Literature review

Strategy:
- Pubmed 1993-2003 (review)
- Key phrases = Infective endocarditis associated with: epidemiology, pathogenesis, clinics, experimental, therapy
- Only studies with ≥ 30 patients

Results:
- 3784 episodes (median pts/study = 156, range 30-415)
- mean age varied 36 – 69 years

Lancet 2004; 363:139-149

Incidence:

(Endocarditis per 100,000 patients/year)

Overall median = 3.6 (range 0.3-22.4)

- in patients < 50 years old: ≤ 5%
- in patients ≥ 50 years old: > 15%

Incidence in the literature:
- 2-6 per 100,000 patients per year

Lancet 2004; 363:139-149

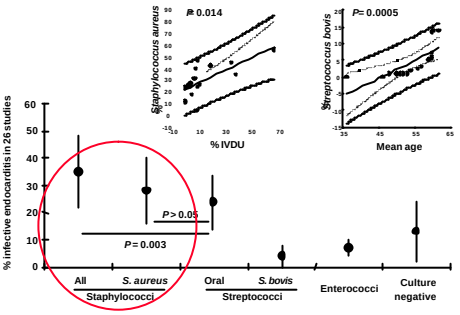
Mortality of Infective Endocarditis

Median in-hospital mortality = 16% (median 11-26)

Study period	Episodes	Native/prosthetic valves (%)	Global mortality	Source
1980-90	210	181/29 (16%)	21.4%	*Watanakunakorn. 1993 Medicine;72:90-102*
1984-88	125	…	23%	*Hogevik et al. 1995 Medicine;74:324-39*
1990…	300	231/69 (30%)	26%	*Mansur et al. 1996. Thorac cardiovasc Surgeon;44 :2-10*

Mortality *S. aureus* PVE = 47.5% (in 61 cases)
(ICE study; Chirouze et al CID 2004;38:1323-1327)

Frequency organisms reported in IE in 26 Studies between1993 and 2003



Lancet 2004; 363:139-149

Frequency of IE by Pathogen (%)

Pathogens	Native valve	IVDU	Prosthetic early	Prosthetic late
Staphylococci	105 (47)	109 (69)	6 (100)	39 (39)
S. aureus	96 (43)	109 (69)	0 (0)	25 (24)
Coag. negative	9 (4)	0 (0)	6 (100)	15 (15)
Streptococci	72 (32)	36 (23)	0 (0)	35 (35)
Enterococci	12 (6)	5 (3)	0 (0)	13 (13)
HACEK	6 (3)	0 (0)	0 (0)	5 (5)
Other bacteria	9 (4)	3 (2)	0 (0)	6 (7)
Fungi	2 (1)	2 (1.5)	NS	NS
Neg. blood cult.	15 (7)	2 (1.5)	NS	NS

Adapted from *Watanakunakorn C. Medicine 1993; Mathew J Arch Intern Med 1995; Sandre RM. Clin Infect Dis 1996; Tornos P. Clin Infect Dis 1997*

Predisposing Factors Have Changed

1970

Rheumatic heart disease	…
Congenital cardiopathy	Congenital cardiopathy
	IVDU
	Elderly patients with valve sclerosis
	Prosthetic valves
	Dialysis patients
	Nosocomial endocarditis

"Liaison Dangereuse"

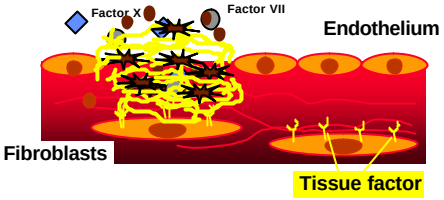
Host
- Tissue factor
- Monocytes
- Endothelium
- Platelets

Bacterium
- Adhesins (MSCRAMMs)
- Fibrinogen/fibronectin-binding proteins
- Regulation

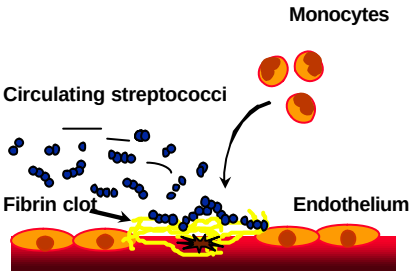
40-60% des personnes > 50 ans ont des lésions valvulaires dégénératives

1. Tissue Factor

- 43 kDa membrane-bound glycoprotein
- Activates factors VII-X and triggers coagulation
- Expressed constitutively on all cells except for the endothelium.

