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Septic Embolism in Endocarditis: Anatomic and Pathophysiologic Considerations

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Abstract

Septic embolism is a relatively common and potentially severe complication of infective endocarditis (IE). Septic emboli (SE), most often described as consisting of a combination of thrombus and infectious material—either bacterial or fungal—can be caused by hematogenous spread from virtually any anatomic site; however, it most commonly originates from cardiac valves. During the past two decades there has been a confluence of various risk factors that, both alone and in combination, led to greater incidence of both IE and SE, including increasing population age, greater use of prosthetic valves, implantation of various intracardiac devices, escalating intravenous drug use, and the high incidence of healthcare associated infections with antibiotic resistant microorganisms. From a clinical standpoint, SE can present at any time during the course of IE and may even be the initial presenting sign. SE may affect virtually any location in the human body, but some organs (e.g., liver, spleen, brain) and anatomic regions (e.g., lower extremity) tend to be more frequently involved. The most important aspect of management involves prompt recognition and proactive therapeutic approach. Given the broad spectrum of clinical presentations, symptoms and complications, SE can be challenging to diagnose and treat. Following the identification of SE, appropriate antibiotic coverage should be immediately instituted followed by supportive and/or interventional management, depending on the severity of presentation and the associated complications. In this chapter we explore the pathophysiology, anatomic origins, diagnostic tools, therapeutic measures, and new developments in SE, focusing predominantly on bacterial infections of cardiac origin.

Keywords: endocarditis, infective endocarditis, morbidity and mortality, septic embolism

1. Introduction

The collective understanding of infective endocarditis (IE) has changed significantly since its early characterization by Sir William Osler [1, 2]. In most low-and-middle income countries, rheumatic fever accounts for approximately two-thirds of all endocarditis cases [3–5], whereas in developed countries it is responsible for less than 10% of instances [6]. Over the past decade the incidence of IE has been increasing, with a recent study showing an overall increase of >30% between 2000 and 2011 [7]. The American Heart Association identified IE and associated complications as a major source of cardiovascular disability [8].

This surge in IE has been linked, in part, to recent medical advances, including increased use of implantable cardiac devices and a growing population of patients with chronic comorbidities [5, 9, 10]. Moreover, 10–35% of newly diagnosed cases of IE are thought to be healthcare associated infections, and hospital-acquired IE attributable to sources other than cardiac surgery is an emerging problem with mortality as high as 30–50% [11, 12]. The above observations can be explained, to some degree, by increases in antibiotic resistance including greater incidence of methicillin-resistant *Staphylococcus aureus* (MRSA), and higher prevalence of comorbidities in an increasingly aging population [2, 5, 12, 13].

In terms of intravenous drug use, injectable heroin has seen significant escalation [14, 15], with an associated incidence of IE growing by 58% between 2000 and 2013 [14]. In addition to the disease burden on individual patients and their families, the health-care system is further taxed with managing this difficult and expensive to treat population [14, 16]. Finally, it is important to recognize that recent years have seen IE presentations becoming more acute in nature, making diagnosis and treatment more challenging at times [5, 17, 18]. Among key complications of acute IE, the development of potentially devastating septic emboli (SE) may be seen. In this chapter, we will focus on the pathophysiology, diagnosis, and management of SE in the context of IE, using a systematic anatomic approach and outlining some of the most recent developments in this fast-changing area of cardiovascular infectious disease.

2. Pathophysiology of septic emboli

When discussing the pathophysiology of emboli of cardiac origin, one must consider both non-infective (Libman-Sacks or autoimmune, Marantic or related to wasting illnesses such as cancer) and infective (e.g., bacterial or fungal) endocarditis [19–21]. As an overarching theme, any condition that results in structural “damage or alteration” of cardiac valves has the potential to trigger an inflammatory reaction leading to the formation of valvular “vegetations” and thromboembolic complications [22]. In contrast to non-infectious valvular etiologies which lead to sterile emboli, IE has the potential to produce SE which typically are composed of a conglomerate of infectious organisms, inflammatory cells, platelets and fibrin [23]. In contrast to non-infectious emboli, SE have the potential to result in both vascular compromise and hematogenous spread of infection [24–26]. Evidence shows that as many as 50–82% of patients with IE may be affected by some form of SE, including both symptomatic and sub-clinical

presentations [27–29]. In terms of valvular propensity for systemic (non-pulmonary) SE development, mitral valve is the most commonly involved [10, 30].

