriasis. Avoid hair-to-hair contact, do not share clothing or towels, and do not lie on beds, couches, pillows, carpets, or stuffed animals that have recently been in contact with an infected person.

FLEAS (ORDER APHANIPTERA)

Examples: human flea (*Pulex irritans*), *Ceratophyllus fasciatus*, and oriental rat flea (*Xenopsylla cheopis*).

Morphology (Fig. 80, *b–d*). Fleas are wingless, laterally flattened insects. Their mouthparts are adapted to feeding on blood. There are short palps and a pair of simple eyes on the head. The last pair of legs is long and well-adapted for jumping.

Life cycle (Fig. 80, *a*). There are four life cycle stages: *egg*, *larva*, *pupa*, *and adult* (complete metamorphosis). Females lay eggs in slits of the floor or in the garbage. In about 3–4 days, eggs hatch and produce larvae that feed on organic debris. The larvae are worm-like and have no limbs. Larvae pupate and develop into adults in 3–4 weeks. Adult fleas must feed on blood before they become capable of reproduction. The life span of fleas is over 1 year.

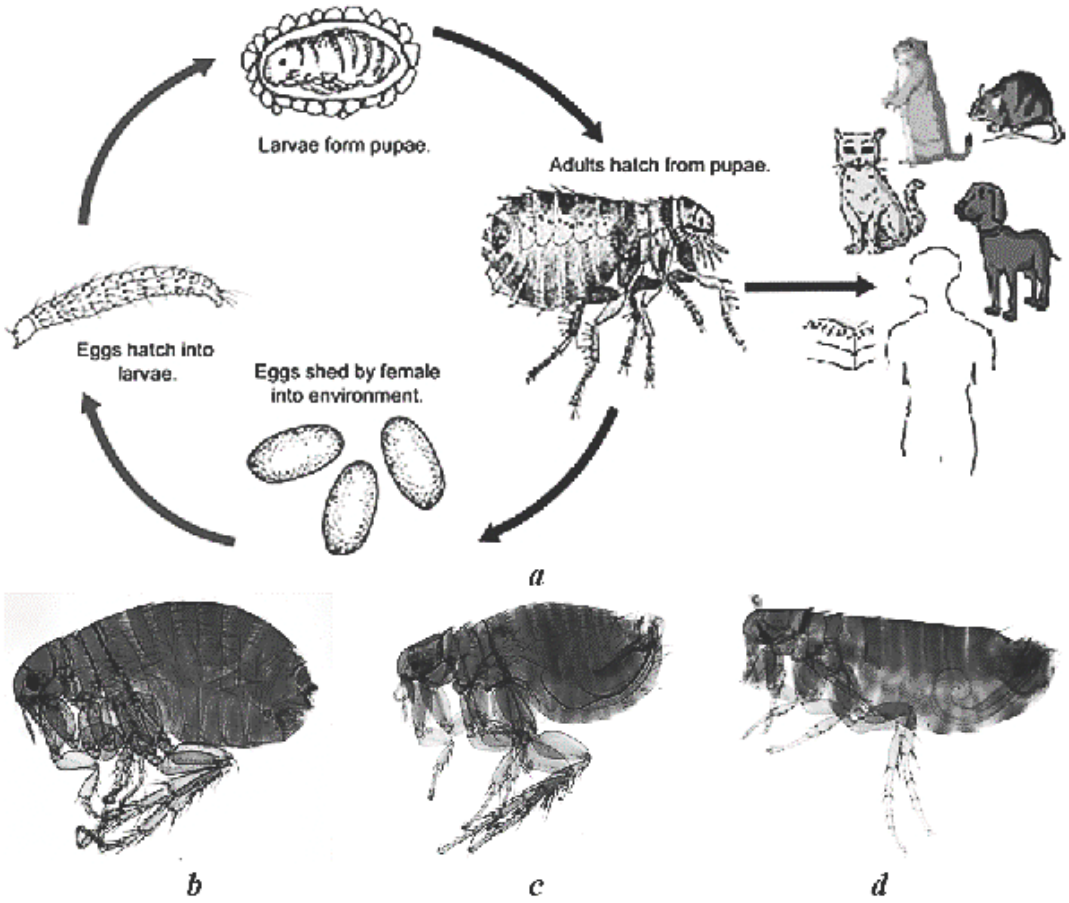


Figure 80. Morphology and life cycle of fleas:
a — life cycle; *b* — Pulex irritans; *c* — Xenopsylla cheopis; *d* — Ceratophyllus spp.

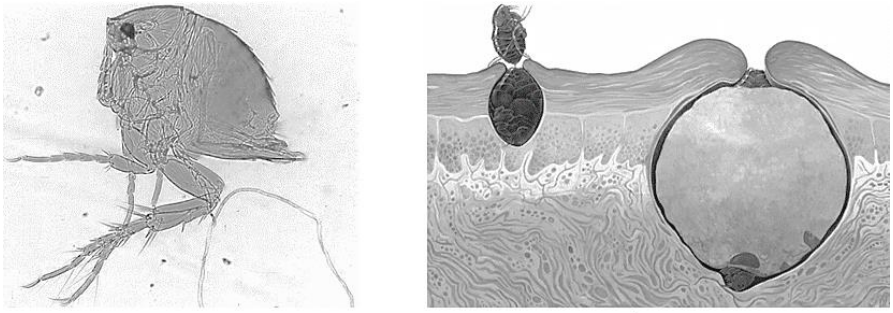
Medical significance. Fleas are temporary ectoparasites (bites cause itching, and dermatitis). Fleas are biological vectors of bacteria causing plague and tularemia. Natural reservoirs of plague are rodents, such as rats, gophers, and marmots. Fleas of the genus *Xenopsylla* are biological vectors of *tularemia* and *murine typhus* (pathogen bacteria of genus *Rickettsia*), they are also intermediate hosts of animal tapeworms.

Jigger flea (*Sarcopsylla penetrans* or *Tunga penetrans*) is the parasite causing *tungiasis* (*sarcopsyllosis*). The disease is a zoonosis and affects humans and animals alike. It is common in countries of South America and Africa.

Morphology: jigger flea is small: about 1 mm long, and has a yellow-grey color. It becomes clearly distinguishable when invades a host (Fig. 81).

Life cycle. Females permanently penetrate into the epidermis of the host and persistently suck blood. A burrowed female jigger flea is fertilized by a male only after it has started to feed on blood. During a period of 4–6 weeks, the flea increases in size and produces eggs, and eventually dies. Eggs are expelled and fall onto the ground.

In a suitable environment, the eggs develop into larvae, pupas, and eventually adults. Transmission occurs when the skin comes into contact with soil or floor where adult sand fleas have developed.



a *b*

Figure 81. Sarcopsylla penetrans:
a — photograph; *b* — diagram of the parasite invading the skin

Diagnosis. The diagnosis of tungiasis is based on the morphological characteristics of the different developmental stages. In the endemic areas, affected individuals, even children, know whether they have tungiasis.

COCKROACHES (ORDER BLATTOIDEA)

Morphology. The body of a cockroach is dorsoventrally flattened and reaches 3 cm in length. There are 2 pairs of wings. The fore wings are thick and resemble leather; the hind wings are thin and membranous. In females, the wings are reduced. Cockroaches have chewing mouthparts (Fig. 82).

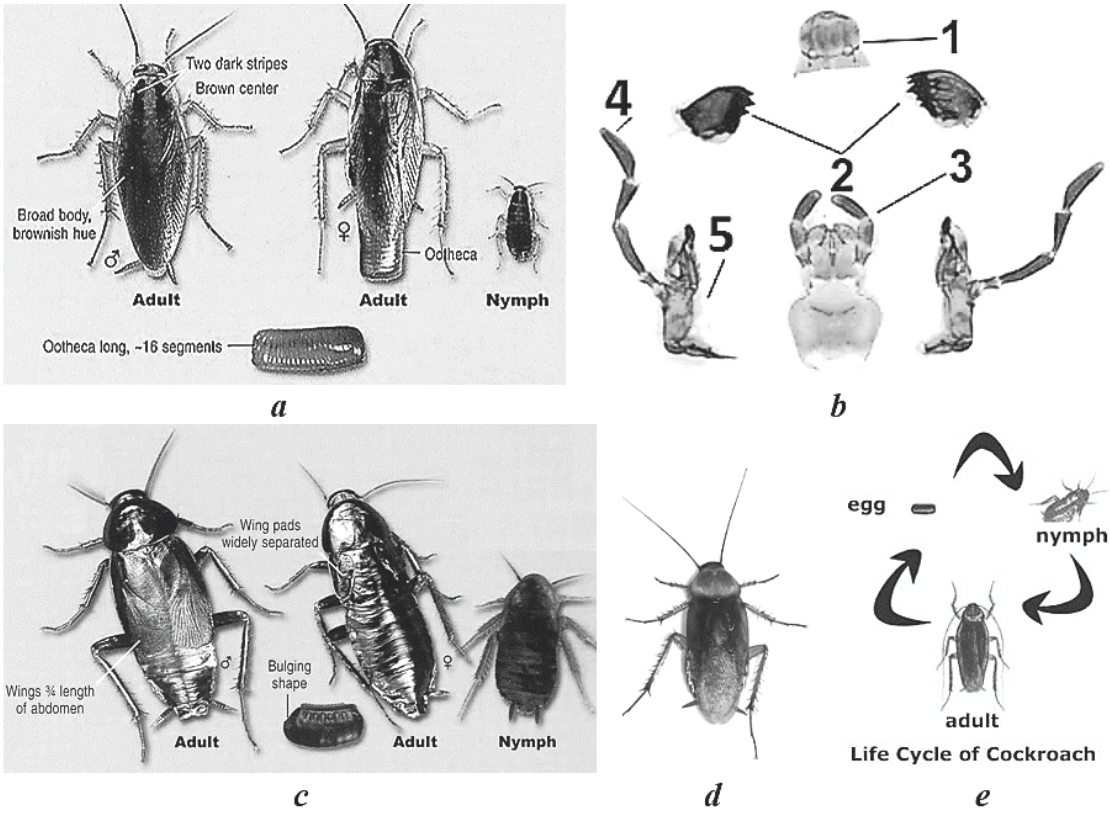


Figure 82. Morphology of cockroaches:
a — Blattella germanica; *b* — mouthparts of an oriental cockroach: *1* — upper lip; *2* — upper jaw; *3* — lower lip; *4* — palps; *5* — lower jaw; *c* — Blatta orientalis; *d* — Periplaneta americana; *e* — life cycle

Females lay eggs in an ootheca, and carry it about 14–15 days. Cockroaches are commonly active at nighttime and hide in the daytime. They feed on almost any foodstuff, food waste, and other organic matter. Their habitat is human dwelling, food factories, and public food services, shops, and canteens. Obligatory conditions for their life in human houses are the presence of water, definite temperature, and food.

Representatives: oriental cockroach (*Blatta orientalis*), the German cockroach (*Blattella germanica*), and the American cockroach (*Periplaneta americana*).

Medical significance. Cockroaches are mechanical vectors of infectious and invasive diseases. They may bite sleeping humans and feed on their skin.

Prevention. Insecticides are used to eliminate cockroaches. It is recommended to clean the rooms and kitchens, not to leave food on the table.

BUGS (ORDER HETEROPTERA)

Bed bug (*Cimex lectularius*). *Cimex lectularius* is a parasitic insect that feeds on the blood of people and animals while they sleep.

Morphology (Fig. 83, *a*). The bug is wingless, dorsoventrally flattened, reddish-brown in color, and 1 to 8 mm in length. Males are smaller than females. Typically, they produce a specific sweet musty smell with their odorous glands.

a ***b***

Figure 83. Morphology of bugs (order Heteroptera):
a — Cimex lectularius; *b* — Triatoma infestans

Life cycle. Bugs have indirect development with incomplete metamorphosis (there is no pupal stage). Eggs hatch into first nymphs (there are five nymphal stages and they look like smaller adults) which feed on the blood of a host and molt into the next stage. The last molting produces adults. Mating occurs off the host. Female bed bugs lay about five eggs.

