Epidemiology of Infectious Endocarditis in Children

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Content

- Change of the epidemiology of infectious endocarditis(IE)
  - Incidence and mortality
  - Microbiology
  - Underlying condition
  - Underlying heart condition
- IE in modern era
- IE after congenital heart surgery
- IE after transcatheter therapy

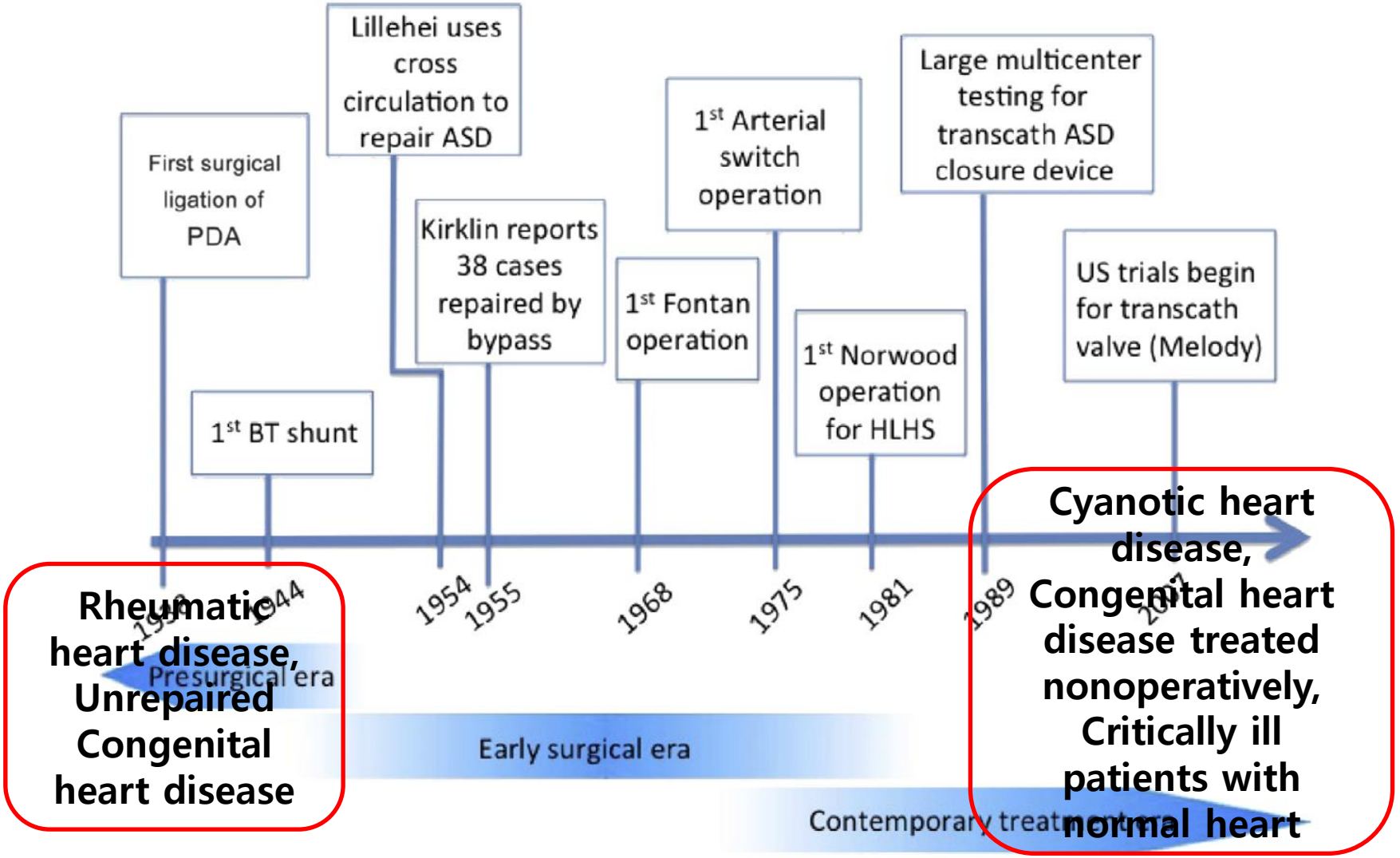


Fig. 1. Selected timeline for advances in surgical and transcatheter treatment of CHD. BT, Blalock-Taussig; HLHS, hypoplastic left heart syndrome; Transcath, transcatheter.

Infect Dis Clin N Am 29 (2015) 513–524

Incidence and mortality

Antibiotics era

		Johnson[1]			Hare[2]	Saiman[3]	Day[4]
Number of subject	23	18	40	68	42	62	1588
Years reviewed	1933-1942	1943-1952	1953-1962	1963-1972	1972-1982	1977-1992	2000, 2003
Incidence (/1000 patients)	Not available	0.22	0.42	0.55	0.78	Not available	0.27 /0.29
Mortality (%)	100	27	7	19	14	21	5

1. Johnson DH, Rosenthan A, Nadas AS. Circulation 1975;51(4):581-8
2. Van Hare GF, Ben-shachar G, Liberman J, et al. Am Heart J 1984;107(6):1235-40
3. Saiman L, Prince A, Gersony WM. 1993;122(6):847-53
4. Day MD, Gauvreau K, Shulman S, et al. Circulation 2009;119(6):865-70

Microbiology of infective endocarditis

- Have changed from viridans streptococci to staphylococci
- Enterococcus nosocomial infection, a small but important portion of most pediatric IE series
- Fungal endocarditis: unusual but can be seen especially in neonates with chronic indwelling central catheter.
- Decreasing culture negative IE

Table 1
Principal pathogenic bacterial agents in pediatric IE series over 8 decades

Series (First Author)	Johnson[1]	Van Hare[3]	Saiman[18]	Day[6]
Number of Subjects	149	42	62	632
Years Reviewed	1933–1972	1972–1982	1977–1992	2000–2003
Organism (%)				
Viridans group streptococci	51	31	23	20
S aureus	28	33	39	57
Coagulase-negative staphylococci	1	14	11	14
Streptococcus pneumoniae	2	7	—	1
Enterococcus species	—	2	2	—
HACEK	—	5	—	1
Other gram-negative rods	3	—	6	2
Other	—	2	10	5
Culture negative	13	2	6	NA
Survival (%)	65[b]	86	89	95

Table 2 Pathogens causing pediatric infective endocarditis (IE) during three eras, 1930–2004

Pathogens	Era 1 1930–1960 ($n = 58$) n (%)	Era 2 1977–1992 ($n = 62$) n (%)	Era 3[a] 1992–2004 ($n = 85$) n (%)
Streptococcal spp.	40 (69)	14 (23)	26 (31)
Staphylococcus aureus	10 (17)	24 (39)	18 (21)
Methicillin-resistant *S. aureus*	0	8	4
Coagulase negative staphylococci	0	7 (11)	18 (21)
Enterococcal species	0	1 (2)	11 (13)
Vancomycin-resistant enterococci	–	–	0
Gram negative bacilli	0	4 (6)	10 (12)
Candida spp.	0	6 (10)	10 (12)
Aspergillus spp.	0	0	2 (2)
Culture negative	3 (5)	4 (6)	1 (1)
No blood culture obtained	5 (9)	0	0

