# Morbus Botulism: Manifestation in digestive system. Misunderstanding in diagnosis and treatment.

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**1.INTRODUCTION —** Botulism is a rare but potentially life-threatening neuroparalytic syndrome resulting from the action of a neurotoxin elaborated by the bacterium Clostridium botulinum.
The microbiology, pathogenesis, epidemiology, clinical manifestations, diagnosis, and treatment of botulism will be discussed here. Here we will discuss too cases in which this pathology can be misdiagnosed. All our attention is concentrated at food borne botulism. It's the first type of botulism that we have wrote below.

**2.TYPES OF BOTULISM —** The modern syndrome of botulism occurs in five forms, differentiated by the mode of acquisition:

- Foodborne botulism — Ingestion of food contaminated by preformed botulinum toxin.
- Infant botulism — The ingestion of clostridial spores that then colonize the host's gastrointestinal (GI) tract and release toxin produced in vivo.
- Wound botulism — Infection of a wound by Clostridium botulinum with subsequent in vivo production of neurotoxin.
- Adult enteric infectious botulism or adult infectious botulism of unknown source — Similar to infant botulism in that toxin is produced in vivo in the GI tract of an infected adult host.
- Inhalational botulism — The form that would occur if aerosolized toxin was released in an act of bioterrorism.

**3.MICROBIOLOGY —** C. botulinum is a heterogeneous group of gram-positive, rod-shaped, spore-forming, obligate anaerobic bacteria. Eight strains of C. botulinum have been distinguished based upon the antigenic specificities of their toxins. The spores of C. botulinum are heat-resistant, easily surviving 100°C at one atmosphere for five or more hours. However, spores can be destroyed by heating to 120°C for five minutes. When appropriate environmental conditions are present, the spores will germinate and grow into toxin-producing bacilli. These environmental parameters include:

- Restricted oxygen exposure (either an anaerobic or semi-anaerobic environment)
- Low acidity (pH >4.6) water
- A temperature of 25 to 37°C for ideal growth; however, some strains may grow in temperatures as low as 4°C.

**4.PATHOGENESIS —** Eight distinct C. botulinum toxin types have been described: A, B, C1, C2, D, E, F, and G. Of these eight, types A, B, E, and rarely F and G cause human disease. The polypeptide toxin is composed of a light and heavy chain with a combined molecular weight of 150 to 165 kDa. Regardless of the route of entry into the body, the toxin disperses widely via the vascular system and binds to a specific receptor (synaptotagmin II) on the presynaptic sides of peripheral cholinergic synapses at ganglia and neuromuscular junctions. The heavy chain of the toxin binds to the receptors, allowing the light chain to translocate into the nerve cell via receptor mediated-endocytosis.
After gaining entrance to the cell's cytoplasm, the toxin produces an irreversible disruption in stimulation-induced acetylcholine release by that presynaptic nerve terminal. Return of synaptic function requires sprouting of a new presynaptic terminal with subsequent formation of a new synapse, a process that requires approximately six months. Adrenergic synapses are not affected by the toxin, nor does the toxin appear to permeate the blood brain barrier, therefore limiting involvement to the peripheral cholinergic nervous system.

**5.EPIDEMIOLOGY-** Botulism is a rare pathology so we do not have statistics about it. In Europe there are a few of sporadic cases. An average of 110 cases of botulism are reported each year in the United States. Approximately 72 percent of these cases are infant botulism, 25 percent are foodborne botulism, and the remaining 3 percent wound botulism. The highest rates of foodborne botulism in the United States occur in Alaska Natives as a result of ingestion of fish and marine mammals that have been aged.

**6.CLINICAL MANIFESTATIONS —** Botulism is classically described as the acute onset of bilateral cranial neuropathies associated with symmetric descending

weakness. The following symptoms are considered as key features of the botulism syndrome:

- Absence of fever
- Symmetric neurologic deficits
- The patient remains responsive
- Normal or slow heart rate and normal blood pressure
- No sensory deficits with the exception of blurred vision

The onset of symptoms in foodborne botulism usually begins within 12 to 36 hours after ingestion of the preformed toxin, but the incubation period may range from several hours to one week. Prodromal symptoms often include nausea, vomiting, abdominal pain, diarrhea, and dry mouth with sore throat, but these symptoms can occur at any time throughout the course of the illness.

