# Acute Bacterial Endocarditis in Intravenous Drug Users: Case Presentation and Review

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### Acknowledgement

Acknowledgment: The Department of Family Medicine and Division of Emergency Medicine University of Alberta, Edmonton, Canada for their assistance in kind.

### Abstract

The diagnosis and treatment of complications of intravenous drug use in the emergency department are challenging. Intravenous drug use is a significant risk factor for the development of acute bacterial endocarditis. Commonly, these patients develop endocarditis on the right sided heart valves; however, left sided involvement is not unusual. The mortality is significantly higher with left sided heart pathology. Fever is the most common symptom associated with this disease. Other signs and symptoms present will depend on the side of the heart involved, site of embolisation of vegetations, and the general medical condition of the patient.

Staphylococcus species are the predominant bacteria associated with acute bacterial endocarditis in these patients. Empiric antimicrobial treatment should consist of an anti-staphylococcal penicillin and an aminoglycoside.

We report the case of an injection drug user with predominantly left sided involvement. The review that follows provides current update on epidemiology, pathogenesis, diagnosis and treatment of this entity.

Emergency physicians should maintain a high clinical suspicion and investigate and treat aggressively patients presenting with fever and a history of intravenous drug use.

### Introduction

The diagnosis of Acute Bacterial Endocarditis (ABE) is relatively uncommon in the Emergency Department (ED) and a missed diagnosis can have severe consequences for the patient.

The overall incidence of ABE is significantly higher in the Intravenous Drug Use Population (IVDU) contrasted with the Non-Intravenous Drug Use (NIVDU) population (150-2000 per 100000 vs. 1.7-6.2 per 100000 people years) (1,2,3). The mortality of this disease in both the IVDU and the NIDVU populations may be as high as 25% (4,5). Within the IVDU population, mortality is a consequence of the infectious agent, as well as the side of the heart involved (4). In the IVDU there is predominantly right-sided heart involvement, with morbidity and mortality associated with cardiac and/or pulmonary complications. In contrast, in the NIDVU population, death and complications are more likely a result of direct cardiac involvement and systemic emboli from left heart.

In this article, we present a case involving an IVDU with left sided cardiac involvement and systemic emboli. A review of the pathophysiology, clinical presentation, and management in the ED of ABE in the IVDU population will complete the article.

### Case Presentation

A 47-year-old female sex worker and known IVDU was brought by Emergency Medical Services (EMS) to the ED of a major hospital. A friend called EMS because the patient was comatose. According to this friend, the patient was last seen 48 hours prior and at that time she was confused and very lethargic. No further history was available from EMS. The initial assessment in the ED revealed a comatose 47 year old female, looking much older than stated age, with vital signs as follows: BP = 127/47, pulse 155 and regular, RR 44, t° = 36.5°C, $O_2$ saturation = 100% on 15 l of $O_2$, GCS of 6\15 and a blood glucose of 26.3 mmol. The patient was intubated in the ED, and the fluid resuscitation with normal saline that was initiated by EMS was continued. A foley catheter and a nasogastric tube were also inserted. After initial resuscitation with normal saline the patients' temperature increased to 38.6°C.

The pertinent positive findings on complete physical examination were as follows: a grade III systolic ejection murmur best heard at the right upper sternum and radiating to the carotids, splinter haemorrhages, and black necrotic lesions up to 1 cm to hands and feet compatible with Janeway lesions (**Figure 1**), lack of movement of the left upper and lower limbs, as well as a up going left Babinski.

