BOTULIZM

(synonyms: ichthyism, allantiism; botulism, allantiasis, sausage-poisoning - English; botulisme, allantiasis - French; Botulismus Wurst-Vergiftung, Fleischvergtftung - German)
(from gr. allantiksa - sausage),
ichthyoism (from gr. ichtis - fish)

Botulism is an acute infectious disease with a leading enteral route of infection, caused by exotoxins of Cl.Botulinum and characterized by a severe course with damage to the nervous system, mainly the medulla oblongata and spinal cord, occurring with a predominance of ophthalmoplegic and bulbar syndromes (characterized by paresis and paralysis of the striated and smooth muscles, sometimes in combination with gastroenteritis syndrome in the initial period.)

History

It is assumed that people have been ill with botulism throughout the entire period of human existence. Thus, the Byzantine emperor Leo VI banned the consumption of black pudding because of the life-threatening consequences.

However, the disease was documented only in 1793, when 13 people who ate black pudding fell ill in Württemberg, 6 of whom died.

Hence the disease got its name - "botulism" (lat. botulus - sausage).

ETIOLOGY

The causative agent of botulism *Clostridium botulinum* belongs to the genus Clostridium, family Bacillaceae.

***Clostridium botulinum* is an anaerobic, Gram positive, spore-forming rod.**

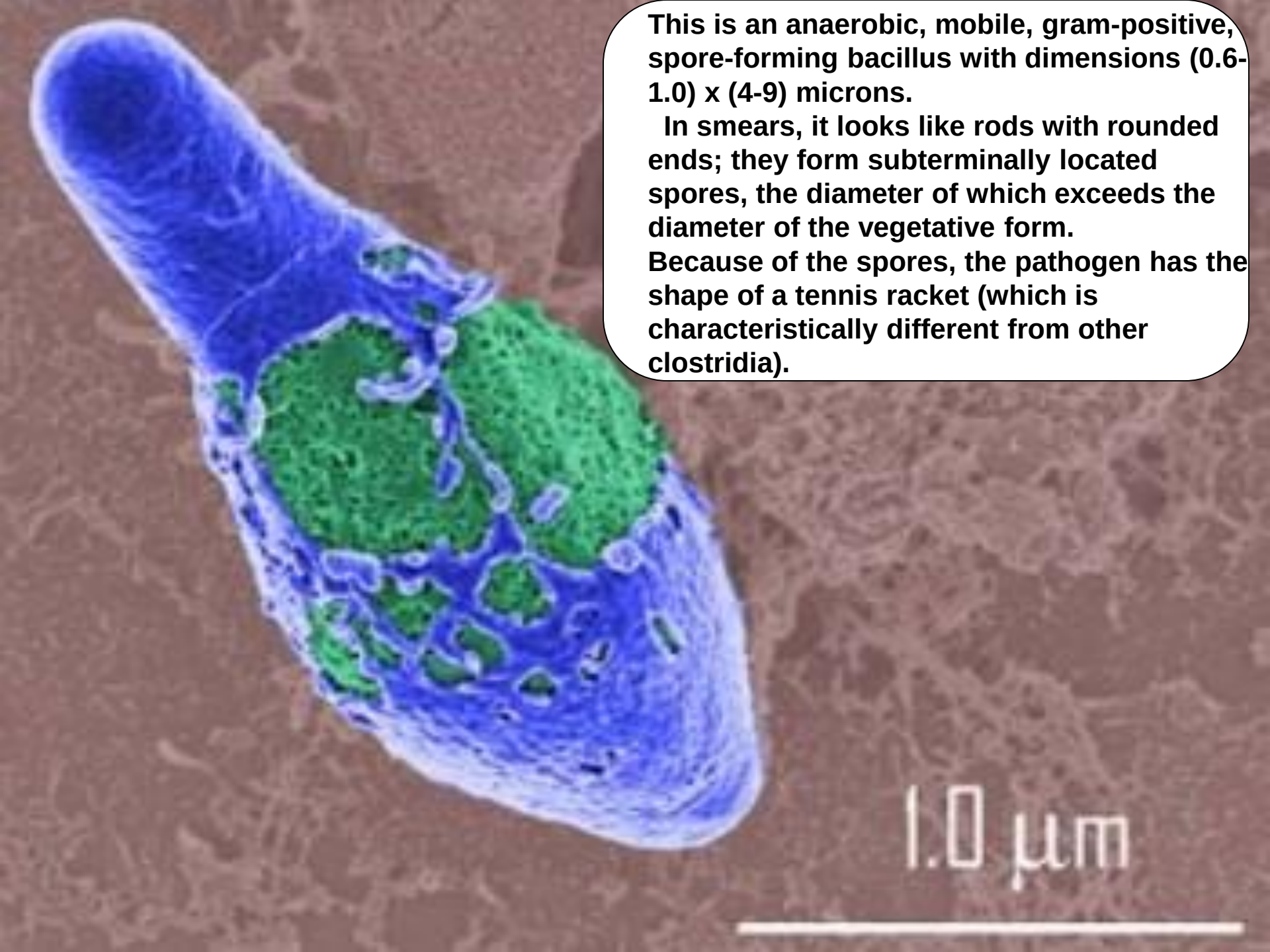
Does not form capsules, mobile, peritrichous, obligate anaerobes, located in random clusters or small chains.

There are eight serological varieties of the bacterium denoted by the letters A to H (labeled as types A, B, C [C1, C2], D, E, F, and G), which are antigenically and serologically distinct but structurally similar.

Human botulism is caused mainly by types A, B, E, and (rarely) F .