Adults live in a sheltered location (spaces of floorboards or baseboards, seams of mattresses). The adults may take several blood meals over several weeks. A blood meal lasts 5–10 minutes. Adults live 6–12 months and may starve for several months.

Medical significance. The saliva of the bed bug causes allergic reactions and inflammation. Bites are painless. Transmission of infections by bedbugs is not observed. The presence of bedbugs can be detected if adults, nymphs, or their chitin exoskeletons are found if their fecal spots are found on bedlinen, or due to specific smell.

Kissing bug (*Triatoma infestans*). *T. infestans*is a parasitic insect feeding on blood. It is found in South America. It has been found in birds' nests, hollow trees, rodent dens, human dwellings, and peridomestic habitats like chicken coops or guinea — pig runs.

Morphology. The kissing bugs are relatively large (1.5–3.5 cm) oval, dorsoventrally flattened, and have wings (Fig. 83, *b*).

Life cycle. The life cycle of *T. infestans* is similar to that of *C. lectularius*. Nymphs hatch and pass through five stages of nymphs and are then sexually mature adults. The typical lifespan of adults is 3 to 12 months.

Medical significance. Kissing bugs are temporal ectoparasites bites of which may cause allergic reactions. The bugs are biological vectors of *Trypanosoma cruzi* which causes *Chagas disease* (see the topic 17) a natural-focal disease common in South America.

Prevention of bug bites. The prevention is based on the usage of insecticides, and the elimination of rodents living near humans, (as they are hosts where bugs may feed). It is also necessary to clean the rooms and to fix slits in a floor, walls, and furniture where bugs may hide.

CHAPTER 14
PHYLUM ARTHROPODA, CLASS INSECTA

FLIES (MUSCIDAE)

House fly (*Musca domestica*) is common worldwide. Adult flies have slightly hairy grey or black bodies reaching up to 7.5 mm in length (Fig. 84, *b*).

There are claws and sticky pads on the legs, due to them flies can move on any surface. Flies have siphoning mouthparts. The saliva contains mucolytic enzymes for the digestion of organic substances which flies "lick" after. They feed on food particles and organic leftovers.

Life cycle. The house fly has a complete metamorphosis with distinct egg, larval or maggot, pupal, and adult stages. The house flies overwinter in either the larval or pupal stage under manure piles or in other protected locations. Warm summer conditions are generally optimum for the development of the house fly, and it can complete its life cycle in as little as seven to ten days. However, under suboptimal conditions, the life cycle may require up to two months.

Medical significance: flies are mechanical vectors of enteric infections (*cholera, typhoid fever, paratyphus, dysentery*), *tuberculosis, diphtheria, eggs of helminthes and cysts of protists*. There are more than 6 million bacteria on the fly's body, and up to 28 million bacteria in the intestine. Cases of myiasis caused by *Musca domestica* are described, but not common.

Control. The more commonly used control measures for house flies are sanitation, use of traps, and insecticides.

Stable fly (*Stomoxys calcitrans*). *S. calcitrans* feeds on blood, takes blood meal predominantly on cattle and horses. In the absence of these animal hosts, they can bite humans and dogs.

Stable fly adults are similar to the house fly (Fig. 84, *a*). The length of an adult stable fly is typically 5–7 mm. Stable flies have long, bayonet-like mouthparts for piercing skin and feeding on blood, whereas house flies have sponging mouthparts for feeding on liquids. The population of flies reaches its maximum in the period of August and September. The life cycle lasts about 28 days. Stable flies are mechanical vectors of *anthrax*.

Control of stable flies is the same as that of the house flies.

Tsetse fly (*Glossina palpalis*) is a large (6 to 14 mm in length) brown fly (Fig. 84, *d*), found in midcontinental Africa. Once inseminated, the female remains fertile for life and rarely mates more often than once in nature. Females deposit a larva on the ground every 7–11 days. The larva develops into pupa into the soil and maturates into an adult in 3–4 weeks. During the whole life, females lay about 6–12 larvae. Tsetse flies feed on the blood of animals or humans and are biological vectors of *African trypanosomiasis.*

Control of tsetse flies: cutting down bushes and trees along river banks near human habitations and along roads. Insecticides are used against mature flies.

Spotted flesh fly (*Wohlfahrtia magnifica*) is common in countries with moderate and hot climates. The size of an adult fly is 9–13 mm, the flies feed on nectar. The thorax is striped greyish and the abdomen's dorsal surface is bright white with a series of contrasting dark black spots (Fig. 84, *c*). Larvae of *W. magnifica* cause *myiasis:* females deposit larvae (about 120–150) in open wounds or cavities of animals and humans (nasal cavity, eyes, ears). Larvae feed on live and necrotic tissue. In 5–7 days larvae drop from the wound and pupate.

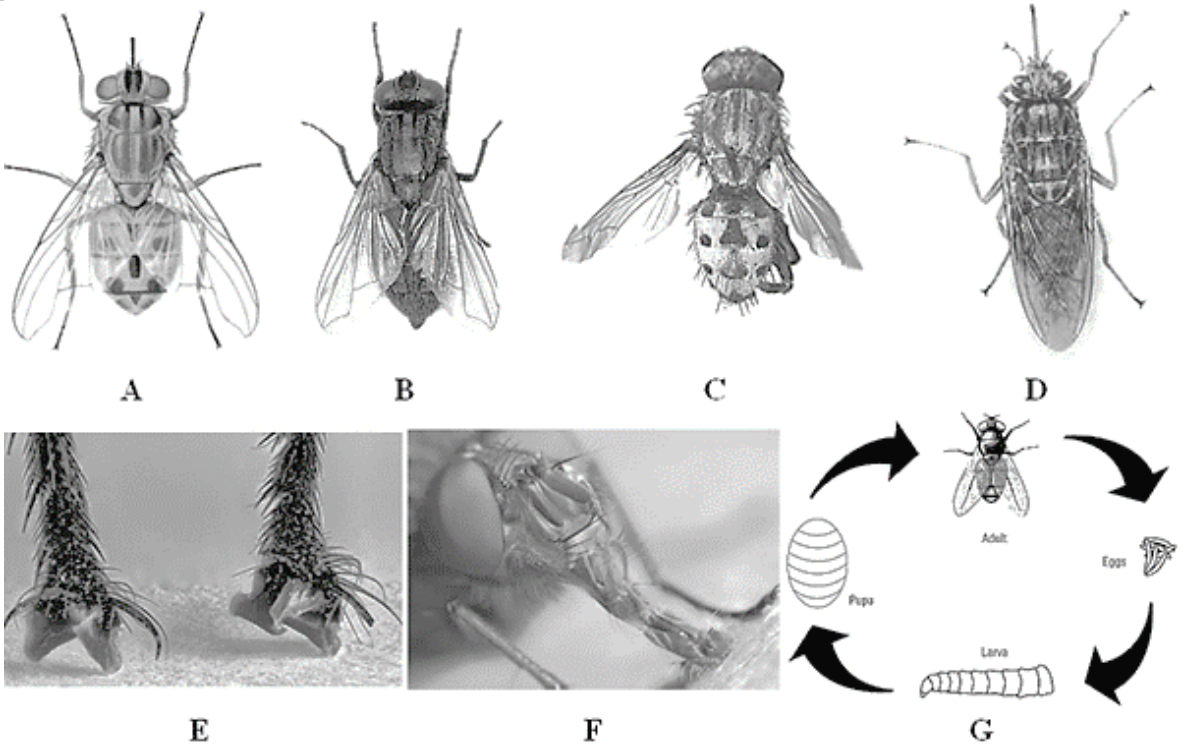


Figure 84. Morphology of flies (family Mucsidae):
A — Stomoxys calcitrans; *B* — Musca domestica; *C* — Wohlfahrtia magnifica; *D* — Glossina palpalis; *E* — claws and sticky pads on the legs; *F* — mouthparts of the house fly; *G* — life cycle of flies

GNAT

Gnat is a complex and diverse complex of two-winged insects sucking the blood of humans and warm-blooded animals. Gnat includes blackflies (*Simuliidae*), biting midges (*Ceratopogonidae*), sand flies (*Phlebotominae*), horse — flies (*Tabanidae*), mosquitoes (*Culicidae*), and some other insects.

Gnats are found everywhere except on the islands of the Arctic and Antarctica. The development and mass reproduction of the components of the gnat is associated with water, standing and flowing, with swampy areas, and with high groundwater levels. Gnat is more typical for tundra and forests. In forest-steppe, especially in the steppe, semi-desert, and desert, mass development of gnats is confined to flood-plains of large rivers, their deltas, and coastal parts of usually strongly saline lakes.

The damage caused by gnat is manifold. People greatly reduce labor productivity, and gnat interferes with normal rest and sleep. Insect saliva that enters the skin causes burning and itching, often inflammation and swelling. Many species of gnats are mechanical and biological vectors of pathogens of a number of human and animal diseases.

Black flies (family Simuliidae) look like small flies. Their sizes are about 2–3 mm (Fig. 85, *a*). Their development occurs in water, females lay eggs on underwater stones and plants. Larvae develop in streaming water. In day time in the open air, females attack animals and humans, bite them and feed on blood. The saliva of black flies is toxic, bites are painful. Black flies are mechanic vectors of tularemia, anthrax, and leprosy. They are intermediate hosts and biological vectors of *onchocerciasis* (river blindness).

Midges (family Ceratopogonidae) are a family of small flies. Their sizes are about 1–2.5 mm. They differ from black flies as they have a more slender body, a longer proboscis, and longer legs (Fig. 85, *b*). They are common everywhere. Only females attack animals and humans in twilight (in the morning or in the evening) and feed on blood. Larvae and chrysalides (pupae) develop in wet soil, forest leaf litter, in small stagnant reservoirs. Midges are mechanic vectors of tularemia, intermediate hosts, and biological vectors of *filariasis*.

Sand flies (subfamily *Phlebotominae*) inhabit regions with a warm climate. They are found close to human habitations or in caves and dens of rodents. Sand flies are 1.5–3.5 mm in length and brown-grey or slightly yellow in color (Fig. 85, *c*). The head, thorax, abdomen, and appendages are covered with hairs. The head is small, the mouthparts are piercing-sucking. Legs are long and thin. Sand flies lay eggs in shadowed places: rodent dens, caves, bird nests, the garbage. Males feed on nectar while females feed on blood (in twilight and at night). Their bites are painful and cause itching and scratching. Sand flies are biological vectors of *leishmaniasis* and *pappataci fever*. Transovarial transmission occurs in sand flies.

Horse-flies (family Tabanidae) are big true flies (their body length is up to 3 cm). They live in a forest and steppe. Males feed on flower nectar. Females have piercing-sucking mouthparts and feed on the blood of animals and humans. They attack more often in hot weather on pasture ground or near water reservoirs. They lay from 200 to 1000 eggs on plant leaves at river banks. Larvae develop in silt on the bottom of reservoirs or in wet soil. Their saliva is toxic, and bites are painful and cause itching. They are mechanic vectors of *tularemia, anthrax and poliomyelitis*, intermediate hosts and biological vectors of *loa loa filariasis*.

Protective measures against gnat: insecticide treatment of human habitations, putting nets on windows, and using repellents.

MOSQUITOES (FAMILY CULICIDAE). GENERA CULEX, ANOPHELES AND AEDES

Morphology (Fig. 85, *D–E*). Mosquitoes are small (3–6 mm) two-winged insects. They have slender bodies, long proboscis projecting forwards from the head, and large compound eyes. Female mosquitoes have piercing-sucking mouthparts and feed on blood. Males feed on the sugary fluids of plants such as nectar.

