Few Cases of Clostridium Difficile Infections

Zoltán Pozsonyi

- 27 y.o. female patient, works in the hospital
  - No relevant medical history;
  - 30. Nov - 5. Dec 2004: Clindamycin before tooth extraction
  - 6. Dec: High fever for two days, stool 6 times daily, later continous diarrhea, fever
  - 13. Dec: Stool culture at family doctor: negative.
  - Use of medical charcoal;

- 20. Dec.: persistent complaints, 6 kg of weight loss, Hospitalisation to Dep. of Infectious Diseases., Szt. László Hospital.
- 22. Dec.: C. difficile toxin pos., 3x500 mg metronidazol for ten days.
- Jan, 2005: no complaints, slow weight gain.

- SZ. B. 68 y.o. male
  - Medical history: HT for ten years, lately diagnosed DM, effort angina for 3 weeks.;
  - 14.Nov, 2004.: ACBG (LIMA-LAD and vein graft on RCA and IVP)
  - 21.Nov: Admission to hospital:
  - **Status**: BW: 78 kg, no fever, pp. healing scars, hs was well,
  - **Lab**: We.:36 mm/h Hb: 125 g/l, WBC: 7.4x10'9/l, HbA1c: 7.1 %.
  - Echo: small amount of pericardial and pleural effusion.

- Medication: ACE-I, aspirin, metoprolol, statin, ibuprofen,
- 26.Nov and 27.Nov diarrhea three times/day, once 38 C fever, but emission on 28/Nov.
- Stool send for culture and C. diff.
- Persistent diarrhea for few days.
- 5.Dec: C. diff. toxin positive. (result arrived)
- 3x500 mg metronidazol for 10 days.
- Becomes asymptomatic

- K. A. 84 y.o. female
  - Medical history: ‘96: ischaemic stroke, HT, mild rheumatic MS and regurg., permanent AF.
  - Admission on 04.May,2004., pedal oedema, weakness, weight loss due to difficulty of chewing, NYHA I-II.
  - Status: cachexia, normal lgl-s, lungs: normal, heart: aa, mild systolic murmur, p: 82/min, RR: 140/90. Abdomen: normal. Mild paresis of the right upper extremity.
  - Medication: digoxin, furosemid, ACE-I, potassium, spironolactone, VKA.

- Epikrízis:
  - Rutin tests for malignancy: negative. Echo: enlarged atria, mild MS.
  - Iv diuretics: got better.
  - VKA discontinued and two teeth extraction. Before the operation infective endocarditis profilaxis was given: 300 mg clindamycin, because of penicillin allergy.
  - Emission: 14.Nov. Other day at home: T: 37.5 C. Stool 4-5 times/day. One week later: C. difficile toxin positive test. 10 day long metronidazol therapy.

- SZ. J. 36 y.o. female
- Medical histrory:
  - M. Crohn since 1998.
  - 2001: Relaps of M. Crohn, sepsis, severe anaemia. Th: azathioprine 2x50 mg, Mesalazine (Salofalk) 3x1500mg, budesonide (Entocort) 3x1.
  - Early in 2004: mild fever,abdominal pain, diarrhea (8-10 times a day), anaemia, CRP: 40-60.
  - C. difficile toxin negative
  - Th: TNF-α receptor blocker (adalimumab) s.c.,

- Getting better, CRP normal, weight gain, fever gone
- Sep, 2004: Abdominal pain, weight loss, CRP elevation, diarrhea.
- Dec, 2004 fever, anaemia, weakness. Th: 3x500 mg metronidazol, 2x500 mg ciprofloxacin.
- 27.Dec, 2004: C. difficile toxin pos.
- Hospitalization

- Very high fever, weakness, severe diarrhea.
- Status: pale, weak, painful abdomen, No fistula. P: 110/min, RR: 100/60 mmHg. T: 39.7 C.
- Lab: Hb 90 g/l, fvs: 8.4x10’9/l, thr: 565x10’9/l, iron: 1.9 umol/l, transferrin: 1.5 g/l, sat: 5%, protein: 68g/l, alb: 29 g/l. CRP 207 mg/l, sediment rate.: 80 mm/h. Electrolytes, renal and kidney function: normal. Occult blood test: neg.

- Abdominal US: thick colon
- Colonoscopy: terminal ileum normal, sigma: patchy, hyperaemic, regions with scar formation.
- Th: 4x250 mg p.o. Vancomycin. CRP lower, diarrhea better. Th: Folic acid, iron,
- Emmission after two weeks.