The toxin from all of these acts in the same way and produces similar symptoms:

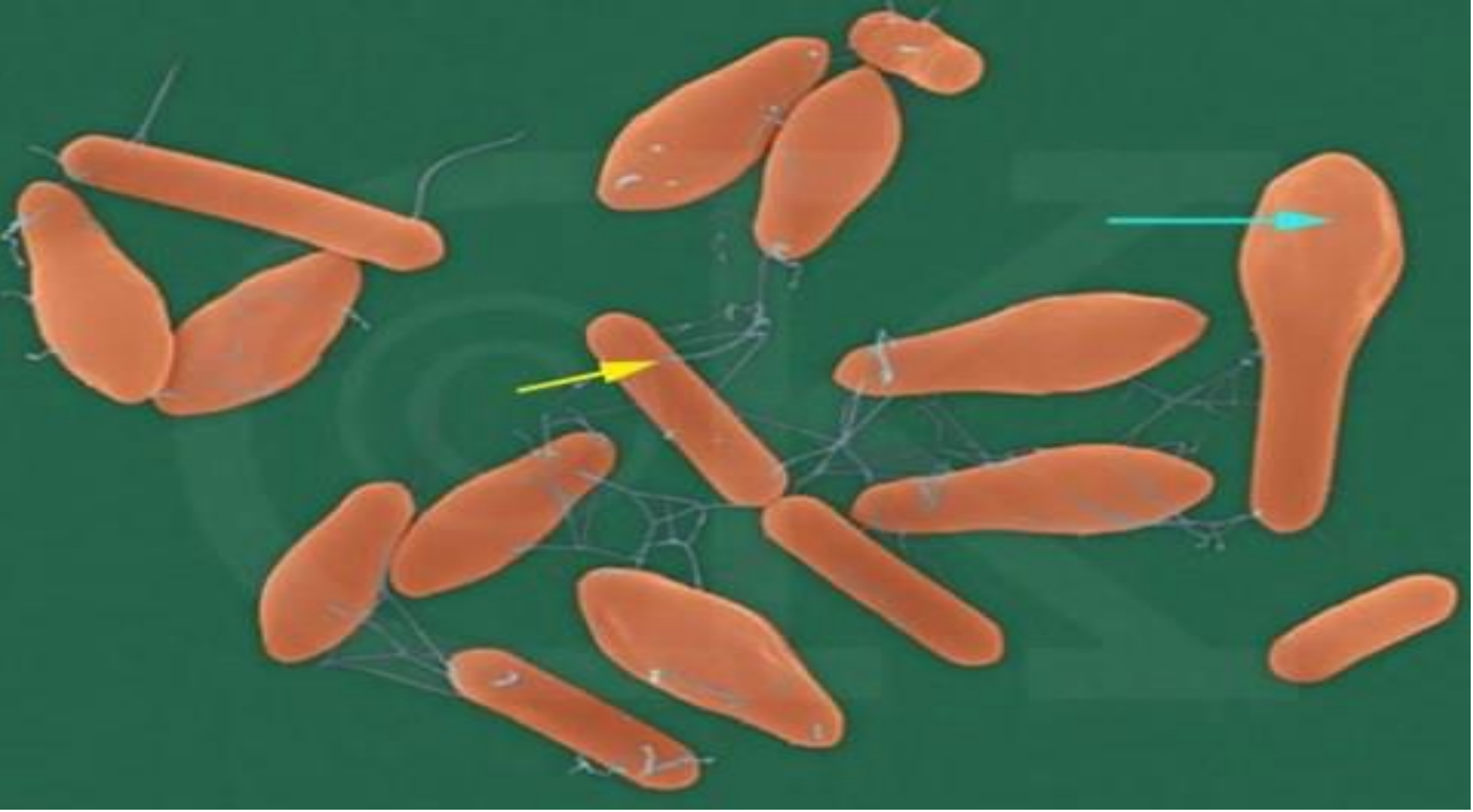
the motor nerve endings are prevented from releasing acetylcholine, causing flaccid paralysis and symptoms of blurred vision, ptosis, nausea, vomiting, diarrhea or constipation, cramps, and respiratory difficulty.



This is an anaerobic, mobile, gram-positive, spore-forming bacillus with dimensions (0.6-1.0) x (4-9) microns.

In smears, it looks like rods with rounded ends; they form subterminally located spores, the diameter of which exceeds the diameter of the vegetative form.

Because of the spores, the pathogen has the shape of a tennis racket (which is characteristically different from other clostridia).



vegetative

spore

• The pathogen can be in two forms - vegetative (indicated by a yellow arrow in the figure below) and spore (blue arrow) - this is important for preventive measures, because vegetative forms are the most pathogenic and less resistant to harmful factors. Spore form - the ability to spore formation, i.e. the emergence of almost unshakable stability. The spore is formed terminally, that is, almost at the end, the pathogen takes the form of a “tennis racket”.

The bacterium multiplies and produces a toxin in the process of life.
Toxins are produced by vegetative forms.
The optimal conditions for the growth of vegetative forms are an extremely low residual oxygen pressure (0.40–1.33 kPa) and a temperature regime in the range of 28–35 °C.
In the process of vital activity, gas formation, which is characteristic of most Clostridia, occurs (visually, on canned products, it is defined as a 'bombing' - swelling of a lid or can).

The vegetative forms of bacteria die at 80 °C within 30 minutes, when boiled - within 5 minutes, however, its spore forms are able to survive for several hours at a temperature of 100 °C, and, once in a favorable environment, pass into vegetative forms.

Of interest is the phenomenon of the formation of so-called "dormant spores" from vegetative forms with insufficient heating, capable of germinating only after 6 months.

Spores are resistant to freezing and drying, to direct ultraviolet radiation.

