



**MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE**

DISTANCE LEARNING CENTRE

**DEPARTMENT OF INFECTIOUS DISEASES, EPIDEMIOLOGY,
PARASITOLOGY AND TROPICAL MEDICINE**

**PRACTICAL EXERCISE № 6 –
PRELIMINARY EXAMINATION. BOTULISM.
THESIS**

**FOR E- LEARNING IN INFECTIOUS DISEASES
ENGLISH MEDIUM COURSE OF TRAINING**

SPECIALTY OF MEDICINE

ACADEMIC DEGREE: MASTER

PROFESSIONAL QUALIFICATION: DOCTOR OF MEDICINE

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PRACTICAL EXERCISES – THESES

PLEVEN, 2020

I. Aim of the practical exercise – after completed exercise, the students must be able to take informative history and physical examination of patients with botulism, to group symptoms in syndromes, to prepare plan for diagnosis (and differential diagnosis), to be familiar with major principles of etiological and supportive treatment of botulism.

II. Tasks for achievement of mentioned above aim:

1. Preliminary examination about gastrointestinal and CNS infectious diseases.
2. Repetition of microbiological characteristics of genus *Clostridium* with emphasizing on specific features of *Clostridium botulinum*.
3. Discussion on specific features of history in botulism.
4. Importance of epidemiological part of history.
5. Information about past history and comorbidity.
6. Discussion on physical examination from medical record of a patient with botulism.
7. Discussion about syndromes in botulism and their diagnostic value.
8. Discussion about diagnosis and differential diagnosis of botulism.
9. Discussion about management of patient with botulism emphasizing on etiologic and supportive treatment.

III. Theoretical part of the exercise:

INTRODUCTION

The genus *Clostridium* includes over 60 species. The most common pathogens are *C. perfringens*, *C. difficile*, *C. botulinum*, and *C. tetani*. Clostridia are Gram-positive rods, spore forming, motile (except *C. perfringens*), obligate anaerobes.

Botulism is an acute life-threatening infectious disease with specific paralysis caused by exotoxin, produced from *Clostridium botulinum*.

ETIOLOGY

Causative agent is *Clostridium* – **Gram-positive** peritrichial rod, spore forming, and anaerobe. It is not resistant in the environmental. Eight serotypes *C. botulinum* exist but pathogenic for human are serotypes A, B and E, seldom F and G. *C. botulinum* produces heat labile exotoxin – the most potent biological poison. The exotoxin contains neurotoxin and hemagglutinin. The neurotoxin has double stranded structure – the one strain causes damages, but other is responsible for binding to the receptors and penetration into the cells.

EPIDEMIOLOGY

Major reservoir are heat blood animals, especially livestock, cattle, horses, swine etc. Less common sources of infection are fishes and shellfish. The animals eat spores with food, and spores in the stomach grow to vegetative forms that shed by animal feces transforms to spores that contaminate the soil, grass, vegetables and fruits. The spores are too resistant in the environmental.

Human infects by consumption of spores-contaminated foods. Other rare modes are after contamination of wounds (**wound botulism**), after consumption of contaminated honey (**infant botulism**), or inhalation of aerosol (**as biological weapon**).

DETERMINANTS OF PATHOGENICITY OF *C. botulinum*

Eight types of *C. botulinum* are distinguished (A – G).

- Types A, B, and E account for nearly all human cases;
- Types F and G are rare.
- Types C and D are chiefly responsible for botulism in domestic and wild fowl. Toxin production by types C and D depends on the presence of specific prophages.
- Type E is nearly always associated with fish.

Spores of *C. botulinum* are more resistant to heating than those of other pathogenic clostridia. They can survive up to 2 hours of boiling (100°C), but are killed rapidly at autoclave temperatures (120°C).

The toxin produced by *C. botulinum* is generically designated as botulin; however, the various strains of *C. botulinum* actually produce eight toxins (A, B, C_a, C_b, D, E, F, and G).

These toxins are structurally homologous – an active (A) region and binding (B) region can be defined in all of them.

Generally, each of strains produces only one toxin. Human pathogenic strains most frequently produce toxins A, B, and E.

Toxin A through F are neurotoxins that interfere with neurotransmission at the peripheral cholinergic synapses by preventing the release of acetylcholine (Ach), causing flaccid paralysis.

Toxin G is the only one with which no disease is associated.

Although the toxins are considered exotoxins, they are only released when the bacterium undergoes autolysis. Some require partial digestion by proteolytic enzymes to become active. In cultures the toxin first appears as a prototoxin, which is subsequently activated by a trypsin-like enzyme.