[a] Twelve subjects had polymicrobial infections

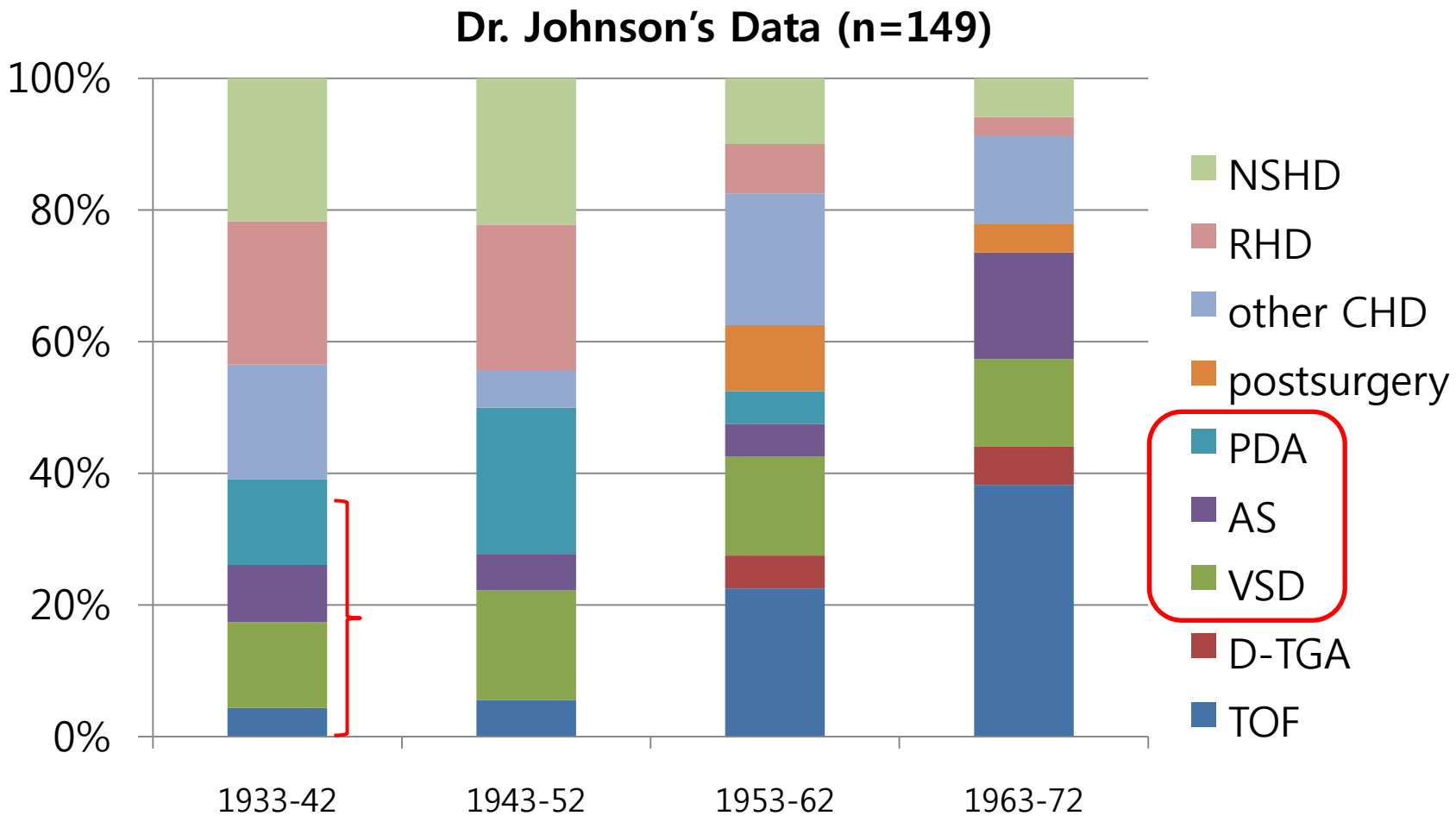
Pediatr Cardiol (2010) 31:813–820

Underlying conditions

	Johnson	Hare	Saiman	Day
Years reviewed	1933 -1972	1972 -1982	1977 -1992	2000, 2003
Congenital heart disease(CHD) (%)	79.2	76.2	64.5§	33.7
Rheumatic heart disease(RHD) (%)	9.4	7.1	4.9	3.4
Other preexisting heart disease (%)				4.7‡
Nonstructural heart disease(NSHD) (%)	11.4*	16.7	30.6†	58.3

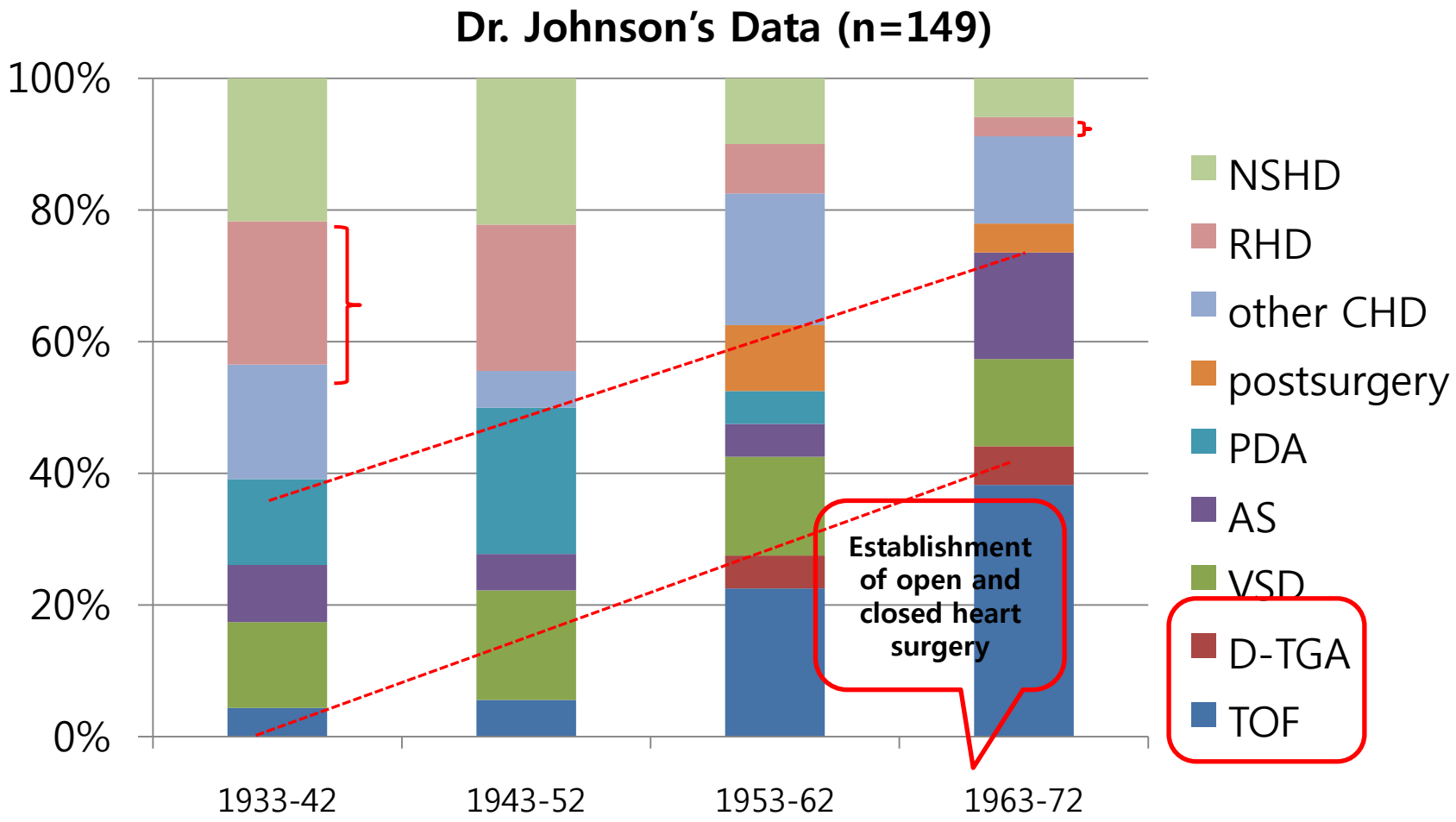
* Mortality of nonstructural heart disease: 64.7%
§ 50% of them were complex cyanotic heart disease with palliative shunts, conduits, or prosthetic valves
† 68.4% hospital acquired endocarditis, among them, 81% central venous catheters, 53.8% premature infants
‡ Others: cardiomyopathy, intracardiac devices