Under anaerobic conditions or close to them, the causative agents of botulism produce a specific lethal neurotoxin, which is the only but exceptional pathogenicity factor. Specially purified, brought to a crystalline form, botulinum toxin can contain millions of lethal doses. Botulinum toxins of a protein nature under normal environmental conditions persist for up to 1 year, in canned foods - for years. They are stable in an acidic environment, are not inactivated by digestive tract enzymes, and the toxic properties of botulinum toxin E under the influence of trypsin can be enhanced hundreds of times. Botulinum toxins withstand high concentrations (up to 18%) of table salt, are not destroyed in products containing various spices.

Toxins are relatively quickly inactivated under the influence of alkalis, when boiled, they completely lose their toxic properties for more than 30 minutes, and under the influence of small concentrations of potassium permanganate, chlorine or iodine - within 15-20 minutes.

Botulinum toxin is one of the most powerful natural poisons (lethal dose for humans is 5-50 ng/kg of body weight).

More than 60 years ago, research began on the possibility of using the toxin as a biological weapon. The botulinum toxin is the most powerful toxin known - it is **375,000** times stronger than the venom of a rattlesnake, and one gram of the toxin sprayed into the air is enough to kill more than 1 million people.

Epidemiology.

Botulism is classified as a saprozoonosis. The main reservoir of the causative agent of botulism are herbivores and, less often, cold-blooded animals (fish, mollusks, crustaceans) that absorb spores of Cl. botulinum with water and food. Carnivores are usually resistant to this pathogen.

A person becomes infected with botulism by eating food contaminated with spores. Most cases of botulism are associated with the use of home canned products - mushrooms, vegetables, fish, meat, lard, etc.

Rarely, wound botulism and infant botulism occur.

Botulism is one of the rare diseases, and incidence rates do not exceed a fraction of a percent, although the incidence of botulism is currently recorded in all countries of the world.

The most common cause of botulism infection is home-made canned food, the type of which depends on the commitment of the population.

The dangers of home canning are obvious: the heat resistance of spores allows them to endure even long-term (up to 6 hours) boiling at 100 ° C, while the concentrations of salts and vinegar used in canning do not prevent toxin formation, and subsequent sealing of jars with home-made canned food leads to the creation of anaerobic conditions.

At the same time, canned food containing toxin does not change either its appearance or organoleptic properties - in an already lethal concentration, botulism toxin does not change either the taste, color, or smell of the products containing it.

If the infected product is solid-phase (sausage, smoked meat, fish), then "nested" infection with botulinum pathogens and the formation of toxins are possible in it. Therefore, there are outbreaks in which not all people who used the same product get sick.

Currently, diseases caused by poisoning with toxins A, B or E predominate.

Thus, the main route of infection is food, due to the use of home-canned food.

For complete destruction,
fractional pasteurization-tyndalization
is used.

Anaerobic conditions can be created in the food product as a result of the presence of additional aerobic flora, such as oxygen-consuming Staphylococcus aureus.

According to WHO recommendations, there are four categories of botulism:

- **foodborne**
- **wound**
- **infant**
- **unspecified**

Food botulism (the disease occurs after eating foods containing accumulated botulinum toxin);
Wound botulism (develops when the wound is contaminated with soil, in which the conditions necessary for the germination of Clostridium botulinum that have fallen from the soil and subsequent toxin formation are created);
Infant botulism (occurs in children mainly up to 6 months, when they are infected with spores of Clostridium botulinum);
Botulism of an unspecified nature (it is not possible to establish any connection between the disease that has arisen and the food product).

Iatrogenic botulism can happen if too much botulinum toxin is injected for cosmetic reasons, such as for wrinkles, or medical reasons, such as for migraine headaches.

Adult intestinal toxemia (also known as adult intestinal colonization) botulism is a very rare kind of botulism that can happen if the spores of the bacteria get into an adult's intestines, grow, and produce the toxin (similar to infant botulism). Although we don't know why people get this kind of botulism, people who have serious health conditions that affect the gut may be more likely to get sick.

All kinds of botulism can be fatal and are medical emergencies.

In Azerbaijan, diseases associated mainly with the use of home-canned vegetables (tomatoes, cucumbers) are more often recorded;
in Russia - home-canned mushrooms, smoked or dried fish, in European countries - meat and sausage products, in the USA - canned beans. These products often cause group, "family" outbreaks of diseases.

Much less common are cases of the disease as a result of infection only with spores of pathogens Cl. Botulinum.

These include so-called wound botulism and infant botulism.

Wound botulism may occur due to contamination of wounds, which subsequently create conditions close to anaerobic.

At the same time, vegetative forms germinate from spores that have fallen into the wound, which produce botulinum toxins.

During their resorption, typical for botulism develops neurological disorders.

A peculiar form of wound botulism is botulism in drug addicts.
Infection occurs as a result of injections or even skin scarifications of "black heroin"
("black tar"), the starting material for which is contaminated with soil and thus contaminated with spores.
In the case of abscessing of injection sites, prerequisites for the development of the disease are created, as in wound botulism.

Infant botulism occurs predominantly in children during the first six months of life.
Most of the patients were on partial or full artificial feeding..

Honey is a known dietary reservoir of *C. botulinum* spores and has been linked to infant botulism. For this reason, honey is not recommended for infants less than one year of age.