Life cycle. Mosquitoes pass through the stages of egg, larva, pupa (or chrysalis), and adult (Fig. 86).

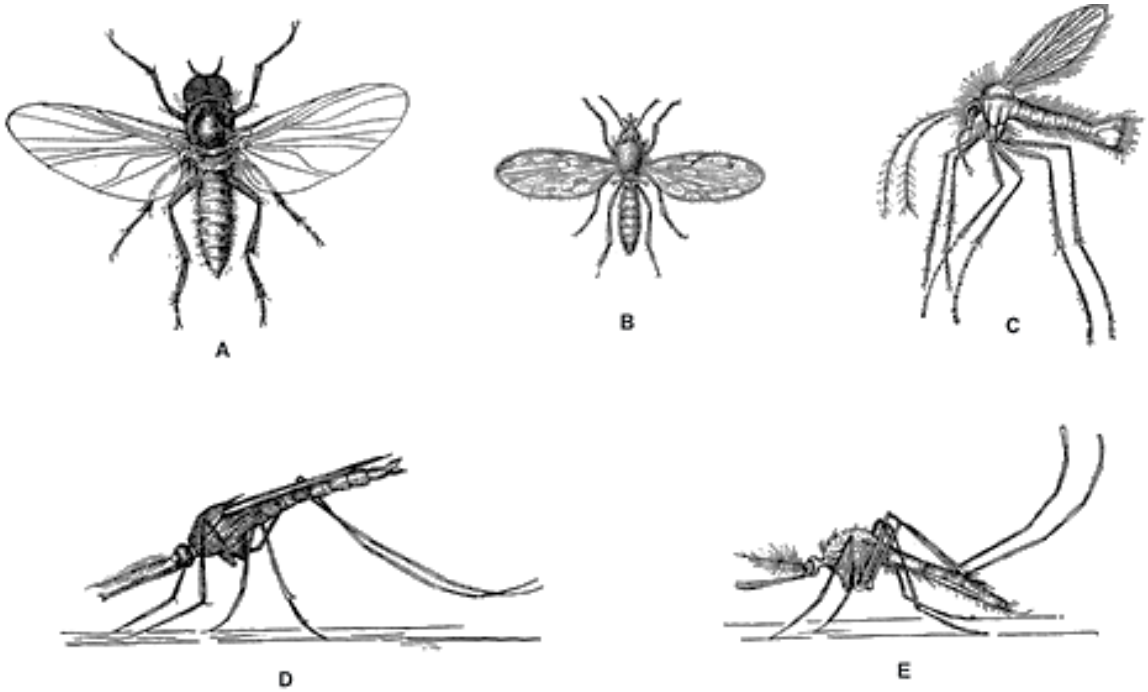


Figure 85. Components of gnat:
A — black fly (Simuliidae); *B* — biting midge (Ceratopogonidae); *C* — sand fly (Phlebotomiodae); *D* — mosquito of the genus Anopheles; *E* — mosquito of the genus Culex

Eggs are laid in water where they float on the surface. They hatch within several days and produce larvae. Larvae have well-developed heads with mouth brushes used for feeding on microorganisms and organic matter in the water. Larvae molt and grow larger several times and ultimately produce pupas (chrysalis; resting, non-feeding stage).

Such pupa is comma-shaped when viewed from the side. As with the larvae, pupas must come to the surface frequently to breathe. Oxygen supply occurs through a pair of respiratory trumpets on the dorsal side of the cephalothorax. When the development of the pupa is complete, the pupal skin splits and the adult mosquito emerges.

The newly emerged adult rests on the surface of the water for a short time to allow itself to dry and all its body parts to harden. The wings have to spread out and dry properly before they can fly.

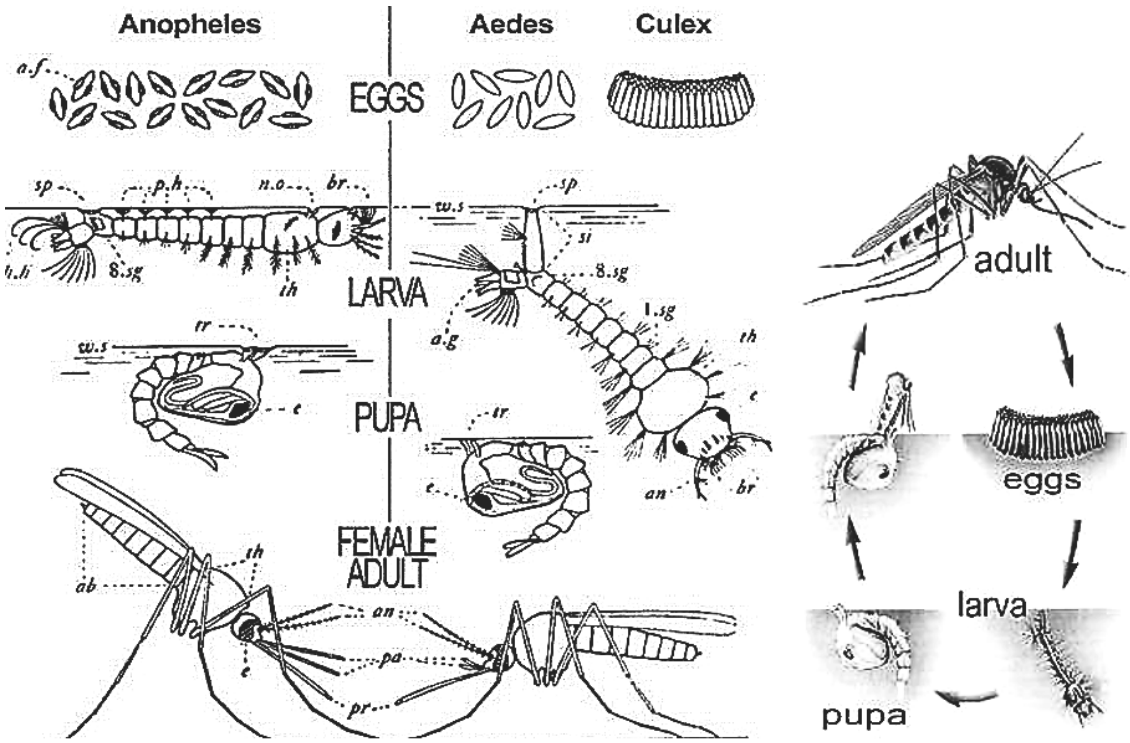


Figure 86. Life cycle of mosquitoes

Morphological peculiarities of mosquitoes of the genera ***Culex***, ***Anopheles,*** and ***Aedes*** are shown in the Table 7, Fig. 87.

Table 7

Morphological peculiarities of mosquitoes

Genus	***Culex***	***Aedes***	***Anopheles***
Eggs	Lay eggs on the surface of stagnant water. Eggs have no air floats and are stacked together	Lay eggs into temporary reservoirs: (puddles or tree hollows). Eggs are oval, float separately and have no air floats	Lay eggs in stagnant or slowly running clean water where they float separately. Eggs have lateral floats with air
Larvae	Larvae form an ~45-degree angle with the water surface, and have respiratory siphon tubes for breathing		Larvae have no siphon and lie parallel to the water surface to get a supply of oxygen
Pupas	Breathe through a pair of the straight tube-shaped respiratory trumpets		Breathe through a pair of the funnel-shaped respiratory trumpets
Male adult	Palps are longer than the proboscis. Antennae are bush-like with multiple long fibers		Palps are as long as the proboscis and have thickenings at ends. Antennae are bush-like with multiple long fibers
Female adult	Palps are much shorter ($^1/_3$–$^1/_4$) than the proboscis. Antennae are bush-like with multiple short fibers		Palps are as long as the proboscis. Antennae are bush-like with short fibers

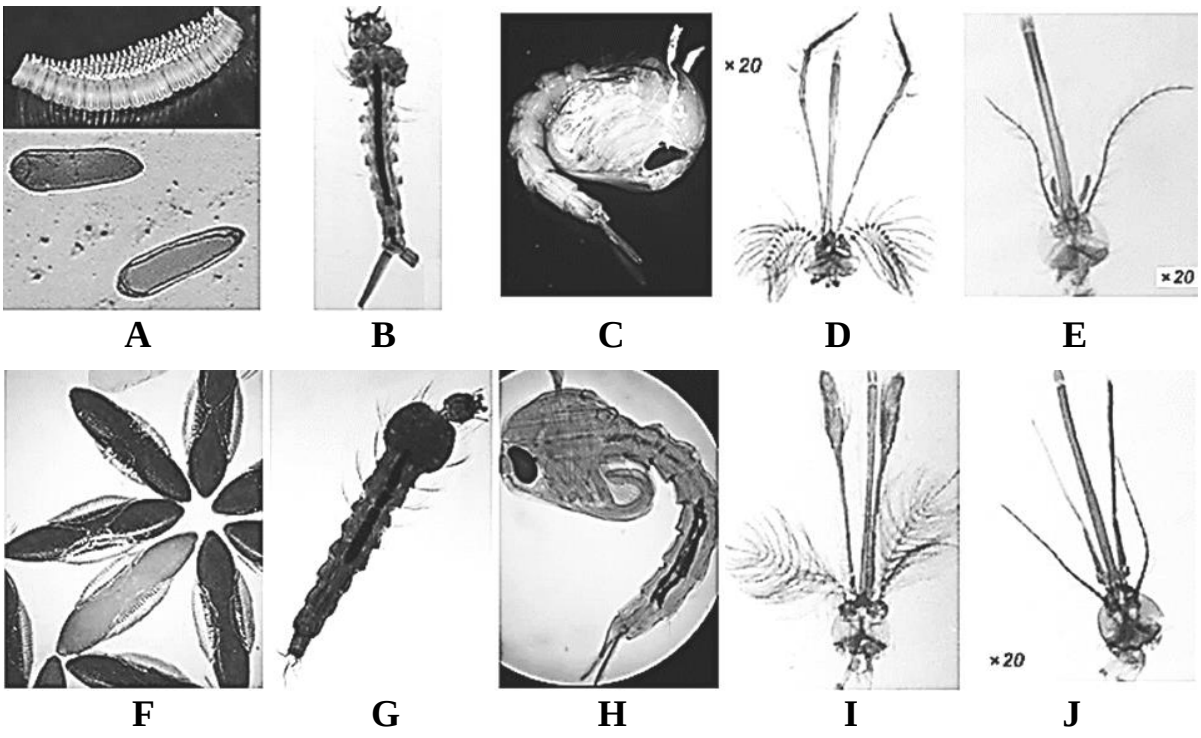


Figure 87. Morphology of mosquitoes: Genus Culex:
A — eggs; *B* — larva; *C* — chrysalis; *D* — head of a male; *E* — head of a female; Genus Anopheles; *F* — eggs; *G* — larva; *H* — chrysalis; *I* — head of a male; *J* — head of a female

Medical significance: mosquitoes are temporary ectoparasites and vectors of diseases:

• ***Anopheline*** mosquitoes are biological vectors and principal hosts of *malaria parasites*, biological vectors and intermediate hosts of filaria (nematodes *Wuchereria bancrofti, Brugia malayi, Dirofilaria repens*).

• ***Aedes*** mosquitoes are biological vectors of *Japanese encephalitis*, *yellow fever*, *dengue fever*, *lymphocytic choriomeningitis*, *anthrax, tularemia*, *filariases* (nematodes *Wuchereria bancrofti*, *Brugia malayi, Dirofilaria repens*).

• ***Culex*** mosquitoes are biological vectors of *Japanese encephalitis*, *tularemia,* and *filariases* (caused by *Wuchereria bancrofti and Dirofilaria repens*).

OESTRIDAE

Botflies (family *Oestridae*). Botflies are common everywhere. Mature botflies live for several days and do not eat. They lay eggs or produce living larvae that cause *myiasis*.