Cranial nerve involvement most commonly marks the onset of symptomatic illness and can include blurred vision, diplopia, nystagmus, ptosis, dysphagia, dysarthria, and facial weakness. Descending muscle weakness usually progresses to the trunk and upper extremities, followed by the lower extremities. Urinary retention and *constipation are common resulting from smooth muscle paralysis*. Respiratory difficulties, requiring intubation and mechanical ventilation are common, caused by diaphragmatic paralysis, upper airway compromise, or both. Despite the evidence of neurologic involvement, cerebrospinal fluid analysis is normal.

**7.DIAGNOSIS —** The most important issue in the diagnosis is the initial consideration of the disease. A careful history and physical examination are essential. Patients presenting with clinical signs and symptoms of foodborne botulism should have serum analysis for toxin. Demonstration of toxin in the blood is diagnostic. This laboratory test is performed by special laboratories. Analysis of stool, vomitus, and suspected food items may also reveal toxin. EMG studies may be useful in these patients as well, but are not generally required.

**8.TREATMENT —** Any patient with clinical signs, symptoms, or history suspicious for botulism should be hospitalized immediately and meticulously monitored for signs of respiratory failure.

Monitoring — Monitoring should include pulse oximetry, spirometry, arterial blood gas measurement, and clinical evaluation of ventilation, perfusion, and upper airway integrity. Intubation should be considered for those patients with inadequate or worsening upper airway competency. Severe adult cases may require prolonged mechanical ventilation. Supportive care in these cases should also include small volume continuous nasogastric feedings.

**Antitoxin**- There are two botulism antitoxin therapies available for use. The equine serum botulism antitoxin and the human derived botulinum immune globulin.

***The treatment in the cases with botulism is done only with the antitoxins which vary in the type of botulism and in the intensive care.***

**Other treatments —** In cases of foodborne botulism, laxatives, enemas may be given, provided no significant ileus is present. Guanidine, a drug that increases acetylcholine release at the neuromuscular junction, and plasmapheresis are experimental therapies that remain unproven in clinical trials.

**9.PREVENTION-** Prevention of foodborne botulism is based on good practice in food preparation particularly preservation and hygiene. Botulism may be prevented by the inactivation of the bacterial spores in heat-sterilized. Commercial heat pasteurization (vacuum packed pasteurized products, hot smoked products) may not be sufficient to kill all spores and therefore the safety of these products must be based on preventing bacterial growth and toxin production. The WHO Five Keys to Safer Food serve as the basis for educational programmes to train food handlers and educate the consumers. The Five Keys are: keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials.

***Introduction***

*In our country, clinical cases diagnosed with food-borne botulism are very rare. This makes this disease difficult to be diagnosed, increasing chances of misdiagnosing. Through this clinical case we want to bring under attention this nosology to increase its awareness. Also in analogy we want to add that after a detailed research we found a case like ours which is treated by our colleges in Canada in 2008 in the University of Toronto and in the Sunnybrook Health Sciences Centre in Toronto. Below you will find both cases.*

***Canadian clinical case***

*A 45-year-old man who was previously healthy presented to the emergency department with acute-onset abdominal distension and mild blurry vision. Despite self-induced vomiting, his abdominal distension worsened. A small-bowel obstruction was diagnosed based on his clinical presentation and the results of radiography.A computed tomography scan of the patient's abdomen confirmed the obstruction, but did not add any further information. Despite nasogastric suctioning for 12 hours, the patient's abdomen continued to distend, bowel sounds became diminished and signs of peritonitis (tenderness) appeared. To avoid bowel perforation, an exploratory laparotomy was performed. No obvious cause of the obstruction was identified. A neurologist was consulted 5 days later to assess the patient's worsening neurologic symptoms, including ptosis, diplopia, dysphagia, aphonia and dry mouth. On examination, the patient's vital signs were normal. Performing the Valsalva manoeuvre did not change his heart rate The patient had bilateral paralysis of cranial nerves 3, 4, 6, 7, 9 and 10. The patient's pupils were initially dilated but they were sluggishly reactive to light. One day later, his pupils were unreactive to light. Neck flexion was weak. A neurophysiological assessment with repetitive nerve stimulation was performed, which showed an electro-incremental response on high-frequency stimulation, which was suggestive of a presynaptic disorder.Botulism was highly suspected based on the clinical presentation and the neurophysiological findings. Serum, stool and gastric contents*

