

# Infective Endocarditis

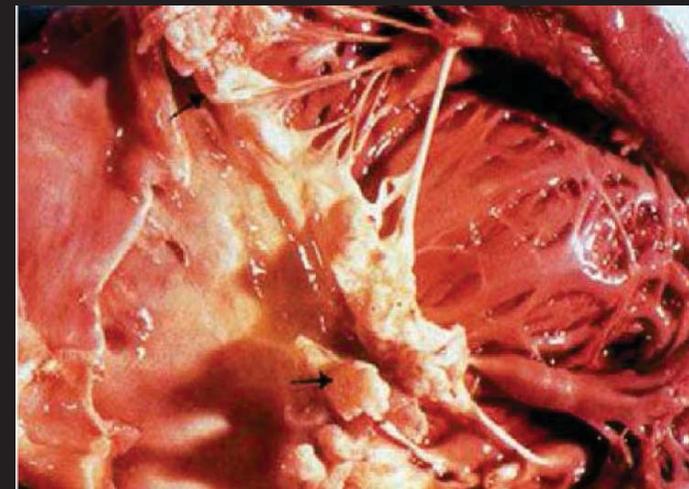
Pattaya Riengchan M.D.  
MAR 16, 2017

## Definition

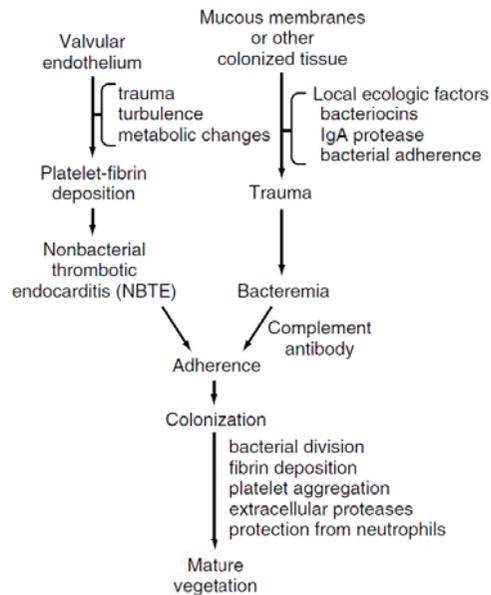
- **Acute endocarditis** : fulminant course, death within less than 6 weeks. *S.aureus*, *S.pneumoniae*, *S.pyogenes*, *N.gonorrhoeae*.
- **Subacute to chronic endocarditis** : mainly caused by viridans streptococci

## Definition

- Infection of **endocardial surface** of the heart and implies the physical presence **microorganisms in the lesion**
- **Heart valves** are most commonly affected, also may occur in septal defects or on the mural endocardium
- Microorganisms : chlamydiae, mycoplasma, rickettsiae, fungi and viruses



**Vegetation : mass of platelets, fibrin, microcolonies of microorganisms and scant inflammatory cells**



## NBTE

- Found in patients with malignancy (pancreas, gastric or lung)
- Other chronic wasting disease
- Rheumatic and congenital heart disease
- Uremia and connective tissue disease
- Placement of intracardiac catheter
- Found in 2.4% of 3,404 autopsies especially in elderly with chronic wasting disease

Angrist AA., JAMA 1963;183:249  
Chino F., Am Heart J; 1975;90:190

## NBTE

- NBTE is most common on the low-pressure side of cardiac valve
- Hypercoagulable states may contribute to the development and propagation of NBTE
- In 1,024 cases autopsies, valvular lesions were found in :  
mitral valve 86%, aortic 55%, tricuspid 19.6 and pulmonic 1.1%

Kupferwasser LI. Am J Coll Cardiol. 1999;33:1365  
Lepeschkin E. Am J Med Sci. 1952;224:318

## Incidence of bacteremia after various procedures

procedure		% positive blood culture
Dental	Dental extraction	18-85
	Periodontal surgery	32-88
	Chewing candy or paraffin	17-51
	Tooth brushing	0-26
	Oral irrigation device	27-50
Upper airway	Bronchoscopy (rigid scope)	15
	Tonsilectomy	28-38
	Nasotracheal suction/intubation	16
Gastrointestinal	Upper GI endoscopy	8-12
	Sigmoidoscopy/colonoscopy	0-9.5
	Barium enema	11
	Percutaneous needle biopsy of liver	3-13