Horse botfly (*Gasterophilus intestinalis*) lays eggs on the hair of horses (Fig. 88). Larvae penetrate into the skin and cause itching. During scratching itching sites with teeth horses swallow larvae. Larvae get into the soil with horse feces and pupate. Sometimes a female horse botfly lays eggs on human hair. Larvae permeate into the skin of the face or chest, where they make passages 3–5 cm long and parasitize for about 1 or 2 months.

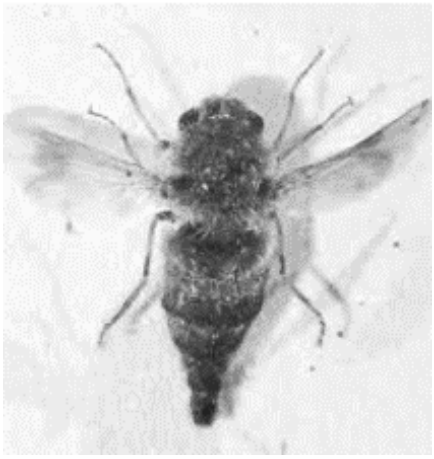


Figure 88. Horse botfly (Gasterophilus intestinalis)

Warble fly (*Hypoderma bovis*) lays eggs on the hair of animals, sometimes on human hair. Then larvae develop and migrate into tissues to complete their development in the subcutaneous adipose tissue on the back, arms, and face. Pupation occurs in soil.

Sheep botfly (*Oestrus ovis*) and Russian botfly (*Rhinoestrus purpureus*). Females are viviparous, they throw out a stream of fluid containing larvae into the nostrils or eyes of animals or humans. The development of larvae occurs in nasal cavities, sinuses, eyes, or in the cranial cavity. They leave the host through nostrils before pupation and enter the environment. Larvae of horseflies in the human body can be removed surgically.

CHAPTER 15
POISONOUS AND VENOMOUS ORGANISMS

POISONOUS FUNGI: CLASSIFICATION, CHARACTERISTICS OF MYCOTOXINS, FIRST AID AND PROPHYLAXIS OF POISONINGS

There are two morphological groups of fungi: micro- and macromycetes.

The *micromycetes* are microscopic fungi. They are the most frequent agents of severe food intoxication caused by fungi (aspergillus, penicillium, fusarium, ergot).

Macroscopic fungi are *macromycetes*. They usually cause intoxication when eaten by mistake (amanita, gyromitra).

According to edibility, macromycetes (commonly known as mushrooms) are: edible, edible after proper cooking (blewit, sharp agaric), unpalatable, and poisonous (death cap amanita, fly amanita, gyromitra).

Characteristics of the poisons. The poison of death cup amanita contains bicyclic polypeptides, *amanitins*, and *phalloidins.* Fly amanita contains *muscarine* (acts on muscarinic acetylcholine receptors) and hallucinogens (bufotenin, muscarine, and others). Gyromitra contains *gyromitrin* which is similar to toxins of death cup amanita.

Symptoms of poisoning. The symptoms of poisoning with fly amanita may include vomiting, diarrhea, elevation of temperature, tachycardia, hallucinations, and convulsions. The poisoning with death cup amanita incoercible vomiting, diarrhea, and thirst. Death is caused by hepatic and renal failure.

First aid: gastric lavage with suspending of activated carbon, 1 % potassium permanent, usage of saline laxatives.

POISONOUS PLANTS: CLASSIFICATION, CHARACTERISTICS OF PHYTOTOXINS, FIRST AID AND PROPHYLAXIS OF POISONINGS

There are plants that produce and accumulate poisons that can cause toxication and even death of animals or humans in various types of contact. More than 10 000 species of poisonous plants are described. Such plants are lily of the valley, blister buttercup, marsh tea, and others. There are extremely poisonous plants such as devil's trumpets, black henbane, belladonna, Zwerg–Holunder and others. Some plants can be poisonous only when grow in certain conditions.

Characteristics of the poisons: plant poisons contain different groups of chemical compounds such as alkaloids, saponins, essential oils, glycosides, flavonoids, tannins, resinous substances, carboxylic acids, cyanic compounds, and others.

The toxicity of plant poisons is associated with a number of factors. Cardiac glycosides are not destroyed for a long time, are excreted through kidneys and affect them. Alkaloids have a toxic effect on the liver. Many glycosides are hydrolyzed and then broken into hydrocyanic acid which causes adverse effects.

Symptoms: The most clinically important syndromes in case of acute poisonings are: psychoneurological, respiratory, cardiovascular, gastrointestinal, hepatic, and renal syndromes.

Clinical presentation of poisoning with *Papaver somniferum* includes vomiting, dizziness, hallucinations, retention of urine and bowel movement, and respiratory depression up to failure.

Clinical presentation of poisoning with cannabis may include a vinose state, verbal and motor excitement, hallucinations, and merriment passing into sleep with dreams. Chronic intoxication may cause psychological functional disturbances leading to the disintegration of personality.

The essential oils of marsh tea cause local irritative effects and may cause throat irritation, nausea, and vomiting.

First aid in case of poisonings with phytotoxins:

1. *Removal of toxins from the organism*: gastric lavage, vomiting, removal of the intestinal content, usage of adsorbents such as activated carbon.

2. *Antidotes*: substances with opposite effects on the organism can be used for some toxins.

3. *Detoxication*: artificial diuresis, replacement transfusion, dialysis, hemosorption.

4. Relief of symptoms: *antishock therapy*, *normalization of work of respiratory, cardiovascular, central, and peripheral nervous systems*.

CLASSIFICATION OF POISONOUS AND VENOMOUS ANIMALS

Venom is a toxic secretion of animals that is injected into the prey via bite or sting.

Poison is a toxic secretion or metabolite which is contained in a poisonous animal or exposed to its body surface.

Animals can produce their own toxins or accumulate them from the environment, there can be toxic metabolites or toxins produced by specialized glands, some animals can bite the victim while others cannot. These factors are the basis for the classification of animal toxicity.

According to the presence of specific apparatus for injecting venom into the victim (“armed”), animals are divided into venomous and poisonous.

- *Primarily-toxic* animals have special glands to *produce* toxins or toxic metabolites (jellyfish, scorpions, snakes).
- *Secondarily-toxic* animals *accumulate* exogenous toxins from the environment. Such animals are *poisonous* if they are eaten by other organisms (pufferfish accumulates toxins produced by marine bacteria).

The primarily-toxic animals are divided according to the ways used for the production of toxins.

- Actively-toxic animals have specialized glands producing toxins. They are called venomous (“*armed*”) if have a specialized apparatus for biting or

stinging: thread cells on tentacles of jellyfishes, stingers in bees, wasps or scorpions, stingers of cone snails, chelicerae of spiders, spines of sea urchins or sting rays, fangs in snakes and etc. Venom is injected into the body of the victim parenterally (avoiding the digestive tract). The actively-toxic animals that have no apparatus for biting or stinging ("*unarmed*") are not venomous, but poisonous. Secretions of their glands commonly poison the victim in case of direct contact with its skin (skin glands of some amphibians, anal glands of insects).

• *Passively-toxic* animals (fishes with poisonous caviar) do not have specialized glands but may have toxic metabolites that are accumulated in various organs and tissues. They are dangerous only when eaten by a victim.

PHYSIOLOGICAL CHARACTERISTICS OF TOXINS OF INVERTEBRATES (JELLYFISH, ARACHNIDS, HYMENOPTERANS), THEIR EFFECT ON THE HUMAN BODY; THE FIRST AID AND PROPHYLAXIS OF BITES AND POISONINGS

Characteristic of animal toxins. Animal toxins (zootoxins) are biologically active substances that actively interact with the biological structures of the body. Zootoxins are diverse in their chemical structure (alkaloids, histamine, various enzymes, and their inhibitors).

There are various types of zootoxins such as:

– neurotoxins affecting predominantly the nervous system;

– cytotoxins damaging cells and tissues;

– hemorrhaging impairing normal permeability of blood vessels;

– hemolysins destroying erythrocytes.

The clinical presentation of toxication in humans depends on the composition of the poison or venom, the site of bite, sting, or contact with a poison, the season of the year, and the time of the day (animals can change their toxicity) as well as on the overall condition of the person.

Coelenterates (Orange-striped jellyfish and Physalia) refer to *actively-venomous* animals. Thread cells release toxins with neurotoxic effects.

Clinical presentation. In sites of the sting by tentacles of the orange-striped jellyfish appears sharp pain, erythema, and rash. Symptoms temperature rise, rapid decrease of muscle tone, pains in extremities and lumber area, impairment of consciousness, hallucinations, delirium, respiratory and cardiac affection, in severe cases — death.

First aid. It is required to remove parts of tentacles and striking threads from the skin and treat the affected sites with alcohol or a solution of soda.

Prophylaxis. Not to bathe in the thicket of water plants and in places of jellyfish gatherings.

Phylum Arthropoda, class Arachnida, order Scorpions (yellow, Italian, black scorpions). They are actively-venomous and have venomous glands located in the last segment of the abdomen. They excrete neurotropic venom that blocks neuromuscular synapses.

Clinical presentation. severe pain, edema, and hyperemia appear at the site of a bite. Symptoms: headache, weakness, confusion, and tachycardia. Lethal outcomes may happen in children.

First aid. Sucking off the venom, applying cold to the site of a bite, taking pain-killers. Injection of specific antiserum.

Prophylaxis. Protection from bites: an examination of dwellings, bedding, clothes, and shoes.

Order Arachnida. Spiders are actively-venomous. Ducts of their venomous glands open on chelicerae.

Karakurt (black widow) has neurotropic venom that blocks neuromuscular synapses.

Clinical presentation. At a bite site pain and numbness of extremities appears. Symptoms: pain quickly spreading throughout the body, headaches, breathlessness, heartbeat, bronchial spasms, vomiting, and impairment of consciousness. Lethal outcomes are possible.

First aid. Sucking off the venom, injection of an antikarakurt serum can be used. *Prophylaxis.* Prevention from getting karacurts to the places of human lodging for the night.

Tarantulas venom contains cytotoxins and hemorrhagins and impairs the permeability of capillary walls.

Clinical presentation. Pain, hyperemia, and edema in the bite area. Symptoms: malaise, sleepiness, chills, pulse acceleration, perspiration.

First aid. To treat the site with disinfectants, ensure rest, abundant drinking, pain-killers for the patient. *Prophylaxis:* protection from bites.

Class Insecta, order Hymenoptera (bees, wasps). These insects are actively-venomous, and have toxic glands and a sting at the end of the abdomen. The venom has a neurotropic and cytotoxic action and is a strong allergen.

Clinical presentation. After a bite **—** pain, edema, erythema. Possible symptoms: allergic reactions.

PHYSIOLOGICAL CHARACTERISTICS OF TOXINS OF VERTEBRATE ANIMALS (FISHES, AMPHIBIANS, REPTILES), THEIR EFFECT ON THE HUMAN; THE FIRST AID AND PROPHYLAXIS OF BITES AND POISONING

Toxic **fishes** are divided into 2 groups:

1. Venomous species having toxic glands; the secretion of these glands is injected into the wound made by fin rays, teeth, or thorns of branchial covers. Representatives: sting ray, sea dragons, ruffs and perches, moray eels, devilfish, and firefish. They are spread predominantly in tropic latitudes of the Pacific and Atlantic Oceans.

Pathogenic action and clinical presentation. Toxins pass into the organism through a wound on the skin. At the moment of a prick, the victim feels pain that quickly spreads to the whole extremity. Then appear fear, breathlessness,

heart pain, vomiting, and sometimes loss of consciousness. Inflammation, sometimes ulcers, and tissue necrosis develop at the bite site. A severe poisoning ends with death within a day.