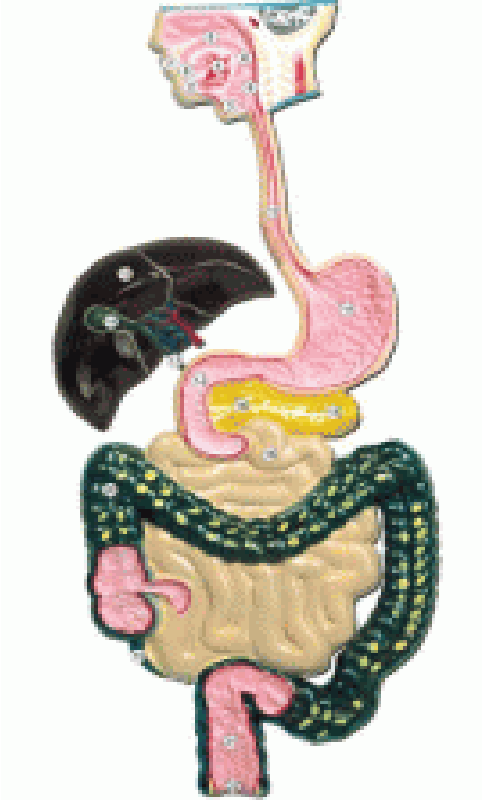
It is assumed that the spores are brought with dust into the nectar, which is processed by bees into honey, which is subsequently used in nutrient mixtures.

The same spores were found in the environment of the child - the soil, household dust and even on the skin of nursing, mothers. Attention is drawn to the fact that infant botulism is recorded exclusively in socially disadvantaged families living in unsatisfactory sanitary and hygienic conditions. Many infant botulism patients have been demonstrated to live near a construction site or an area of soil disturbance Due to the peculiarities of the intestinal microflora of infants, it is believed that those caught in child's gastrointestinal tract spores are found favorable conditions for germination in vegetative form and production of toxins.

Thus, the epidemiology of botulism is very complex. The disease can develop due to the ingestion of only botulinum toxins, toxins and pathogens, or only spores.

Pathogenesis.

In the pathogenesis of botulism, the leading role belongs to the toxin.
With a normal infection (food route), it enters the body along with food, which also contains vegetative forms of pathogens - poison producers. The absorption of botulinum toxin occurs through the mucous membrane of the proximal gastrointestinal tract, starting from the oral cavity. But the most significant is the entry of the toxin through the mucous membrane of the stomach and small intestine, from where it enters the lymph and subsequently into the blood, which spreads throughout the body. It has been established that botulinum toxin is strongly bound by nerve cells. In this case, both nerve endings and motor neurons of the anterior horns of the spinal cord are affected.



Botulinum toxin selectively affects the cholinergic parts of the nervous system, as a result of which the release of acetylcholine into the synaptic cleft, and therefore the neuromuscular transmission of excitations (paresis, paralysis) is disturbed. Cholinesterase activity in synapses remains virtually unchanged. First of all, the innervation of muscles that are in a state of constant and highly differentiated functional activity (oculomotor apparatus, muscles of the pharynx and larynx) is disturbed. The result of the defeat of motor neurons is also the inhibition of the function of the main respiratory muscles up to paralysis.

The effect of botulinum toxins is reversible and over time motor function is fully restored. The inhibition of cholinergic processes is preceded by an increase in the content of catecholamines. Due to a violation of the autonomic innervation, the secretion of the digestive glands decreases (the secretion of saliva, gastric juice), and persistent paresis of the gastrointestinal tract develops. The pathogenic effect of botulinum toxins is greatly enhanced when they enter the blood again, against the background of radioactive exposure or after it.

Paresis or paralysis of the intercostal muscles, the diaphragm leads to acute ventilatory respiratory failure with the development of hypoxia and respiratory acidosis. Violation of lung ventilation contributes to the inhibition of the function of the muscles of the pharynx and larynx, the accumulation of thick mucus in the supra- and subglottic space, aspiration of vomit, food, water.

With botulism, due to the indirect or direct action of the toxin, all types of hypoxia develop –

hypoxic, histotoxic, hemic and circulatory.

Ultimately, it determines the course and outcome of the disease.

The pathogenesis of wound botulism and infant botulism differs in that infection occurs with spores that germinate under the anaerobic conditions of the wound or due to the characteristics of the flora and enzymatic activity of the intestines of infants into vegetative forms that produce toxins. The entry of botulinum toxin into the blood gives a neurological picture of the disease typical of botulism. In such cases, there are no syndromes of gastroenteritis, general infectious intoxication.

Clinical features

The incubation period for botulism lasts up to a day, less often up to 2-3 days, and very rarely (in single descriptions) up to 9 or even 12 days.

It is possible that a longer incubation period corresponds to the manifestation of latent manifestations of the disease due to the additional intake of botulinum toxin from the gastrointestinal tract.

With a shorter incubation period, a more severe course of the disease is observed, although not always.

Drinking alcohol, as a rule, does not affect the course of the disease, and intoxication can obscure the first manifestations of botulism, preventing its timely diagnosis.

It should be emphasized that the body temperature in botulism remains normal, less often subfebrile.