## Incidence of bacteremia after various procedures

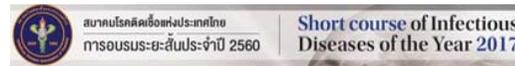
procedure		% positive blood culture
Urologic	Urethral dilatation	18-33
	Urethral catheterization	8
	Cystoscopy	0-17
	Transurethral prostatic resection	12-46
Obstetric/gynecologic	Normal vaginal delivery	0-11
	Punch biopsy of the cervix	0
	Removal/insertion of IUD	0



Everett ED., Medicine(Baltimore). 1977;56:61

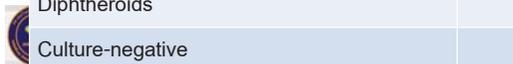
## Transient bacteremia

- Usually with low-virulence flora, sterile in 15-30 minutes
- Ability of certain organisms to adhere to the lesion plays important role in IE
- Both direct impact and reaction with platelet to form vegetation



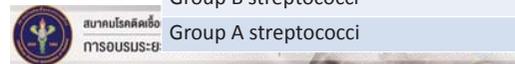
## Organisms causing native valve endocarditis (%)

organism	Community-acquired (n=1,718)	Health care associated (n=1,110)
Streptococci	40	13
Pneumococci	2	-
Enterococci	9	16
<i>Staphylococcus aureus</i>	28	52
Coagulase-negative staphylococci	5	11
HACEK group	3	-
Gram negative bacilli	1	1
<i>Candida</i> spp.	< 1	1
Polymicrobial/miscellaneous	3	3
Diphtheroids	-	< 1
Culture-negative	9	3



## Ratio of IE and non-IE bacteremia for various Streptococci and Enterococci

Organisms	IE:non-IE ratio
<i>Streptococcus mutans</i>	14.2:1
<i>Streptococcus bovis</i> I	5.9:1
Dextran-positive <i>Streptococcus mitior</i>	3.3:1
<i>Streptococcus sanguinis</i>	3:1
<i>Streptococcus mitior</i>	1.8:1
Unclassified viridans Streptococci	1.4:1
<i>Enterococcus faecalis</i>	1:1.2
Miscellaneous streptococci	1:1.3
<i>Streptococcus bovis</i> II	1:1.7
<i>Streptococcus anginosus</i>	1:2.6
Group G streptococci	1:2.9
Group B streptococci	1:7.4
Group A streptococci	1:32



## The Modified Duke Criteria, Major

### 1. Positive blood culture with typical microorganism from two separate blood culture

Viridans streptococci, *Streptococcus gallolyticus*, HACEK group

organism, *Staphylococcus aureus*, or community-acquired enterococci

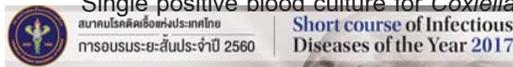
in the absence of primary focus, or

microorganisms consistent with IE from **persistently positive blood cultures**

Blood culture drawn > 12 h apart

All of 3 or majority of  $\geq 4$  separate blood cultures, first and last drawn at least 1 h apart

Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1:800



## The Modified Duke Criteria, Major

### 2. Evidence of endocardial involvement

Positive echocardiogram

**Oscillating intracardiac mass** on valve or supporting structures or in the part of regurgitant jets or in implanted material, in the absence of an alternative anatomic explanation, or

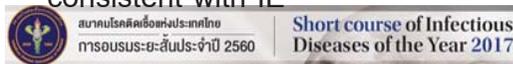
Abscess or new partial dehiscence of prosthetic valve

New valvular regurgitation (increase or change in preexisting murmur not sufficient)



