Sexually transmitted infections and blood borne pathogens

MB Champions

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Internal Medicine, Medical Microbiology & Infectious Diseases and Community Health Sciences

Manitoba HIV Program

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Land Acknowledgement

The National Collaborating Centre for Infectious Diseases (NCCID) is hosted at the University of Manitoba, situated on the ancestral lands of the Anishnabeeg, Anishniniwak, Dakota Oyate, Denesuline and Nehethowak/Inninwak Nations. It is also in the heart of the homeland of the Métis Nation.

At NCCID, we strive to honour the lands and their original caretakers in our work. We acknowledge that we are on Treaty One land. We recognize that this and other treaties, have been implemented as part of the process of colonization intended to benefit some while harming others. We are committed to working with our partners towards reconciliation.

Outline

- Epidemiology
- Pathogenesis/pathology
- Microbiology
- Diagnosis
- Focus on *staphylococcus aureus*
- Unusual organisms

Epidemiology- IE general

Prevalence 2-4/100.000

Age > 60 increased frequency

Male to female ratio 2-3/1

Changing epidemiology: a disease of medical progress

- increased device related
- prosthetic material
- less virulent organisms
- commonly hospital associated

Epidemiology

- Most common predisposing valvular lesion for NVE: MVP
- Studies among persons experiencing houslessness are limited
- US study -351 patients - 170 patients (48%) having history of IVDU-associated endocarditis
- From 2014 to 2018, there was a 630% increased incidence of patients with IVDU-associated endocarditis. significant number of patients with IVDU-associated endocarditis were homeless
- A study from US showed an increase from 0.2% of IE to 2.4% between 2000 and 2017

-Khan MZ, Munir MB, Khan MU, Kuprica T, Balla S. Am J Med Sci. 2021 Jul;362(1):39-47.
-Nguyen H et al. Stroke , 2021, Vol.52 (Suppl_1)

ICE-international collaboration

AGENT	CASES (%)
Staphylococcus	
Staphylococcus aureus	31.6
Coagulase-negative staphylococci	10.5
Streptococcus	
Viridans-group streptococci	18.0
Streptococcus bovis	6.5
Other streptococci	5.1
Enterococci	10.6
HACEK group	1.7
Non-HACEK gram-negative bacteria	2.1
Fungi	1.8
Polymicrobial	1.3
Other species	3.1
Culture negative	8.1

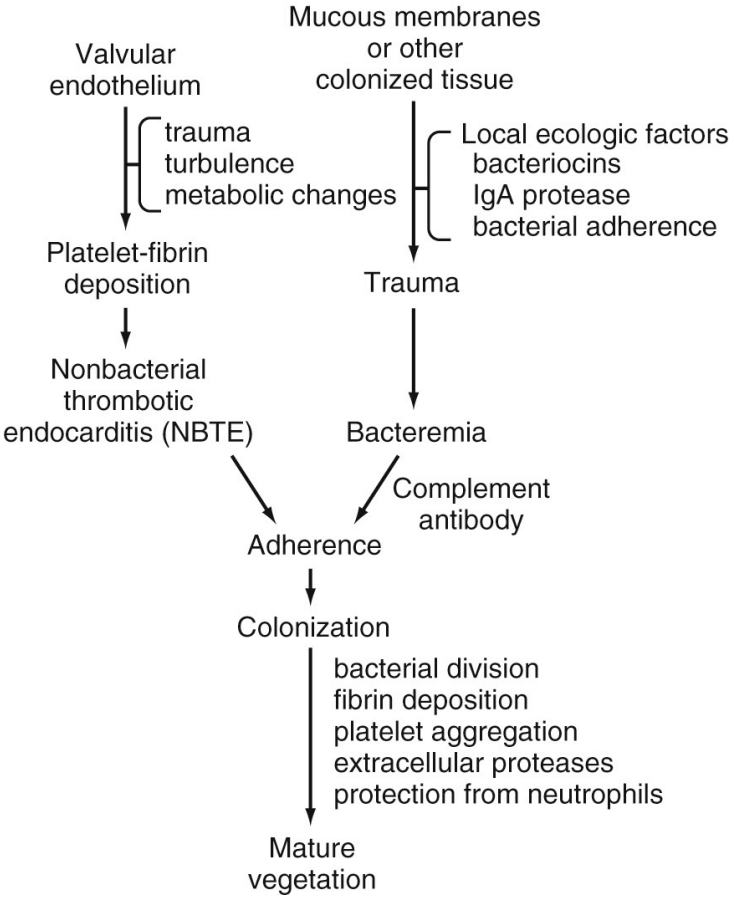
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases

