

Blood stream infection

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Blood stream infection

- Cause
 - Secondary BSI
 - Source from other organs
 - Catheter related infection
 - CRBSI/CLABSI
 - Different definition/purpose
 - Primary bacteremia
 - Unknown source

Definition

Transient bacteremia → tooth brushing, biopsy



Intermittent bacteremia → abscess

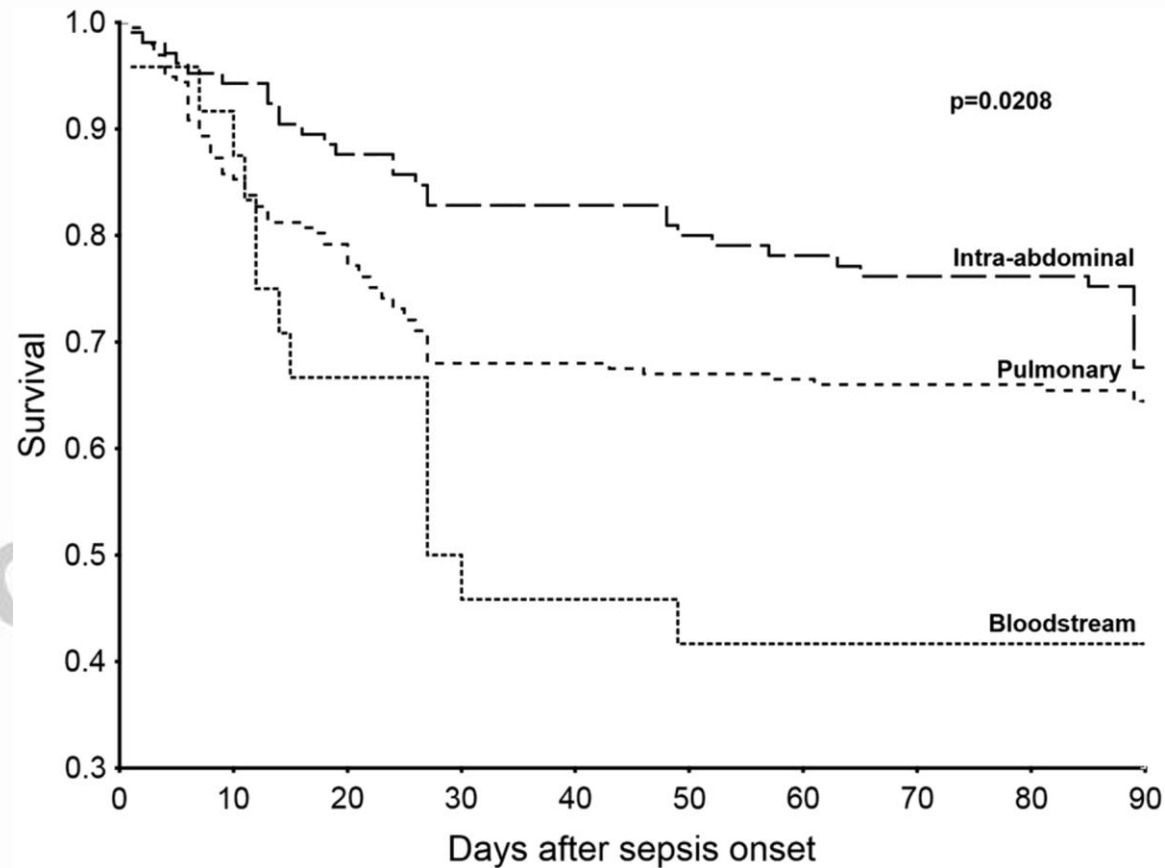


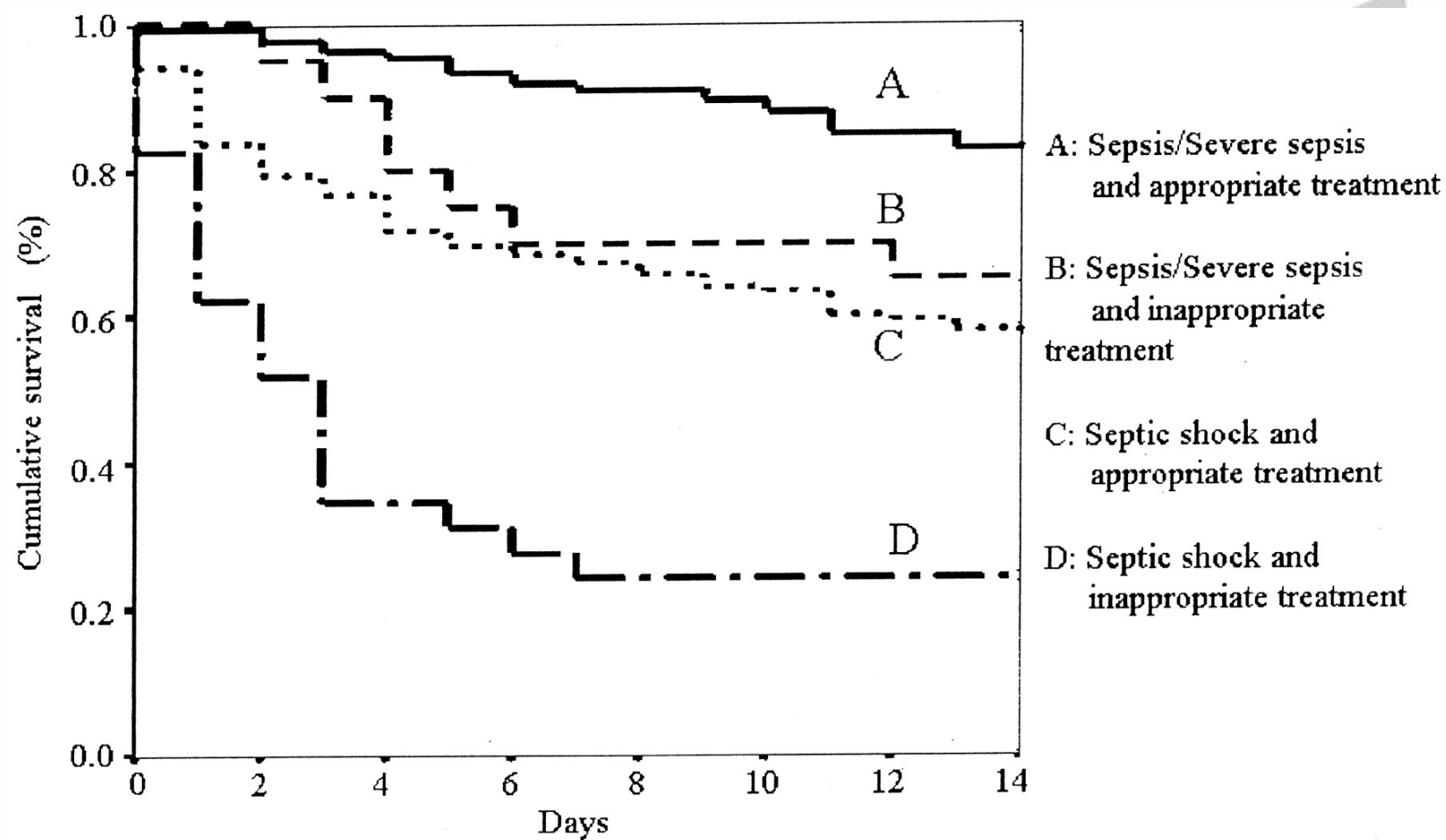
Persistent/sustained bacteremia → intravascular



- Bacteremia : present of microorganisms in blood
 - Transient : associated with procedure
 - Intermittent : associated with close space infection
 - Persistent/sustained : endovascular infection, brucellosis, typhoid fever

Importance for empirical ABT





Why so important?

- Estimated mortality rate for BSI pt in USA is 16-40%
- Appropriate ABT is crucial, reduce mortality rate from 34 to 20%
- Finding the source of infection and identify causative organisms are also important
- Also included other intervention; drainage

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Leibovici L et al, J Int med. 1998;244(5):379-86.

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Blood culture?