## The Modified Duke Criteria, Minor

1. **Predisposition** : predisposing heart conditions or injection drug use
2. **Fever**  $\geq 38.0^{\circ}\text{C}$  ( $\geq 100.4^{\circ}\text{F}$ )
3. **Vascular phenomena** : major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
4. **Immunologic phenomena** : glomerulonephritis, Osler's nodes, Roth's spot, rheumatoid factor
5. **Microbiologic evidence** : positive blood culture but not meeting major criterion, or serologic evidence of active infection with an organism consistent with IE



## Definition of IE according to the modified Duke Criteria

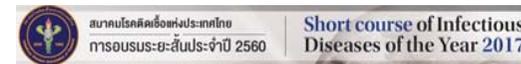
### • Definite

#### Pathological criteria

Microorganisms demonstrated by culture or histological examination of a vegetation, a vegetation that has embolized or an intracardiac abscess specimen, or a pathological lesion, vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

#### Clinical criteria

**2 major criteria, 1 major and 3 minor criteria or 5 minor criteria**



## Definition of IE according to the modified Duke Criteria

- Possible IE

1 major and 1 minor criteria, or 3 minor criteria

- Rejected

Alternative diagnosis explaining evidence of IE; or resolution of IE syndrome with antibiotic therapy for  $\leq 4$  days, or does not meet criteria for possible IE as above

- IE is a heterogeneous disease with highly variable clinical presentations, the use of these criteria alone will never suffice

- The Duke criteria are meant to be a guide for diagnosis IE and must not replace clinical judgment

[AHA Scientific statement. Circulation 2015]



### Demographic and clinical characteristics of patients with IE in Khon Kaen, Thailand and Rennes, France

	Khon Kaen (N = 58)	Rennes (N = 58)	P value
Median age, years (range)	47 (18–75)	70 (17–86)	< 0.001
Male	72%	67%	0.69
Lives in rural area	91%	49%	< 0.001
Animal contact	86%	21%	< 0.001
Received antibiotics during the week before admission	71%	48%	0.01
Blood culture-positive	31%	79%	< 0.001
RHD	31%	4%	0.001
Prosthetic heart valve	9%	35%	0.001

History/exposure	Possible disease
IVDU	<i>S.aureus</i>
Inhalation/ingestion/contact with goat, sheep, cattle, cat, others	<i>C.burnetii</i>
Contact with infected sheep, goat, others Ingestion dairy products	Brucellosis
Contact to swine, fish	<i>Erysipelothrix rhusiopathiae</i>
Contact to cat, mammals	<i>Bartonella</i> spp.
Abdominal surgery	Fungus, esp. <i>Candida</i> spp.

### Findings in more than 2,700 patients with definite IE

signs	Patients (%)
Fever	96
Heart murmur	85
Changing murmur	20
New murmur	48
Vascular embolic event	17
Osler's nodes	3
Splinter hemorrhages	8
Janeway lesion	5
Splenomegaly	11
Roth's spot	2
Hematuria	26
Conjunctival hemorrhage	5