Underlying cardiac abnormalities- 1933-1972



- PDA: patent ductus arteriosus, AS: aortic stenosis, VSD: ventricular septal defect, D-TGA: Dextrotransposition of the great arteries, TOF: tetralogy of Fallot

Underlying cardiac abnormalities- 1933-1972



- PDA: patent ductus arteriosus, AS: aortic stenosis, VSD: ventricular septal defect, D-TGA: Dextrotransposition of the great arteries, TOF: tetralogy of Fallot

Characteristics of Children Hospitalized With Infective Endocarditis

Michael D. Day, MD; Kimberlee Gauvreau, ScD; Stanford Shulman, MD;
Jane W. Newburger, MD, MPH

Background—Infective endocarditis in children is rare, and most reports describe the experience in referral centers. The purpose of our study was to assess the characteristics of children with infective endocarditis in a large national sample.

Methods and Results—We analyzed hospital discharge records with *International Classification of Diseases*, ninth revision, codes indicating infective endocarditis among admissions of patients <21 years of age in the Kids' Inpatient Databases 2000 and 2003; analyses for the 2 years were combined. In 1588 hospitalizations, the age distribution was bimodal, with peaks in infancy and late adolescence. The organism was coded in 632 admissions; *Staphylococcus aureus* was most common (57%), followed by the viridans group of streptococci (20%). Preexisting heart disease was present in 662 patients admitted (42%), among whom 81% had congenital heart disease, 8% had prosthetic valve endocarditis, and 5% had rheumatic heart disease. In-hospital mortality occurred in 84 patients (5%), 38 with preexisting heart disease. Death occurred in 12 of 25 patients (48%) with tetralogy of Fallot and pulmonary atresia, and 4 of 54 (8%) with prosthetic valve endocarditis. Among 46 deaths without preexisting heart disease, *S aureus* was the causative organism in 13 of 14 patients (93%) beyond infancy; among 32 infants who died, 10 (31%) were premature.

Conclusions—In 2000 and 2003, we found a continuing shift in the epidemiology of pediatric infective endocarditis toward a higher proportion of children without preexisting heart disease. Risk factors for mortality included some forms of congenital heart disease and, among patients without preexisting heart disease, premature/neonatal age and *S aureus* as an etiologic agent. (***Circulation*. 2009;119:865-870.**)

***Circulation*. 2009;119:865-870.**

IE-nationwide study

- 2000, 2003
- 1588 hospitalization
- Peaks in infancy and late adolescence
- *S aureus* (57%), viridans group of streptococci (20%)
- Mortality in 5%, among them, 45% with preexisting heart disease
- Death without preexisting heart disease
  - 93%: *S aureus*
  - 70%: infants, 22%: premature

Circulation. 2009;119:865-870

Preexisting heart disease (662/1588)

- 33.7%(535 of 1588): CHD
- 4.7%(75): previous RHD
- 3.4%(54): prosthetic valves
- 3.1%(49): cardiomyopathy
- 1.4%(22) intracardiac devices, comprising defibrillators or pacemakers
- 33.8%(224 of 662); cardiac surgery performed on the same admission
- 55.4% of the cardiac surgeries : CHD surgery

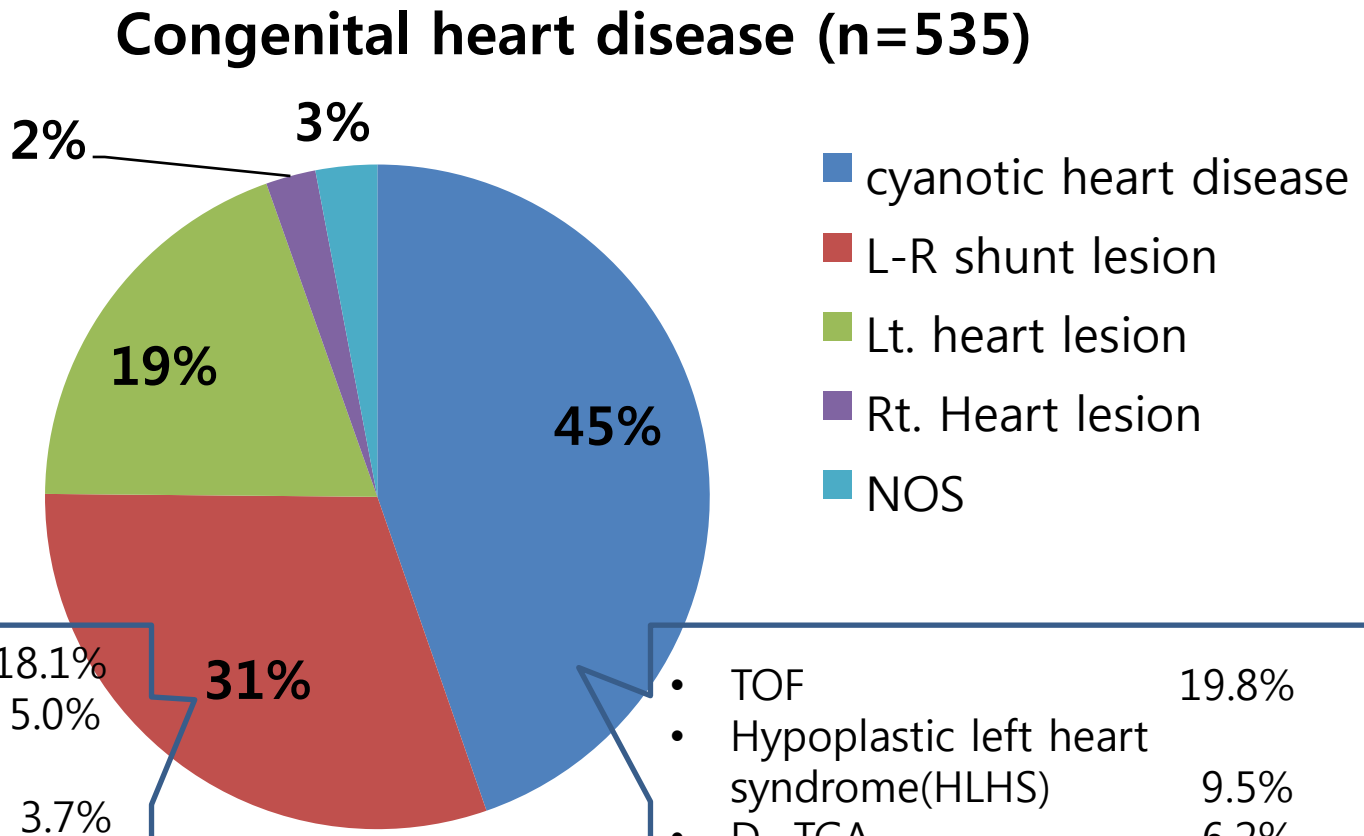
Circulation. 2009;119:865-870

Without preexisting heart disease (926/1588)

- 9.5%(88 of 926): neoplasm
- 5.8%(54): prematurity
- 5.6%(52): connective tissue disorders
- 2.4%(22): diabetes mellitus
- 10.5%(97): cardiac surgery during the same hospitalization
- 30.9% of them, aortic valve(AV) surgery

Circulation. 2009;119:865-870.