*were sent for testing. A detailed history revealed no exposure to suspicious foods, and he had no sick contacts. Public health was notified immediately. We administered antitoxin based on his clinical presentation and the the progression of his pupillary symptoms. There was no subsequent progression of his symptoms. The patient's bowel sounds returned 6 days after the exploratory laparotomy. The patient received nutrition through a nasogastric tube until his neurologic deficits improved. Speech sounds and other deficits gradually improved over several weeks. Two fecal samples, taken about 2 and 8 weeks after the onset of symptoms, both tested positive for viable C. botulinum type B. The patient received no further therapy because his symptoms were improving. He remained in hospital with supportive care for 1 month until his dysphagia resolved.*

***Our Clinical Case***

*In August 2015, a 23 old patient with F.D. initials, presented in the surgery emergency unit of the regional hospital of Vlora with a 10 days history of abdominal pain, nausea, vomiting, stool arrest and abdominal distention, complaints that were getting worse gradually. The surgeons there decided to have the surgery with the diagnoses of intestinal suboclusion. During laparotomy they did not find any obvious cause to justify the preoperative diagnose. After the surgery the patient is transported to the University Hospital Center "Mother Theresa", in the Intensive Care Unit, as the general clinical situation of the patient was getting worse. During hospitalization, was seen that the patient had signs of diplopia, ophtalmoplegia, dysphagia, kserostomia and bad word articulation. During a careful medical history taking, our patient referred that 2 weeks before he had consumed some canned food (canned fish). During neurological examination were seen signs of bilateral cranial nerve deficits and ophthalmoplegy. The patient remained in the intensive care unit were Botulism disease was suspected and its management started immediately.*

***Discussion***

*As seen above, our clinical case was presenting an atypical clinical presentation for botulism disease, presenting first gastrointestinal signs, what actually made doctors make an inadequate diagnose and naturally a late diagnose and inappropriate treatment at first. In cases of atypical clinical presentation and a vague symptomatology of the disease, with signs of abdominal discomfort and abdominal pain, nausea and vomiting etc., before those of neurologic deficits, increases the risk of misdiagnoses or at least a late diagnosis. In our case, were the gastrointestinal findings similar to those of an intestinal suboclusion that lead doctors to a wrong diagnose and eventually a late diagnosing. It was only when neurological signs got intensified, when doctors attention was directed to the diagnosis of botulism, and immediate measures were taken in its laboratory confirmation and treatment with antitoxin. Our patient got fully recovered from this situation after being treated with the anti-toxin vaccine.*

***As a conclusion, as seen from our case, there is a need to increase the medical awareness towards this disease in all our medical system to prevent and avoid other cases of misdiagnosing or late diagnosing of food-borne botulism. Rapid diagnoses, provision and management with aggressive supportive care are essential and lifesaving.***

## REFERENCES


1. Kerner, J. Neue Beobachtungen uber die in Wurtemburg so haufig vorfallen Vergiftung durch den Genuss gerauchter Wurst. Tubingen, 1820. Quoted in: Damon, SR, Food Infections and Food Intoxications. Williams and Wilkins, Baltimore 1928. p.67.
2. Abrutyn, E. Botulism. In: Principles of Internal Medicine, 14th ed, Fauci, AS, Isselbacher, KJ, Braunwald, E, et al (Eds), McGraw-Hill, New York 1998. p.904.
3. Dowell VR Jr. Botulism and tetanus: selected epidemiologic and microbiologic aspects. Rev Infect Dis 1984; 6 Suppl 1:S202.
4. Bleck, TP. Clostridium botulinum (botulism). In: Principles and Practice of Infectious Diseases, 6th ed. Mandell, GL, Bennett, JE, Dolin, R, (Eds), Churchill Livingstone, Philadelphia, PA 2005, p. 2822.
5. Aureli P, Fenicia L, Pasolini B, et al. Two cases of type E infant botulism caused by neurotoxigenic Clostridium butyricum in Italy. J Infect Dis 1986; 154:207.
6. Jin R, Rummel A, Binz T, Brunger AT. Botulinum neurotoxin B recognizes its protein receptor with high affinity and specificity. Nature 2006; 444:1092.
7. Chai Q, Arndt JW, Dong M, et al. Structural basis of cell surface receptor recognition by botulinum neurotoxin B. Nature 2006; 444:1096.
8. Black JD, Dolly JO. Interaction of 125I-labeled botulinum neurotoxins with nerve terminals. II. Autoradiographic evidence for its uptake into motor nerves by acceptor-mediated endocytosis. J Cell Biol 1986; 103:535.
9. Sugiyama H. Clostridium botulinum neurotoxin. Microbiol Rev 1980; 44:419.
10. Middlebrook, JL. Relative lethality of selected toxins. Figure In: Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning, 2nd ed, Ellenhorn, MJ, Schonwald, S, Ordog, G, et al (Eds), Williams and Wilkins, Baltimore 1997. p.1055.
11. Mcnally, RE, Morrison, MB, Berndt, JE, et al. Effectiveness of medical defense interventions against predicted battlefield levels of botulinum