The genesis of SE is predicated on the appearance of a thrombus in a critical cardiac (usually valvular, **Figure 1**) location. This is usually associated with the presence of infected pacemaker leads, prosthetic valve, or some form of anatomic (acquired or congenital) abnormality of the native valve [30]. Bacterial species that feature specific adhesion matrix molecules are particularly likely to attach onto the damaged valvular surfaces, endocardium, or exposed prosthetic material [30–32]. Simultaneous presence of inflamed tissue and microorganisms leads to further accumulation of fibrin-platelet-microorganism complexes, contributing to the growth of infectious vegetations [33, 34]. If fragments of such vegetations—in whole or in part—are released into the circulation, SE is said to have occurred [5, 31, 32]. Microorganisms most often implicated include *Staphylococci*, *Beta-hemolytic Streptococci*, *Haemophilus*, *Actinobacteria*, *Caridobacterium*, *Eikenella*, and *Kingella*. The latter 5 are often listed under the acronym, “HACEK”, and are less likely to cause IE than *Staphylococci* and *Streptococci* [10, 32, 35, 36]. Identifying the causative organism is critical to instituting prompt treatment with the most appropriate antibiotics. It is important to recognize that SE may affect any organ system or anatomic location, although certain patterns of involvement tend to be more common than others. This chapter will review key clinical evidence and developments regarding the diagnosis and management of SE. The authors will organize the current discussion according to regional/anatomic considerations in order to systematize and simplify the review process.

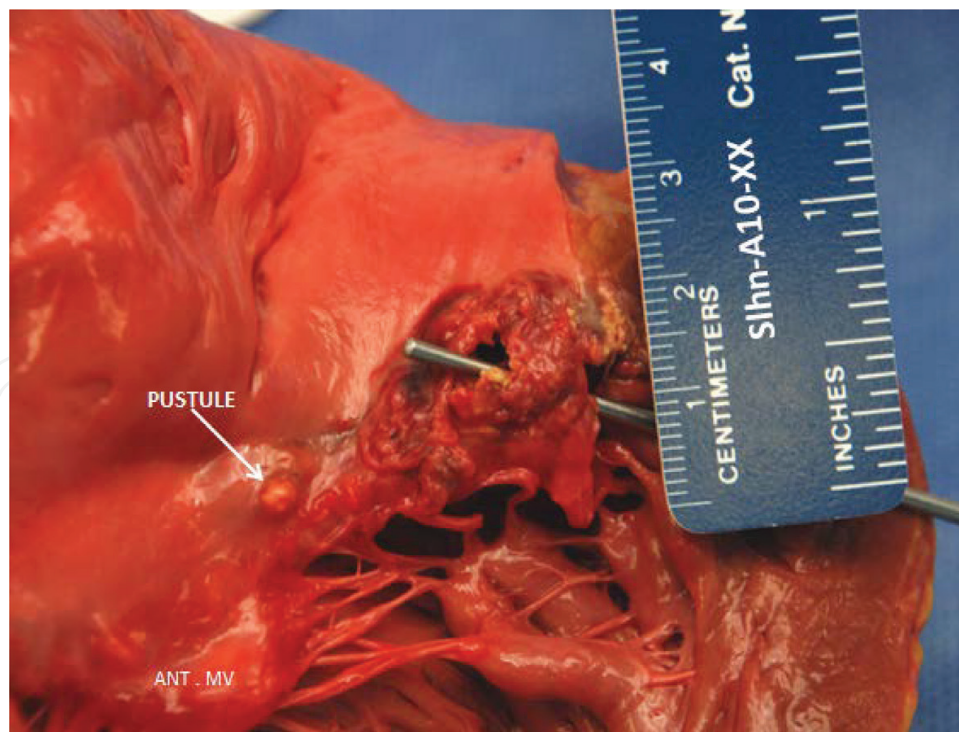


Figure 1. An example of a large necrotic bacterial vegetation, leading to the replacement of the entire posterior mitral valve leaflet. A pustule can be seen in the immediate vicinity of the vegetation. Also note the normal-appearing leaflet, chorda tendinea, and papillary muscles of the anterior leaflet (labeled as ANT. MV).