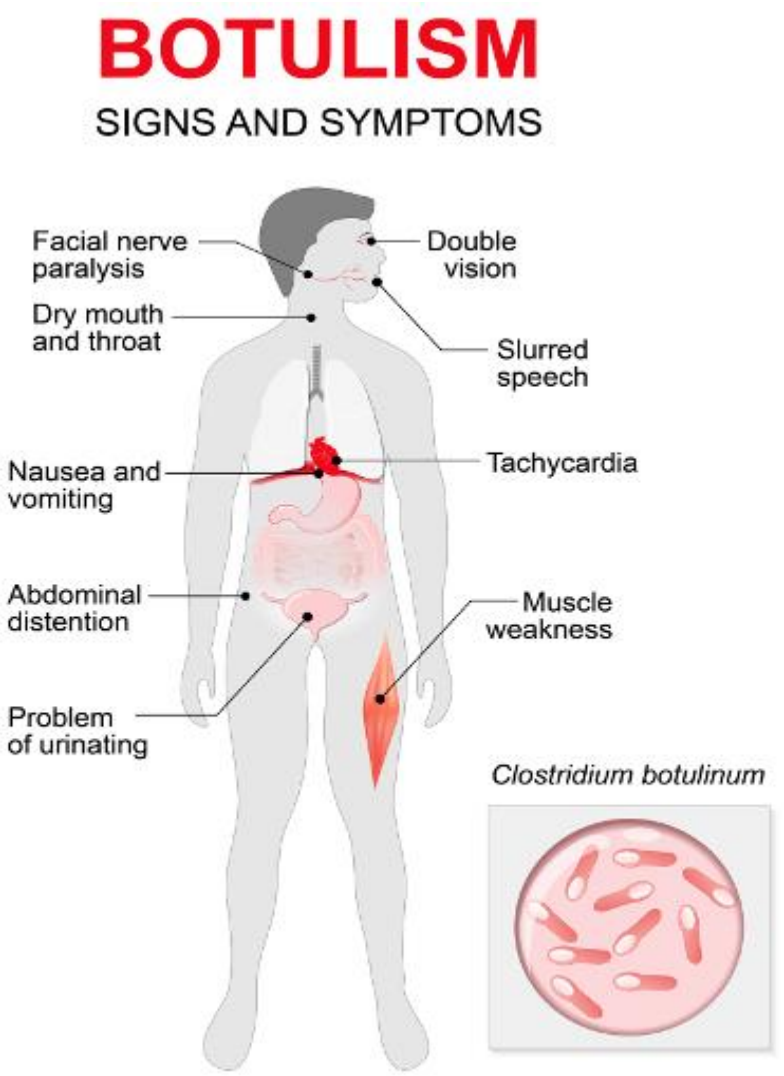
The main syndromes of botulism are:

intoxicating

dyspeptic

paralytic

Intoxication syndrome is the least specific and is accompanied by general weakness, malaise, headache dizziness, etc.



In 1/3 of patients, the disease may begin with dyspeptic syndrome.

In such cases, patients usually complain of acute pain in the abdomen, mainly in the epigastric region, followed by repeated vomiting and loose stools without pathological impurities, no more than 10 times a day, more often 3-5 times. Sometimes, against this background, there is a headache, malaise, there is an increase in body temperature from subfebrile

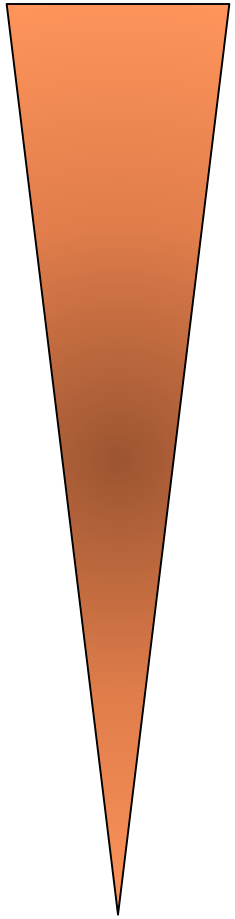
up to 39-40°C.

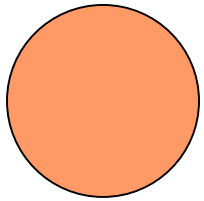
By the end of the day, hypermotility of the gastrointestinal tract is replaced by persistent atony, body temperature becomes normal.

The main neurological signs of the disease begin to appear.

Damage to the nervous system in botulism is often symmetrical. Complete paralysis is not observed, because in addition to large motor neurons, there are also small motor neurons that continue to function normally

The sensitive area is not affected





The leading diagnostic syndrome is paralytic. Of the cranial nerves, botulism does not affect only sensitive ones (olfactorius (I), opticus (II), vestibulo-cohlaris (VIII)). The earliest and deepest changes are recorded on the part of the oculomotor nerves (oculomotorius (III), trochlearis (IV), abducens (VI)). Damage to these pairs of cranial nerves accompanied by the following symptoms:

Ptosis (drooping of the upper eyelid due to impaired innervation of m. levator palpebrae superioris)