- How many specimens? 1,2,3,4 or more
- Usually 2-3 spp are sufficient
- But some pathogens need more than 2

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Number of blood cultures required to detect common microorganisms causing unimicrobial bacteremia and fungemia

Microorganism(s)	Four blood cultures obtained					Three blood cultures obtained			
	No. of BSI episodes	Cumulative % detected by culture no.:				No. of BSI episodes	Cumulative % detected by culture no.:		
		1	2	3	4		1	2	3
<i>S. aureus</i>	100	93	97	100		75	87	93	100
Coagulase-negative staphylococci	66	64	85	100		41	71	98	100
<i>Enterococcus</i> spp.	36	67	80	89	100	47	68	87	100
Streptococci	26	77	85	100		20	85	100	
<i>Escherichia coli</i>	43	72	91	95	100	20	65	90	100
<i>Klebsiella pneumoniae</i>	40	78	90	98	100	25	76	88	100
<i>P. aeruginosa</i>	15	60	85	100		16	62	94	100
<i>C. albicans</i>	20	60	85	95	100	15	60	83	100
<i>Candida glabrata</i>	8	75	88	100		10	80	100	

Source and cause of BSI

- Study in 1990 from USA
 - 843 specimens
 - Primary BSI 44.7%
 - Catheter associated 19.1%
 - Unknown 25.6%
 - Others : GU 17.4%, Respiratory 12.3%, intraabdominal 12.1%, SSS 6.3%
- Study from France in 2001 has similar results

TABLE 2. SOURCES OF BACTEREMIA AND MICROORGANISMS INVOLVED IN 111 PATIENTS WITH ICU-ACQUIRED BACTEREMIA

	Source of Bacteremia			All Episodes (n = 111)
	29% Primary (n = 32)	26% Catheter Related (n = 29)	45% Other Secondary (n = 50)	
Gram-positive cocci	15	12	17	44
<i>S. aureus</i>	4	4	11	20
Coagulase-negative staphylococci	7	7	1	15
Enterococci	4	0	4	8
Streptococci	0	0	1	1
Gram-negative bacilli	10	8	26	44
Enterobacteriaceae	4	5	19	28
Aerobic gram-negative	6	3	7	16
Anaerobes	1	0	2	3
<i>Candida</i>	4	2	2	8
Polymicrobial	2	7	3	12
Total organisms	34	36	53	123

TABLE 6. CASE-CONTROL STUDY (96 PAIRS) OF MORTALITY AND LENGTH OF STAY (LOS) ATTRIBUTABLE TO ICU-ACQUIRED BACTEREMIA, ACCORDING TO ITS SOURCE

	Catheter-related Bacteremia		Primary Bacteremia	
	Cases	Controls	Cases	Controls
Mortality, n (%)	10/26 (38.5)	7/26 (26.9)	14/28 (50)	6/28 (21.4)
Attributable, % [95 CI]	11.5 [−14.5, 37.5]		28.6 [5.6, 51.6]	
p Value	0.095		0.11	
LOS, d				
All pairs, median	32.5	17.5	21.5	20
Surviving pairs, [IQR]	33 [21–58]	19 [11–40]	29 [24–50]	21 [11–32]
p Value	0.23		0.016	
	Secondary Bacteremia		All Bacteremias	
	Cases	Controls	Cases	Controls
Mortality, n (%)	26/42 (61.9)	3/42 (7.1)	50/96 (52.1)	16/96 (16.7)
Attributable, % [95 CI]	54.8 [35.9, 73.6]		35.4 [23, 48]	
p Value	0.006		0.0002	
LOS, d				
All pairs, median	24	21	24.5	19
Surviving pairs, [IQR]	29 [24–54]	22 [13–52]	31 [23.5–56]	21.5 [13–36]
p Value	0.13		0.01	

Nosocomial vs Community BSI

Source of infection ^a	No. (%) of cases	
	Nosocomial BSI (<i>n</i> = 216)	Community-onset BSI (<i>n</i> = 165)
Catheter	57 (26)	43 (26)
Genitourinary tract	31 (14)	32 (19)
Gastrointestinal or biliary tract	27 (13)	18 (11)
Respiratory tract	20 (9)	12 (7)
SSTI	9 (4)	15 (9)