Treatment: sucking off the venom from the wound, applying a rope, symptomatic treatment. Prophylaxis includes putting on special clothes if dealing with the fish.

2. Fishes that are poisonous when eaten (moray eels, thons, perciformes, pufferfish). When these fishes are used as food, poisoning develops in 20–30 minutes. There appears numbness of the tongue and fingers, nausea, vomiting, breathlessness, respiratory and speech affection. The treatment is symptomatic. As prophylaxis, the mentioned fishes should be excluded from the diet.

Amphibians. There are some toxic substances in the skin of some amphibians. The most virulent poison is produced by African tree frogs and tree toads. The toxin of the Columbian cocoa frog (the length of 2–3 cm, the weight is a bit more than 1 g) is 50 times stronger than a tetanus toxin. Other toxic amphibians are not dangerous for humans (they have no mechanism for injecting the toxin into tissues). When their poison gets on the skin or mucous membranes, erythema, and inflammation are observed. These symptoms are relieved by washing with water. It is necessary to take care lest amphibians' poison gets to the eyes.

Class Reptilia. Families of elapids and sea serpents (king cobra and Indian cobra, long-glanded coral snakes, sea kraits). These are primarily-toxic actively-venomous animals. They have toxic immobile fangs with canals for the venom on the anterior part of the maxilla.

Pathogenic action and clinical presentation. The venom contains neurotoxins, cytotoxins, and hemolysins. At a bite site pain, edema, and inflammation develops. Symptoms: excitation and then depression of CNS; swallowing, speech, and breathing are impaired. Lethal outcomes are possible.

Family Viperidae (blunt-nosed viper, phoorsa, Orsini's viper, copperhead snake, rattlesnakes). They are primarily-toxic actively-venomous animals. They have toxic glands and fangs with canals.

Pathogenic action and clinical presentation. The venom contains neurotoxins, cytotoxins, and hemolysins, they stimulate blood coagulation. At a bite site pain, edema, and tissue necrosis develops. Symptoms: weakness, nausea, dizziness, impairment of blood coagulation. Lethal outcomes are possible.

First aid. The bite site should be treated with an antiseptic and a compressing bandage should be applied. The patient should be transported in a lying position. Injection of snakes' antitoxins should be done.

Prophylaxis: in places of snakes' inhabitance one should not touch them and wear high boots.

CHAPTER 16
HOMEOSTASIS AND CHRONOBIOLOGY

HOMEOSTASIS AND ITS MAINTENANCE

Living organisms are constantly in contact with their environment. Environmental factors of their habitation are changing all the time. Any organism adapts to them and strives to maintain the constancy of its own morphology and physiology, physical and chemical properties of cells, tissues, interstitial fluid, and blood.

Homeostasis is the property of living systems to maintain stability and relative constancy of their internal environment in changing environmental conditions. The term "homeostasis" (Greek *homois* — identical; *stasis* — immobility) was introduced into biology by an American physiologist W. Cannon in 1932.

Mechanisms of homeostasis. Mechanisms of homeostasis provide thermoregulation, regulation of blood pressure, and concentration of ions in various media of the organism.

Homeostasis depends on:

1. *Substances* that perform various functions in cells (proteins, fats, carbohydrates, oxygen, inorganic compounds, etc.).

2. *Environmental factors* that have an effect on cells (osmotic pressure, temperature, concentration of ions).

3. *Mechanisms* providing integrity of the body (immunobiological reactivity, regeneration, repair, and others).

In the context of Cybernetics (science of control and communication) a living organism is a system in which input variables (a stimulus, irritant, cause) and output variables (an effect, reaction, response) interact. A system is a sum of all elements obeying definite behavioral law. The basis of the system functioning is the registration of deviations in output variables depending on the information received at the input. For all that, the system behavior changes according to the information coming to the control block through feedback channels.

Positive feedback enhances the action of input variables. This connection changes the system to extreme states and ultimately causes its instability. Negative feedback weakens the action of input variables. Negative feedback is the most spread type of feedback in living organisms as it increases its stability.

Levels of homeostasis:

– *molecular-genetic*: DNA repair, regulation transcription;

– *cellular, tissue, organ*: regeneration (cristae of mitochondria, myofibrils, cisternae of Golgi complex, an increase of the number of organelles, cell division, modifications in cells and intercellular substance);

– *organism*: neurohumoral regulation and the organizing role of the NS;

– *population-specious*: Hardy–Weinberg principle;

– *biocenotic*: self-regulation of the population number;

– *biospheric*: provides a dynamic balance of living systems with the environment by trophic connections (food chains) and circulation of substances in nature.

Adaptation of a biological system to changing conditions of the internal or external environment is based on "metabolic adaptation" — quantitative changes of metabolic process in cells.

Maintaining the constancy of an organism's internal environment and continuous adaptations to a constantly changing external environment occurs by means of nervous and endocrine systems. *The nervous system* provides quick changes in the organism. The effect of *hormones* is slower but lasts longer.

Immune mechanisms of homeostasis provide the organism with defense from foreign genetic information (viruses, bacteria, protists, helminths, proteins, and modified cells of the organism itself). Homeostasis is regulated by the immune system consisting of the thymus, spleen, lymphatic nodes, and red bone marrow.

The organism reacts to unusual and strong effects of the external environment with *stress reaction*, which changes the work of most organ systems. The stress reaction involves the cerebral cortex, hypothalamus, hypophysis, and adrenal glands (secrete adrenalin).

Stages of a stress reaction:

1. Activation of defensive mechanisms.
2. Increasing the resistibility of the organism.
3. Attenuation of defensive mechanisms.

The 1st and 2nd links of this chain preserve mechanisms of homeostasis; the 3rd one causes the failure of homeostatic mechanisms and the development of pathologic changes in the organism.

Mechanisms of homeostasis are maximally reliable in mature age. In childhood and in the course of aging, their efficiency decreases and the general resistance of the organism during these periods of ontogenesis is low.

CHRONOBIOLOGY AND ITS MEDICAL ASPECTS

Living organisms are surrounded by inanimate nature characterized by rhythmic processes. Rhythms are alternating deviations and restorations of an initial state of a system that occur at equal time intervals. For example, alternation of day and night, and alternation of seasons. Living organisms have adapted to them by means of the rhythmicity of their vital activity or biological rhythms (biorhythms). Rhythmic processes are observed at all levels of life from the molecular-genetic level to the biospheric one. C. Barr was the first who formulated the problem of biological time in 1861. The time associated

with live phenomena is biological time. Chronobiology studies biological time and biorhythms (Greek *chromos* — time).

When rhythms are regulated by external factors, they are *exogenous* rhythms. *Endogenous rhythms* are regulated by internal factors. In fact, rhythms depend on both endo- and exogenous factors.

In many cases the main external factor regulating the functional rhythmic activity of living organisms is the duration of the light day (*photoperiod*). For example, flowers of the majority of plants open in the morning and close at night; Drosophilae come out of a chrysalis at dawn; 59 % of deliveries happen at night.

There are 5 types of biorhythms:

The 1st type: *rhythms of high frequency* last from fractions of a second to 30 minutes. Examples: heart contractions, respiration movements, peristalsis.

The 2nd type: *rhythms of moderate frequency* or *circadian rhythms* that last from 30 minutes to 28 hours. Examples: changes in respiration and growth in plants; changes of activity in animals (day-time and night-time animals). About 69 physiological processes in the human body are associated with circadian rhythms. They can change 3–5 and more times during the day. Examples of such changes in humans:

– contractile function of the myocardium is higher in the day-time;
– the maximal temperature of the body is reached at 18 o'clock;
– arterial pressure in the human is higher in the day-time and lower at night;
– blood coagulation is higher in the day-time;
– speed of cell division is more in the morning than at night.

People can be divided according to their workability (Table 8).

Table 8

Peoples' workability

	larks	**doves**	**owls**
♀	25 %	50 %	25 %
♂	50 %		50 %

Such differences in men and women can be explained by the fact that the gene regulating circadian rhythm is located in an X-chromosome.

The regulation of circadian rhythms is accomplished at a hypothalamus level.

The 3rd type is *month rhythms* (for example periods in women).

The 4th type is *annual or seasonal* (from some months to 1 year): depending on the light day is its synchronizer. Examples: transmigration of birds; winter and summer hibernation in animals; maximal activity of adrenal glands in summer; arterial pressure is higher in an autumn-winter period; incidence of bronchial asthma attacks is higher in January and April and less in summer months.

The 5th type — *rhythms of low frequency*: 3, 7, 11, 80–90-year changes of solar activity. With them are associated:

– 3-year rhythms of tuberculosis recurrence incidences in humans;

– epidemics of some infectious diseases; cardio-vascular and psychic diseases (their number increases at maximum solar activity). The dependence of physiological processes on solar activity cycles is studied by *heliobiology*.

There is much data about the influence of the Moon and its phases on living organisms in literature. The Moon phases repeat every 29.53 days. The Earth's surface ascends 35.6 cm maximum and descends 17.8 cm under the influence of the Moon. Under the influence of the Sun, ascending of the surface is 16.4 cm, and descending — 8.2 cm. Such "breathing" of the Earth is caused by gravitation.

There are data that human workability, irritability of the nervous system, and irritation increase at a full moon; at a new moon there is weakness, lowering of activity, creative energy, and abilities. The association of psychic diseases with the Moon phases was authentically proved. The least frequency of childbirth is marked on the new moon and the highest is on the full moon.

From the moment of birth, three activity cycles are observed in every human:

– *physiological* activity (23-day periodicity);

– *emotional* activity (28-day periodicity);

– *intellectual* activity (33-day periodicity).

There is a critical (zero) day in the middle of every period.

The first half of the cycle is a positive period, and the 2nd half of the cycle is a negative period. All the critical days coincide once a year.

Applied sections of Chronobiology are Chronomedicine and more common sections — Chronopathology, Chronopharmacology, Chronotoxicology, and Chronotherapy.

A *chronobiological* approach allows predicting exacerbations of chronic diseases and acceleration of patients' recovery.

Chronomedicine studies the biological rhythms of a healthy and sick organism.

Chronopathology studies changes in the organism in the impairment of biorhythms. Discordance of biorhythms — *desynchronosis* — may be a sign of pathology in the organism or may lead to some pathology. It contributes to gastritis, ulcers, tumors, and nervous disturbances. Desynchronosis produces a considerable effect on a person's workability.

Chronopharmacology studies various efficiency of medicines at different times of the day — sensitivity may fluctuate from 0 to 100 %. Studying the organism's sensitivity to medicines at different times of the day is the subject of *chronotoxicology*. For example, the application of cyclophosphan at 18 o'clock increased the frequency of curing mice from leucosis 5 times as

compared to its effect at 9 o'clock. Taking into consideration chronobiology, chronotherapy should revise medicines' doses, and their administration at times when they are most effective. For example, to prevent cardiac asthma and lung edema, which occur more often at night, the increasing of glycosides and prednisolone doses should be done not in the morning but in the evening.

Achievements of chronobiology and chronomedicine are used for elaborating *chronoprophylactic measures*:

– a compilation of day chronograms of a norm;

– taking into account biorhythms for making up a rational regimen of work and rest, rational nutrition of people of various occupations — workers of night shifts, pilots, and cosmonauts;

– prognosis of exacerbations of various diseases; settling the problems of acclimatization and adaptation.

CHAPTER 17
EVOLUTION OF ORGAN SYSTEMS

CONNECTION OF THE ONTOGENESIS AND PHYLOGENESIS, BIOGENETIC LAW, A. N. SEWERTZOFF'S THEORY ABOUT PHYLEMBRYOGENESES

Ontogenesis is the individual development of an organism or all the development processes of an individual from the moment of zygote formation to death. This development proceeds due to the expression of genetic information received from parents. Environmental conditions have a considerable effect on this expression and development of characters.

Phylogenesis is the evolutionary history of a species.