### Other findings

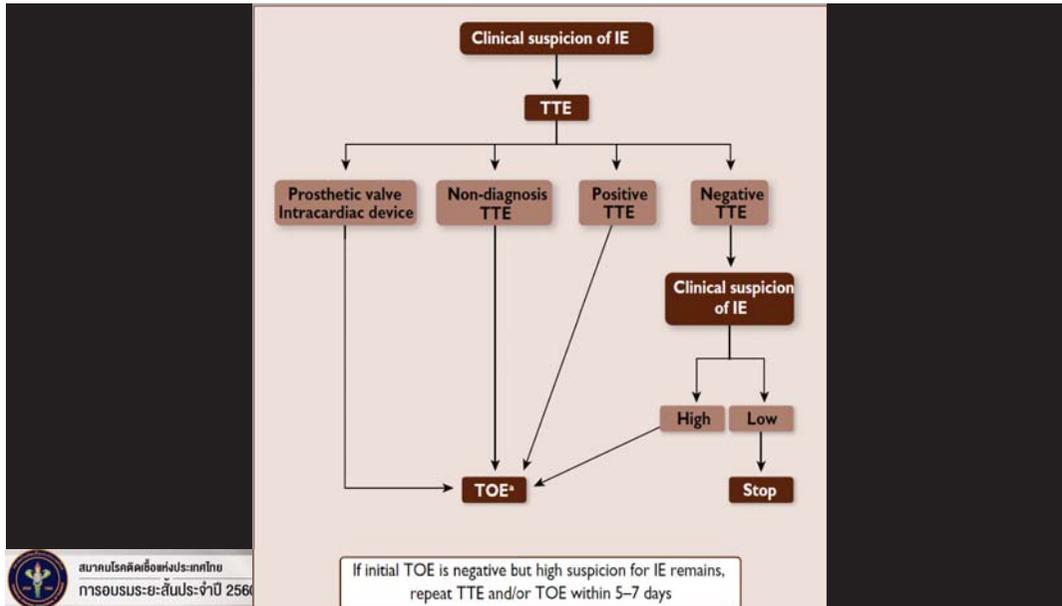
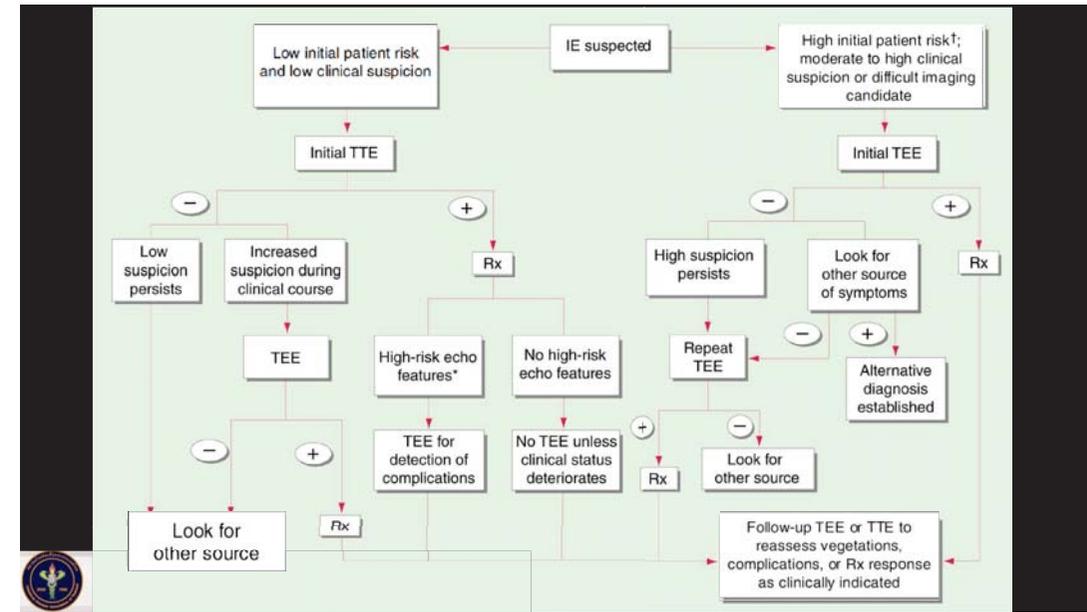
- Anemia is almost always present (70-90%) (NCNC)
- Leukocytosis in 20-30% (rare in subacute variety), thrombocytopenia 5-15%
- False positive VDRL 0.2%
- Abnormal urinalysis is common, proteinuria (50-65%), microscopic hematuria (30-60%), red blood cell cast (12%)
- Elevated ESR (60%), hypocomplementemia (5-15%)

### Blood culture obtaining

- Three set of optimally filled blood cultures (10 ml;ESC 2015) from different peripheral sites
- Sampling of intravascular line should be avoided
- Antibiotic therapy may need to be stopped 7-10 days before blood culture become positive
- Do not need to be timed with peak of fever

## Culture negative endocarditis

- Prior antibiotic treatment
- Slow growth or fastidious organism : anaerobes, nutritionally variant streptococci, brucellosis
- Obligate intracellular parasite : Rickettsiae, Chlamydia, *T. whipplei*, virus
- Subacute right sided IE, mural IE, as in VSD



## Echocardiography

- TTE has a sensitivity of 50-90% and a specificity of 90% for suspected native valve endocarditis
- Diagnosis, detection of complication and assesses cardiac function