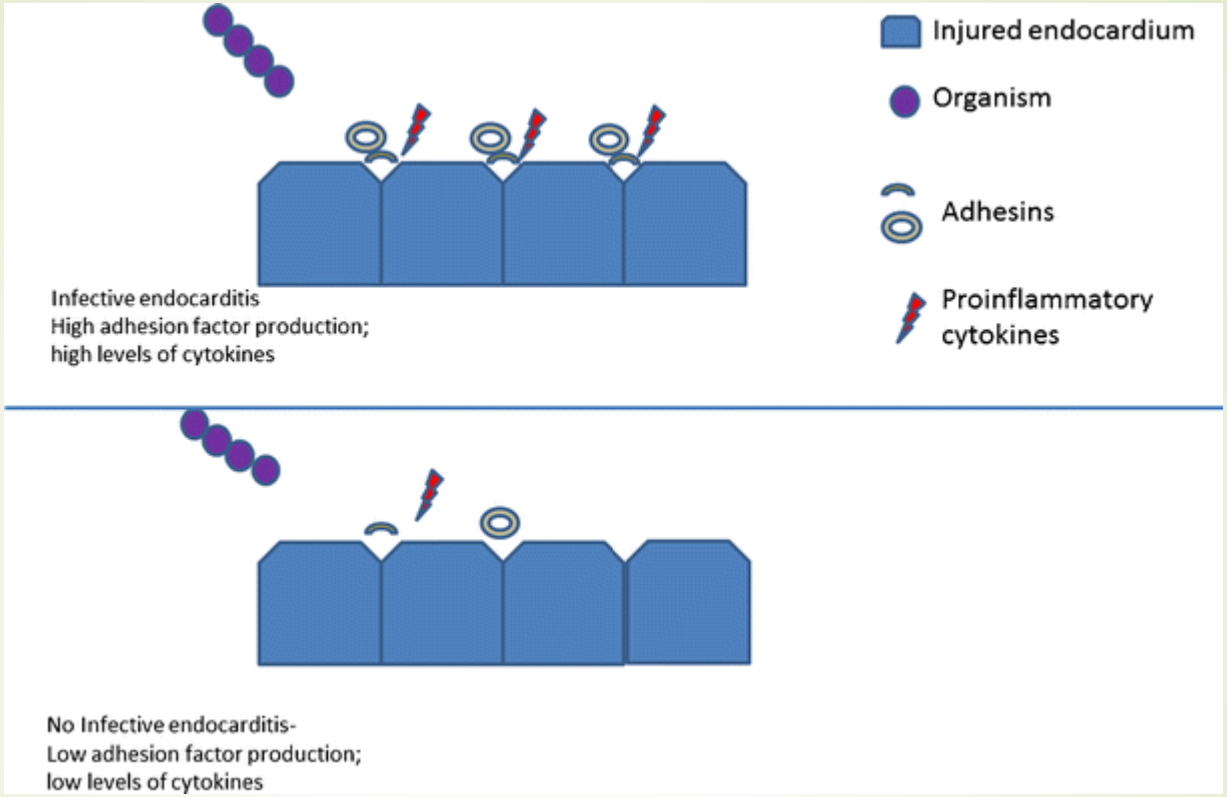
Microbiology of IE

Etiology	Total (N = 1779)	Native Valve IE (n = 1247)		Intracardiac-Device IE (n = 362)	
	n (%)	PWID (n = 158) n (%)	General Population (n = 1089) n (%)	PVIE (n = 307) n (%)	PM/ICD IE (n = 55) n (%)
S. aureus	558 (31.6)	107 (67.7)	295 (27.3)	64 (21.1)	22 (41.5)
Viridans group strep	318 (18.0)	16 (10.1)	235 (21.8)	44 (14.5)	3 (5.7)
S. bovis	114 (6.5)	2 (1.3)	82 (7.6)	18 (5.9)	1 (1.9)
Other strep	59 (3.3)	2 (1.3)	43 (4.0)	10 (3.3)	1 (1.9)
Enterococci	186 (10.5)	9 (5.7)	128 (11.9)	36 (11.9)	3 (5.7)
Culture negative	136 (7.8)	7 (4.4)	79 (7.3)	30 (9.9)	5 (9.4)