Ontogenesis and phylogenesis are closely connected. Knowledge of phylogenesis explains ontogenesis and the mechanism of malformations that can develop during prenatal ontogenesis.

The correlation of ontogenesis and phylogenesis was shown by Karl Ernst von Baer in 1828 when he formulated the following laws:

Law of embryonic similarity — the embryo of a higher form (i.e. higher animal) never resembles any other form, but only its embryo.

Law of successive appearance of characters — the more general characters of a large group appear earlier in the embryo than the more special characters.

Law of embryonic divergence — every embryo of a given animal form, instead of passing through the other forms, rather becomes separated from them.

These laws state that the early stages of embryogenesis of vertebrates (such as fishes, birds, and mammals) are very similar. In the course of time, they get differentiated and acquire traits of their classes, then those of their orders and etc.

In 1866 Ernst Haeckel formulated the ***biogenetic law:*** *ontogenesis is a short and fast repeat of phylogenesis.* Though not adult ancestral stages are repeated but traits of their embryos.

Ch. Darvin confirmed the correlation between onto- and phylogenesis and developed the theory of recapitulations. ***Recapitulation*** is a repeat of ancestral characters in embryos. For example, lying down and development of the respiratory system in a mammal embryo undergoes the stages when gill slits, only then the lungs are formed.

A. N. Severtsev elaborated on the theory of phylembryogeneses. This theory explains the relationship between ontogenesis and phylogenesis.

Phylembryogenesis is an embryonic reconstruction that is preserved in adults and has adaptive nature. There are 3 types of phylembryogeneses:

1. **Archallaxis** — an early deviation from the ancestral developmental pattern that occurs simultaneously with the formation of the organ anlage (an example is the development of a hair coat in mammals). Mutated genes get

involved in morphogenesis at its initial stages and make the new course for the development of the organ (recapitulations are absent);

2. **Deviation** — a development that begins in accordance with the ancestral pattern and deviates in the middle of the course (an example is the development of scales in reptiles). Initially morphogenesis proceeds according to ancestral patterns (partial recapitulation) but later on mutated genes activate and make a new course for the organ's development.

3. **Anaboly** — a development that follows ancestral patterns up to its last stage and then new stages are added (a two-chambered heart into a four-chamber heart). At first, all the stages of organ development recapitulate, and then new genes start to work to form a new character.

In cases of some malformations, an organ or body part may acquire some characteristics similar to that of other orders or classes of chordates. They develop due to ontophylogenetic mechanisms such as recapitulations and parallelisms.

Recapitulations occur as a result of incomplete anaboly or its absence. Examples of such disorders are a three-chambered heart, preservation of embryonic vessels, two aortal arches, arrested development of kidneys, and duplication of ureters.

Parallelism is the independent development of similar characters in closely related species during their evolution (humans and animals that have similar origins). An example of parallelism in humans is polymastia (abnormal number of nipples).

EVOLUTION OF THE NERVOUS SYSTEM IN CHORDATES

The nervous system originates from the ectoderm and forms as a nerve tube. **Basic directions of evolution:**

1. Differentiation of the nerve tube into the brain and the spinal cord.

2. Evolution of the brain:

– transformation of 3 brain vesicles into 5 brain vesicles and therefore 5 brain regions;

– appearance of the cerebral cortex and enlargement of its surface due to its sulci (grooves) and gyri (folds);

– transformation of the ichthyopsidian brain into sauropsidian one and ultimately into mammalian brain.

3. Differentiation of the peripheral nervous system.

The CNS of the lancelet is a nerve tube. Its anterior part is dilated and has an olfactory pit. Photosensitive cells (Hesse organs) are located throughout the whole length of the tube.

The brain of mammals consists of 5 regions. It undergoes the same stages during its formation. At first, the nerve tube is formed and 3 brain vesicles appear in its anterior end: forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon). Then the forebrain and hindbrain divide to form

5 brain vesicles which transform into a certain brain region: cerebrum (*telencephalon*), interbrain (*diencephalon*), midbrain (*mesencephalon*), pons and cerebellum (*metencephalon*) and medulla oblongata (*myelencephalon*). There are cavities in the brain (cerebral ventricles) that are followed by the spinal canal in the spinal cord. The part of the brain located above the ventricles is called the *roof* and the part below is the *floor* of the brain.

The brain of **fish** is small. The cerebrum is not divided into hemispheres. The roof is epithelial; the floor of the brain consists of striate bodies. Olfactory lobes are small. The interbrain consists of the thalamus and hypothalamus. The midbrain is large as it is the integrating center of the CNS (*ichthyopsidian* type of the brain). A flexure appears in the area of the midbrain. The cerebellum is developed well. There are 10 pairs of cranial nerves (Fig. 89).

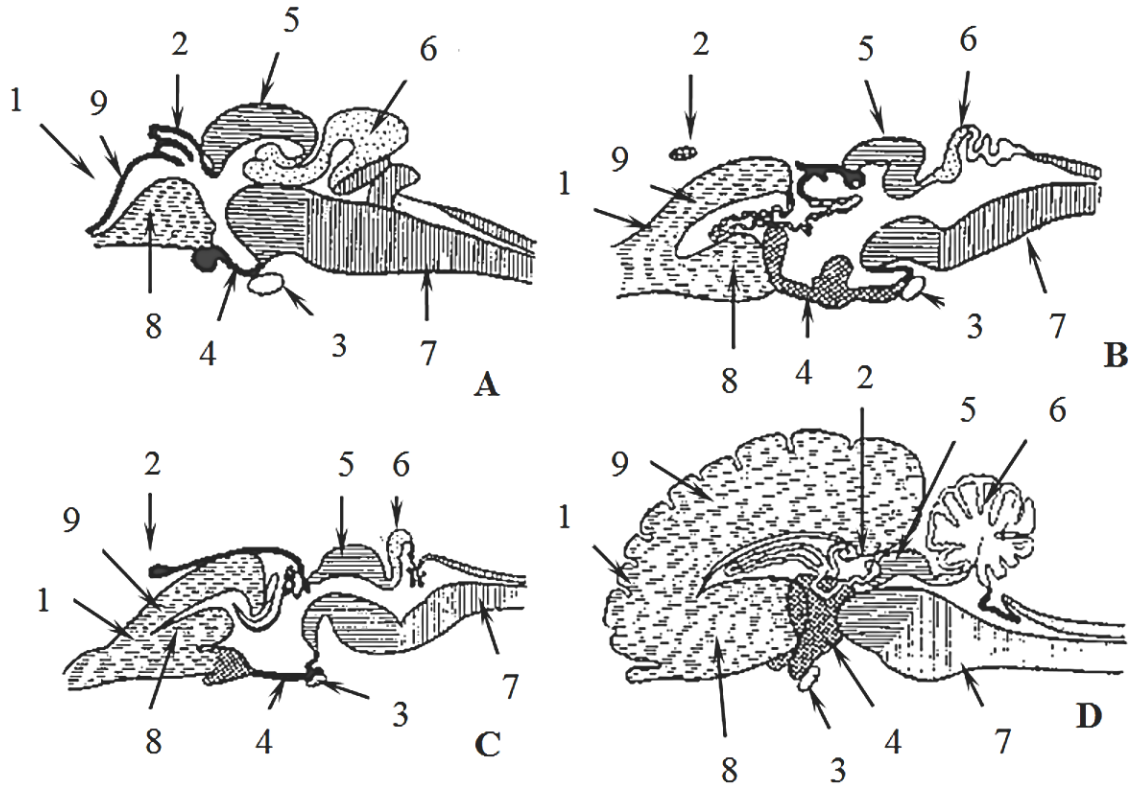


Figure 89. The brain of vertebrates (longitudinal section):
A — bony fish; *B* — amphibian; *C* — reptile; *D* — mammal: *1* — forebrain; *2* — epiphysis; *3* — hypophysis; *4* — interbrain; *5* — midbrain; *6* — cerebellum; *7* — medulla oblongata; *8* — striated bodies; *9* — roof

In **amphibians:** 1) volume of the forebrain increases; 2) the cerebrum divides into 2 hemispheres; 3) nervous tissue appears in the brain roof; 4) striated bodies are well developed. Olfactory lobes are separated from the hemispheres. The interbrain consists of the thalamus and hypothalamus. The midbrain is large and still serves as the integrating center. The cerebellum is poorly developed. The medulla oblongata is developed the same as in fish. There are 10 pairs of cranial nerves.

In **reptiles**, the cerebrum is the largest brain region. Large olfactory lobes are differentiated, and parietal lobes are separated. Hemispheres of the brain have a primordial cortex on their lateral surfaces. The structure of the cortex is primitive (3 layers of cells) — *archipallium*. The striated bodies of the forebrain serve as the integrating center. Such a type of the brain is called *sauropsidian (striatal)*. The size of the midbrain is lower than in amphibians (it is no longer the integrating center of the brain). The cerebellum is considerably larger than that of amphibians. The medulla oblongata forms a sharp flexure in the vertical plane. There are 12 pairs of cranial nerves.

In **mammals**, the forebrain reaches maximal development due to the secondary cortex (*neopallium*). In lower mammals the surface of the cortex is smooth, in higher mammals it has sulci and gyri. The secondary cortex is an integrating center (mammalian type of the brain). The forebrain covers the interbrain. The size of the midbrain decreased. This region consists of quadrigemina (2 superior colliculi are subcortical centers of vision, and 2 inferior colliculi are subcortical centers of hearing). The cerebellum is considerably larger. It is differentiated into two hemispheres with the vermis in the middle. The brain has 12 cranial nerves.

There are 3 flexures of the brain:

1) cephalic flexure at the level of the midbrain,

2) cervical flexure in the region where the medulla oblongata passes into the spinal cord,

3) pontine flexure in the area of the hindbrain.

EVOLUTION OF THE CIRCULATORY SYSTEM OF CHORDATES

The circulatory system originates from the mesoderm. **Basic directions of evolution:**

1. Appearance and differentiation of the heart (change of two-chambered heart into the four-chambered one).

2. The appearance of the 2^{nd} (pulmonary) circulation and complete separation of venous and arterial blood.

3. Transformation of branchial arteries (arterial arches) and differentiation of vessels following from the heart.

Lancelet has one circulation. The abdominal aorta carrying venous blood forms afferent branchial arteries (their number corresponds to the number of branchial arches — up to 150 pairs), where it gets enriched with oxygen. Through efferent branchial arteries, blood flows to the left and right branches of the dorsal aorta. Anterior parts of the branches proceed into carotid arteries and carry blood to the anterior region of the body; posterior parts of the branches join together and form the dorsal aorta that divides into multiple arteries carrying blood to all organs (Fig. 90).

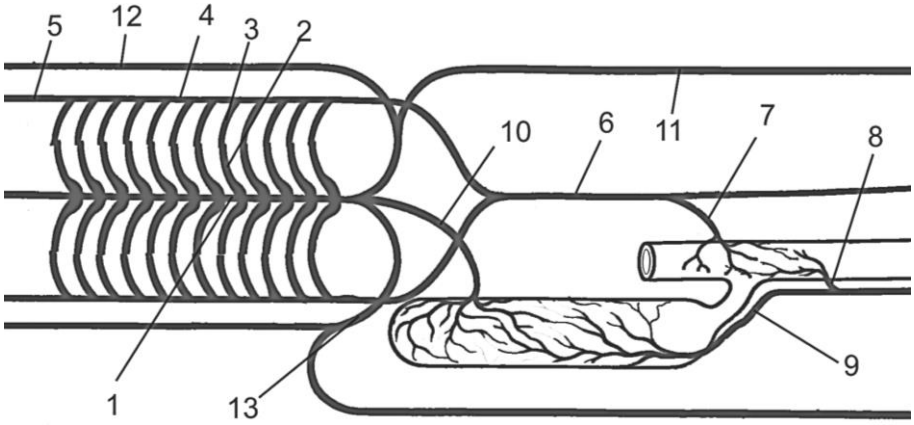


Figure 90. The circulatory system of the Lancelet:
1 — abdominal aorta; *2* — afferent branchial arteries; *3* — efferent branchial arteries; *4* — branches of a dorsal aorta; *5* — carotid arteries; *6* — dorsal aorta; *7* — intestinal artery; *8* — subintestinal vein; *9* — liver portal vein; *10* — hepatic vein; *11* — right posterior cardial vein; *12* — right anterior cardial vein; *13* — left Cuvier's duct

After the gas exchange, the venous blood accumulates in paired anterior and posterior cardial veins located symmetrically. The anterior and posterior cardial veins join together into the Cuvier's ducts. They empty into the abdominal aorta. The portal system is formed near the hepatic cecum. Blood from there passes through the hepatic vein into the abdominal aorta.