Underlying cardiac abnormalities- 2000, 2003



- VSD 18.1%
- PDA 5.0%
- Atrial septal defect(ASD) 3.7%
- Complete atrioventricular septal defect(CAVSD) 3.0%

- TOF 19.8%
- Hypoplastic left heart syndrome(HLHS) 9.5%
- D- TGA 6.2%
- Tricuspid atresia 3.4%
- Truncus arteriosus 2.1%
- etc

Circulation. 2009;119:865-870.

Infective Endocarditis in Children With Congenital Heart Disease

Cumulative Incidence and Predictors

Dinela Rushani, MSc; Jay S. Kaufman, PhD; Raluca Ionescu-Ittu, PhD; Andrew S. Mackie, MD, SM; Louise Pilote, MD, MPH, PhD; Judith Therrien, MD; Ariane J. Marelli, MD, MPH

Background—The American Heart Association guidelines for prevention of infective endocarditis (IE) in 2007 reduced the groups of congenital heart disease (CHD) patients for whom antibiotic prophylaxis was indicated. The evidence base in CHD patients is limited. We sought to determine the risk of IE in children with CHD.

Methods and Results—We performed a population-based analysis to determine the cumulative incidence and predictors of IE in children (0–18 years) with CHD by the use of the Quebec CHD Database from 1988 to 2010. In 47 518 children with CHD followed for 458 109 patient-years, 185 cases of IE were observed. Cumulative incidence of IE was estimated in the subset of 34 279 children with CHD followed since birth, in whom the risk of IE up to 18 years of age was 6.1/1000 children (95% confidence interval, 5.0–7.5). In a nested case-control analysis, the following CHD lesions were at highest risk of IE in comparison with atrial septal defects (adjusted rate ratio, 95% confidence interval): cyanotic CHD (6.44, 3.95–10.50), endocardial cushion defects (5.47, 2.89–10.36), and left-sided lesions (1.88, 1.01–3.49). Cardiac surgery within 6 months (5.34, 2.49–11.43) and an age of <3 years (3.53, 2.51–4.96; reference, ages 6–18) also conferred an elevated risk of IE.

Conclusions—In a large population-based cohort of children with CHD, we documented the cumulative incidence of IE and associated factors. These findings help identify groups of patients who are at the highest risk of developing IE. (***Circulation*. 2013;128:1412-1419.**)

IE in children with CHD

- Quebec CHD database from 1988 to 2010
- 47,518 children for 458,108 patient-years
- 185 cases of IE
- 6.1/1000 children with CHD
- Highest risk of IE
  - Cyanotic CHD, CAVSD, left-sided lesions
  - Cardiac surgery within 6 months, an age of < 3 years

Circulation. 2013;128:1412-1419

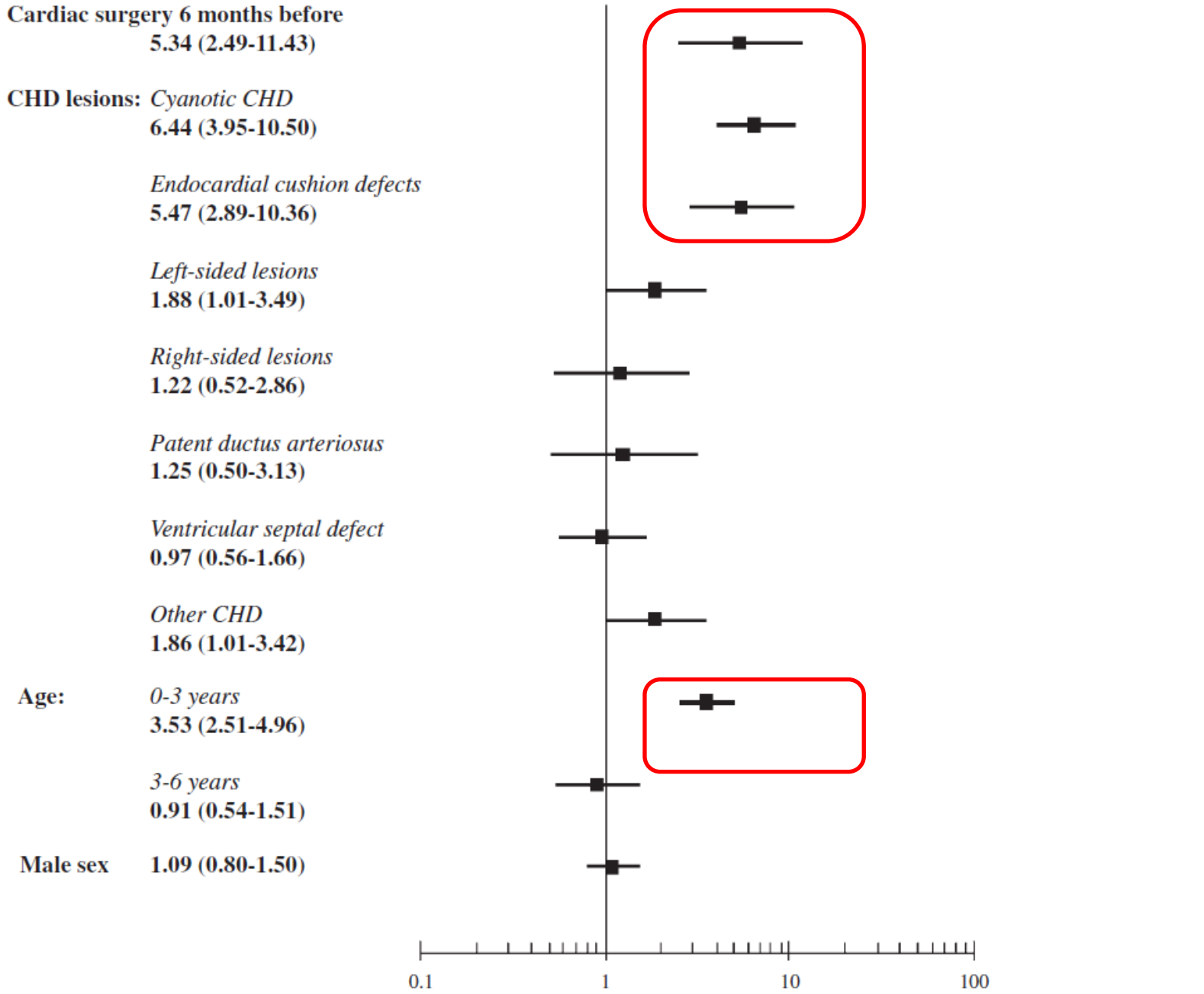
Table 2. Lesion Group–Specific Cumulative Incidence and Incidence Rate of IE in Children With CHD

CHD Lesions	Cumulative Incidence (95% CI) per 1000 Children			Incidence Rate (95% CI) pe 10 000 Person-Years
	0–6 y	0–12 y	0–18 y	
Cyanotic CHD	16.8 (11.9–23.8)	23.3 (17.0–31.8)	31.0 (22.5–42.7)	20.7 (15.4–27.7)
Endocardial cushion defects	5.5 (2.3–13.1)	8.7 (4.1–18.6)	11.1 (5.4–22.9)	7.7 (3.9–15.4)
Left-sided lesions	2.7 (1.3–5.7)	4.8 (2.6–8.7)	7.9 (4.4–14.0)	4.4 (2.6–7.4)
Right-sided lesions	2.3 (1.0–5.5)	2.3 (1.0–5.5)	4.2 (1.5–11.5)	2.9 (1.3–6.5)
Patent ductus arteriosus	3.2 (1.4–7.1)	3.2 (1.4–7.1)	3.2 (1.4–7.1)	3.5 (1.6–7.7)
Ventricular septal defect	2.0 (1.2–3.2)	2.4 (1.5–3.8)	3.2 (1.9–5.3)	2.4 (1.5–3.7)
Atrial septal defect	1.9 (1.3–2.9)	2.2 (1.5–3.4)	3.0 (1.9–4.8)	2.3 (1.6–3.4)
Other CHD	2.9 (1.4–5.8)	3.7 (1.8–7.3)	5.5 (2.9–10.6)	3.7 (2.0–6.7)
Overall	3.2 (2.6–3.9)	4.2 (3.5–5.1)	6.1 (5.0–7.5)	4.1 (3.5–4.9)

CHD indicates congenital heart disease; CI, confidence interval; and IE, infective endocarditis.