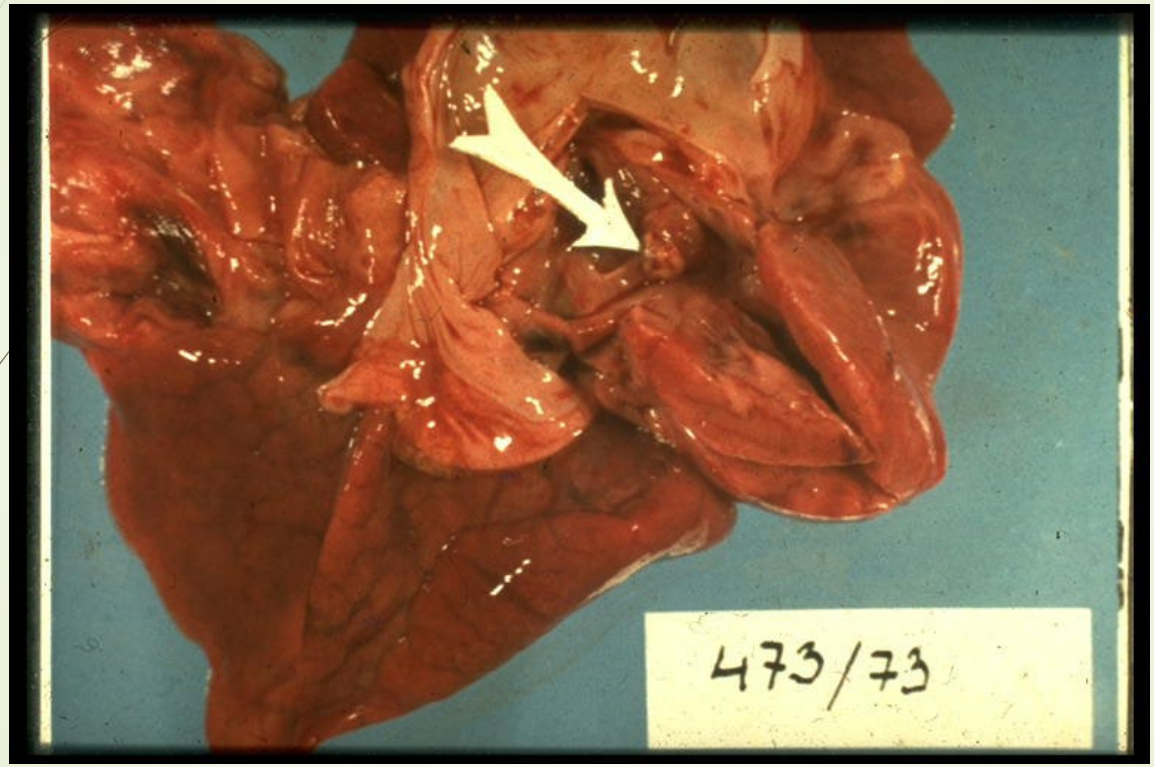
Fowler VG et al. *JAMA* 2005

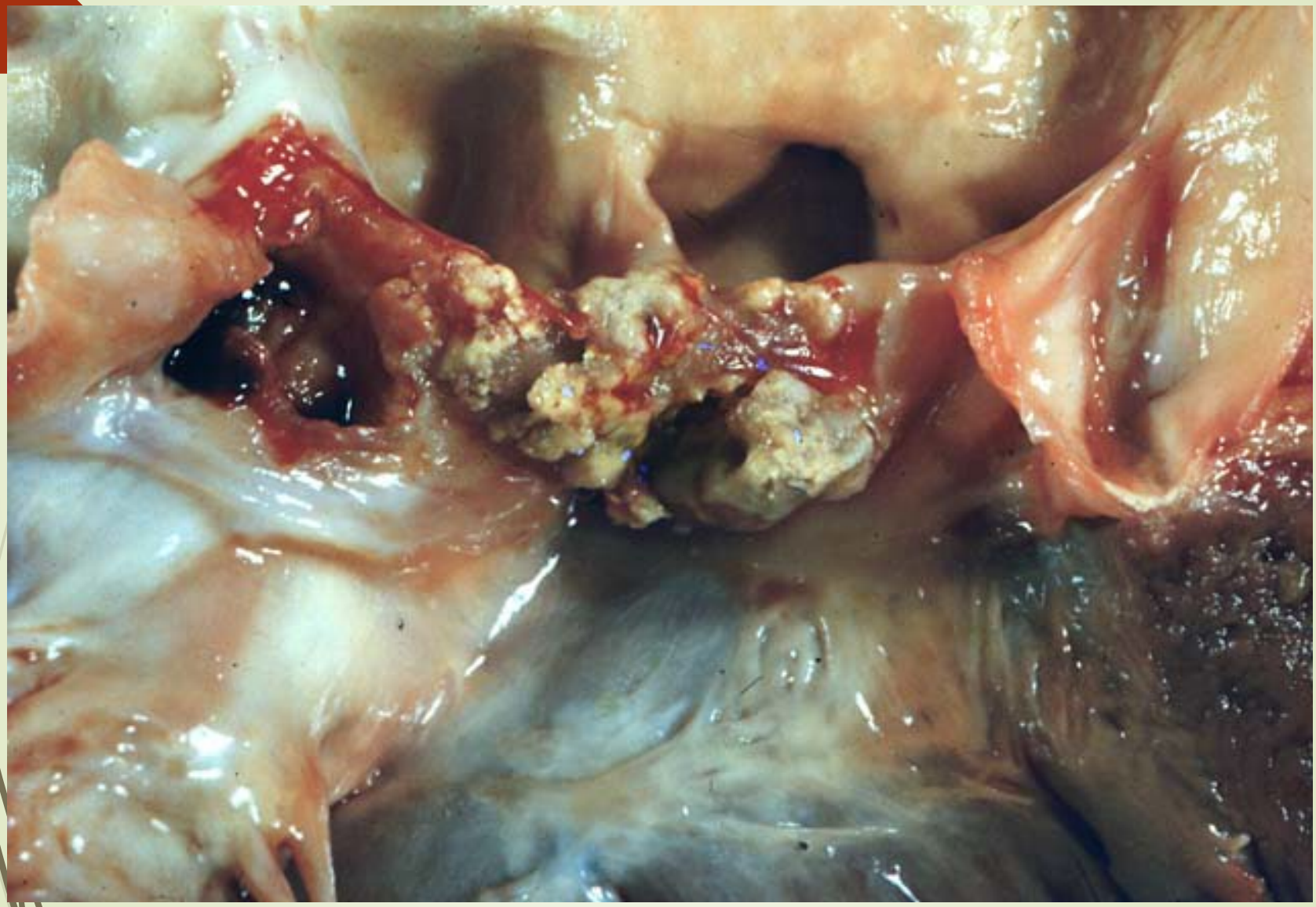
Pathogenesis





Curr Infect Dis Rep. 2013 Aug;15(4):342-6


473/73