**Table 1** Studies comparing the sensitivity and specificity of transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE) in the diagnosis of vegetations

	No.	Sensitivity (%)		Specificity (%)	
		TTE	TOE	TTE	TOE
Shapiro <i>et al</i> <sup>6</sup> 1994	64	60	87	91	91
Erbel <i>et al</i> <sup>7</sup> 1988	96	63	100	98	98
Shively <i>et al</i> <sup>8</sup> 1991	66	44	94	98	100

Prendergast. Heart 2004;90(6):611

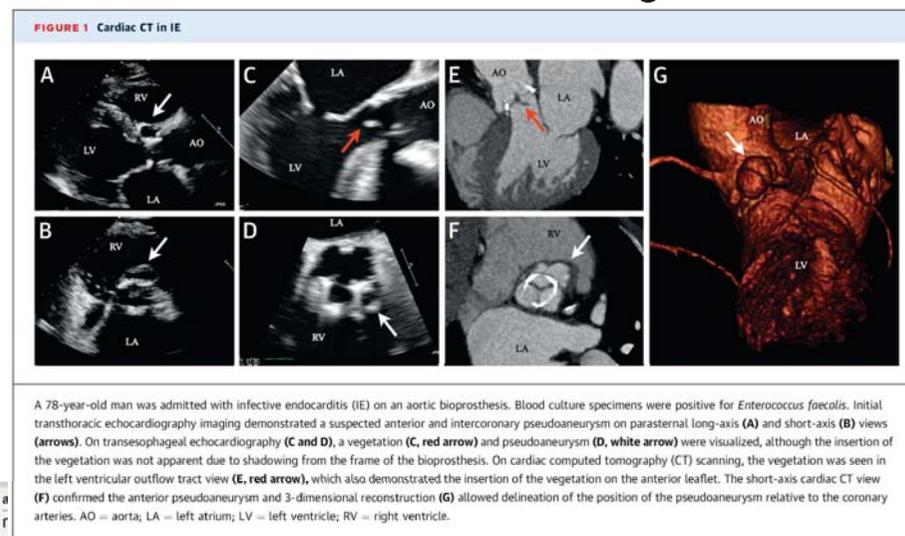
## Limitation of TTE

- Chronic obstructive lung disease, previous thoracic or cardiovascular surgery, morbid obesity
- False-negative: small vegetation (<5mm), presence of pre-existent lesions ;mitral valve prolapse, degenerative lesions, prosthetic valves
- False-positive: cardiac tumors, thrombi, fibrous
- Limit to detect complication of IE; abscess, valve perforation, pseudoaneurysm

## Limitation of TEE

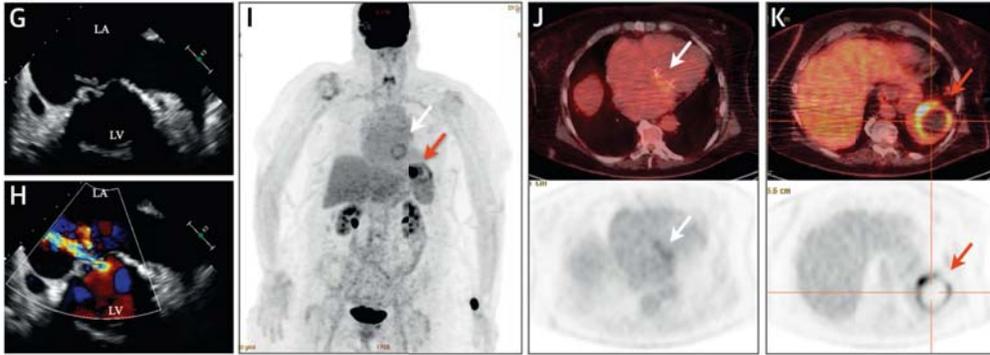
- Availability
- Not candidate in patient who have eaten within preceding 6 hours
- Quantifying hemodynamic dysfunction, ventricular dysfunction, and elevated left and right ventricular filling pressure and pulmonary artery pressure
- Tricuspid vegetation, abnormality of RV outflow tract