- Lt-sided lesions: coarctation of the aorta, aortic stenosis/insufficiency, mitral stenosis/insufficiency

Circulation. 2013;128:1412-1419



Circulation. 2013;128:1412-1419

Table 4. CHD Lesions at Elevated Risk of IE Stratified by History of Cardiac Surgery

CHD Lesions	IE Cases, n (%)	Controls, n (%)	Adjusted Rate Ratio (95% CI)
Cyanotic CHD	45	178	
Unoperated	27 (60)	100 (56)	7.56 (4.03–14.18)
Operated	18 (40)	78 (44)	9.22 (4.39–19.34)
Endocardial cushion defects	8	84	
Unoperated	5 (63)	51 (61)	3.00 (1.06–8.51)
Operated	3 (37)	33 (39)	–*
Left-sided lesions	14	253	
Unoperated	13 (93)	233 (92)	2.35 (1.16–4.73)
Operated	1 (7)	20 (8)	–*

Circulation. 2013;128:1412-1419

Thirty-Year Incidence of Infective Endocarditis After Surgery for Congenital Heart Defect

Cynthia D. Morris, PhD, MPH; Mark D. Reller, MD; Victor D. Menashe, MD

Context.—The incidence of infective endocarditis after surgical repair of congenital heart defects is unknown.

Objective.—To determine the long-term incidence of endocarditis after repair of any of 12 congenital heart defects in childhood.

Design.—Population-based registry started in 1982.

Setting.—State of Oregon.

Participants.—All Oregon residents who underwent surgical repair for 1 of 12 major congenital defects at the age of 18 years or younger from 1958 to the present.

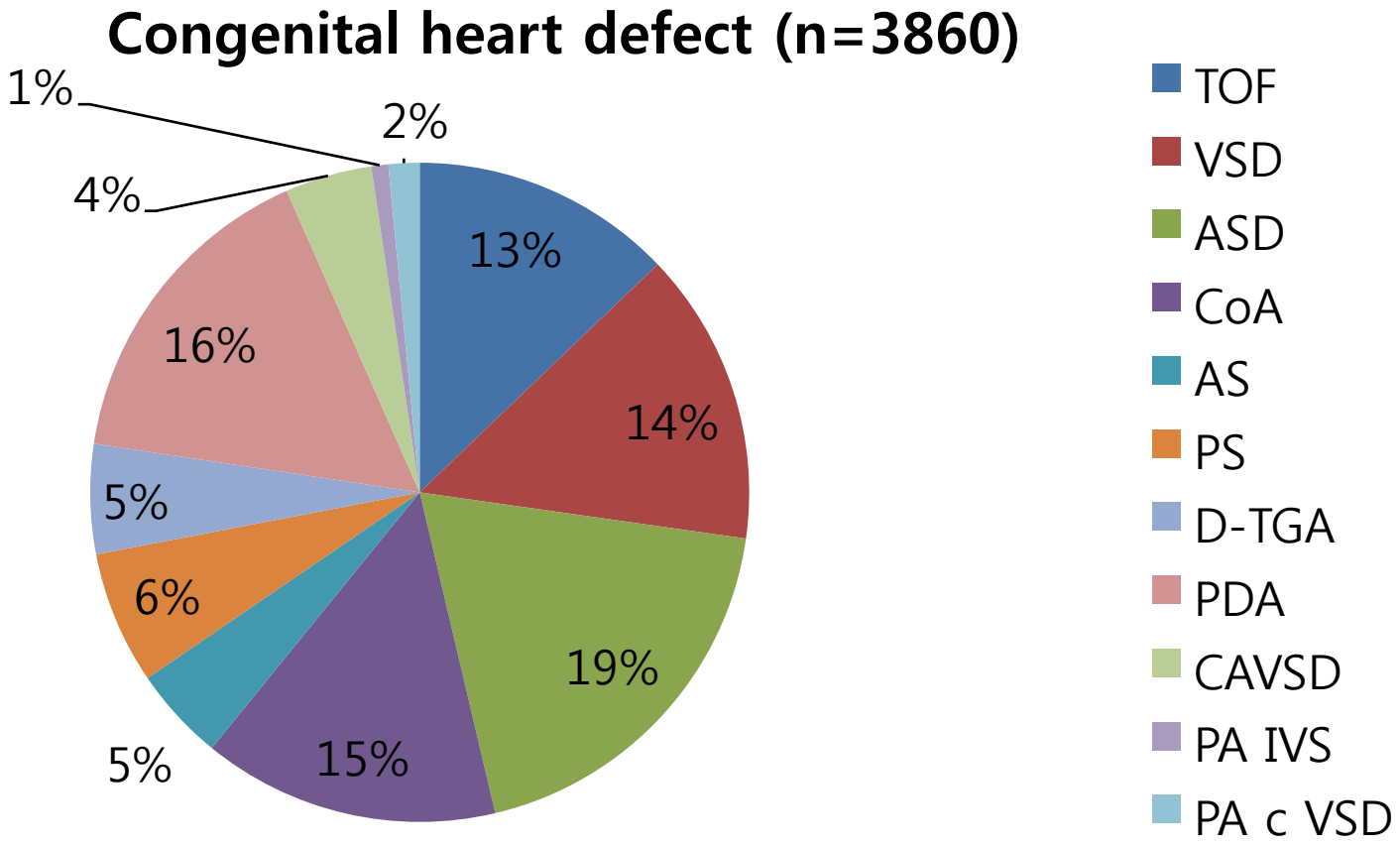
Main Outcome Measure.—Diagnosis of infective endocarditis confirmed by hospital or autopsy records.

Results.—Follow-up data were obtained from 88% of this cohort of 3860 individuals through 1993. At 25 years after surgery, the cumulative incidence of infective endocarditis was 1.3% for tetralogy of Fallot, 2.7% for isolated ventricular septal defect, 3.5% for coarctation of the aorta, 13.3% for valvular aortic stenosis, and 2.8% for primum atrial septal defect. In the cohorts with shorter follow-up, at 20 years after surgery the cumulative incidence was 4.0% for dextrotransposition of the great arteries; at 10 years, the cumulative incidence was 1.1% for complete atrioventricular septal defect, 5.3% for pulmonary atresia with an intact ventricular septum, and 6.4% for pulmonary atresia with ventricular septal defect. No children with secundum atrial septal defect, patent ductus arteriosus, or pulmonic stenosis have had infective endocarditis after surgery.