3. Head and neck

3.1. Brain

It is well known that there are many different central nervous system (CNS) manifestations of SE [37]. However, proving direct cause-and-effect relationship has been more challenging. Evidence suggests that septic cerebral embolic events may complicate as many as 40% of cases of IE, with recurrence rates for SE reaching 50% [38]. Cumulatively, manifestations of SE within the cerebral circulation can be divided into cerebral infarction (purely ischemic, purely hemorrhagic, or combined), CNS infection (encephalitis, meningitis, and abscess formation); and vasculopathy (vasculitis, mycotic aneurysm formation), with widely varied clinical presentations [38]. Summary of potential CNS manifestations of IE is provided in **Table 1**.

Involvement of SE within the CNS can be broadly categorized into cerebrovascular and non-cerebrovascular event types. Given that approximately 20% of cardiac output is dedicated to supplying the cerebrovascular system, it is no surprise that the brain is among the most commonly involved organs in IE. In fact, it is not uncommon for a cerebrovascular event to precede the formal diagnosis of IE, and to be the trigger for subsequent cardiac work-up [39]. Consistent with the above information, the greatest risk factor for a cerebral SE is left-sided IE, especially when due to *Staphylococcus aureus* infection. For embolic strokes, symptomatology heavily depends on the final resting point of the embolus. In one extreme case, complete cortical blindness followed the rupture of bilateral occipital mycotic aneurysms [40]. Even among patients with a limited duration of initial clinical symptoms, the risk of recurrent brain infarction may be as high as 80% [41]. **Figure 2** demonstrates septic embolism to the brain originating from mitral valve endocarditis.

Among patients experiencing CNS complications due to SE, approximately 50–60% have ischemic lesions, with the middle cerebral artery distribution being most commonly affected [42, 43]. Associated symptoms may include contralateral hemiplegia, homonymous hemianopia, dysarthric or aphasic speech, neglect, and sensory loss. It is difficult to differentiate

Cerebrovascular	Infections	Secondary complications	Rare complications
Ischemic stroke	Meningoencephalitis	Toxic-metabolic encephalopathy	Myeloradiculitis
Intracerebral hemorrhage	Cerebritis	Seizure	Spinal cord infarction
Subarachnoid hemorrhage	Abscess formation	Headache	Discitis/osteomyelitis
Mycotic aneurysm formation	Ventriculitis		Cranial neuropathies
	Ependymitis		Mononeuritis multiplex
			Myalgia

Adopted from Ref. [6].

Table 1. Central nervous system manifestations of infective endocarditis.