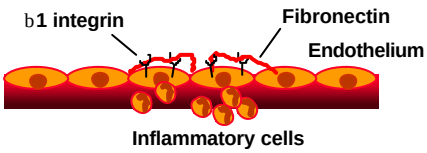


Colonization of endothelial lesions

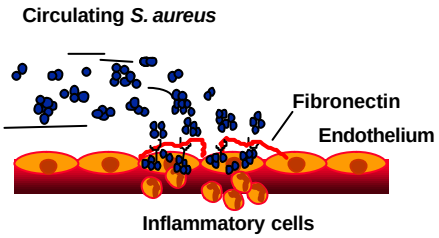


Host: Endothelium

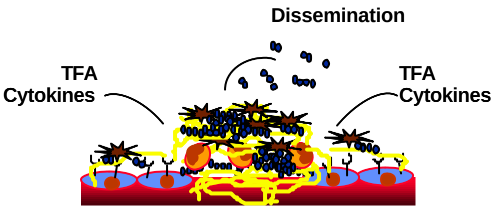
Colonization of intact endothelium



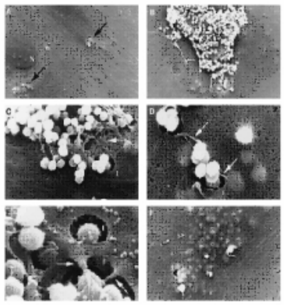
Colonization of intact endothelium



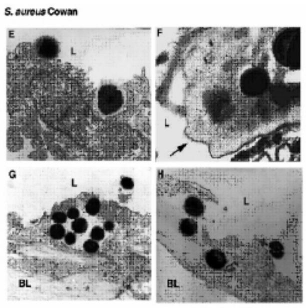
Colonization of intact endothelium



Internalization of S. aureus into HUVEC in vitro



Vriesema et al. I&I 2000; 68: 165-72



Que et al, submitted

S. aureus adhesins (MSCRAMMs) involved in IE pathogenesis

Adherence substrate	MSCRAMM	Gene or function	Demonstrated in experimental IE	References
Fibrinogen/ fibrin	Clumping factor A Clumping factor B Coagulase Extracellular fibrinogen binding protein Fibrinogen-binding protein A	*clfA* *clfB* *coa* *efb* (formerly *fib*) *fbpA*	**Yes** No No No No	45;49;53 46 45;47 106;107 108
Fibronectin	Fibronectin-binding protein A and B	*fnbA*, *fnbB*	**Yes** **no**	53;54
Collagen	Collagen-binding protein	*cna*	No	109
Broad spectrum ECM	MHC class II analog (Map or Eap) Serine-aspartate repeat proteins (SDR)	*map* or *eap* *sdr* gene family	No No	110;111 112

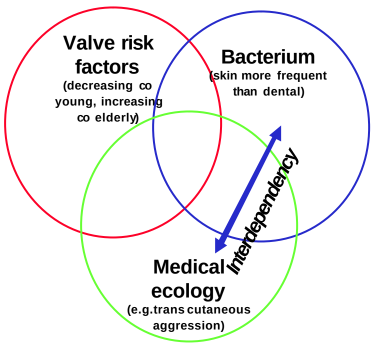
Infect. Dis. Clin. North Am. 2002; 16:297

Risk of invasive *Staphylococcus aureus* infection

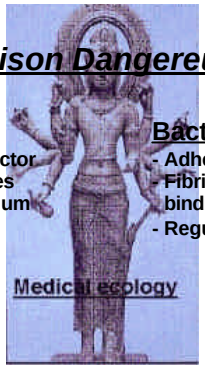
Underlying condition	No. of patients with ISA infection (*n* = 226)	Annual incidence, per 100,000	Relative risk (95% confid. int.)	*P* value
Hemodialysis	24	7692	257.2 (160-393.6)	<.001
Peritoneal dialysis	3	4918	150.0 (30.5-44l.1)	<.001
HIV nfection	4	778	23.7 (6.4-61.4)	<.001
Solid organ transplantation	3	683	20.7 (4.2-61.3)	<.001
Heart disease	114	362	20.6 (15.8-27.0)	<.001
Cancer	47	348	12.9 (9.1-17.8)	<.001
Illicit intravenous drug use	13	321	10.1 (5.3-17.7)	<.001
Alcohol abuse	31	241	8.2 (5.4-12.0)	<.001
Diabetes mellitus	48	192	7.0 (5.0-9.7)	<.001
Stroke	16	200	6.4 (3.6-10.6)	<.001
Chronic obstructive pulmonary disease	26	120	3.9 (2.5-5.9)	<.001
Systemic lupus erythematosus	2	80	2.4 (0.3-8.7)	.3
Rheumatoid arthritis	5	[illegible]	[illegible]	[illegible]

Laupland et al. J Infect Dis 2003;187(9):1452-9.

Conditions taken into account for infective endocarditis



"Liaison Dangereuse"



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Medical ecology