Conclusion.—The continuing incidence of endocarditis after surgery for congenital heart defect, particularly valvular aortic stenosis, merits education about endocarditis prophylaxis for children and adults with repaired congenital heart defects

JAMA. 1998;279:599-603

Sample size by heart defect



- CoA: coarctation of the aorta, PA IVS: pulmonary atresia with intact ventricular septum, PS: pulmonic valve stenosis
- Children with palliative surgery only are excluded

JAMA. 1998;279:599-603

Table 2.—Annualized Risk of Endocarditis Within This Population

Risk for Endocarditis	No. of Cases per 1000 Patient-Years
High	
Pulmonary atresia with ventricular septal defect	11.5
Tetralogy of Fallot with palliative systemic-to-pulmonary shunt	8.2
Aortic valve stenosis*	7.2
Pulmonary atresia*	6.4
Unoperated ventricular septal defect	3.8
Moderate to low	
Primum atrial septal defect with cleft mitral valve*	1.8
Coarctation of the aorta*	1.2
Complete atrioventricular septal defect*	1.0
Tetralogy of Fallot*	0.7
Dextrotransposition of the great arteries*	0.7
Ventricular septal defect*†	0.6
No documented risk	
Atrial septal defect*	0
Patent ductus arteriosus*	0
Pulmonic stenosis*	0

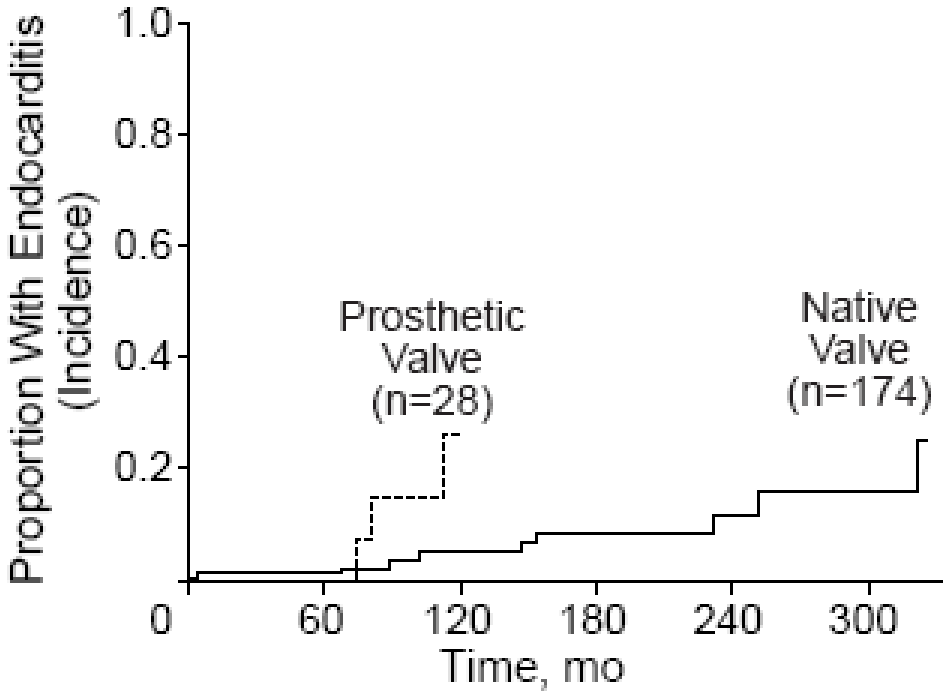
JAMA. 1998;279:599-603

Cumulative incidence of endocarditis by heart defect

Defect	Cumulative incidence follow-up interval					
	1m	1y	5y	10y	20y	30y
TOF	0.2(0.2)	0.7(0.4)	1.0(0.5)	1.3(0.6)	1.3(0.6	1.3(0.6)
VSD	0	0.2(0.2)	0.2(0.2)	0.5(0.4)	0.5(0.4)	4.1(2.1)
CoA	0.4(0.3)	0.8(0.4)	1.0(0.5)	1.0(0.5)	2.3(1.0)	3.5(1.6)
AS	0	1.2(0.9)	1.9(1.1)	6.1(2.3)	13.3(3.8)	20.7(7.7)
PA VSD	2.6(2.6)	2.6(2.6)	6.4(4.4)	6.4(4.4)		

- Values reported are cumulative incidence (SE)

JAMA. 1998;279:599-603



In the cohort with aortic valve stenosis, the incidence of endocarditis is shown by time after surgery for individuals after aortic valve replacement and with a native valve.

JAMA. 1998;279:599-603

IE after transcatheter therapy

- Following placement of foreign material(eg, vascular plug, ASD device, PDA device), IE prophylaxis for 6 months
- Sporadic case reports of IE among patients with devices

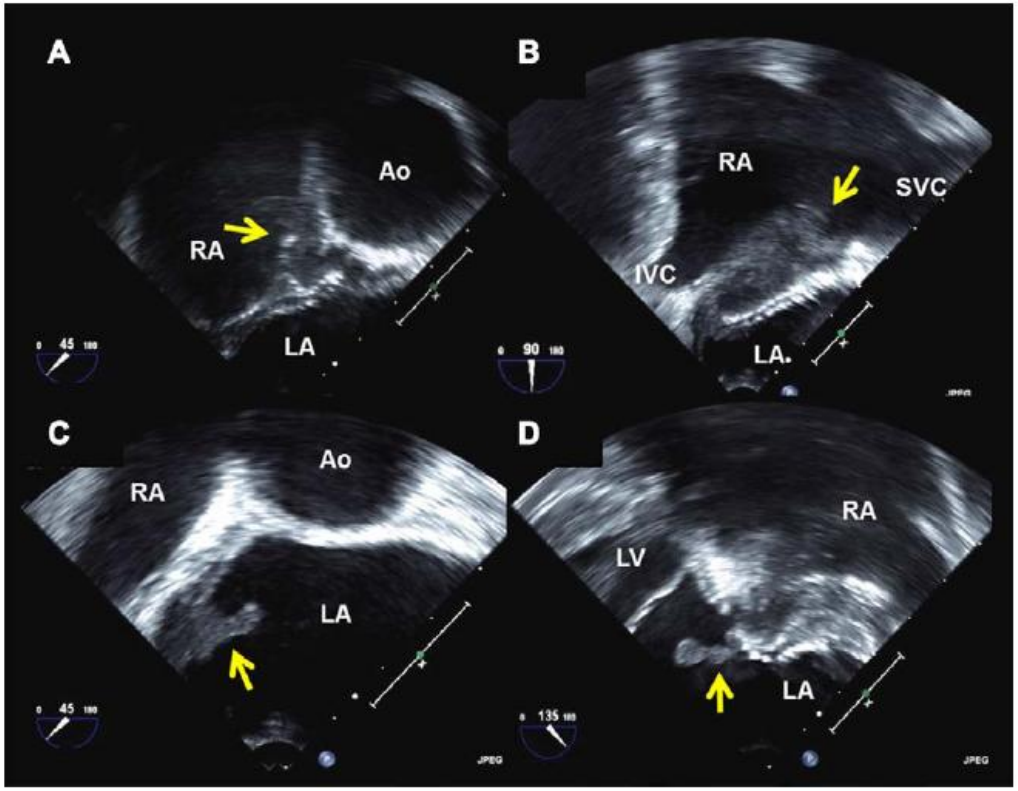
Case reports of IE with ASD device

- Incomplete endothelialization of an Amplatzer septal occluder(ASO) device followed by meningitis and late acute bacterial endocarditis