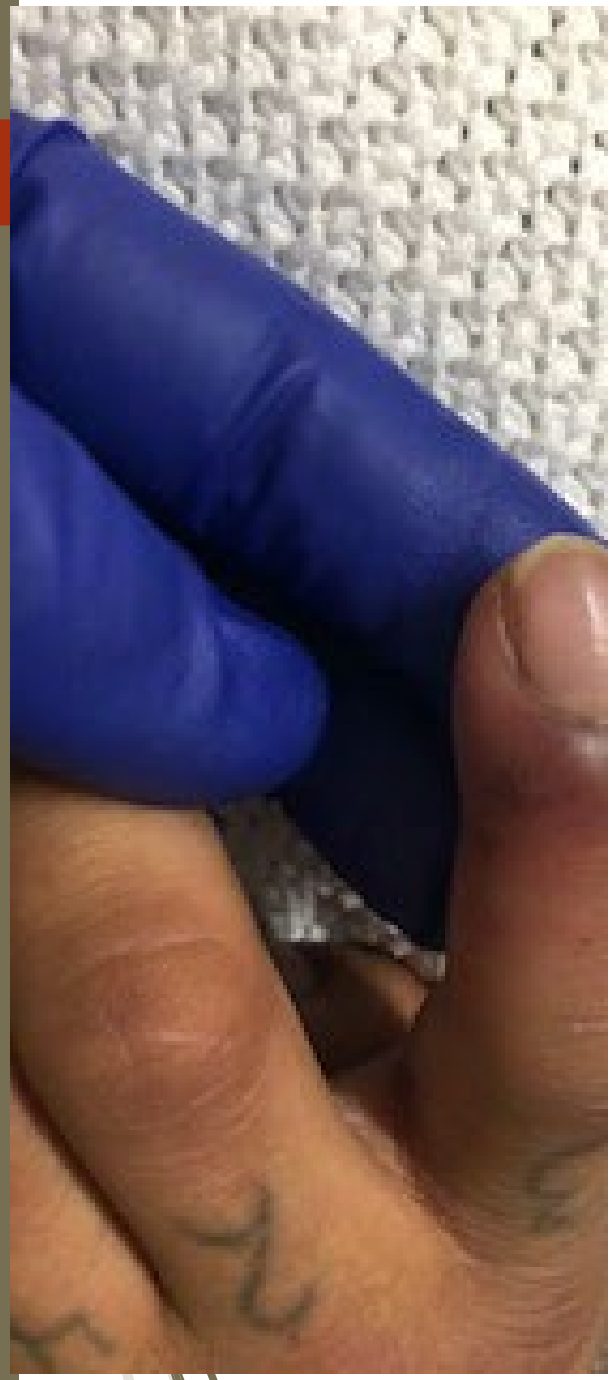


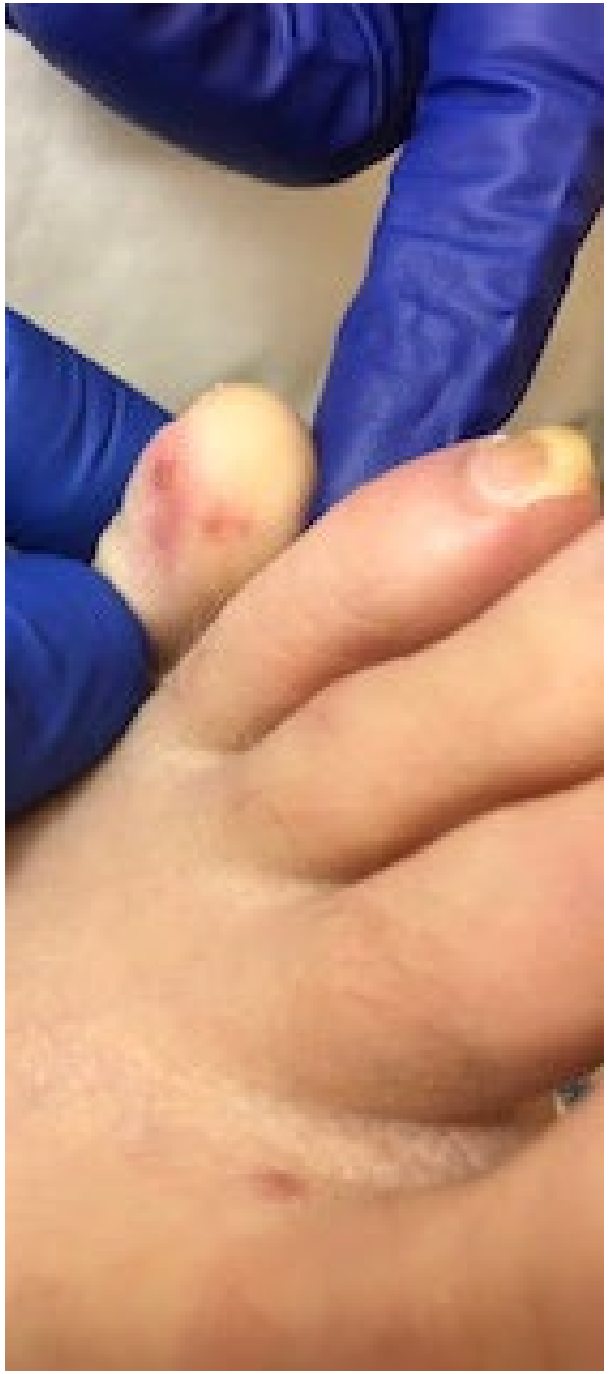
Clinical and Laboratory Findings on Admission in 2781 Patients With Definite Endocarditis