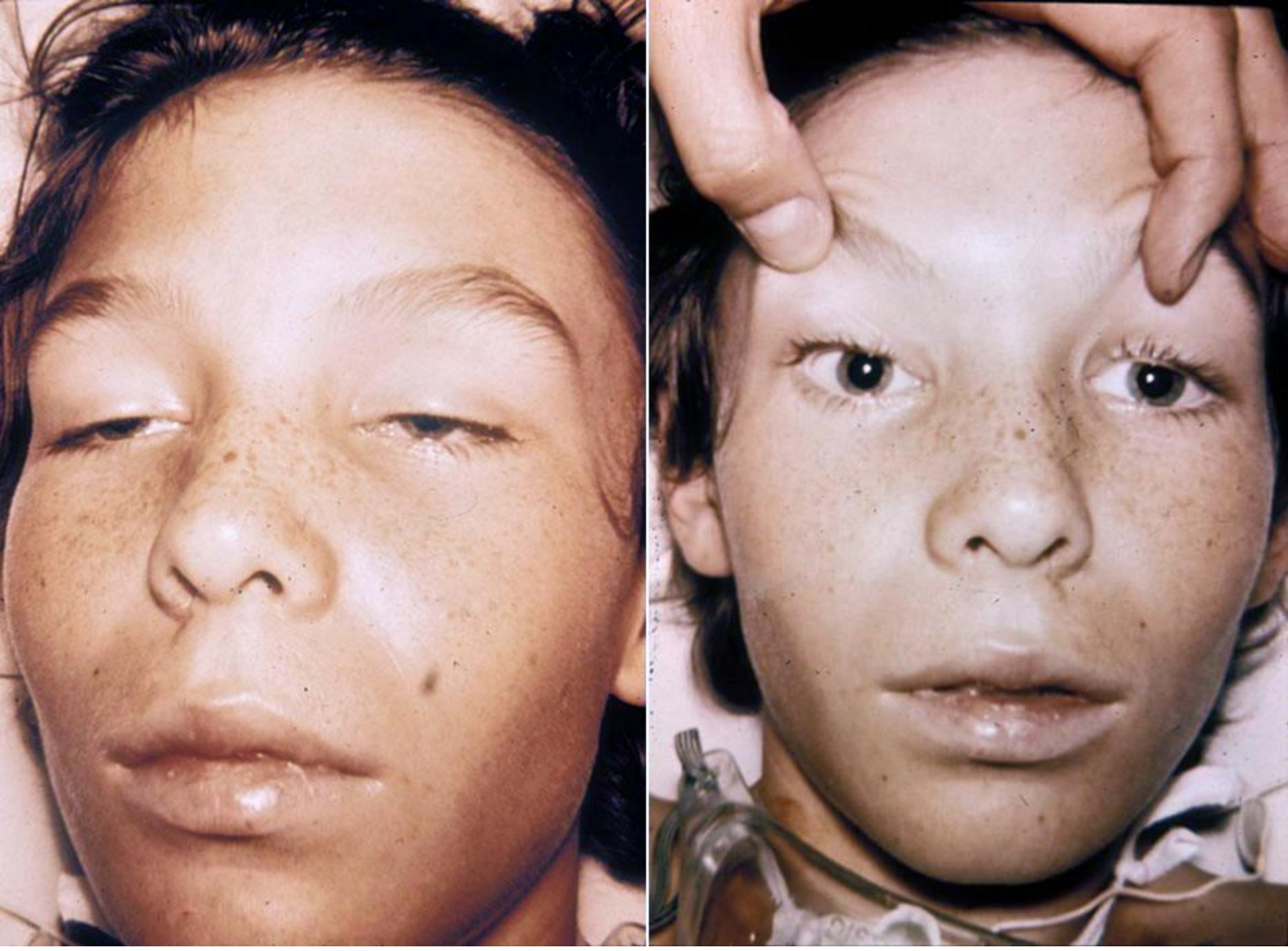
Mydriasis (dilation of the pupil due to impaired innervation of m. dulatator pupillae)

Disorders of reactions of pupils to light (due to impaired innervation of m. dulatator pupillae)

Violation of accommodation (due to impaired innervation of m. ciliaris)

Restriction of the movement of the eyeballs and gaze paresis (due to impaired innervation of the oculomotor muscles)

The patient is also concerned about a number of subjective sensations: fog and a grid before the eyes, doubling of objects, etc.



When the motor nuclei n. trigeminus (V), are damaged weakness of the masticatory muscles is noted, in more severe cases the patient cannot close his mouth.

When n. facialis (VII) is damaged there is a weakness of mimic muscles up to amimia.

When the bulbar group of nerves (glosso-pharyngeus (IX), vagus (X), hypoglossus (XII)) is damaged, the innervation of the muscles of the pharynx, soft palate, larynx, vocal cords, saliva secretion decreases, and visceral innervation suffers.

Clinically, this manifests itself

- **dry mouth**
- **bloating,**
- **weakening of intestinal motility,**
- **constipation**
- **as well as the development of bulbar syndrome.**

The bulbar syndrome is characterized by

Dysphagia

violation of swallowing (liquid food is poured out through the nose, when swallowing solid food, the patient feels difficulty and chokes, the pharyngeal reflex is depressed or absent)

Dysphonia

phonation disorder (hoarse voice or aphonia)

Dysarthria

- speech disorder (nasal tone of voice, slurred speech)

All of the above neurological symptoms appear in various combinations, sequences and severity.

Some of them may be missing.

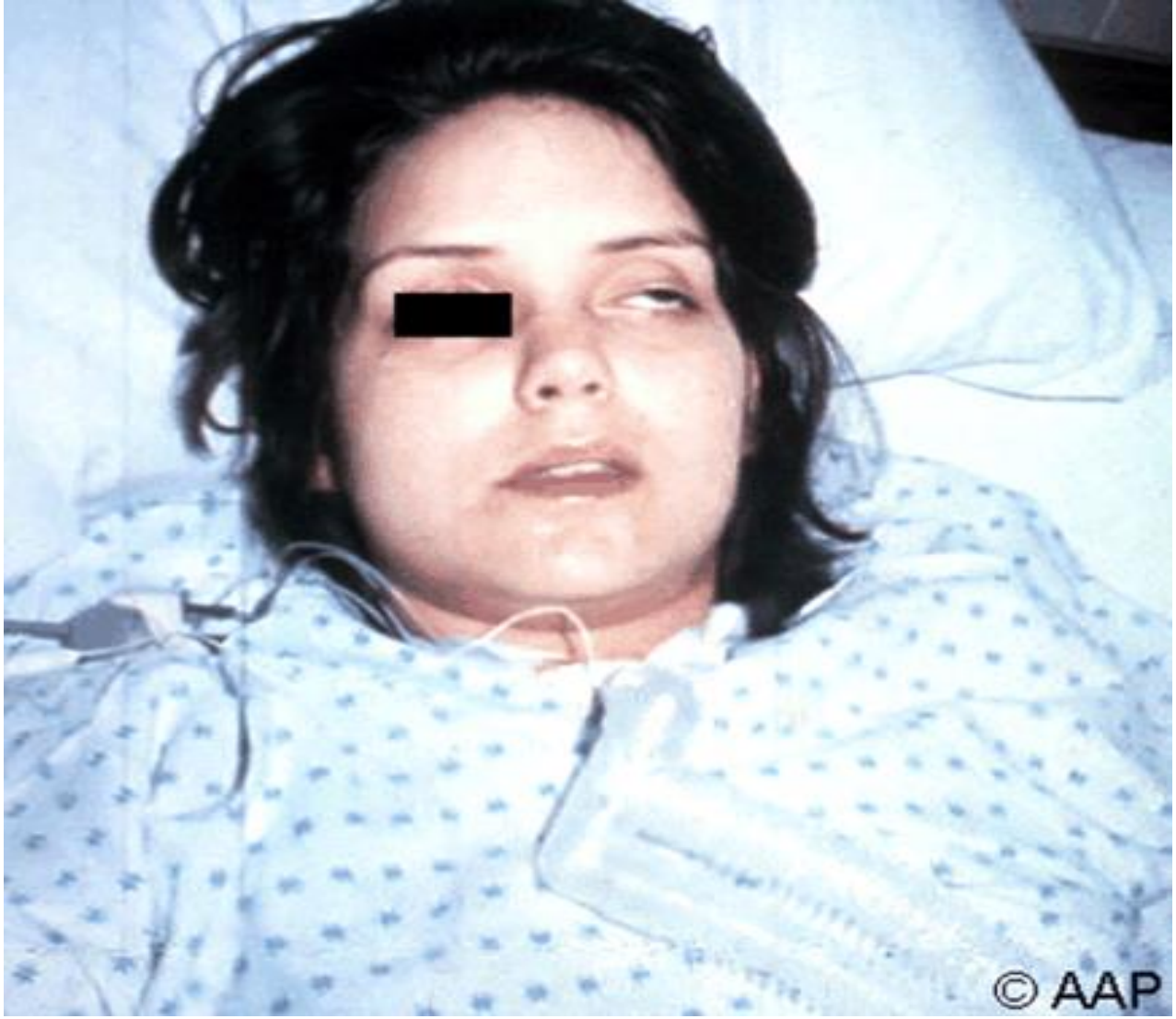
However, the obligatory background for them is