Cardiol Young 2016;26:808-10

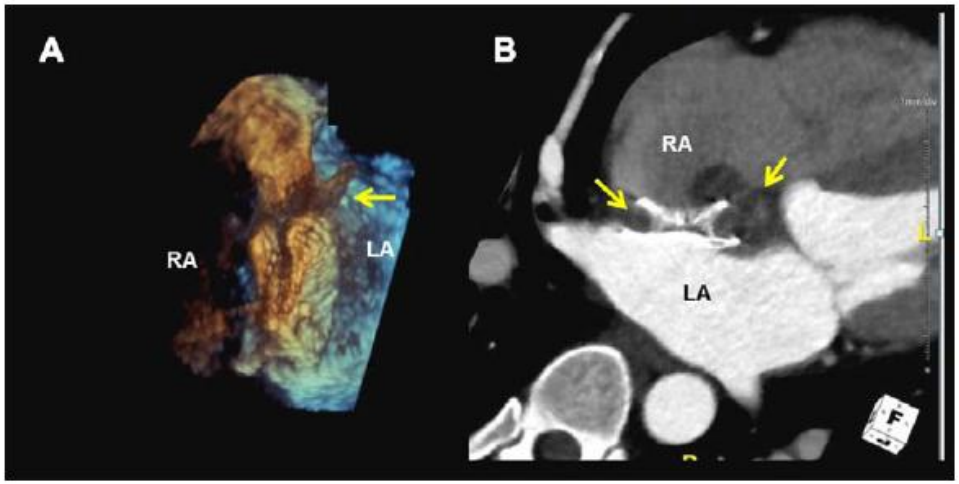
- Late bacterial endocarditis and abscess formation after implantation of an Amplatzer septal occluder device

Circulation 2015;131:e536-e538

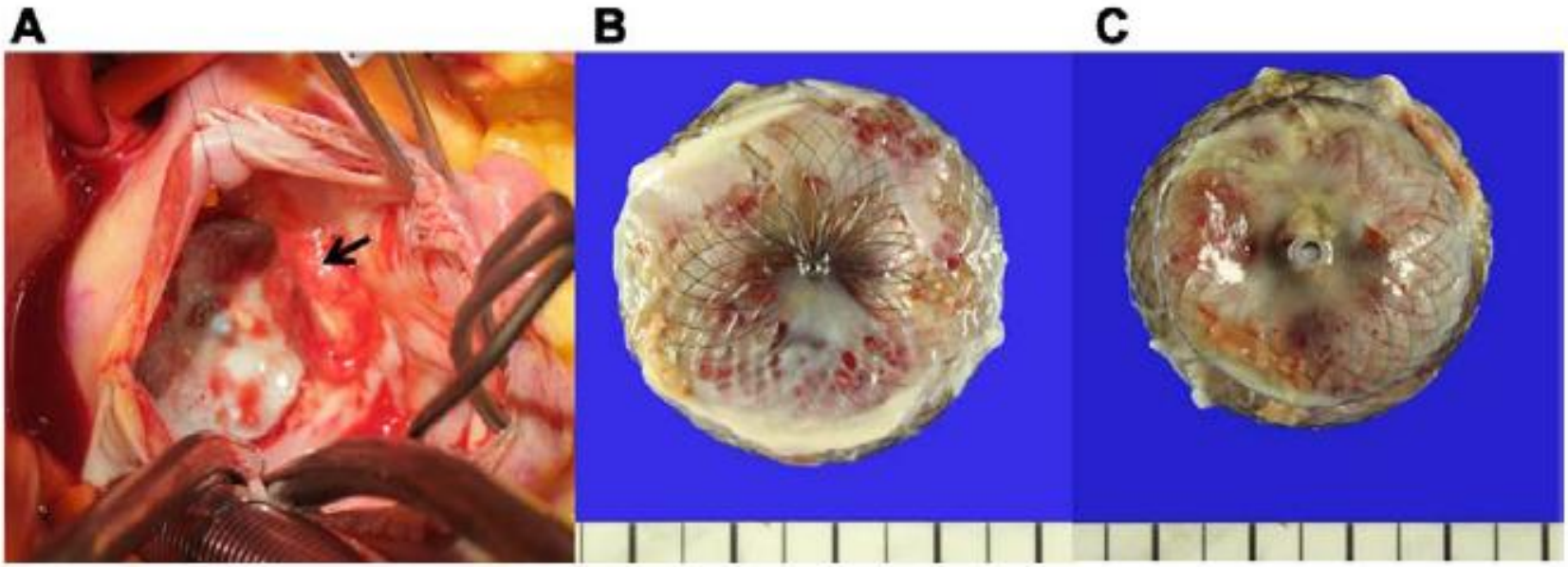


- 37-year-old man
- Fever, Janeway lesions
- ASD device closure four years ago
- Periodontal scaling without IE prophylaxis before 1 month
- Methicillin-sensitive *Staphylococcus aureus* on blood culture

- **A, B** 2.1 x 1.4 cm nonmobile hyperechogenic mass attached to the right atrial side of ASO -> aortic root abscess
- **C, D** 1.6cm length elongated hypermobile echogenic material to the left atrial side of the device



(*Circulation*. 2015;131:e536-e538.



- **Treatment**: removal of the ASD through a right atrial approach
  repair of inflamed and partially ruptured noncoronary sinus
- **A** arrow : abscess pockets and necrotic debris around the device rim
- **B** The removed ASO -> incomplete endothelialization on the left atrial surface of the metallic mesh
- 6 weeks of antibiotics after surgery with nafcillin + rifampin + gentamicin

(*Circulation*. 2015;131:e536-e538.