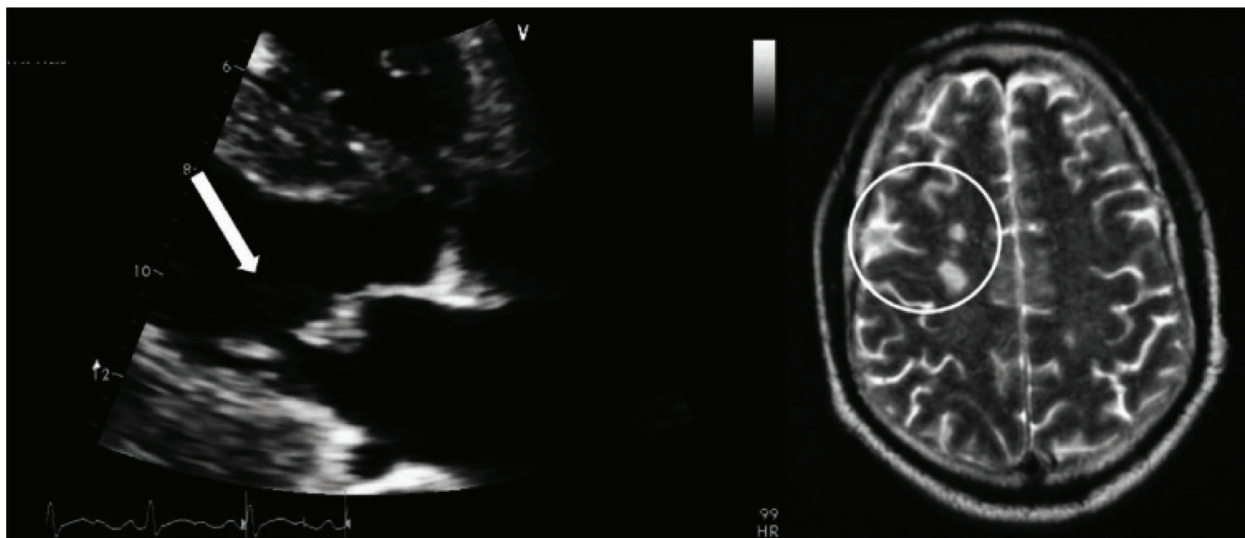


Figure 2. An example of septic embolization to the brain (circled) originating from an infected vegetation on the mitral valve (arrow) (source: Ref. [29]. Image used under the terms of the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported license).

between intracerebral hemorrhage and ischemic infarction based on clinical symptoms alone, and importantly, the American Stroke Association recommends against the use of intravenous Alteplase in cases of suspected ischemic stroke due to SE because of elevated potential for hemorrhagic conversion [23]. At the time of this publication there is no specific recommendation for or against intra-arterial intervention (e.g., thrombectomy) in the setting of SE causing large vessel occlusion and cerebral infarction, and cases should be evaluated on an individual basis.

Risk factors for mortality in stroke caused by SE include MRSA infection, older patient age, and larger vegetation size [44]. Patients with right-sided IE can also experience cerebral SE although it is very uncommon and occurs through the so-called “paradoxical embolus” pathway [45, 46]. Prompt evaluation for cerebral SE is critical in any patient presenting with focal neurologic symptoms, and usually starts with computed tomography (CT) of the brain to rule out bleeding, and potentially CT-Angiography to evaluate the cerebral circulation for patency. One must keep in mind that, regardless of clinical symptoms, the majority of patients with IE have some evidence of cerebral SE on magnetic resonance imaging (MRI) [47, 48].

Patients with cerebral SE have elevated mortality rates compared to patients presenting with stroke from other etiologies. In fact, baseline mortality of approximately 8–9% may reach nearly 40% in the presence of meningitis, hemorrhage, or brain abscess [39]. In the setting of mild cerebral ischemia, immediate antibiotic therapy combined with valve surgery within 48 h results in improved outcomes, including fewer systemic embolic events and more favorable mortality profile [49]. Recent studies also suggest that an ischemic stroke secondary to IE is unlikely to transform into a hemorrhagic stroke [50]. Primary indications for surgery in the setting of IE include the emergence of heart failure, uncontrolled infection, and embolism prevention [49]. Note that antithrombotic therapy is somewhat controversial in this setting. The American Heart Association guidelines for surgical intervention state that in the absence of severe neurological deficits, cardiac surgery should be considered urgently [50, 51]. In cases

of severe ischemic stroke, it is recommended to delay surgery by at least 4 weeks, and with hemorrhagic stroke (usually a more severe complication) at least 4 weeks are recommended prior to proceeding with cardiac surgery [50].

3.2. Eyes

Septic embolization involving ocular and facial structures is extremely rare. There is, however, fragmentary case-based evidence for such occurrences. In one example, Dadu et al. [52], described SE involving the ophthalmic artery and the inferior muscular artery, resulting in diplopia due to medial rectus muscle paralysis. In that particular case, IE of the mitral valve was causative. In another rare occurrence, Cumurcu et al. [53], describe a case of a septic metastasis to the iris, resulting in iris abscess and endophthalmitis.