toxin A. Science Applications International Corp, Joppa, MD 1994.
12. Wannemacher, RW Jr, Dinterman, RE, Thompson, WL, et al. Treatment for removal of biotoxins from drinking water. Fort Detrick, Frederick, MD: US Army Biomedical Research and Development Laboratory. Technical report 9120.
13. Pickett J, Berg B, Chaplin E, Brunstetter-Shafer MA. Syndrome of botulism in infancy: clinical and electrophysiologic study. N Engl J Med 1976; 295:770.
14. Dodds, KL. Worldwide incidence and ecology of infant botulism. In: Clostridium botulinum: Ecology and control in foods, Hauschild, AHW, Dodds, KL (Eds), Marcel Dekker, New York 1993. p108.
15. Werner SB, Passaro D, McGee J, et al. Wound botulism in California, 1951-1998: recent epidemic in heroin injectors. Clin Infect Dis 2000; 31:1018.
16. Chertow DS, Tan ET, Maslanka SE, et al. Botulism in 4 adults following cosmetic injections with an unlicensed, highly concentrated botulinum preparation. JAMA 2006; 296:2476.
17. Passaro DJ, Werner SB, McGee J, et al. Wound botulism associated with black tar heroin among injecting drug users. JAMA 1998; 279:859.
18. Sam AH, Beynon HL. Images in clinical medicine: Wound botulism. N Engl J Med 2010; 363:2444.
19. Yuan J, Inami G, Mohle-Boetani J, Vugia DJ. Recurrent wound botulism among injection drug users in California. Clin Infect Dis 2011; 52:862.
20. Roblot F, Popoff M, Carlier JP, et al. Botulism in patients who inhale cocaine: the first cases in France. Clin Infect Dis 2006; 43:e51.
21. Sobel J, Tucker N, Sulka A, et al. Foodborne botulism in the United States, 1990-2000. Emerg Infect Dis 2004; 10:1606.
22. Townes JM, Cieslak PR, Hatheway CL, et al. An outbreak of type A botulism associated with a commercial cheese sauce. Ann Intern Med 1996; 125:558.
23. Centers for Disease Control and Prevention (CDC). Botulism associated with commercial carrot juice--Georgia and Florida, September 2006. MMWR Morb Mortal Wkly Rep 2006; 55:1098.
24. Sheth AN, Wiersma P, Atrubin D, et al. International outbreak of severe botulism with prolonged toxemia caused by commercial carrot juice. Clin Infect Dis 2008; 47:1245.
25. Zhang S, Wang Y, Qiu S, et al. Multilocus outbreak of foodborne botulism linked to contaminated sausage in Hebei province, China. Clin Infect Dis 2010; 51:322.
26. Centers for Disease Control and Prevention (CDC). Notes from the field: Botulism caused by consumption of commercially produced potato soups stored improperly--Ohio and Georgia, 2011. MMWR Morb Mortal Wkly Rep 2011; 60:890.
27. Fagan RP, McLaughlin JB, Castrodale LJ, et al. Endemic foodborne botulism among Alaska Native persons--Alaska, 1947-2007. Clin Infect Dis 2011; 52:585.
28. Austin JW, Leclair D. Botulism in the North: a disease without borders. Clin Infect Dis 2011; 52:593.
29. Centers for Disease Control and Prevention (CDC). Botulism from home-canned bamboo shoots--Nan Province, Thailand, March 2006. MMWR Morb Mortal Wkly Rep 2006; 55:389.
30. Kongsaengdao S, Samintarapanya K, Rusmeechan S, et al. An outbreak of botulism in Thailand: clinical manifestations and management of severe respiratory failure. Clin Infect Dis 2006; 43:1247.
31. Sobel J. Botulism. Clin Infect Dis 2005; 41:1167.
32. Sobel J, Malavet M, John S. Outbreak of clinically mild botulism type E illness from home-salted fish in patients presenting with predominantly gastrointestinal symptoms. Clin Infect Dis 2007; 45:e14.
33. Varma JK, Katsitadze G, Moiscrafishvili M, et al. Signs and symptoms predictive of death in patients with foodborne botulism--Republic of Georgia, 1980-2002. Clin Infect Dis 2004; 39:357.
34. Hughes JM, Blumenthal JR, Merson MH, et al. Clinical features of types A and B food-borne botulism. Ann Intern Med 1981; 95:442.
35. Mechem CC, Walter FG. Wound botulism. Vet Hum Toxicol 1994; 36:233.
36. O'Suilleabhain P, Low PA, Lennon VA. Autonomic dysfunction in the Lambert-Eaton myasthenic syndrome: serologic and clinical correlates. Neurology 1998; 50:88.
37. Roland EH, Ebelt VJ, Anderson JD, Hill A. Infant botulism: a rare entity in Canada? CMAJ 1986; 135:130.
38. Arnon SS, Schechter R, Maslanka SE, et al. Human botulism immune globulin for the treatment of infant botulism. N Engl J Med 2006; 354:462.