- **desorders of salivation (dry mouth),**
- **progressive muscle weakness**

and

- **persistent constipation.**

On the part of other organs and systems, no changes typical of botulism are determined. Sometimes there may be urinary retention. Studies of peripheral blood do not reveal any special deviations from the norm, with the exception of monocytosis, which also does not always occur. Leukocytosis, neutrophilia, accelerated ESR should be alert for a possible purulent complication of botulism.



Clostridial Infections, Botulism and Infant Botulism (*Clostridium botulinum*). Botulism with ocular muscle paralysis in a preadolescent female. She also had respiratory muscle weakness but did not require ventilatory support.

Distinguish according to severity

- mild,
- moderate and
- severe form of the disease.

Mild cases of botulism are characterized by blurred or monosymptomatic neurological manifestations. Accommodation disorders, slight ptosis, sometimes changes in the timbre of the voice against the background of moderate muscle weakness, hyposalivation are more often observed. Duration from several hours to several days.

With moderate botulism, there are all clinical neurological symptoms, the severity of which is not the same, and the damage to the muscles of the pharynx and larynx does not reach the degree of aphagia and aphonia. There are no life-threatening respiratory disorders. The duration of the disease is 2-3 weeks.

Severe forms of the disease are characterized by a rapid increase in lesions of the oculomotor, pharyngeal and laryngeal muscles, a sharp inhibition of the function of the main respiratory muscles. In the absence of adequate therapy, death usually occurs from respiratory failure on the 2-3rd day of illness.

Recovery comes slowly.

One of the early signs of improvement is the return of salivation. Gradually, neurological symptoms regress. Later than all, there is a complete restoration of visual acuity and muscle strength. Intermittent visual disturbances can be observed for several months. Despite the most severe, sometimes incompatible with life neurological disorders, those who have recovered from botulism do not have any consequences and any persistent dysfunctions of the nervous system or internal organs.

With regard to outcomes, the division of the disease according to severity is rather arbitrary, because even with a mild and even more moderate course of the disease, cases of sudden respiratory arrest are observed.

Some features differ wound botulism and infant botulism.

In both cases, there is no gastrointestinal syndrome and general infectious intoxication.

With wound botulism, a longer incubation period (4-14 days).

Botulism is characterized by neurological symptoms.

It should be noted that these patients do not eating foods that might contain botulinum toxin.

The incubation period is unknown and cannot be established. The first manifestations of the disease may be lethargy in children, weak sucking or refusal to suck, stool retention. Infant botulism (also referred to as floppy baby syndrome) was first recognized in 1976, and is the most common form of botulism in the United States. Infants are susceptible to infant botulism in the first year of life, with more than 90% of cases occurring in infants younger than six months. Infant botulism results from the ingestion of the *C. botulinum* spores, and subsequent colonization of the small intestine. The infant gut may be colonized when the composition of the intestinal microflora (normal flora) is insufficient to competitively inhibit the growth of *C. botulinum* and levels of bile acids (which normally inhibit clostridial growth) are lower than later in life.

DIAGNOSTICS

Botulism is diagnosed on the basis of epidemiological and characteristic clinical manifestations (eating canned foods, the appearance of visual disorders, violations of swallowing, sucking, changes in voice, respiratory failure, etc.).

Diagnosis is simplified if the disease occurs against the background of normal body temperature, accompanied by severe myasthenia gravis, mydriasis, general pallor, dryness of the oral mucosa, thirst, dizziness, without impaired consciousness.

For laboratory confirmation, the detection of a toxin and a pathogen in biomaterials taken from a patient (blood, vomit, gastric lavage, feces, urine, etc.), as well as in food products, is used.

The simplest method for determining botulinum toxins is the neutralization reaction of fecal filtrates or blood serum of patients with specific anti-botulinum sera.

For express indication of toxins, IHAR is performed with an antibody diagnosticum (erythrocytes sensitized with antitoxins of the corresponding types).