3.3. Thyroid

The possibility of SE to the thyroid has been proposed in 1959 by Richie while describing acute suppurative thyroiditis in a child [54]. Cabizuca et al. [55], reported an unusual case of IE leading to acute thyroiditis, presumably due to septic embolization. Although undoubtedly uncommon, the paucity of literature reports in this area is likely due to limited awareness and under-recognition of similar clinical presentations.

4. The thorax

Given the pathophysiologic factors discussed earlier in the chapter, SE of cardiac origin tend to follow the pattern of “cardiac output.” Consequently, a generalization can be made that the higher the blood flow to a specific organ or anatomic region, the higher the chance of SE traveling there. Within the thorax, there are two commonly described types of septic emboli—those originating on the “left side” of the heart and involving the coronary arterial circulation or thoracic aorta [56, 57], and those originating from the “right side” and involving the pulmonary arterial circuit [58–60].

4.1. Coronary circulation

First described in the 1910s and 1920s, septic coronary embolism continues to be under-recognized as a cause of acute coronary ischemia [56]. These types of emboli predominantly originate from bacterial valvular vegetations [61]. A high index of clinical suspicion is required because electrocardiographic (ECG) and laboratory changes characteristic of myocardial ischemia can easily be misinterpreted as being due to more typical coronary artery thrombosis [29]. The diagnosis is established through the performance of a comprehensive work-up, including trans-thoracic and trans-esophageal echocardiography (TEE), with subsequent angiography as indicated [62, 63]. Management may include a variety of both non-interventional and interventional procedures, up to and including surgical cardiac revascularization at the time of valve replacement [29].

4.2. Thoracic aorta

Mycotic aneurysms of the aorta have been described as a consequence of septic emboli from infective endocarditis [64]. Clinical management of these lesions is challenging, partly due to the presence of active infection within the aneurysm itself, and partly due to the associated inflammatory changes and altered (e.g., diminished) structural integrity of the involved aorta [65]. Mycotic aortic aneurysms are associated with significant mortality and complications, including the potential for the development of aortoesophageal or aortotracheobronchial fistula [66, 67].

4.3. Pulmonary artery

Pulmonary artery aneurysms (PAA) of infectious etiology are among less frequently seen complications of endocarditis [68, 69]. They are similar to mycotic aneurysms, with the main difference being the location of occurrence [70]. PAAs (also referred to as Rasmussen's aneurysms) can be seen in patients with tuberculosis. However, there have been recent cases with PAAs being associated with endocarditis [70, 71]. These aneurysms require prompt surgical treatment given published mortality rates of approximately 50% [72]. Patients with aneurysms that are symptomatic or >6 centimeters in size are candidates for surgery [73]. Data regarding surgical treatment are limited; however, recent studies have shown that steel coil embolization may be applicable in this setting [70, 74–76]. While PAAs are uncommon in endocarditis, they should be considered in patients with IE that present with pulmonary symptoms.

4.4. Pulmonary circulation

Pulmonary SE are relatively common complications of right-sided IE (RSIE). As outlined in previous sections, any areas through which large volume of blood transits will be inherently susceptible to SE. The pulmonary arterial circuit is no exception in this regard. From an anatomic standpoint, evidence suggests that septic pulmonary emboli (SPE) involve both upper and lower lobes, with bilateral upper lobes involved in >70% of patients, and peripheral or subpleural zones involved in >90% of cases [58]. Centrally located lesions were noted in only about 25% of instances [58]. SPE are distinct from other types of pulmonary emboli because of their tendency to form cavitory lesions with air-fluid levels [77]. A significant proportion of patients with RSIE are intravenous drug users [78, 79], although there is an increasing number of patients with SPE who present with IE due to implanted cardiac devices [80, 81]. SPE in intravenous drug users can manifest with empyema, and is most likely to be associated with endocarditis due to *S. aureus* infection [82]. Other common complications of SPE include pulmonary abscess and pulmonary nodules [77]. If patients with either empyema or a pulmonary abscess are identified, it is crucial to continue intravenous antibiotics and preform an incision and drainage prior to any required valve surgery [83]. Waiting is not recommended as a strategy in these patients, mainly because of the risk of further complications associated with therapeutic delays [83, 84]. Pulmonary and perivalvular abscess should be suspected in intravenous drug users who fail to respond to antibiotic administration [84].