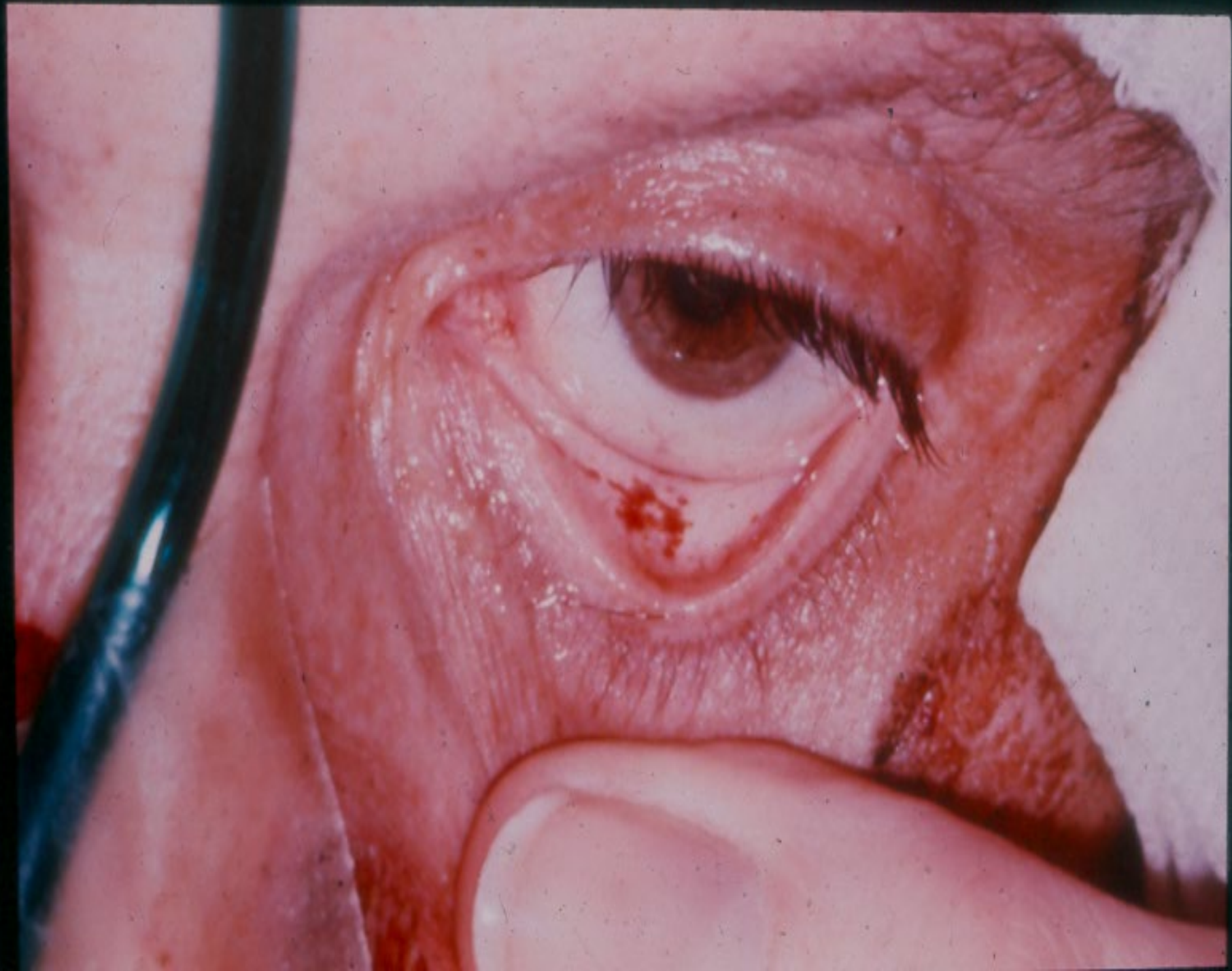
Murdoch et al. *Arch Intern Med*,

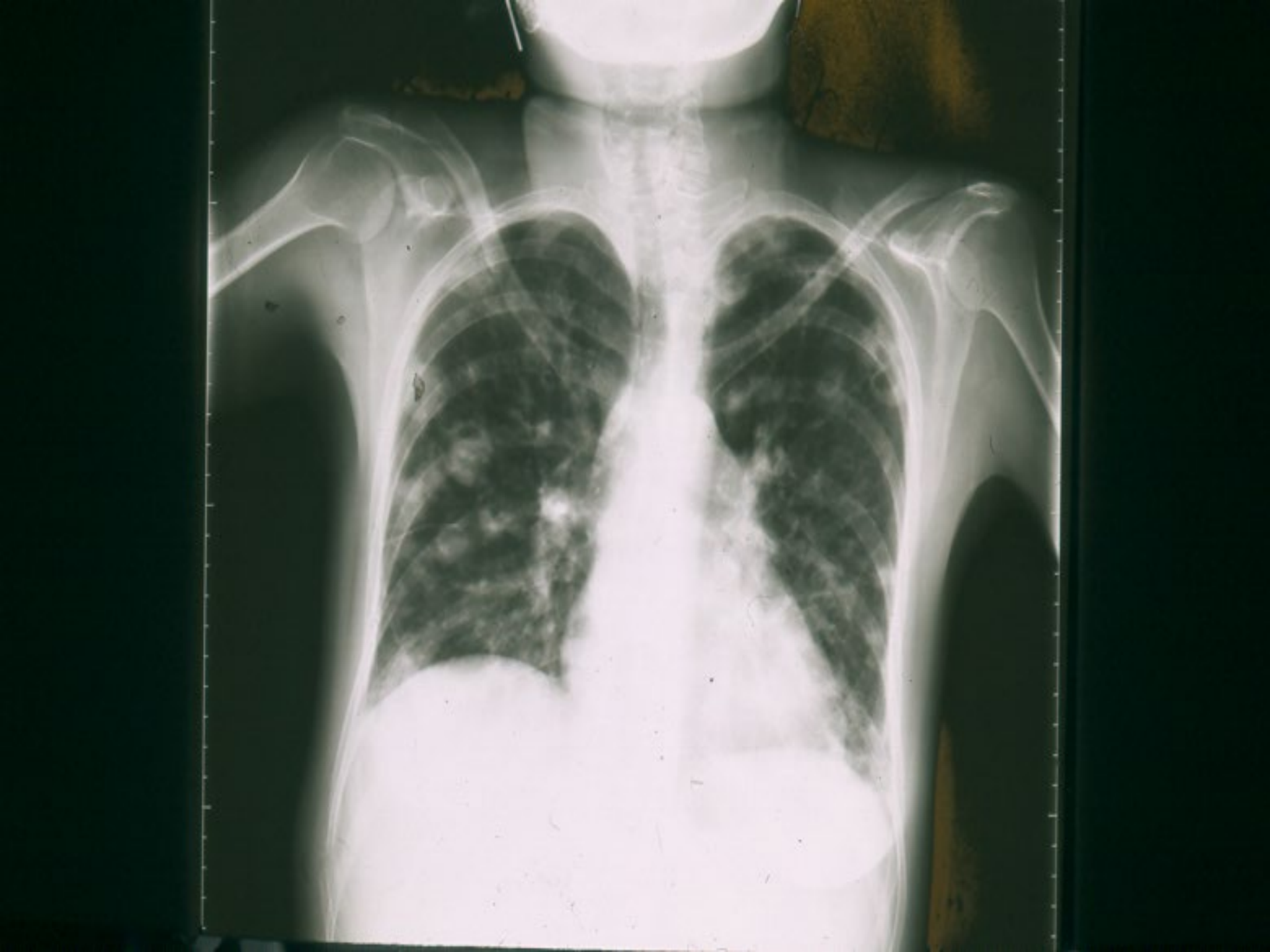
Mar 2009-169: 463 - 473

Symptom/sign/lab	No (%) of patients
Fever, temperature 38°C	2322/2428 (96)
Splinter hemorrhages	213/2655 (8)
Osler nodes	77/2648 (3)
Janeway lesions	123/2650 (5)
Roth spots	50/2649 (2)
Vascular embolic event	456/2665 (17)
Conjunctival hemorrhage	122/2655 (5)
New murmur	1068/2232 (48)
Worsening of old murmur	359/1787 (20)