Antibiotics Associated Colitis
C. difficile Induced Colitis
Pseudomembranosus Colitis

- C. difficile: rezistant, anaerob, Gram pozitiv bacterium;
- faeco-oral infections;
- Common in hospitals and social institutes;
- Disease is caused by the toxin;
- Most common antibiotics:
  - clindamicin;
  - amoxicillin, ampicillin;
  - cephalosporins;
  - erythromycin, sulfonamid, tetracyclin, fluoroquinolons;

- Risk factors:
  - Bowel surgery;
  - Intestinal ischaemia;
  - Chemotherapy, bone marrow transplantation;
  - M. Crohn;
  - Childhood, elderly;
  - Long hospitalisations;
  - Severe diseases;
  - Most common cause of nosocomial diarrhea;

- Pathology
  - Odema or inflammation in the mucous membrane of the colon, but may be normal,
  - Ulsers in the mucous membrane; may mimic micro- és macroscopic idiopathic colitis
  - Extrem cases: yellow exsudativ inflammation, „pseudo membranes”
  - No invasion in the deep tissue

Figure 2: A: Normal colonic mucosa. B: Mucosa showing yellow pseudomembrane.

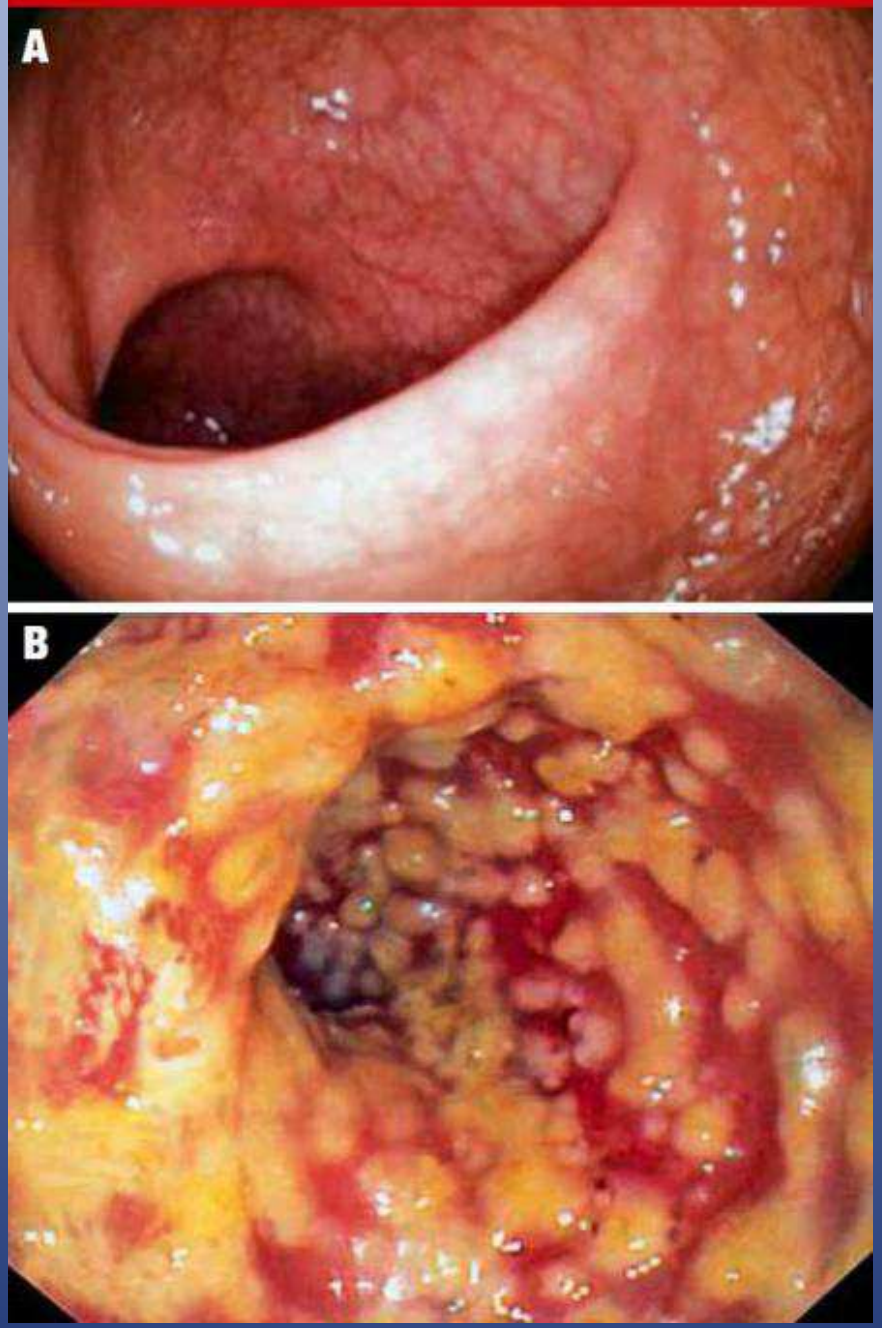
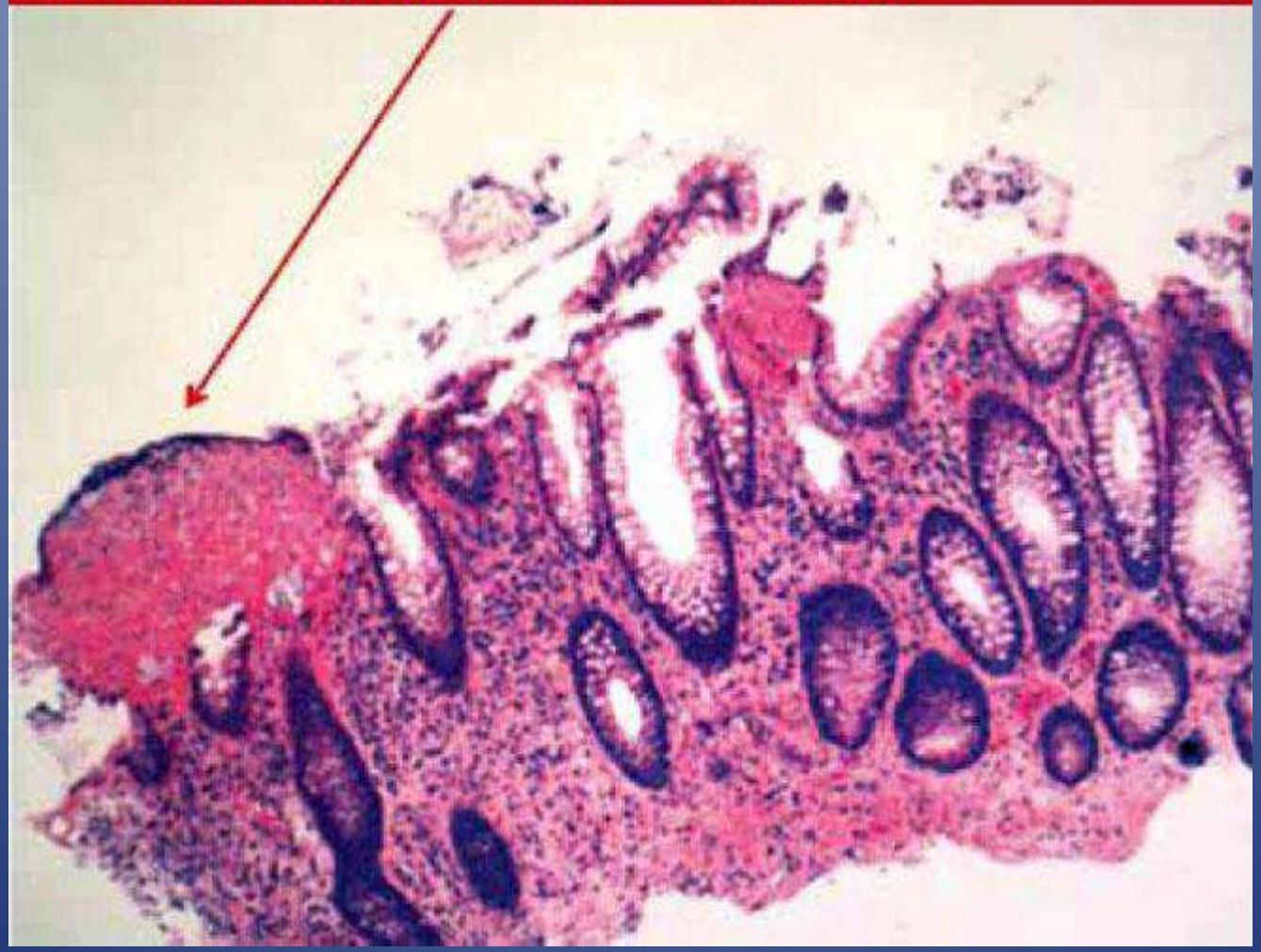
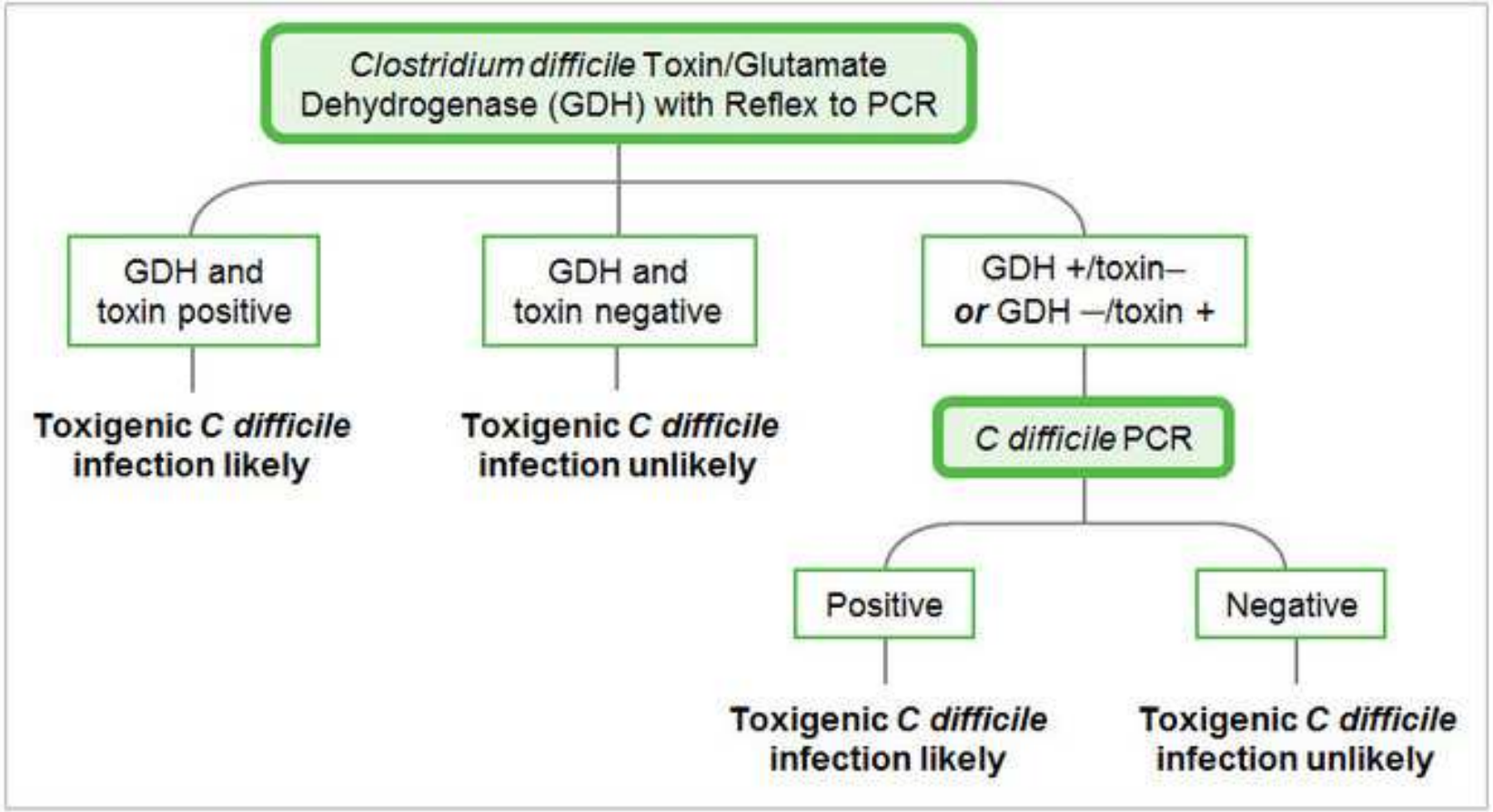