## Cardiac CT scanning



## 18FDG-PET/CT imaging

FIGURE 2 Continued



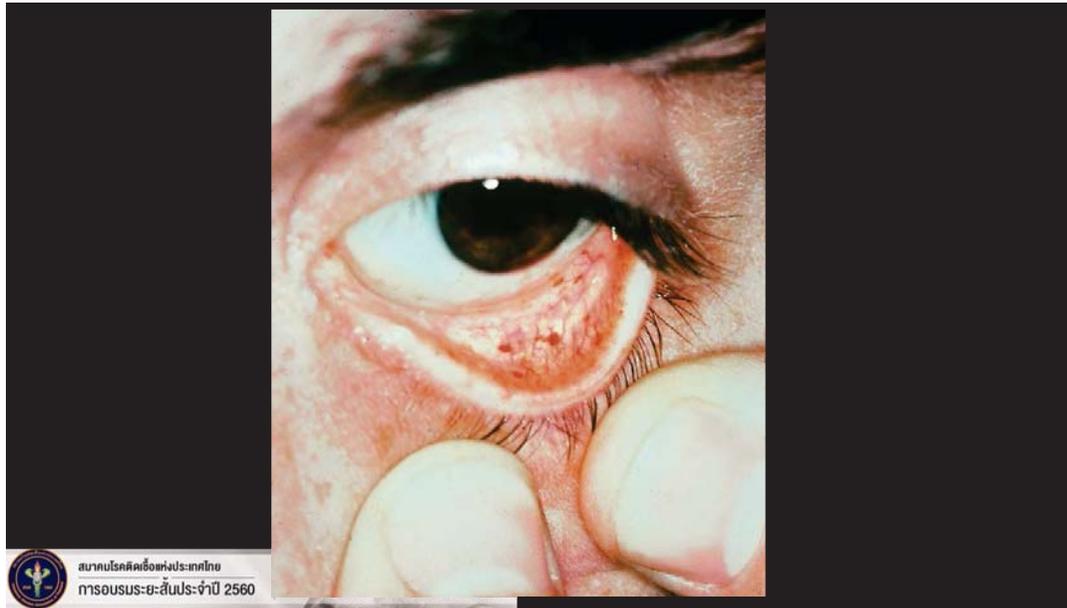
Panels G to K: A 65-year-old woman with a mitral bioprosthesis was diagnosed with *S. aureus* IE. TEE revealed a mobile vegetation with leaflet prolapse and severe regurgitation (G and H). On 18FDG-PET/CT imaging, there was 18FDG signal from the mitral bioprosthesis (I and J, white arrow) and evidence of a splenic abscess (I and K, red arrow). 18-Fluorodeoxyglucose positron emission tomography (18FDG-PET/CT)



Septic emboli from *S. aureus* endocarditis



Janeway lesions in patient with *S. aureus* IE



## Embolic phenomena

- 15-35%, most frequently involving renal, splenic, coronary or cerebral circulation
- Major vessels occlusion by large emboli can be found in fungal IE, marantic endocarditis and intracardiac myxoma
- Mycotic aneurysms are more common in viridans streptococci IE, tend to occur at bifurcation point, commonly in the cerebral vessel



## Immunologic phenomena

- Rheumatoid factor in 50% of patients after 6 weeks duration and 24% less than 6 weeks duration
- Circulating immune complexes may develop a diffuse glomerulonephritis
- Osler's nodes as result of circulating immune complexes deposition

Table 2. Bacterial species identified in 60 patients with infective endocarditis, Khon Kaen, Thailand, January 2010–July 2012\*