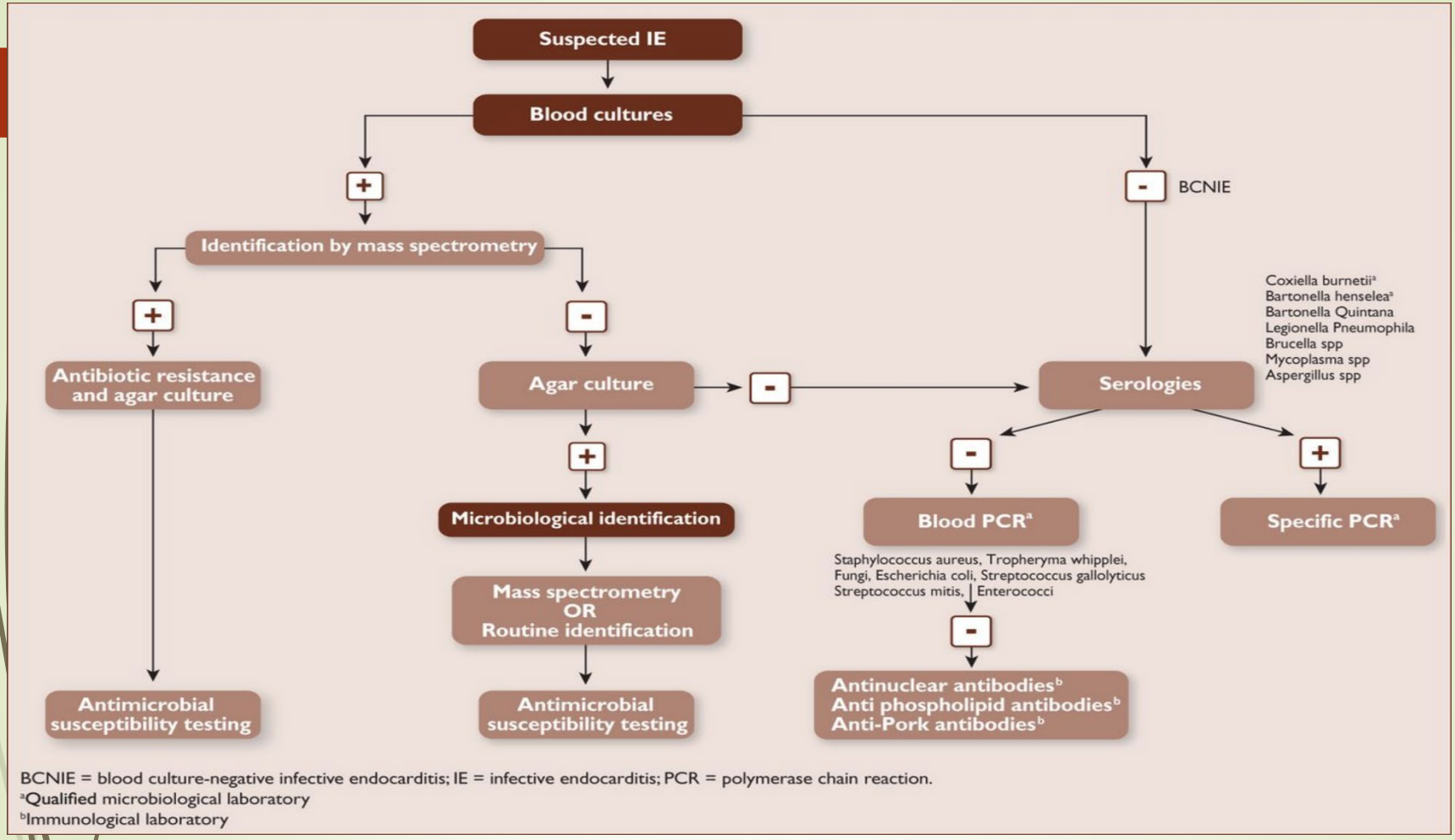
Prognostic factors- outcome

Patient characteristics
- Older age
- Prosthetic valve IE
- Diabetes mellitus
- Comorbidity (e.g., frailty, immunosuppression, renal or pulmonary disease)

Clinical complications of IE
- Heart failure
- Renal failure
- >Moderate area of ischaemic stroke
- Brain haemorrhage
- Septic shock

Microorganism
- *Staphylococcus aureus*
- Fungi
- Non-HACEK Gram-negative bacilli

Echocardiographic findings
- Periannular complications
- Severe left-sided valve regurgitation
- Low left ventricular ejection fraction
- Pulmonary hypertension
- Large vegetations
- Severe prosthetic valve dysfunction
- Premature mitral valve closure and other signs of elevated diastolic pressures



From: 2015 ESC Guidelines for the management of infective endocarditisThe Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

Eur Heart J. 2015;36(44):3075-3128. doi:10.1093/eurheartj/ehv319

Echocardiography

- **TEE is the method of choice for the diagnosis of IE**

- Higher sensitivity than TTE, especially in patients with poor ultrasound transmission through the thoracic wall.
- Increased sensitivity in the diagnosis of vegetations (TEE 90% vs TTE:70%) especially in small vegetations (<5 mm) where only 25% of the vegetations may be detected with TTE.
- TEE assists diagnosing intra-cardiac abscesses that are more frequent in PVE