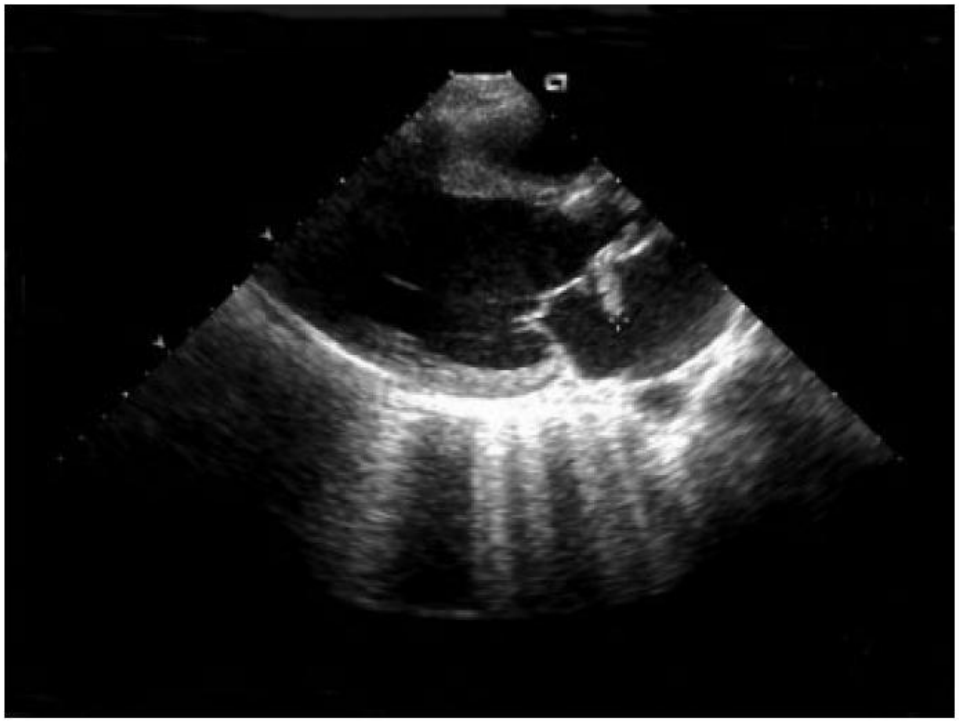
Case reports of IE with VSD device

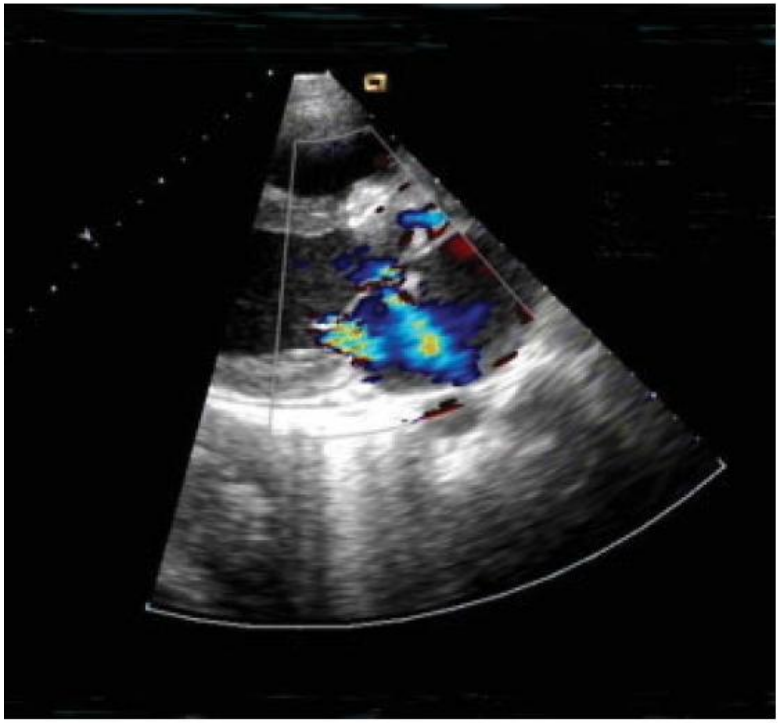
- Endocarditis after closure of ventricular septal defect by transcatheter device

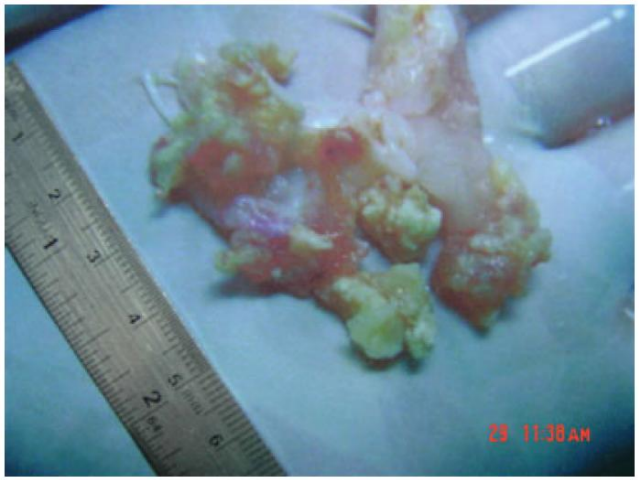
Pediatrics 2006;117:e1256-8

- Complication associated with transcatheter closure of perimembranous ventricular septal defects
  - 210 patients using the Amplazter PmVSD between 2005 and 2006
  - One case of infectious endocarditis
  - 7 months after the initial procedures
  - Fever, new systolic murmur
  - A vegetation on color Doppler
  - Surgical removal

Catheter Cardiovasc Inverv 2008;71:559-563







- **7 months after** the initial procedure
- Fever, palpitation, tachypnea, murmur
- No splinter hemorrhage or Roth's spots
- A 18x 8 mm **vegetation on the mitral valve** on color Doppler
- Blood culture negative
- Surgical removal after antibiotics for 2 weeks
- **Vegetations on the MV and AV on surgical finding**

Case report of IE with PDA device

- Residual shunt after ductus arteriosus occluder implantation complicated by late endocarditis
  - 20-year-old woman
  - PDA closure with a **Rashkind occluder at 4 years of age**
  - **A small residual shunt** at 6 month follow-up
  - Dental procedure with IE prophylaxis before 4 months
  - *Streptococcus acidominimus*
  - 5 x 8mm vegetation on the left pulmonary artery with attachment to the Rashkind occluder
  - Another vegetation on the main pulmonary artery along the persistent left-to-right shunt
  - Antibiotics and surgical removal

Circulation;2012;125:840-2

Bloodstream Infections Occurring in Patients With Percutaneously Implanted Bioprosthetic Pulmonary Valve

A Single-center Experience

Jonathan Buber, MD; Lisa Bergersen, MD, MPH; James E. Lock, MD; Kimberlee Gauvreau, ScD; Jesse J. Esch, MD; Michael J. Landzberg, MD; Anne Marie Valente, MD; Thomas J. Sandora, MD, MPH; Audrey C. Marshall, MD

Background—Percutaneous pulmonary valve implantation using a stent-based bioprosthetic valve provides an alternative to surgery in select patients. Systemic infections in Melody valve–implanted patients with and without identified valve involvement have been reported, yet the incidence is unknown, and risk factors remain unidentified.

Methods and Results—Between 2007 and 2012, a total of 147 consecutive patients with congenital heart disease underwent Melody percutaneous pulmonary valve implantation at our institution. Demographic and clinical variables were collected at baseline and at follow-up and analyzed as predictors. The occurrence of bloodstream infection (BSI), defined as a bacterial infection treated with ≥4 weeks of antibiotics, served as our primary outcome. The mean age at implantation for the study population was 21.5±11 years, and tetralogy of Fallot was the cardiac condition in 59%. During a median follow-up of 19 months, 14 patients experienced BSI (9.5%; 95% confidence interval, 5.3%–15%). Of these, 4 (2.7%) patients had Melody valve endocarditis. Two patients died during the event, neither of whom had known valve involvement. The median procedure to infection time was 15 months (range, 1–56). In univariate analysis, male sex, previous endocarditis, in situ stents in the right ventricular outflow tract, and presence of outflow tract irregularities at the implant site were associated with BSI occurrence.

Conclusions—In this cohort, 9.5% of patients who underwent Melody percutaneous pulmonary valve implantation experienced subsequent BSI, occurring 1 to 56 months after implant, and 2.7% of patients had prosthetic endocarditis. Our findings suggest that patient and nonvalve anatomic factors may be associated with BSI after percutaneous pulmonary valve implantation. (***Circ Cardiovasc Interv*. 2013;6:301-310.**)

Transcatheter pulmonary valve

- Bloodstream infection(BSI) occurring in patients with percutaneously implanted bioprosthetic pulmonary valve - a single-center experience
  - 147 patients between 2007 and 2012
  - During a median follow up of 19 months, 14 patients -> BSI
  - 4 (2.7%) patients had Melody valve endocarditis
  - 2 patients died (*Staphylococcus aureus*)
  - The median procedure to infection time: 15 months
  - Male, previous endocarditis, in situ stents, outflow tract irregularity

Circ Cardiovasc Interv 2013;6:301-310

Change of the epidemiology of infectious endocarditis (IE)

- Decreased mortality d/t antibiotics, early defection, surgical management, advances in postoperative care
- Bacterial species from viridans streptococci -> staphylococci
- Underlying condition from unoperated congenital heart disease(CHD) and rheumatic heart disease(RHD) to postoperative CHD and no heart disease with intravascular cannulae
- IE and CHD treated nonoperatively remains a concern

Infect Dis Clin N Am 29 (2015) 513–524

Thank you for attention!