Disease type, organisms	No. (%) cases
<b>Zoonoses</b>	<b>15 (25)</b>
<i>Coxiella burnetii</i> †	5
<i>Bartonella henselae</i> †	4
<i>Streptococcus suis</i>	4
<i>Erysipelothrix rhusiopathiae</i> †	1
<i>Campylobacter fetus</i> †	1
<b>Nonzoonoses</b>	<b>45 (75)</b>
<i>Enterococcus faecalis</i>	6
<i>Enterococcus</i> spp.	4
<i>Staphylococcus aureus</i>	5
Coagulase-negative <i>Staphylococcus</i> sp.	2
Viridans streptococci	5
<i>Streptococcus agalactiae</i>	4
<i>Streptococcus anginosus</i>	4
<i>Streptococcus gordonii</i>	2
<i>Streptococcus gallolyticus</i> †	2
<i>Streptococcus mitis</i>	2
<i>Streptococcus dysgalactiae</i>	1
<i>Streptococcus oralis</i>	1
<i>Streptococcus diffcilis</i> †	1
<i>Streptococcus pneumonia</i>	1
<i>Streptococcus sinensis</i> †	1
<i>Streptococcus</i> spp.	1
<i>Corynebacterium diphtheriae</i>	1

### The first reported cases of Q fever endocarditis in Thailand

Orathai Pachirat,<sup>1</sup>  
 Pierre-Edouard Fournier,<sup>2</sup>  
 Burapha Pussadhamma,<sup>1</sup>  
 Suthep Taksinachankij,<sup>1</sup>  
 Viraphong Lulitanond,<sup>1</sup>  
 Henry C. Baggett,<sup>3</sup>  
 Somsak Thamthitawat,<sup>3</sup> George Watt,<sup>3</sup>  
 Didier Raoult,<sup>2</sup> Susan A. Maloney<sup>3</sup>

<sup>1</sup>Departments of Medicine and Cardiovascular Surgery, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; <sup>2</sup>Unite de Recherche sur les Maladies Infectieuses et Tropicales Emergentes, Faculte de Medicine, University of the Mediterranean, Marseille, France; <sup>3</sup>International Emerging Infections Program, Thailand MOPH-US CDC Collaboration, Nonthaburi, Thailand

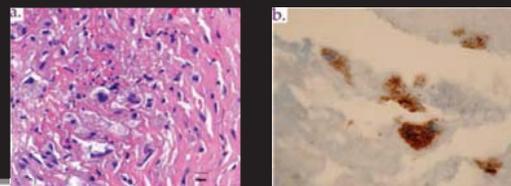
### Case Report #1

A 52-year old male rice and cattle farmer presented to hospital with a history of recurrent episodes of congestive heart failure during the previous two months. On admission, he was afebrile and had signs of severe aortic regurgitation. A transthoracic echocardiogram demonstrated severe aortic as well as mitral valve regurgitation. Six sets of blood cultures were negative. The patient underwent aortic valve replacement, and an aortic root abscess and perforation of the right coronary cusp were found intraoperatively. Serology was diagnostic for chronic Q fever, with a serum IgG antibody titer of 1:25,600 to phase I antigens of *Coxiella burnetii*, the causative agent of Q fever. IgG titers greater than 1:800 to phase I *C. burnetii* are considered diagnostic of chronic Q fever.<sup>4</sup> The resected aortic valve tested positive by 16S rRNA PCR for *C. burnetii*. Immunohistochemical staining demonstrated the causative organism within a background of chronic granulomatous inflammation (Figure 1).

### Case Report #2

A 42-year old male shoe salesman was admitted to hospital for aortic valve replacement. Past medical history was notable for chronic aortic valvular disease of 8 years duration. During the year prior to admission, the patient had experienced several episodes of congestive heart failure without fever. Three months prior to admission, the patient was referred to hospital because of severe aortic stenosis, aortic regurgitation and congestive heart failure and was treated for heart failure as an outpatient while awaiting surgery. On admission the patient was afebrile and had no stigmata of infective endocarditis. A transthoracic echocardiogram demonstrated no vegetative lesions. The patient underwent aortic valve replacement because of congestive heart failure but intraoperatively the aortic valve was noted to be badly damaged with multiple perforations, so the patient was referred for evaluation of possible infective endocarditis. The resected aortic valve was not tested by either

PCR or immunohistochemistry for *C. burnetii*. After blood cultures were obtained, the patient was placed on broad-spectrum antibiotic therapy. Blood cultures were negative but serology was diagnostic for chronic Q fever, with a serum anti-*C. burnetii* IgG1 antibody titer of 1:6,400. Although the patient did not raise cattle, several neighbors raised livestock, and exposure to these cattle is suspected.