Variable	Non-*S. aureus* (N = 1221)	*S. aureus* (N = 558)
Complications/outcomes		
Stroke	175 (14.3%)	119 (21.3%)
Systemic embolization other than stroke	228 (18.7%)	151 (27.1%)
Congestive heart failure	389 (31.9%)	161 (28.9%)
Intracardiac abscess	195 (16.0%)	71 (12.7%)
Persistent bacteremia	64 (5.2%)	95 (17.0%)
In-hospital death	178 (14.6%)	125 (22.4%)

Variable*	Methicillin-susceptible *S. aureus* N = 279	Methicillin-resistant *S. aureus* N =137
Outcome		
Systemic embolization other than stroke	73 (26.2%)	23 (16.8%)
Surgery this episode	105 (37.6%)	54 (39.4%)
Persistent bacteremia	**25 (9.0%)**	**60 (43.8%)**
In-hospital death	66 (23.7%)	42 (30.7%)

MSSA NV endocarditis

Requires >4 wks of intravenous antimicrobial therapy

Cloxacillin 2gr q4h

Or cefazolin 2gr q8h

MRSA endocarditis

Vanco 4-6 w 30-60mg/kg trough target 15-20 mcg/ml

Alternative: Daptomycin 8-10mg/kg

Depends on MIC, if MIC >1 - difficult to attain AUC/MIC >400 (Kullar et al.)

Staphylococcus aureus Endocarditis

The most common causative agent

Increased in persons undergoing procedures and in context of prosthetic device

Increasing prevalence of MRSA complicating management

Blood stream infection in HSC- Tertiary centre in Winnipeg

- Interrupted time series retrospective study for substance use disorder (SUD) adult patients aged >18 years admitted to Health Science Center with bloodstream infection (BSI) and IE between January 2005- December 2007, January 2012 – December 2014, January 2016 – October 2018
- Baseline characteristics, type of substance use, microbiology of the infection and outcomes were reviewed and compared in the three periods
- Of 190 cases recorded with BSI, 22 cases between 2005-2007, 57 between 2012-2014 and 111 between 2016-2018

Blood stream infection in HSC- Tertiary centre in Winnipeg

- Of 190 cases recorded with BSI, 22 cases between 2005-2007, 57 between 2012-2014 and 111 between 2016-2018
- The median age of patients was 37
- More alcohol use disorder between 2012-2014 in comparison to 2016-2018 (60.7 % vs. 34.9 %; $p<0.007$)

Blood stream infection in HSC- Tertiary centre in Winnipeg

- Between 2016-2018, methamphetamine use was by far the most common drug of choice
- *Staphylococcus aureus* was by far the most common pathogen in the three periods

- **Of 74 cases recorded with IE, the median age was 33 and methamphetamine use was the substance of choice either alone or part polysubstance use disorder**

Tsybina et al. Harm Reduct J (2021) 18:44
https://doi.org/10.1186/s12954-021-00492-6

Harm Reduction Journal

RESEARCH Open Access

Hospital admissions and mortality due to complications of injection drug use in two hospitals in Regina, Canada: retrospective chart review

Polina Tsybina[1*], Sandy Kassir[2], Megan Clark[3] and Stuart Skinner[4]

Table 5 Drugs used

Substance	Number of admissions	Percentage of admissions (%)
Opioids	70	47
Methamphetamines	52	35
Methylphenidate	22	15
Cocaine	30	20
Benzodiazepines	8	5
Unreported	20	13
Multiple drugs reported	60	40

Table 3 Diagnoses responsible for admission

Diagnosis	Number of admissions	Percentage of admissions (%)
SSTIs	44	30
Bacteremia/sepsis	33	22
IE	26	17
Talcosis	23	15
Epidural abscess/diskitis	16	11
Septic arthritis	14	9
Osteomyelitis	10	7
Psychosis or other psychiatric diagnosis	3	2
Intoxication	3	2
Overdose	2	1
Withdrawal	1	1
AIDS	1	1

Improving outcomes of IE among persons who inject drugs

- Younger age and fewer comorbid conditions
- Lower mortality rate reported in most studies;
- Receipt of medication for opioid use- any methadone, buprenorphine, or naltrexone, within 3 months after hospital discharge excluding discharge month for IDU-IE
- Reduced mortality in the months of receipt of medication for opioid
- Lower rates of surgery even when surgical indications exist

Kimmel et al. JAMA Netw Open. 2020 Oct 1;3(10):e2016228

Improving outcomes of IE among persons who inject drugs

- Study from SF- 80 of 340 (24%) of hospitalizations for invasive *S. aureus* infections among persons who use drugs involved patient-directed discharge (PDD); of PDD- 59% were experiencing houselessness.
- More than half of PDD required readmission for persistent or recurrent *S. aureus* infection
- Only 11% completed planned course of Abx (compared to 88% in those who stayed)
- One-year cumulative mortality was 15% after patient-directed discharge
- More than half of deaths in the patient-directed discharge group (58%) were due to drug overdose; none was due to *S. aureus* infection

Appa A et al. Am J Med. 2022 Jan

Long acting Abx

- largest study investigating the use of dalbavancin in complicated Gram-positive infections in a high-risk population- long acting requires 1 weekly dosing
- 40 individuals, 60% unstable housing, 58% IDU
- Complicated bloodstream infections; MRSA 57.5% and MSSA 30%

- Good outcomes with dalbavancin

Lueking et al. Microbiol Spectr. 2022 Dec 20

Case 1- culture negative IE

- A 57-year-old man presented presenting with decompensated congestive heart failure
- He had a history ofeasy fatigability over several months and reports itchy rash on legs
- Unstably housed
- PMHx: HIV and HCV, IDU-crystal methamphetamine
- Reported heavy alcohol consumption