Clue from identify microorganisms

Species	Implications and/or underlying infectious disease
<i>Staphylococcus aureus</i>	IE and vertebral osteomyelitis
<i>Staphylococcus epidermidis</i>	Device-related BSI and IE
<i>Streptococcus anginosus</i>	Abscess (brain, lung, liver, or gastrointestinal)
<i>Streptococcus sanguinis</i>	IE
<i>Streptococcus bovis</i>	IE
<i>Enterococcus faecalis</i>	IE, urinary tract infection, and intra-abdominal source
<i>Clostridium septicum</i>	Fatal sepsis in immunocompromised patients
<i>Burkholderia pseudomallei</i>	Melioidosis
<i>Salmonella enteritidis</i>	Gastrointestinal tract infection and extraintestinal focus of infection, such as osteomyelitis, abscess, or mycotic aneurysm
<i>Fusobacterium necrophorum</i>	Lemierre syndrome (often fatal)

Examples of syndromes associated with less common bacteremia and fungemia

Microorganism(s)	Associations ^a
<i>Streptococcus bovis</i> Group G streptococci <i>Corynebacterium</i> JK	Carcinoma or villous adenoma of the colon Acute endocarditis; malignancy or alcoholism Central vascular access line infections in granulocytopenic cancer patients
<i>Erysipelothrix rhusiopathiae</i> <i>Haemophilus parainfluenzae</i> , <i>H. aphrophilus</i> , <i>Cardiobacterium hominis</i> , and <i>Actinobacillus actinomycetemcomitans</i>	Aortic valve endocarditis in males with history of exposure to animals Endocarditis with embolic occlusion of major arteries
<i>Providencia stuartii</i> <i>Citrobacter freundii</i> <i>Pseudomonas cepacia</i> <i>Aeromonas hydrophila</i> <i>Pasteurella multocida</i> <i>Vibrio vulnificus</i> <i>Campylobacter fetus</i>	Urinary tract obstruction or paraplegia in elderly men Disease of the gallbladder or small intestines Contaminated fluids or equipment; nosocomial outbreaks Exposure to fresh water; malignancy or cirrhosis Cat bites; malignancy or cirrhosis Ingestion of raw oysters; males with cirrhosis Endocarditis; mycotic aneurysm; lower-extremity thrombophlebitis or cellulitis in immunocompromised patients
DF-2 <i>Clostridium septicum</i> <i>Lactobacillus</i> species <i>Fusobacterium necrophorum</i>	Dog bites; fulminant septicemia in asplenic persons Septicemia with distant myonecrosis; carcinoma of the colon Endocarditis with embolism in patients with underlying heart disease Occult abscess of the oral cavity or upper respiratory tract; suppurative thrombophlebitis of the internal jugular vein
<i>Malassezia furfur</i> <i>Salmonella</i> species, <i>Cryptococcus neoformans</i> , <i>Histoplasma capsulatum</i> , and <i>Mycobacterium avium</i> - <i>M. intracellulare</i>	Seriously ill patients receiving hyperalimentation Persistent fever in patients with AIDS