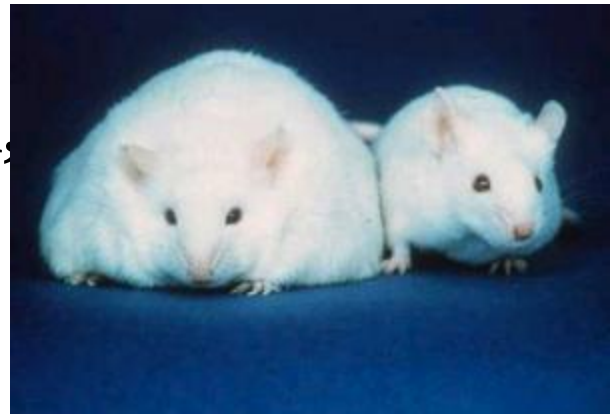
Modern promising methods are based on the indication of antigens in ELISA, or PCR.

Identification of botulism toxins

The classic method for botulism is a biological test on mice.

A batch of 5 animals is selected for the experiment. The first is infected only with the test material, the rest - with the test material using 2 ml of 200 IU antitoxic serum types A, B, C and E.

In the presence of a toxin in the material, the animal that received the antiserum that neutralized the toxin of the corresponding type survives.



Differential Diagnosis

Despite a clearly defined clinical picture, a fairly large number of errors are made due to the fact that the disease is relatively rare, and doctors are not familiar with it enough.

Most often, instead of the diagnosis of "botulism" is diagnosed

food poisoning,

cerebrovascular accident, hypertensive crisis,

encephalitis,

mushroom poisoning,

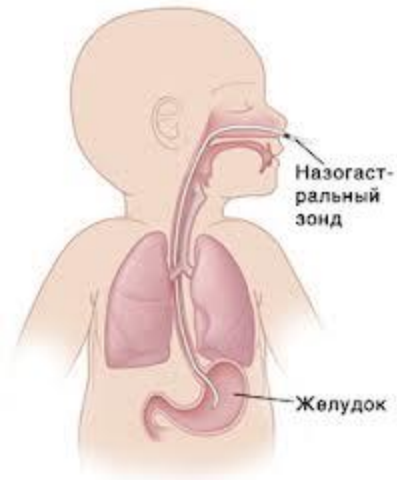
myasthenia.

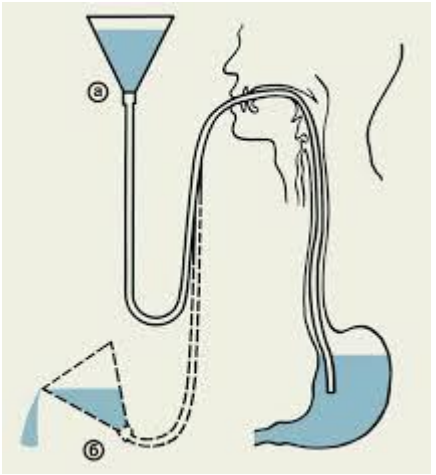
Treatment

Due to the threat to life, hospitalization of patients is necessary in all cases, even if botulism is suspected.

Patients are referred to any hospital where there is equipment for mechanical ventilation. Supportive care for botulism includes monitoring of respiratory function. Respiratory failure due to paralysis may require mechanical ventilation for 2 to 8 weeks, plus intensive medical and nursing care. After this time, paralysis generally improves as new neuromuscular connections are formed.

Therapeutic measures begin with gastric lavage with a thick probe; during the procedure, it is necessary to make sure that the inserted probe is in the stomach, given the fact that in the absence of a pharyngeal reflex, the probe can be inserted into the respiratory tract.





2. **In order to neutralize the toxin circulating in the blood, anti-botulinum antitoxic serum is used.**

In cases where the type of pathogen is unknown, polyvalent serum is administered. One therapeutic dose of it includes 10,000 AU of type A and E serum, as well as 5 type B serum.

In a mild form - on the first day - two doses, the next day one dose, each of the three types of serum A, B, C. In total, 2-3 doses per course of treatment.

In the moderate form - on the first day, 4 doses of serum of each type are administered intramuscularly with an interval of 12 hours, later - according to indications. The course of treatment is 10 doses.

In severe form - 6 doses on the first day, 4-5 doses on the second day. The course of treatment is 12-15 doses. Enter intramuscularly with an interval of 6-8 hours.

Simultaneously with the use of anti-botulinum serum, massive detoxification therapy is carried out, including intravenous drip infusion solutions. It is desirable to use compounds based on polyvinylpyrrolidone (hemodez, rheopolyglucin, etc.), which adsorb freely circulating botulinum toxin well and excrete it through the kidneys with urine.

Due to the fact that the patient cannot swallow, he is fed through a thin probe.
Food should be not only complete, but also necessarily liquid, passed through the probe.
It is undesirable to leave the probe until the next feeding, since with dry mucous membranes, the rapid development of bedsores is possible.

Given the toxic-infectious nature of the disease and the possibility of developing vegetative forms of the pathogen from spores in the gastrointestinal tract, the patient is prescribed antibiotics.

The drug of choice is levomycetin at a daily dose of 25 mg/kg/day in 4 doses, tetracycline at the same dose for a course of 7-8 days.

Increasing the dose of antibiotics is not advisable, as they can cause increased decay of vegetative cells and aggravate the child's condition.

Activities in the epidemic focus

Hospitalization of the patient is carried out according to clinical indications. It is recommended to discharge patients from the hospital no earlier than 7-10 days after clinical recovery.

If cases of the disease are detected, suspicious products are subject to seizure and laboratory examination, and the persons who used them are subject to medical observation for 10-12 days. It is advisable to give them intramuscular anti-botulinum serum containing 2000 IU to toxins A, B and E, as well as the appointment of enterosorbents.

Active immunization has not found wide application.