Figure 1: Histology: Pseudomembrane consisting of a dense inflammatory infiltrate on the surface of the colonic mucosa (H&E ×10).

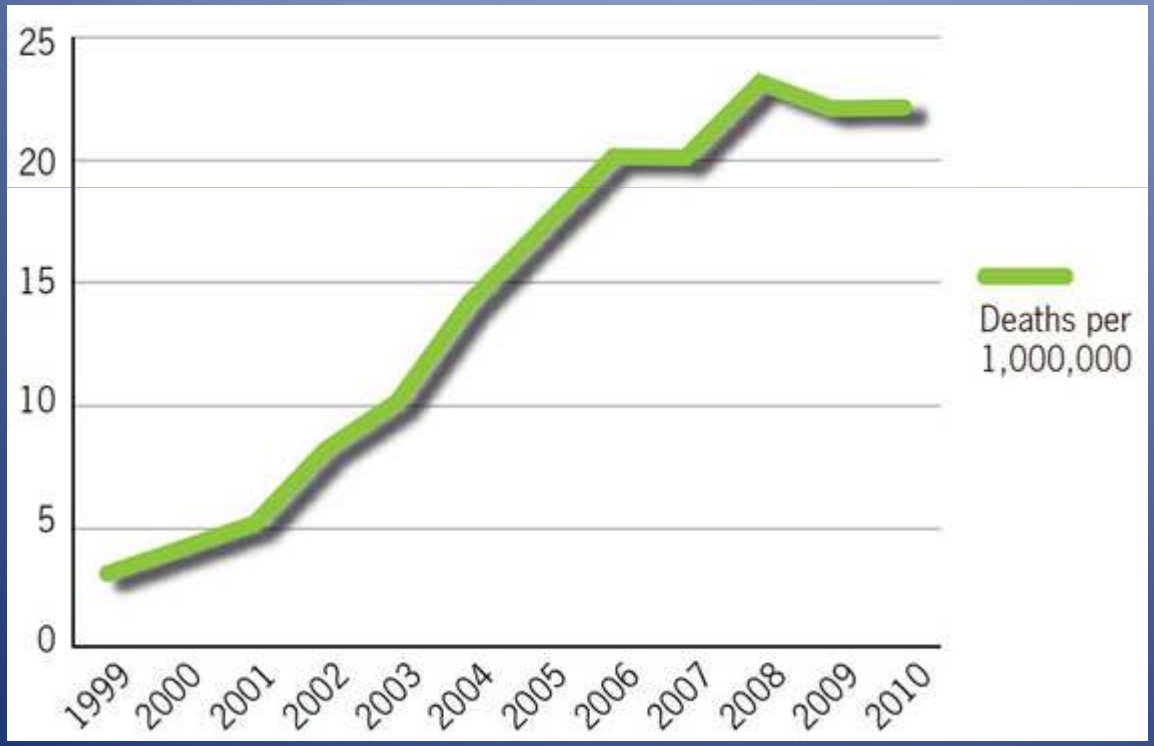


- Symptomes:
  - During or after the antibiotic treatment (1-10 days, max 6 weeks)
  - Mild to very severe
    - Most severe: pain, bloody stool, fever, dehydration, toxic megacolon, perforation, sepsis)
  - Sometimes reactive arthritis.