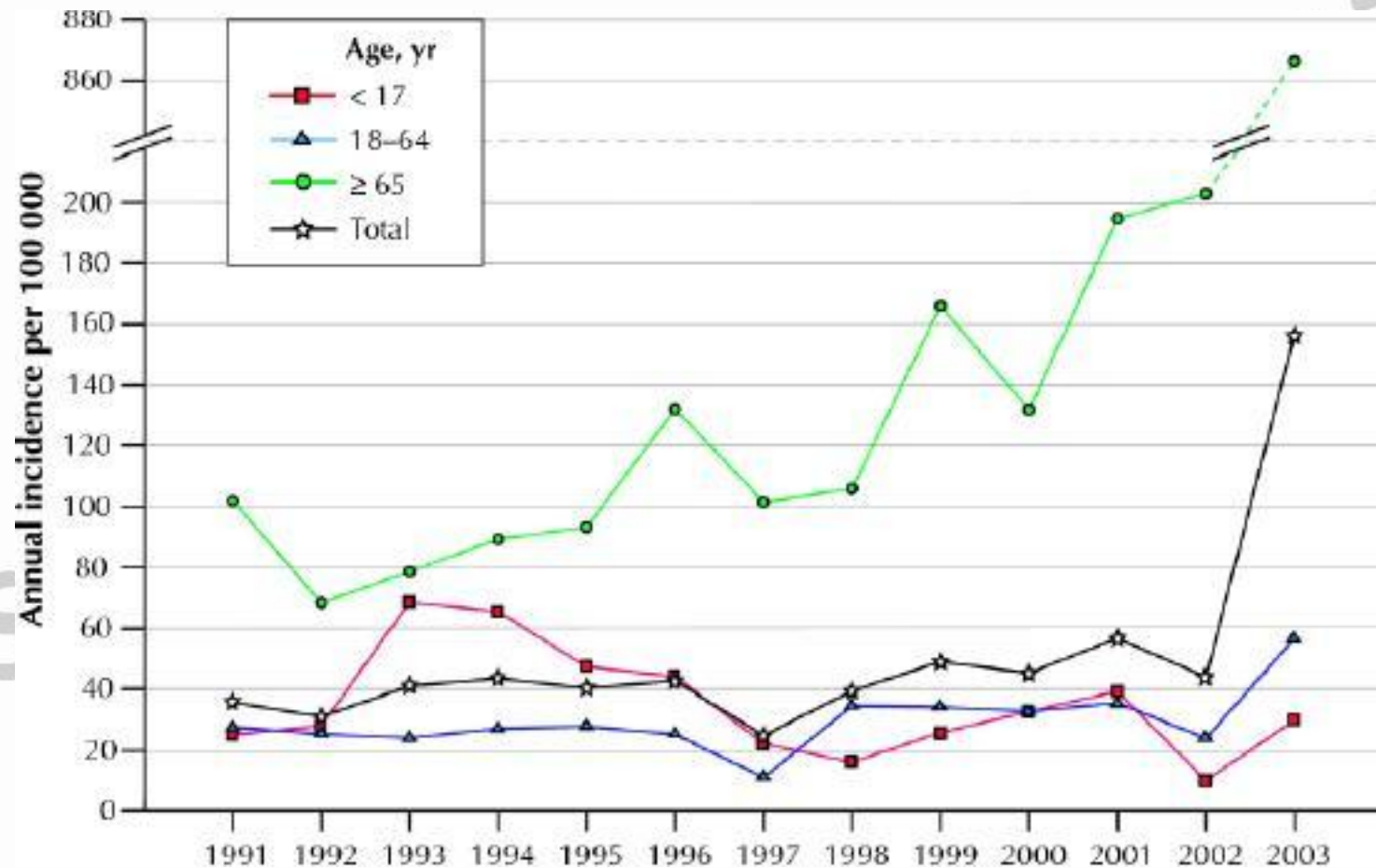
Management

- ABT plus remove infected devices
- Pt with catheter : empiric cover G+ if pt neutropenia consider cover MDR GNB
- Recommended agents : Vancomycin, Daptomycin (MRSA MIC>2 ug/mL), Lenizolid is not recommended
- For GNB : consider in neutropenia, severe sepsis, Hx of colonize organisms
 - Depend on local sensitivity : 4th generation cephalosporin, carbapenem, beta-lactam/beta-lactamase inhibitor with Aminoglycoside
- Consider antifungal (echinocandin or fluconazole) in
 - TPN
 - Prolonged broad spectrum ABT
 - Hematologic malignancy
 - Transplant
 - Candida colonization