39. Fagan RP, McLaughlin JB, Middaugh JP. Persistence of botulinum toxin in patients' serum: Alaska, 1959-2007. J Infect Dis 2009; 199:1029.
40. Wheeler C, Inami G, Mohle-Boetani J, Vugia D. Sensitivity of mouse bioassay in clinical wound botulism. Clin Infect Dis 2009; 48:1669.
41. Schreiner MS, Field E, Ruddy R. Infant botulism: a review of 12 years' experience at the Children's Hospital of Philadelphia. Pediatrics 1991; 87:159.
42. Centers for Disease Control and Prevention (CDC). Investigational heptavalent botulinum antitoxin (HBAT) to replace licensed botulinum antitoxin AB and investigational botulinum antitoxin E. MMWR Morb Mortal Wkly Rep 2010; 59:299.
43. United States Centers for Disease Control and Prevention. Botulism in the United States 1899-1996: Handbook for Epidemiologists, Clinicians & Laboratory Workers, 1998. file://www.cdc.gov/ncidod/dbmd/diseaseinfo/files/botulism.pdf (Accessed April 12, 2010).
44. Tacket CO, Shandera WX, Mann JM, et al. Equine antitoxin use and other factors that predict outcome in type A foodborne botulism. Am J Med 1984; 76:794.
45. Sellin LC. Botulism--an update. Mil Med 1984; 149:12.
46. American Academy of Pediatrics. Botulism and infant botulism. In: Red Book: 2009 Report of the Committee on Infectious Diseases, 28th ed, Pickering, LK (Ed), American Academy of Pediatrics, Elk Grove Village, IL 2009. p.259.
47. Santos JI, Swensen P, Glasgow LA. Potentiation of Clostridium botulinum toxin aminoglycoside antibiotics: clinical and laboratory observations. Pediatrics 1981; 68:50.
48. Reddy, P, Bleck, TP. Clostridium botulinum (Botulism). In: Principles and Practice of Infectious Diseases, 7th ed, Mandell, GL, Bennett, JE, Dolin, R (Eds), Churchill Livingstone Elsevier, Philadelphia 2010, p. 3097.
49. Gottlieb SL, Kretsinger K, Tarkhashvili N, et al. Long-term outcomes of 217 botulism cases in the Republic of Georgia. Clin Infect Dis 2007; 45:174 Brook I. Botulism: the challenge of diagnosis and treatment. *Rev Neurol Dis* 2006;3:182-9. [PubMed]
50. Public Health Agency of Canada. Notifiable diseases summary. *Can Commun Dis Rep* 2002;28:50.
51. Public Health Agency of Canada. Notifiable diseases summary. *Can Commun Dis Rep* 2004;30:182. [PubMed]
52. Public Health Agency of Canada. Notifiable diseases summary. *Can Commun Dis Rep* 2005;31:238.
53. Public Health Agency of Canada. Notifiable diseases summary. *Can Commun Dis Rep* 2006;32:200.
54. Cai S, Singh BR, Sharma S. Botulism diagnostics: from clinical symptoms to in vitro assays. *Crit Rev Microbiol*2007;33:109-25. [PubMed]
55. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2565713/ -Shapiro RL, Hatheway C, Swerdlow DL.
56. Botulism in the United States: A clinical and epidemiologic review. Ann Intern Med 1998;129:221-8
57. -Shapiro R, Hatheway C,Becher J, Swerdlow DL. Botulism surveillance and emergency response: a public health strategy for a global challenge. JAMA 1997;278:433-5.
58. -Doyle M, editor. Foodborne bacterial pathogens. New York: Marcel Dekker; 1989. Clostridium botulinum; p. 112-89.
59. -Hatheway CL. Clostridium botulinum and other clostridia that produce botulinum neurotoxin. In: Hauschild AHS, Dodds KL, editors. Clostridium botulinum: ecology and control in foods. New York: Marcel Dekker; 1992. p. 3-20.
60. -Hatheway CL. Clostridium botulinum. In: Bartlett JG, Blacklow NR, editors. Infectious diseases. Orlando: Saunders Company; 1991. p. 1583-6.
61. -Centers for Disease Control and Prevention (CDC). Botulism in the United States, 1899–1996, handbook for epidemiologists, clinicians and laboratory workers. Atlanta, GA*:* CDC*;* 1998.
62. -Chia JK, Clark JB, Ryan CA, Pollack M. Botulism in an adult associated with food-borne intestinal infection with Clostridium botulinum. N Engl J Med
63. -Therre H. Botulism in the European Union. Euro Surveill 1999;4:2–7
64. -McLauchlin J, Grant KA, Little CL. Food-borne botulism in the United Kingdom. J Public Health 2006;28:337–42
65. -Aureli P, Di Cunto M, Maffei A, De Chiara G, Franciosa G, Accorinti L, et al. An outbreak in Italy of botulism associated with a dessert made with