CLINICAL MANIFESTATIONS

The incubation time is 12- to 72 hours following ingestion of contaminated food.

1. History

a. The first symptoms may suggest gastrointestinal tract illness: nausea, vomiting, abdominal bloating, and dryness in the mouth and throat. Some patients have nervous complaints initially, such as dizziness, unsteadiness on standing, diplopia, and blurred vision.

b. Subsequently the difficulties progress to include difficulty with speech or swallowing, weakness or paralysis in the limbs, and generalized weakness and lassitude. The dryness of the mouth may become as severe as to cause pain in the tongue and throat. Eventually there may be difficulty holding up the head, constipation, urinary retention, and progressive difficulty in breathing.

2. Physical examination

Negative findings in botulism are pertinent. Higher mental functions are preserved, although sometimes patients have been drowsy. Sensation is intact. **Fever is unusual.**

Cranial signs reflect involvement of the autonomic and motor nervous system.

- The mouth is dry and the tongue is furrowed.
- Lateral rectus weakness in the eyes produces internal strabismus. Failure of accommodation is common and the pupils may be fixed in mid position or dilated and unresponsive to light. Ptosis, weakness of other extra ocular muscles, and inability to protrude the tongue or to rise to shoulders are other early findings.
- Weakness in the limbs is of the flaccid, lower motor-neuron type and deep tendon reflexes are initially preserved.
- Facial muscles may be spared; gag and corneal reflexes are not lost. Even if not presents initially, weakness of the respiratory muscles can develop later and deterioration can be very rapid.

Hypotension without compensatory tachycardia, intestinal ileus, and urinary retention are evidence of the widespread autonomic paralysis. Patients are described whose symptoms and signs are virtually confined to the autonomic nervous system.

OTHER CLINICAL FORMS

1. Infant botulism is the most common presentation of botulism today. Infants between 3 and 29 weeks of age are most commonly affected.

Feeding of honey containing *Clostridium* spores is believed to be involved. The toxin cannot be detected in serum but it is assumed that the symptoms are caused by the release of toxin into the intestine by proliferating *C. botulinum*. The lack of detection probably results from a combination of factors: low level synthesis or poor intestinal absorption and quick removal from the circulation by high affinity binding at the neuromuscular junctions.

Symptoms. Affected children present with weakness and flaccid paralysis (“floppy infant” syndrome. Electromyography shows muscle conduction patterns typical of botulism.

Some **protective immunity** must develop, because *C. botulinum* can be isolated from feces weeks after recovery from a clinical infection.

2. Wound botulism, which has clinical symptoms identical to those of food poisoning, is caused by toxin released from infected wounds.

DIAGNOSIS

The diagnosis in the first case of an outbreak is often missed because cranial-nerve symptoms and signs may be ignored in what as apparently a gastrointestinal disturbance.

Diagnosis is primarily by clinical presentation. Culture and isolation of *C. botulinum* take a few days. The diagnosis can be confirmed by testing for botulinum toxin in the patient’s serum, and urine or stomach contents. Mice are inoculated intraperitoneally with 0.5 ml of sample, with and without mixing with polyvalent botulinum antitoxin. The mice are then observed for signs of botulism.

Electromyography can be helpful in confirming a diagnosis of botulism. Single or low-frequency stimuli evoke muscle potentials that are reduced in amplitude. In contrast, tetanic or rapid stimuli produce an enhanced response.

Clinical findings are characteristic and the differential diagnosis usually lies between botulism and the descending form of acute inflammatory polyneuropathy or Guillain-Barre syndrome. Other diagnoses that may come to mind include diphtheria, intoxication with atropine and organophosphorus compounds, myasthenia gravis, and cerebrovascular disease involving the brain-stem and producing bulbar palsy; paralytic rabies, tick paralysis, and neurotoxic snake bite.

MANAGEMENT AND TREATMENT

1. Etiologic treatment

a. Penicillin is the antibiotic of choice, but its usefulness is limited (particularly when the disease is caused by the ingestion of preformed toxin).

b. Antitoxin – trivalent (types A, B, and E) – 10 000 U anti-A, 10 000 U anti-E, and 5 000 U anti-B

Administration is i.m. after test for sensitivity. First dose is given immediately, second – 6 hours after the first, and third – 24 hours after the second. The serotherapy must begin no later than in sixth day from the onset of illness.

No aminoglycoside – potentate neuromuscular blockade!

2. Supportive treatment is bynivalin and prostigmin for improving of intestinal motility, aspiration by nasogastric tube, enema, parenteral nutrition; in respiratory failure – intubation, mechanic ventilation; in retention of urine – urinary catheter.

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