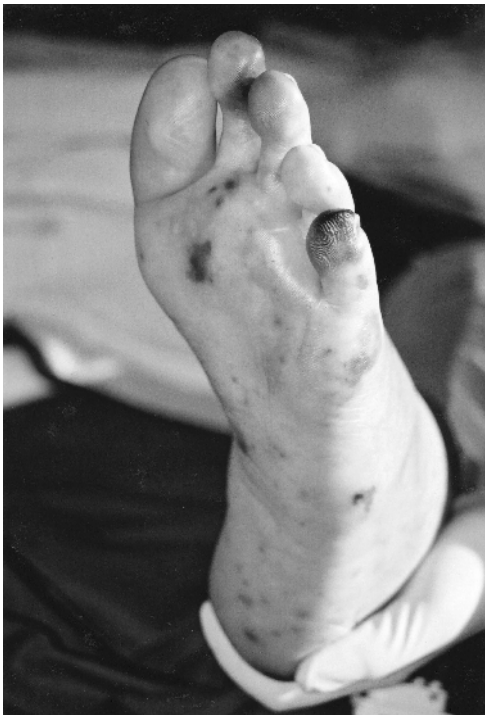

*Figure 1: Janeway lesions in ABE*

In the ED, initial blood work ordered consisted of the following: arterial blood gas, complete blood count, electrolytes, PT, PTT, BUN, creatinine, fibrinogen, blood cultures, serum lactate, CK, CKMB, type and screen, toxicology screen of ethanol, salicylate, and acetaminophen, barbiturates, hepatitis B, C and HIV serology. Urinalysis, urine myoglobin and urine osmolality were also requested. An ECG, chest x-ray and CT head were ordered.

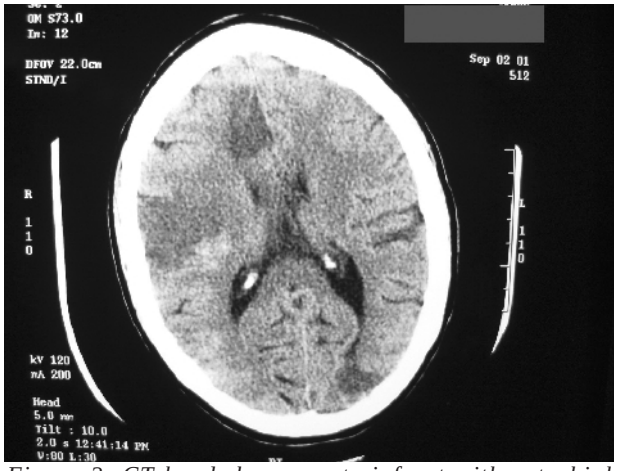


*Figure 2: CT head: large acute infarct with petechial haemorrhage involving the right anterior and right middle cerebral artery territories*

Initial laboratory investigations demonstrated (SI units): A Hb of 148, WBC 23.7, and neutrophils of 19.9. Platelets on admission were 8. Initial electrolytes in the ED were sodium 128mmol, potassium 2.3mmol, chloride 98mmol and bicarbonate 19.2mmol. Blood gas drawn after intubation revealed a pH of 7.42, pCO2 26, pO2 392, bicarb 19.2 and a saturation of 99%. Additionally her BUN was 17.5, creatinine 193, CK 3873 and lactate 5.8. The remainder of the blood work available in the ED was normal. Urinalysis demonstrated concentrated urine, positive for myoglobin and protein. ECG revealed sinus tachycardia at 155 and chest x-ray was reported as normal. CT head demonstrated a large acute infarct with petechial haemorrhage involving the right anterior and right middle cerebral artery territories (**Figure 2**).

Initial diagnosis of this patient was septic shock, secondary to ABE with multiple systemic emboli, and therefore presumably left sided cardiac involvement. Additionally, the patient was in renal failure secondary to dehydration.

Antimicrobial therapy initiated in the ED prior to blood work results consisted of Ceftazidime and Gentamycin.

The patient was admitted to the Intensive Care Unit (ICU). Transesophageal echocardiography demonstrated severe aortic insufficiency secondary to a bicuspid aortic valve and associated acute ABE. Blood cultures drawn in the ED grew Staphylococcus Aureus. Serology demonstrated the patient was Hep C positive and Hep B and HIV negative.

While in the ICU, the patient's condition continued to deteriorate with the development of complete renal failure and fungal septicaemia. In consultation with the family, active treatment was withdrawn three weeks after presentation

to the ED. The patient died 24 hours later. A post-mortem examination was not performed.

## Methodology

Two independent electronic database searches were carried out by one of the authors using Pub med in March 2002 and March 2003. The search was conducted using the Mesh terms ABE, intravenous drug use and sepsis. A total of 323 articles were identified in the English language literature between Jan 1979 and March 2003. Article selection criteria included relevance for current practice in areas of epidemiology, pathogenesis, diagnostic and therapeutic interventions. The final references selected for this case report and review were published after 1979, and include case presentations and narrative review articles.