Fishes have one circulation. The heart is located beneath the mandible and consists of two chambers (atrium and ventricle) filled with venous blood. A venous sinus borders upon the atrium; an arterial cone follows by the ventricle and passes into the abdominal aorta.

Anlages of 5^{th}–7^{th} pairs of branchial arteries are formed during embryogenesis but then the 1^{st}, 2^{nd}, and 7^{th} are reduced, and only the 3^{rd}–6^{th} pairs continue functioning.

Due to the appearance of lungs, 2^{nd} circulation develops in **amphibians**. The heart consists of two atria and one ventricle. A venous sinus borders upon the right atrium, and an arterial cone follows by the ventricle (Fig. 91).

The atria open into the ventricle with one aperture. Venous and arterial blood come from the right and left atria. Blood in the right part of the ventricle is venous, mixed in the center, and arterial in the left part.

The blood is distributed into 3 pairs of vessels through the arterial cone: venous blood goes to the skin and lungs through the pulmocutaneous arteries; mixed blood goes to all organs through aortal arches; arterial blood goes to the brain through carotid arteries.

Anlages of 6^{th}–7^{th} pairs of branchial arteries are formed in embryogenesis and then the 1^{st}, 2^{nd}, 5^{th} and 7^{th} are reduced.

The 3^{rd} one transforms into carotid arteries, the 4^{th} one forms arches of the aorta, and the 6^{th} — pulmocutaneous arteries (Fig. 92).

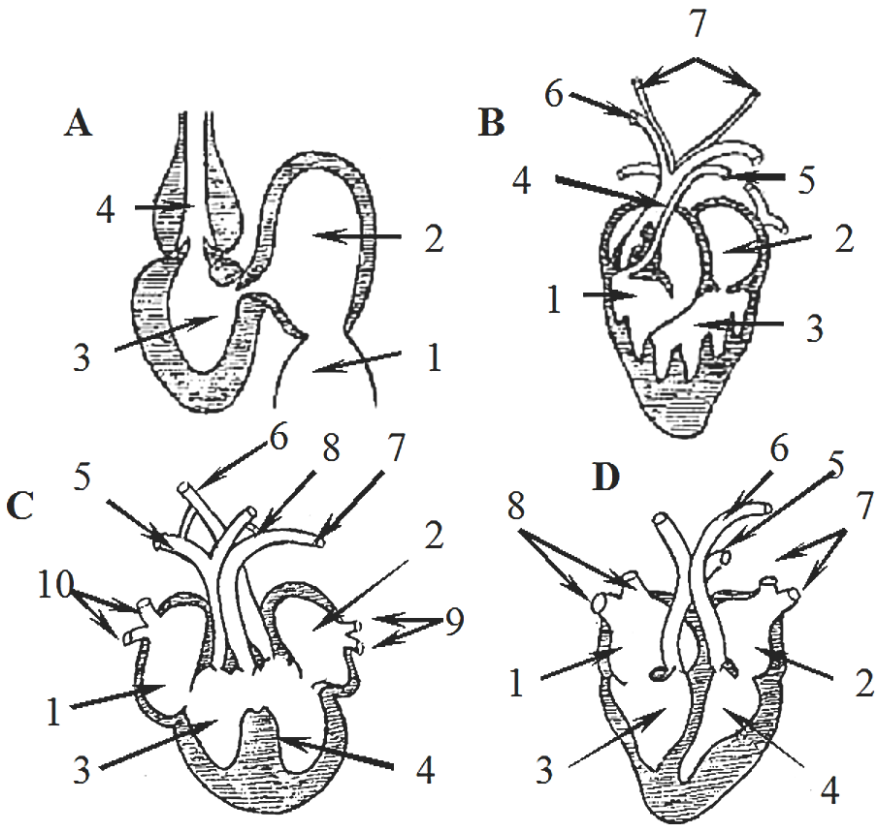


Figure 91. Heart evolution of vertebrates:
A — fish: *1* — venous sinus; *2* — atrium; *3* — ventricle; *4* — bulb of aorta;
B — amphibian: *1* — right atrium; *2* — left atrium; *3* — ventricle; *4* — arterial cone; *5* — left pulmocutaneous artery; *6* — right arch of the aorta; *7* — carotid arteries;
C — reptiles: *1* — right atrium; *2* — left atrium; *3* — ventricle; *4* — interventricular septum; *5* — right pulmonary artery; *6* — right arch of the aorta; *7* — left arch of the aorta; *8* — left Botallo duct; *9* — pulmonary veins; *10* — vena cava;
D — mammal: *1* — right atrium; *2* — left atrium; *3* — right ventricle; *4* — left ventricle; *5* — left pulmonary artery; *6* — left arch of the aorta; *7* — pulmonary veins; *8* — vena cava

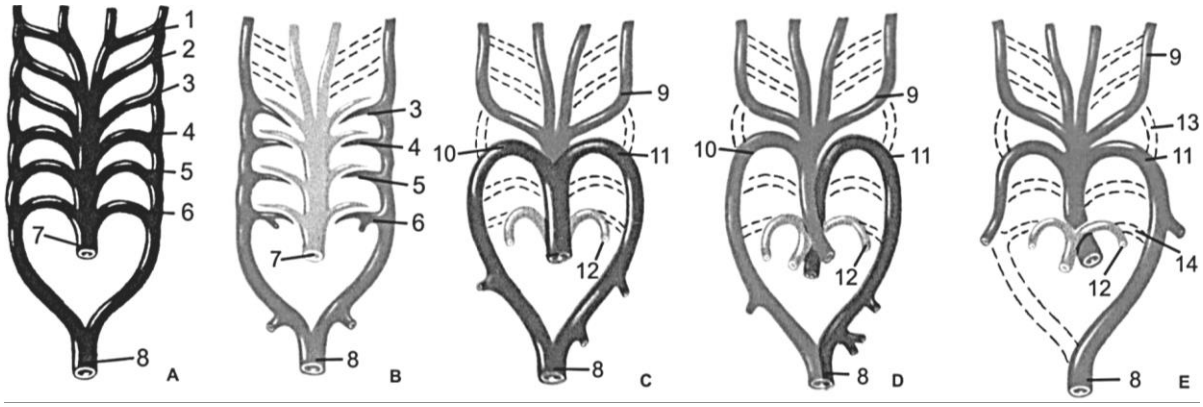


Figure 92. Development of arterial arches in vertebrate animals:
A — anlage in a vertebrate; *B* — fish; *C* — anura amphibian; *D* — reptile; *E* — mammal: *1–6* — arterial (branchial) arches; *7* — abdominal aorta; *8* — dorsal aorta; *9* — carotid arteries; *10* — right arch of aorta; *11* — left arch of aorta; *12* — pulmonary arteries; *13* — carotid duct; *14* — Botallo duct

In **reptiles**, the heart consists of 3 chambers, and an incomplete septum appears in the ventricle.

The pulmonary artery springs from the right part of the ventricle, it carries venous blood to the lungs; from the left part springs the right arch of the aorta that carries arterial blood to the brain and forelimbs. The left arch of the aorta springs from the center of the ventricle, it carries mixed blood. Behind the heart 2 arches of the aorta fuse into one vessel and carry mixed blood to all organs.

Anlages of 6 pairs of branchial arteries are formed. They transform into the same vessels as in amphibians (the 6^{th} pair — into pulmonary arteries).

In **mammals**, the heart is completely divided into the left and right halves to ultimately separate arterial and venous blood.

The right heart contains venous blood while the left one is filled with arterial blood.

The pulmonary circulation starts from the right ventricle with pulmonary arteries and terminates in the left atrium with pulmonary veins.

The systemic circulation starts from the left ventricle with a left arch of the aorta and ends in the right atrium with the vena cava.

Anlages of 6 pairs of branchial arteries are formed in embryogenesis, then in the 1^{st} and 2^{nd} pairs are reduced; the 3^{rd} pair forms carotid arteries; the right one of 4^{th} pair is reduced while the left one forms an arch of the aorta; the 5^{th} pair is reduced; the 6^{th} pair transforms into pulmonary arteries.

EVOLUTION OF THE RESPIRATORY SYSTEM OF CHORDATES

The respiratory system has an endodermal origin. **Basic directions of evolution of the respiratory system:**

1. Transformation of interbranchial septa of lancelets into the gill apparatus of fishes.
2. Enlargement of the respiratory surface due to gill filaments; formation of gill capillaries.
3. Transformation of the gill apparatus into terrestrial respiratory organs (lungs).
4. Development and differentiation of respiratory tract, formation of a bronchial tree.
5. Enlargement of the respiratory surface of the lungs; formation of the chest and appearance of the diaphragm.

A **lancelet** has 100–150 pairs of interbranchial septa piercing the pharynx and gas exchange takes place in their vessels. These are the afferent branchial artery and efferent branchial artery. There are no branchial capillaries.

Fishes have branchiae (gills) in the anterior part of the pharynx. Gas exchange takes place in the capillaries of gill filaments. *Crossopterygians* acquired organs able to breathe with the air-paired outgrowth of the pharyngeal wall at the abdominal side. They are anlagen of the lungs of terrestrial vertebrates.

Anura amphibians have a laryngotracheal chamber, in caudate amphibians it separates into the larynx and trachea (Fig. 93); arytenoid cartilages and vocal folds appear in the pharynx. Anurans have septa in the lungs. The lungs of caudates are presented by two thin-walled sacs without septa. Ventilation of the lungs is low and the skin participates in respiration.

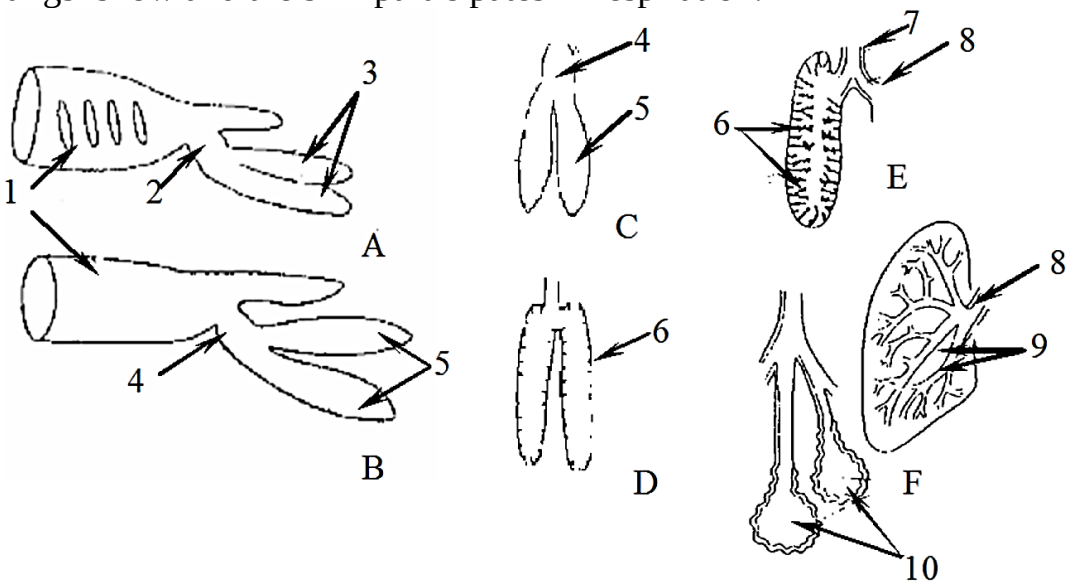


Figure 93. Evolution of the lungs in vertebrates:
A — pharynx and a swimming bladder (lungs) of the crossopterygian fishes; *B* — pharynx and lungs of amphibians; *C* — caudate amphibian; *D* — anuran amphibian; *E* — reptile; *F* — mammal: *1* — pharynx; *2* — unpaired chamber connecting the swimming bladder with the pharynx; *3* — sacs of the swimming bladder; *4* — laryngotracheal chamber; *5* — pulmonary sacs; *6* — intrapulmonary septa; *7* — trachea; *8* — bronchus; *9* — branches of bronchi; *10* — alveoli

In **reptiles** the respiratory surface of the lungs is increased by honeycomb-shaped structures faveoli with blood vessels. There are extrapulmonary bronchi; cricoid cartilage appears in the pharynx, and cartilaginous rings appear in the trachea. There is a chest. Ribs are movably connected to the spine and breastbone, there are intercostal muscles.