mascarpone cream cheese. *Eur J Epidemiol.* 2000;16(10):913-8.

66. -Delbos V, Abgueguen P, Fanello S, et al. Botulism, a clinical diagnosis. Presse Med 2005;34:449–54
67. -Fagan RP, McLaughlin JB, Castrodale LJ, Gessner BD, Jenkerson SA, Funk EA, et al. Endemic foodborne botulism among Alaska Native persons--Alaska, 1947-2007. *Clin Infect Dis.* 2011;52(5):585-92.
68. -Fenicia L, Franciosa G, Pourshaban M, Aureli P. Intestinal toxemia botulism in two young people, caused by Clostridium butyricum type E. Clin Infect Dis 1999;29:1381-7.
69. -Donadio JA, Gangarosa EJ, Faich GA. Diagnosis and treatment of botulism. J Infect Dis 1971;124:108-12
70. -Hughes JM, Blumenthal JR, Merson MH, Lombard GL, Dowell VR,Gangarosa EJ. *Clinical features of types A and B food-borne botulism. Ann Intern Med 1981;95:442-5.*
71. -Fenicia L, Franciosa G, Pourshaban M,Aureli P. *Intestinal toxemia botulism in two young people, caused by Clostridium butyricum type E. Clin Infect Dis 1999;29:1381-7.*
72. -Cowden J. Food-borne Clostridium botulinum intoxication from mass produced foodstuffs in Europe. *Euro Surveill.* 2011;16(49):20033
73. -hapiro R, Hatheway CL, Swerdlow DL. *Botulism in the United States: a clinical and epidemiologic review. Ann Intern Med 1998:129.*
74. -Sobel J, Maslanka S. Botulism. In: Longo DL, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editor(s). Fauci.. *Harrison's Principles of Internal Medicine.* 18th ed. New York: McGraw Hill; 2012. p. 1200-3.