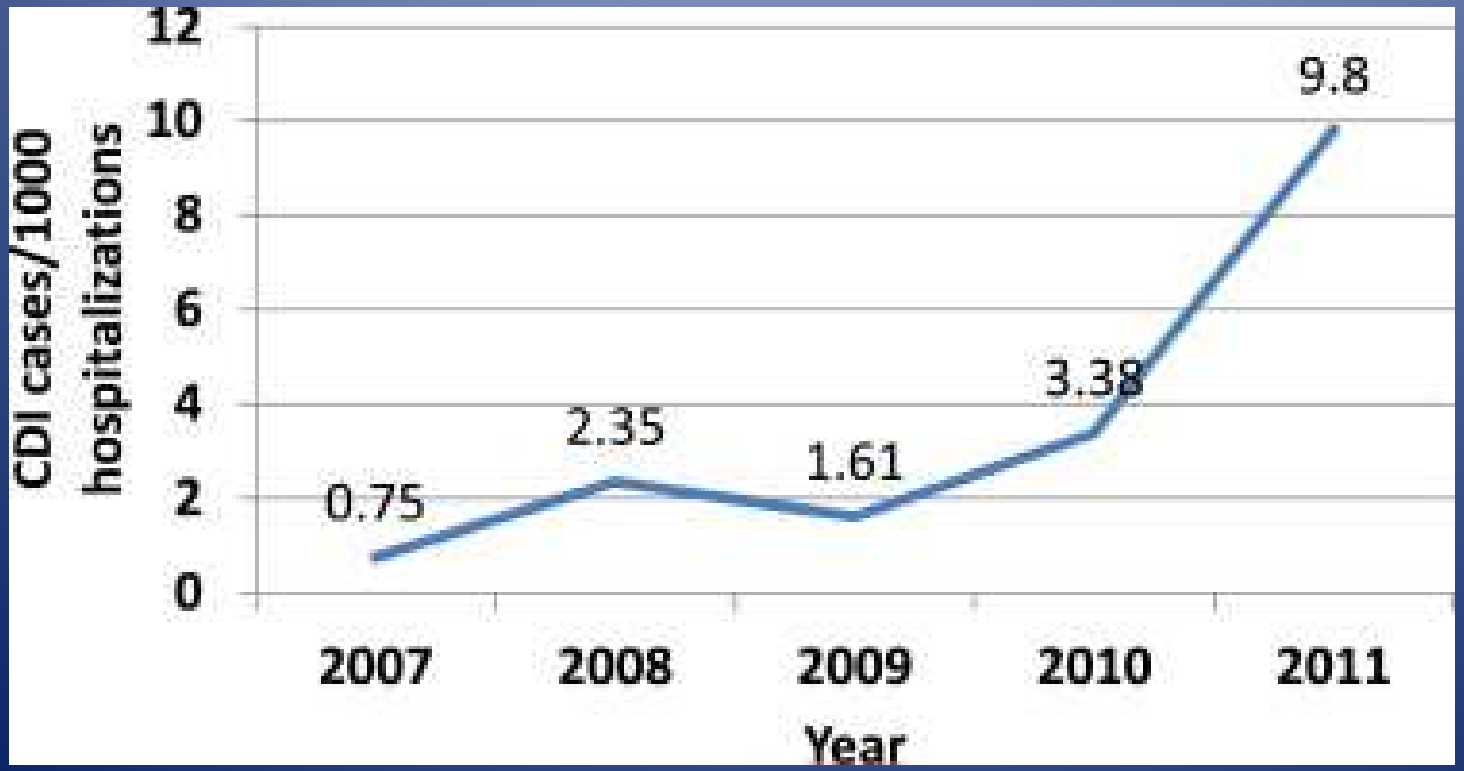
- Diagnosis:
  - Endoscopy (not necessary and may be harmful)
  - Abdominal X-ray (rather for diagnosing the complications: megacolon, perforation)
  - Test for the A or B toxin in the stool (immunoassay),


Clostridium difficile Toxin/Glutamate Dehydrogenase (GDH) with Reflex to PCR
GDH and toxin positive
GDH and toxin negative
GDH +/toxin– *or* GDH –/toxin +
Toxigenic *C difficile* infection likely
Toxigenic *C difficile* infection unlikely
C difficile PCR
Positive
Negative
Toxigenic *C difficile* infection likely
Toxigenic *C difficile* infection unlikely

- C. diff caused mortality, USA



- Incidence of *Clostridium difficile* infection-related hospitalizations per 1000. all-cause hospitalizations, by year from 2007 to 2011.



- Prevention:
  - Lower the use of AB-s;
  - Hand wash;
  - Hygenie
  - Isolation of the pt

- Treatment
  - AB therapy discontinuation;
  - When there are no toxic symptomes, it passes in 10-12 days;
  - Metronidazol 4x250 mg 7-10 days;
  - 4x125 mg p.o. vancomycin (same effectivness)

- Vancomycin rezistance is known;
- Asymptomatic, but toxin positive patients shuld not be treated;
- Severe case: hospital admission, supportive treatment
- i.v. metronidazol is good, but i.v. vancomycin is not effective;
- Enema with vancomycin
- Enema with healthy stool (Stool transplant)
- Healthy stool capsule
- Sometimes life saving colectomy.

Current CDI Guidelines

2010 SHEA/IDSA C. diff Guidelines:

Severity	Clinical picture	Treatment	S/Q
First episode (Mild/Mod)	WBC <15,000 OR sCr < 1.5 x baseline	Metronidazole 500 mg PO TID x 10-14 days	AI
First episode (Severe)	WBC >15,000 OR sCr > 1.5 x baseline	Vancomycin 125 mg PO QID x 10-14 days	BI
First episode (Severe/Complicated)	Hypotension, shock, ileus, megacolon	Vancomycin 500 mg PO/NG QID PLUS Metronidazole 500 mg IV Q8H	CIII
First Recurrence	…	Same as first episode	AII
Second Recurrence	…	Vancomycin in a tapered or pulsed regimen	BIII

S/Q = Strength of recommendation (A-C)/Quality of Evidence (I-III)

Infect Control Hosp Epidemiol. 2010;31(5):431-55.

- Fidaxomycin p.o. (for recurrent infection, only for C. diff. Infection)