As with any other type of pulmonary embolism (PE), SPE can be life threatening [85–87]. It is important to note that it may be initially difficult to differentiate between the two types of PE. Consequently, diagnosis and management requires high levels of clinical suspicion, appropriate diagnostics (e.g., TEE), and immediate treatment (antibiotics, with surgery if indicated). Most SPE patients present with constitutional symptoms, dyspnea, chest pain, and cough (including hemoptysis) [58]. CT imaging may show the presence of cavitary lesions with an associated “feeding vessel sign,” representing a pulmonary artery coursing directly into the infected area [88].

5. Abdomen and retroperitoneum

5.1. The spleen

Septic embolism to the spleen is well described as a complication of IE [10]. In fact, after SE to the central nervous system (>50%), spleen appears to be the second most commonly involved organ in terms of frequency (approximately 30%), with some variability across sources of reported data [18, 28, 89]. One of most common presentations of SE to the spleen is the appearance of single or multiple abscesses [90], including microscopic lesions that were difficult-to-detect until the advent of advanced CT imaging [89]. Abdominal CT and MRI are the gold standard for diagnosing splenic abscesses [8]. Infected splenic artery aneurysms attributed to embolic sequelae of IE have also been reported [91]. Clinical management involves splenectomy in about 50% of cases, with percutaneous drainage indicated for large isolated abscesses and patients who are poor surgical candidates [29]. In cases of splenic arterial aneurysm and infarction, prompt surgical intervention is recommended. Patients should undergo drainage of the abscess or splenectomy prior to any cardiac surgery. This may help prevent further propagation and/or distant spread of the systemic infectious process [8, 91]. An example of splenic SE is shown in **Figure 3** [92].

5.2. The liver

Septic emboli to the liver are relatively common, occurring in >10% of cases of IE [10]. Similar to SE to the spleen, SE to the liver have the potential to evolve over time, coalescing from smaller “micro-abscesses” into larger collections [10]. Hepatic abscesses can be present in association with either right-sided or left-sided endocarditis [93, 94]; however, it may be difficult to determine whether the origin of the infection is cardiac or extra-cardiac, especially when the involved microorganism has known affinity for both locations [94]. Clinical management should follow established guidelines and practices for the treatment of IE and hepatic abscesses [29]. Similar to splenic abscess management, hepatic abscess should be drained as soon as possible in order to prevent worsening and/or further spread of the systemic infectious process [95].

5.3. The pancreas

Due to its vague clinical presentation, SE to the pancreas has the potential to go unrecognized. This is partially because SE to the pancreas often co-occurs with SE to other organs, potentially leading to “clinical masking” of organ-specific symptoms and/or signs [96]. Clinically, septic emboli to the pancreas may result in a picture resembling acute pancreatitis, and are

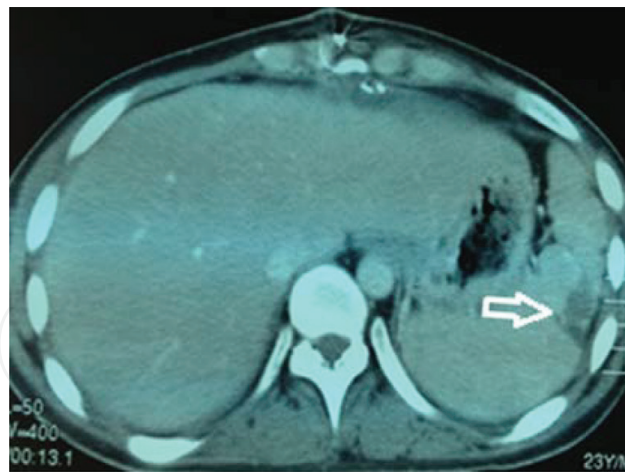


Figure 3. An example of septic embolus to the spleen. In this particular case, the embolus originated from *Corynebacterium diphtheriae* endocarditis (source: Ref. [92]. Image used under the terms of Creative commons Attribution-Noncommercial-NoDerivs Unported license).