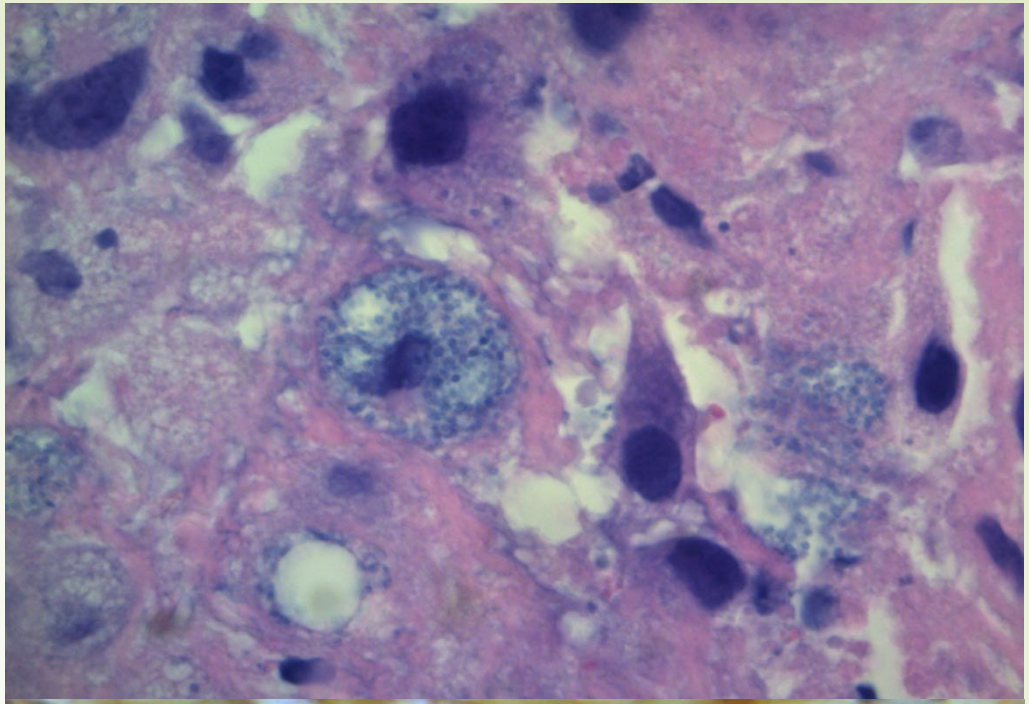
Culture negative endocarditis

- Blood culture-negative IE constitutes 5-30% of all IE cases
- Prior antibiotic treatment- account for 45-60% of CNE
- Q-fever 3-5%, Bartonella 3% of IE (depending on geography)
- *Bartonella* are gram-negative bacilli not identified by routine bacterial culture.

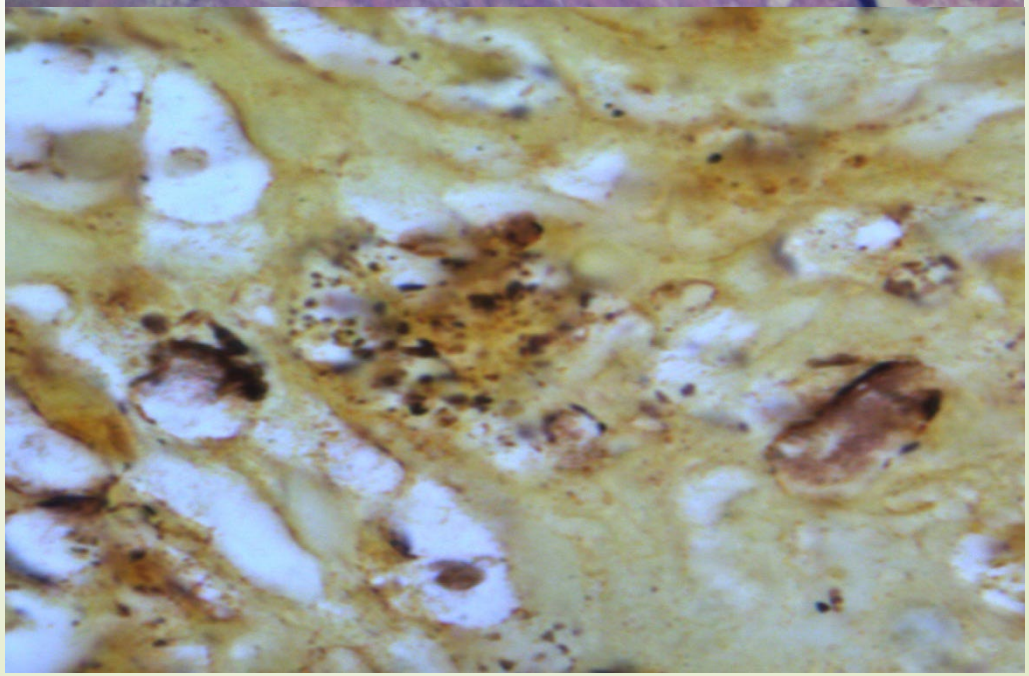
Bartonella endocarditis

- Ten-year retrospective study in MB-1014 *Bartonella* serologic tests
- 24 (2.4%) gave a positive result
- Sixteen adults (12 men and 4 women; mean age 48 yr) seen at a participating hospital had a positive result
- 7/16 houseless; shelter contact
- 10/16 Alcohol use disorder and 4/16 crystal methamphetamine use
- Two patients died; both had multivalvular *B. quintana* endocarditis with ruptured intracranial mycotic aneurysms.

H&E of valve tissue



Steiner stain of valve tissue



Summary

- Endocarditis is an important and potentially fatal infection
- *Staphylococcus aureus* is the most important pathogens
- Higher rates among people who inject drugs; data about shelters is limited but some suggest increased incidence
- Bartonella is an emerging pathogen in urban centres and in Canada among unstably housed individuals
- Endocarditis treatment requires prolonged antimicrobial therapy
- High mortality rate largely attributed to the substance use

For discussion

- Prolonged antimicrobial therapy – potential role of shelters?
- Syndemic conditions- infectious complications
- Opioid substitution and other intervention to decrease IDU related mortality?
- Ectoparasites as vectors of disease among persons experiencing houselessness