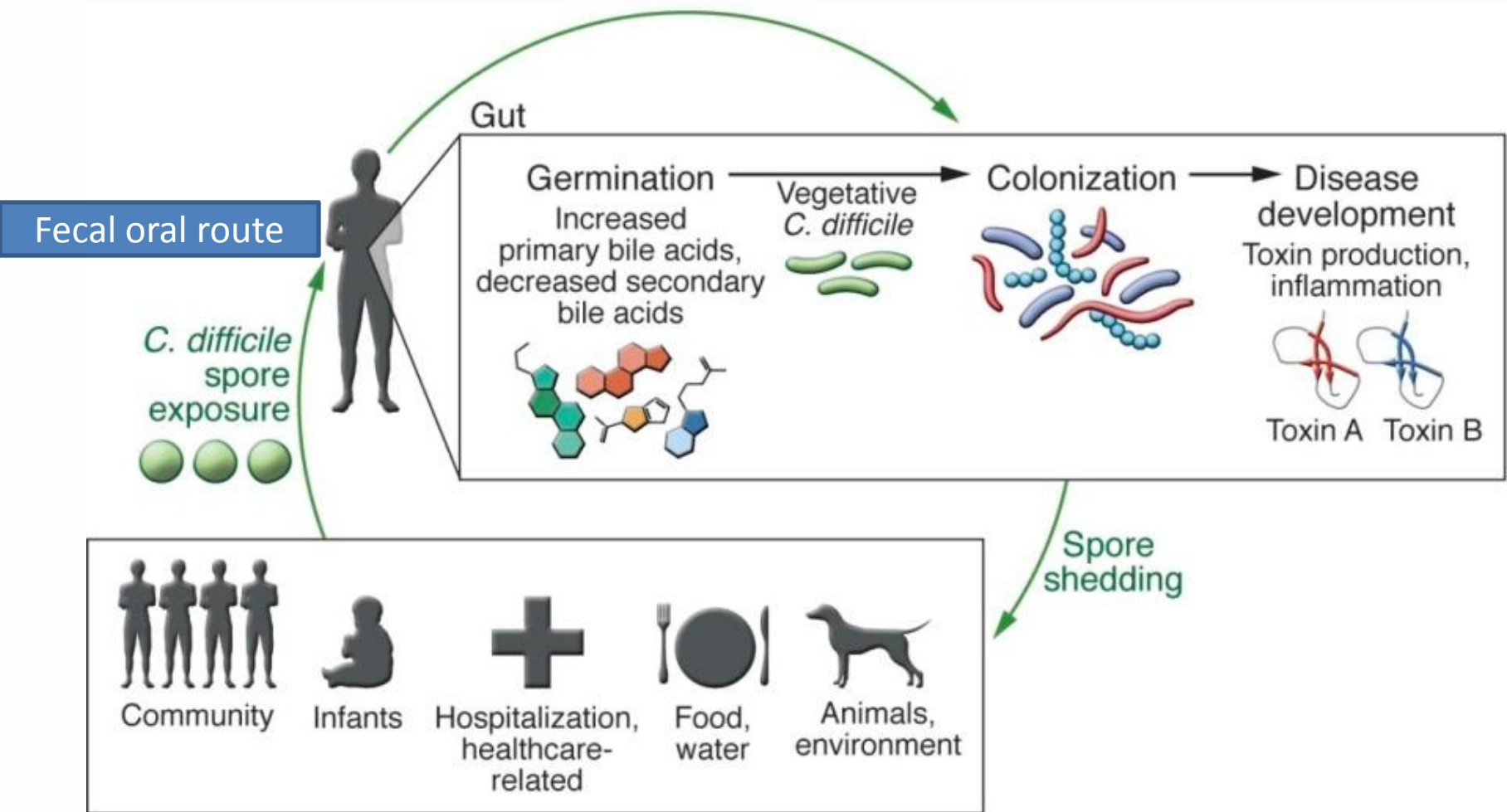
Clostridium difficile infection

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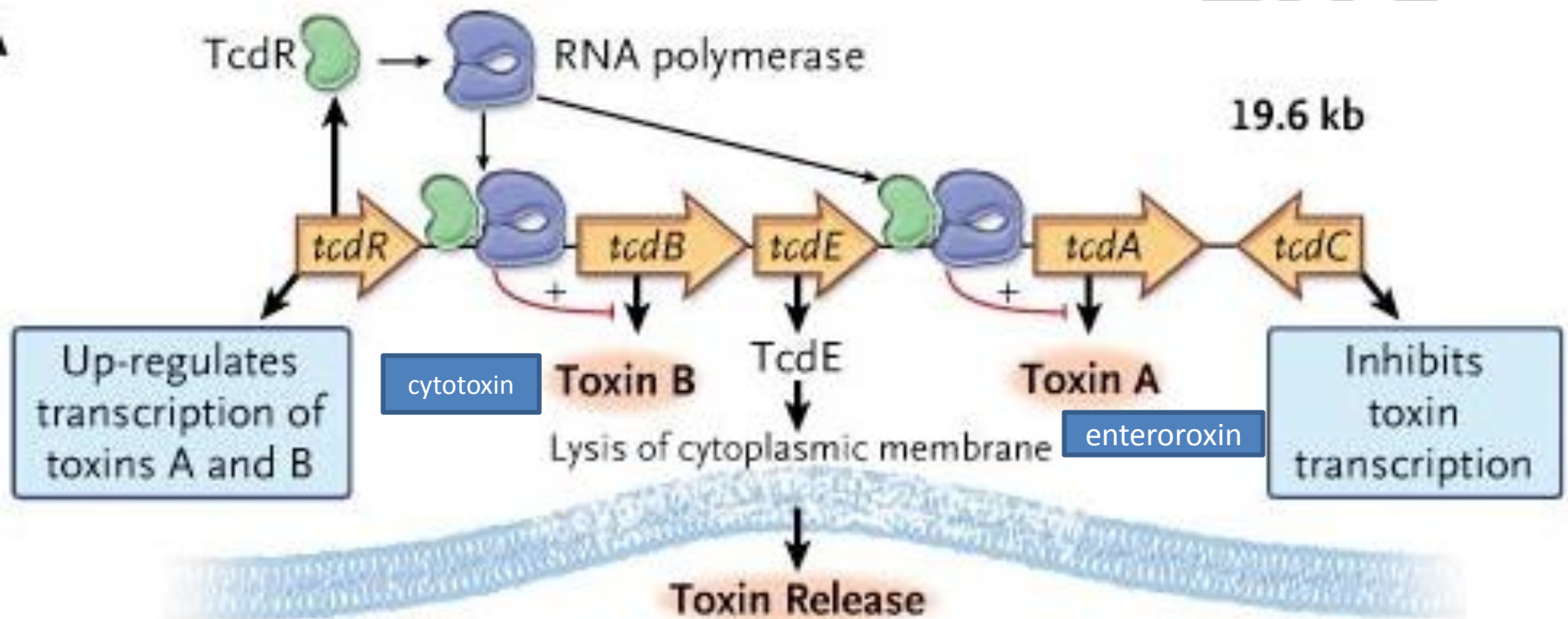
Annual incidence of *Clostridium difficile*-associated diarrhea (CDAD) in Sherbrooke, Que



Pathophysiology



C. difficile gene



Toxin A&B

- Both toxin A&B have C-terminal end (Hydrophilic) → endocytosis → glucosyltransferase to Rho protein → cytoskeleton breakdown → cell lysis

Outbreak of NAP1/BI/027 strain

- Produce binary toxin (CDT) → increase toxicity and quantity of toxin A,B
- Absent of tcdC gene (inhibitory gene)
- Increase resistance to fluoroquinolone (mutation of gyrA)

Risk factors of CDAD

Common

Clindamycin
Ampicillin and amoxicillin
Cephalosporins

Less common

Chloramphenicol
Co-trimoxazole
Erythromycin and other macrolides
Penicillins (other than ampicillin or amoxicillin)
Tetracyclines
Trimethoprim sulfamethoxazole
Quinolones†

Rare or questionable

Bacitracin
Cisplatin
Doxorubicin hydrochloride
Fluorouracil
Methotrexate
Parenteral aminoglycosides
Parenteral metronidazole
Parenteral vancomycin
Rifampin
Sulfonamides
Tacrolimus (FK506)
Teicoplanin

- Most common associated with clindamycin, cephalosporins
- May be associated with some chemotherapy and PPI
- Depend on duration

Clinical manifestation

- Asymptomatic carrier
- Mild diarrhea
- Pseudomembranous colitis
- Extra GI symptoms
 - Reactive polyarticular arthritis, cellulitis, necrotizing fasciitis, osteomyelitis, prosthetic device infection