## Discussion

### Epidemiology

As previously stated, the incidence of ABE is significantly higher in the IVDU population as compared to the NIVDU group. In the IVDU population, the approximate incidence of tricuspid vs. aortic and mitral valvulopathies is 70% and 30% (6). Also in the IVDU group, up to 76% of endocarditis occurs on the right side, in comparison to 9% right-sided involvement in the NIVDU population (7,8).

### Pathogenesis

In previously healthy individuals, IVDU is a significant predisposing factor for the development of ABE. Additionally, the risk of developing ABE is increased by the presence of the following: congenital and acquired heart defects, long-term haemodialysis, diabetes mellitus, poor dental hygiene and mitral valve prolapse (9-11).

In IVDU, increased right-sided ABE is thought to be multi-factorial. These include: bacterial load, differences in valves and cardiac valve endothelium, immunologic differences in this population, drug and particulate matter initiated pulmonary hypertension and increased right-side cardiac turbulence (3).

Staphylococcus Aureus is the most common infectious agent in ABE, being responsible for up to 70 % of the cases (4). Other organisms implicated include a variety of Streptococci (viridans streptococci, group A streptococcus) and enterococci (15- 20%), Pseudomonas aeruginosa, Serratia marcescens, other gram-negative rods (10%) as well as Candida species (2%) (6,12-15).

### Mortality

Mortality is a function of the type of valve involved and the nature of the infective organism.

In ABE with right-sided involvement where Staphylococcus is the bacteria, death occurs in less than 5% of patients, whereas in left sided disease with the same organism, death ensues in 20-30% of the cases (4). In contrast, overall mortality in patients infected with Streptococci viridans and bovis is 4-16% and in Enterococcus 15-25%. Pseudomonas aeruginosa, Enterobacteriacae, and fungi, though rare, carry an overall mortality of more than 50% (5).

Coexisting conditions that increase mortality include: congestive heart failure, neurologic events, renal failure and symptomatic HIV infection (16,17).

### Complications

Cardiac

ABE causes valve damage and this may result in right or left sided congestive heart failure. In rare cases, fragments of vegetations embolise to the cardiac blood supply, causing acute myocardial infarction and congestive heart failure. Coronary artery embolism may also result in pericarditis. Infection involving the aortic valve is more frequently associated with congestive heart failure than mitral valve infection. Cardiac complications include extension of the infection beyond the valve annulus into myocardium also resulting in congestive heart failure and the likely need for cardiac surgery.

Other cardiac complications may involve the septum leading to atrioventricular or bundle branch blocks. Erosion of a mycotic aneurysm can cause pericarditis, fistulas, hemopericardium and tamponade.

Neurological

Stroke syndromes can develop in 20 to 40% of IVDU patients who have left sided infective endocarditis (5).

Other

Systemic embolisation to other areas involves most often the spleen, kidney, liver, and the iliac or mesenteric arteries. Splenic abscesses can be a source for prolonged fever and may cause diaphragmatic irritation and pleuritic or left shoulder pain.

### Diagnosis

In the majority of cases of ABE in the IVDU, the presentation to the ED is not as dramatic as illustrated in our case presentation. Most patients are stable and the diagnosis is considered based on a thorough history and physical examination.

Symptoms:

Symptoms suggestive for right-sided ABE may include: fever, ischemic chest pain, pleuritic chest pain, shortness of breath, and hemoptysis.

Any other symptoms suggestive of end organ embolic events, such as neurological deficits, should raise the suspicion of left-sided ABE.

Non-specific generalized symptoms that may be associated with infective endocarditis include: anorexia, weight loss, malaise, and night sweats (5).

Signs:

Fever is the most common presenting sign in ABE (18,19). Fever may be absent or low grade in patients with congestive heart failure, chronic liver or renal failure, severe disability, previous antibiotic use, or infective endocarditis caused by less virulent organisms (5). Most patients will also have a heart murmur, predominantly tricuspid, followed by aortic and mitral. They may also have petechiae on the skin, conjunctivae, or oral mucosa, as well as other peripheral manifestations such as splinter haemorrhages, Osler's nodes and Janeway lesions (5).