### The first reported case of Bartonella endocarditis in Thailand

Orathai Pachirat,<sup>1</sup> Michael Kosoy,<sup>2</sup>  
 Ying Bai,<sup>2</sup> Sompop Prathani,<sup>1</sup>  
 Anucha Puapairoj,<sup>1</sup> Nordin Zeidner,<sup>2</sup>  
 Leonard F. Peruski,<sup>3</sup> Henry Baggett,<sup>3</sup>  
 George Watt,<sup>3</sup> Susan A. Maloney<sup>3</sup>

<sup>1</sup>Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand;  
<sup>2</sup>Bacterial Diseases Branch, Division of Vector Borne Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado USA;  
<sup>3</sup>International Emerging Infections Program (IEIP), Thailand MOPH-US CDC Collaboration, GDD Regional Center, US CDC SE Asia Regional Office, Nonthaburi, Thailand

### Case Report

A 57-year old male poultry farmer with underlying rheumatic heart disease presented to a local hospital with a 5 day history of fever, muscle pain and shortness of breath. He was found to be in congestive heart failure and was transferred to the regional cardiac referral center, Srinagarind Hospital, Khon Kaen, Thailand. On admission, he had fever of 39.0°C., heart murmurs consistent with aortic stenosis, aortic regurgitation, mitral stenosis and mitral regurgitation, signs of congestive heart failure, anemia and digital clubbing. A transthoracic echocardiogram showed a large, mobile vegetation on the aortic valve (Figure 1) and on the mitral valve.

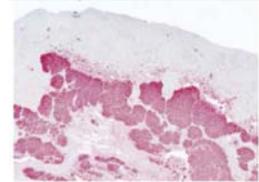
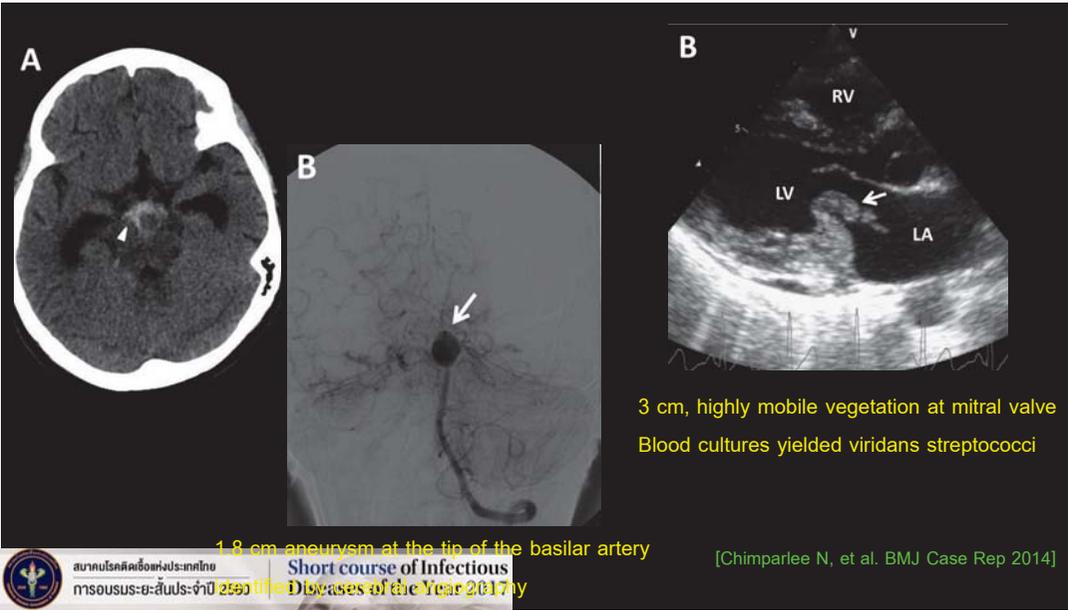


Figure 2. Immunoalkaline phosphatase staining of resected heart valve tissue using a monoclonal antibody reactive only with *Bartonella henselae* shows bacteria staining red (20X magnification).





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