In **mammals** appear the nasal cavity and nasopharynx. Thyroid cartilage appears in the larynx.

The bronchial tree is formed. Bronchioles and alveoli considerably increase the respiratory surface (the number of alveoli is up to 500 million).

The chest is separated from the abdominal cavity by the diaphragm and takes part in respiration.

EVOLUTION OF THE DIGESTIVE SYSTEM OF CHORDATES

The digestive system originates from the endoderm, its beginning and ending regions develop from the ectoderm. **Basic directions of evolution:**

1. Differentiation of the alimentary tube into regions.
2. The appearance of digestive glands.

3. The appearance of teeth and their differentiation.

4. Enlargement of the absorption surface due to the elongation of the intestine and appearance of villi.

Lancelet's digestive system is presented by a straight tube that is differentiated into a pharynx and intestine. The pharynx has gill slits. The alimentary tube forms a hepatic cecum.

Fishes have jaws with homogenous teeth (homodontous animals). There is an esophagus, stomach, small and large intestines. The liver is well developed; there is a gallbladder. The pancreas is differentiated poorly.

Amphibians have an oropharyngeal cavity with homogenous teeth, esophagus, small and large intestine, liver, and pancreas.

A muscular tongue and salivary glands appear. There are no enzymes in saliva. Amphibians have a duodenum and rectum.

The intestine ends with a cloaca.

Reptiles have an oral cavity that is separated from the pharynx, differentiation of teeth begins (fangs), and the walls of the stomach are thick. There is a primordial cecum, the intestine becomes longer and ends with a cloaca.

Mammals are heterodonts (have incisors, canines, and molars); lips appeared. The saliva contains enzymes. The intestine is differentiated into a small and large intestine, the caecum is well-developed and has an appendix.

The rectum ends with an anal opening. The mucous membrane of the intestine has a great number of folds, the small intestine has villi.

EVOLUTION OF THE EXCRETORY SYSTEM OF CHORDATES

The excretory system originates from the mesoderm. It is represented with nephridia in lancelets and by kidneys in vertebrates.

Basic directions of evolution:

1. Substitution of nephridia (lancelet) with kidneys (vertebrates).

2. Transformation of a pronephros (head kidney) into a mesonephros (mesonephric kidney) and ultimately metanephros (pelvic kidney) by increasing the number of nephrons and convergence of the nephrons and blood capillaries, elongation of nephron tubules.

The lancelet has 100–150 pairs of nephridia. They are short tubules that have one end open into a coelom, and the other one — into a peribranchial cavity. A glomerule of capillaries is situated in the coelom wall near tubules.

In the course of evolution, vertebrates successively change 3 generations of kidneys: *pronephros, mesonephros, metanephros*.

A nephron is a basic structural and functional unit of an excretory organ.

The pronephros (in larvae of fishes and amphibians) has 6–12 nephrons. The nephron consists of a funnel (nephrostome) and a short tubule. Nephrostomes open into the coelom and tubules into the ureter of the kidney. The glomerulus is located in the coelom wall near nephrostomes (Fig. 94).

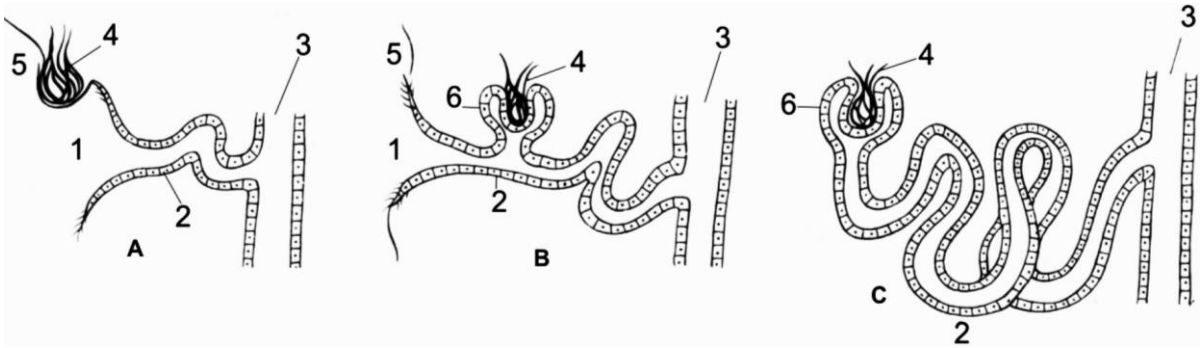


Figure 94. Evolution of the nephron:
A — pronephros; *B* — mesonephros; *C* — metanephros: *1* — nephrostome; *2* — tubule of the nephron; *3* — ureter; *4* — glomerulus; *5* — coelom; *6* — capsule of the nephron

Dissimilation products pass from the blood into the coelom, then through the nephrostome into the tubule, and then into the ureter of the pronephros (pronephric duct). The ureter opens into the cloaca.

The mesonephros (mature fishes and amphibians) contain approximately 100 nephrons. Some glomeruli have an outgrowth of the tubule wall in the shape of a two-walled capsule.

Nephrostomes are preserved.

Dissimilation products are removed from the blood in two ways: from the nephrostome into the tubule or from the glomerulus into the tubule.

During further development of the urinary system, the pronephric duct splits longitudinally into the Mullerian duct and Wolffian duct. In males of lower vertebrates, the Muller duct atrophies but in females it is transformed into an oviduct.

The Wolffian canal transforms into a ureter in females or it functions as both the ureter and seminal duct in males.

Amniotes (higher vertebrates) have metanephros. It contains about 1 million nephrons.

There is no nephrostome, the wall of the tubule completely envelopes the glomerulus (renal corpuscle consisting of a Shumlyansky–Bowman capsule and glomerulus are formed: a), then the tubule is differentiated into a descending part, the Henle loop and an ascending part.

Removal of dissimilation products from the blood occurs directly into a tubule.

Filtration of blood plasma occurs in the glomerulus while tubules perform reabsorption of water, amino acids, and glucose from primary urine. The dilation of the distal part of the ureter forms a urinary bladder.

The phylogenetical relation of the excretory and genital systems:

– the gonads of Vertebrates are germinated as paired folds on ventral parts of the primary kidney;

– canaliculi of the prokidney and its ureter form a funnel and an oviduct in females; a ureter of the primary kidney serves as a semen duct in males (Fig. 95).

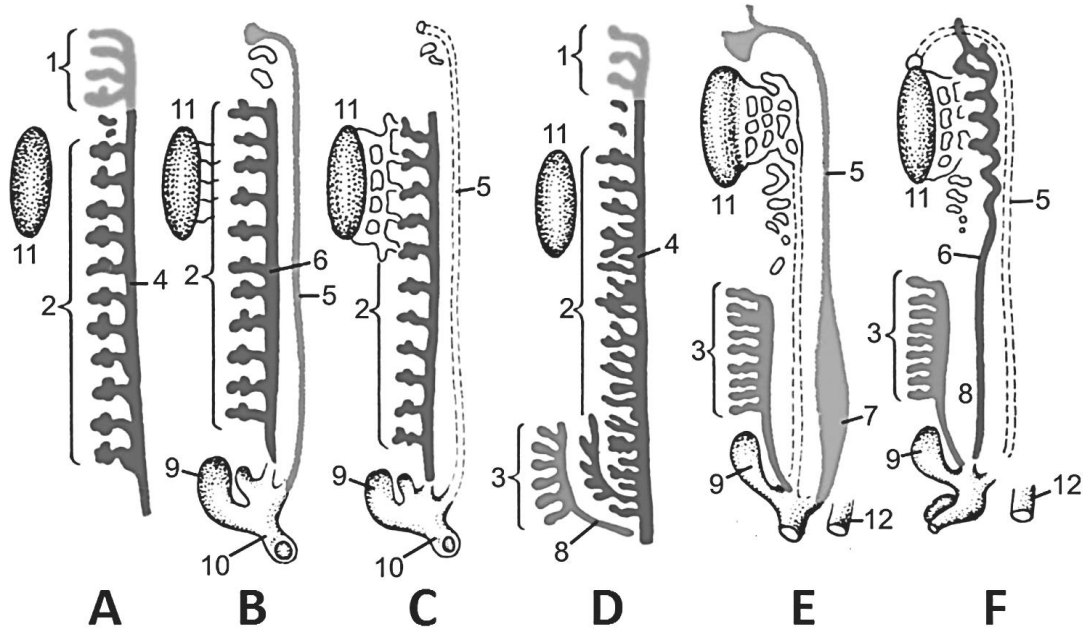


Figure 95. Development of the excretory and genital systems in vertebrates: *A* — neutral embryonic state in a lower vertebrate; *B* — female lower vertebrate; *C* — male lower vertebrate; *D* — neutral embryonic state of a higher vertebrate; *E* — female higher vertebrate; *F* — male higher vertebrate. *1* — pronephros; *2* — mesonephros; *3* — metanephros; *4* — pronephric canal; *5* — Muller duct serving as oviduct in females; *6* — Wolffian duct serving as semen duct in males; *7* — uterus; *8* —ureter; *9* — bladder; *10* — cloaca; *11* — gonad; *12* — anus

ONTOPHYLOGENETIC ETIOLOGY OF MALFORMATIONS IN THE NERVOUS, CARDIOVASCULAR, RESPIRATORY, DIGESTIVE AND UROGENITAL SYSTEMS IN THE HUMAN

Ontophylogenetic etiology of brain malformations (causes are recapitulations): undifferentiation of hemispheres, incomplete separation of hemispheres of the telencephalon (prosencephalia); ichthyopsidian or sauropsidian types of the brain.

Ontophylogenetic etiology of cardiovascular malformations: ventricular septal defect, open Botallo duct, underdevelopment of aortopulmonary septum (incomplete separation of the arterial trunk into an aorta and a pulmonary trunk), transposition of the great vessels, preservation of both aortal arches, etc.

Ontophylogenetic etiology of malformations of the respiratory system: underdevelopment of the pharynx or lungs, cystic lung hypoplasia, abnormal branching of bronchi, hypoplasia of the diaphragm, etc.

Ontophyloigenetic etiology of malformations of the digestive system: cervical fistulae (rupture gill pouch), homodontous teeth, additional lobes of the liver and pancreas, shortening of the intestine.

Ontophylogenetic etiology of urogenital malformations: a pelvic position of kidneys, preservation of a mesonephros, doubling of the ureter, bicornuate uterus, duplex uterus, and vagina (parallelism).

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