Investigations:

In the IVDU with possible ABE, three sets of blood cultures collected by separate venipunctures are an important part of the initial diagnostic evaluation. Non-specific laboratory abnormalities associated with ABE may include anemia, leukocytosis, hematuria, proteinuria, pyuria, hyponatremia, hypokalemia, and an elevated ESR and C-reactive protein level. Therefore a CBC, electrolytes, ESR and C-reactive protein, as well as urinalysis should be considered as initial laboratory investigations. In ABE as a consequence of injection drug use, blood cultures are positive in more than 98 % of cases (8). Radiographs of the chest are abnormal in 55 -76 % of intravenous drug users with right-sided involvement (20,21). Chest x-rays often demonstrate single or multiple rounded or segmented pulmonary infiltrates (4).

Transthoracic echocardiography is a non-invasive test that has an overall sensitivity of less than 60-70% (22,23). Transesophageal echocardiography however, while being more costly and invasive, increases the sensitivity to 75 - 95% and maintains a specificity of 85 - 98% (24-26). The negative predictive value of a negative transesophageal echocardiogram is over 92% (27).

CT and MRI are other diagnostic modalities useful for diagnosis of systemic embolism. MRI is the diagnostic tests of choice for the diagnosis of splenic lesions, with a sensitivity and specificity of 90-95% (28,29).

Diagnosis of ABE involves integration of clinical, laboratory and echocardiographic data and is included in the modified Duke criteria (**Table 1**) (30). Definite diagnosis requires that either 2 major criteria are met, or one major plus three minor or five minor criteria. Probable cases are defined as fulfilling one major and one minor criterion or three minor criteria (30).

**Table 1: Modified Duke criteria for the diagnosis of ABE**

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| Major Criteria<br>Microbiological<br>1. Typical microorganism isolated from two separate blood cultures. Viridens streptococci, Streptococcus bovis, HACEK group*, Staphlococcus aureus, or community acquired enterococcal bacteraemia without a focus OR<br>2. Microrganism consistent with infective endocarditis isolated from persistently positive blood cultures OR<br>3. Single positive blood culture for Coxilla Burnetti or phase I IgG antibody titre for Coxilla Burnetti > 1800<br>Evidence of Endocardial involvement<br>4. New valvular regurgitation (worsening of preexisting not sufficient) OR<br>5. Positive echocardiogram (transesophageal recommended) |
| Minor criteria<br>1. Predisposition to infective endocarditis that includes certain cardiac conditions and injection drug use.<br>2. Fever (temperature > 38 degrees)<br>3. Vascular phenomena (petechiae and splinter haemorrhages excluded)<br>4. Immunologic phenomena (presence of rheumatoid factor, glomerulonephritis, Osler's nodes, or Roth Spots)<br>5. Microbiological findings (positive blood cultures that do not meet major criteria requirements. |

*Adapted from Li et al. (26)*
**HACEK: Hemophylus species, Actinobac*

### *Treatment*

The initial management of endocarditis in the IVDU is based upon patient presentation. Those in extremis need to be urgently resuscitated before any other considerations. Most patients will have a benign presentation and the main concern for treatment will be choice of appropriate antibiotics. This decision is based on the historical prevalence of organism seen in targeted populations. ABE is likely secondary to Staphylococcus aureus and first line therapy, such as nafcillin (unipen) or oxcillin are recommended (31,32). Vancomycin may be substituted in those with a penicillin allergy (33). Additionally, in right-sided infective endocarditis, the use of an aminoglycoside during the first 3-5 days of treatment reduces the duration of fever, leukocytosis and bacteremia (32,34).

Blood cultures drawn in the ED will help identify the infective organism. Therapy may then be adjusted

according to the organisms' susceptibility (32,34,35).

## Conclusions

The overall understanding of the pathogenesis, diagnosis and treatment of ABE has increased significantly in recent years. Patients who present to the ED with a fever greater than 38.5°C and a history of illicit drug injection should be strongly considered to have infective endocarditis. They should be aggressively investigated, and unless another obvious source for their fever is found they should be empirically started on an anti-staphylococcal penicillin

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