Complications

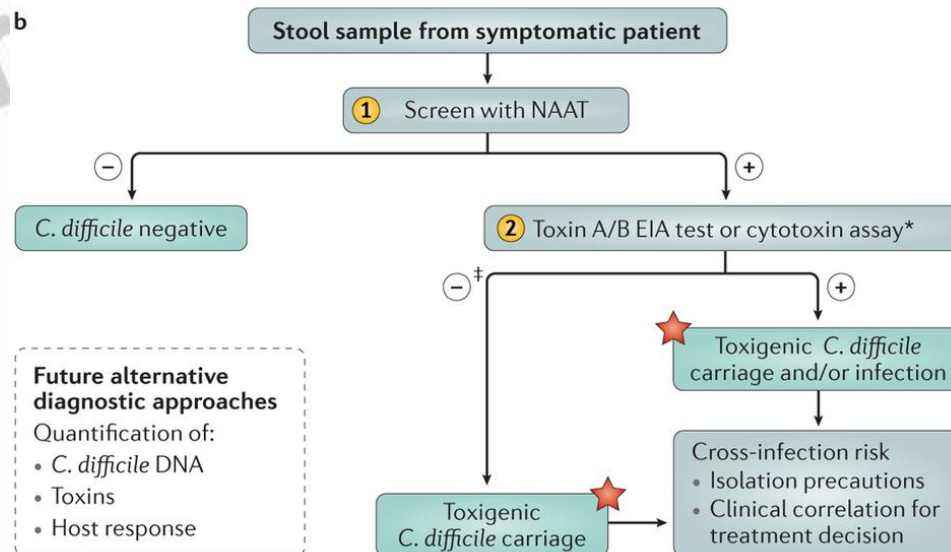
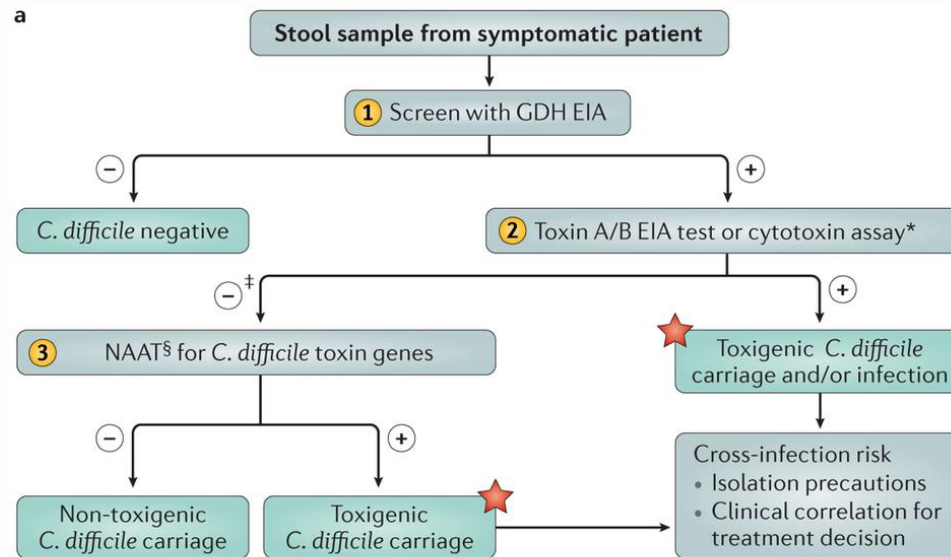
- Fulminant colitis
 - Serious complications may be prolonged ileus, toxic megacolon
 - Severe diarrhea, Diffuse abdominal pain
 - Dehydration, hypotension, oliguria, azotemia
 - High fever, chills, marked leukocytosis
 - May be not diarrhea -Atonic colon
- Toxic megacolon
 - a clinical diagnosis with imaging dilated colon(>7 cm in its greatest diameter)
 - "thumb printing"-submucosal edema
 - May found dilatation of small intestine, Air-fluid levels - intestinal obstruction or ischemia
- Protein losing enteropathy

Diagnosis

- Cannot use only laboratory – cannot differentiate between carrier and patient
- Suitable clinical manifestation : watery diarrhea (>3 times/day) or ileus
- Plus positive toxin or toxigenic gene in stool or pseudomembranous colitis from colonoscopy
- Toxigenic gene
 - Gold standard – toxigenic culture; take time and difficult
 - Glutamate dehydrogenase (GDH)
 - EIA
 - NAATs

Multistep

Multistep algorithm to Dx CDI



Treatment

- Stop unnecessary antibiotics
- Metronidazole 500 mg 3 tid/Vancomycin 125mg qid oral 10-14 days
- Fecal microbial transplant (FMT)
- Probiotics
- Immunoglobulin/monoclonal antibody

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Zar FA et al, Clin Infect Dis Off Publ Infect Dis Soc Am 2007;45(3):302—7.

Kassam Z et al, Am J Gastroenterol 2013;108(4):500—8.

Allen SJ, Infect Dis Clin North Am 2015;29(1):135—44.

Lowy I et al, N Engl J Med 2010;362(3):197—205.