usually characterized by leukocytosis, elevated pancreatic enzymes, peri-pancreatic “stranding” on CT scan, and acute abdominal pain [29]. Most often, pancreatic involvement in the setting of IE and SE tends to be self-limited [10]. At times, the finding of pseudoaneurysms involving adjacent arterial structures may provide a hint that the origin of the observed clinical syndrome is a result of SE [97].

5.4. The kidneys

Similar to the pancreas, SE to the kidneys is most often described in the setting of multi-visceral involvement [29]. Overall, renal SE are relatively frequent in the setting of IE, and their manifestations include infarcts in 31% of cases and glomerulonephritis in 26% [98]. Of interest, glomerulonephritis seen in association with IE has been shown not to feature immune complex deposition [98]. The co-occurrence of SE to other organs with arterial “high-flow” characteristics is exemplified by cases involving simultaneous cerebral, splenic, renal, and intestinal emboli [96]. Clinically, patients with renal SE may be found to have hematuria, glomerulonephritis, and evidence of renal failure [10]. Management focuses on preservation of renal function and is generally supportive, including antibiotic treatment, end-organ support (if required), and percutaneous or open interventions (in cases where abscess drainage is indicated) [98–100].

Etiology of renal injury in patients with IE is not always obvious, especially given the combined effect of cardiac dysfunction, sepsis, and concurrent treatment with potentially nephrotoxic antibiotics [98, 101]. Systemic infection can lead to acute tubular necrosis, while antibiotic treatment can lead to acute interstitial nephritis [102]. It is important to differentiate these conditions from the glomerulonephritis that is seen in IE, with an outline of important differentiating factors provided in **Table 2**.

5.5. The intestines including mesenteric involvement

Given its large surface area and rich vasculature, the bowel receives a significant amount of cardiac output and is highly susceptible to SE originating from IE [10, 29]. Fortunately, when compared to other organs and organ systems outlined above, arterial distribution to the

Type of kidney injury→	Glomerular	Interstitial	Tubular	Vascular
Typical causes	Bacterial endocarditis and vasculitis	Antibiotics	Sepsis and hypovolemia	Renal ischemia
Cast type	Red blood cell casts	White blood cell casts	Granular casts	Tubular epithelial cell casts
Clinical management	Treatment of underlying etiology	Remove inciting substance	Hydration and treatment of underlying condition	Surgical correction of underlying pathology

Table 2. Types of kidney injury, including their associated differentiating characteristics [102].

bowel appears to be less commonly affected (e.g., superior mesenteric artery in 3%, inferior mesenteric in <1%) [103]. This may be, at least in part, due to the presence of some degree of redundancy within the mesenteric vasculature, as opposed to a lack of such redundancy in the kidney or spleen. Occlusion of the superior mesenteric artery by SE is relatively well described in the setting of mitral valve endocarditis [104]. Mesenteric pseudoaneurysm attributable to SE has also been described [105]. In cases of acute arterial occlusion, bowel infarction may follow without prompt restoration of adequate blood flow to the involved segment(s) of bowel [106].

5.6. Reproductive organs

The involvement of reproductive organs in septic embolic complications is very uncommon. However, the authors believe that at least a brief overview of this under-recognized topic is warranted. In terms of testicular involvement, symptomatic presentation, including swelling, has been reported in conjunction with right-sided endocarditis [107]. It is thought that the this unusual clinical picture may result from SE [52, 107]. In another case, pneumococcal pulmonary valve endocarditis has been circumstantially linked to epididymo-orchitis and a scrotal abscess [108], although the directionality of causation may be difficult to prove except for the fact that *Streptococcus pneumoniae* isolated from the epididymo-orchitis is seldom a primary cause of scrotal infection. Equally uncommon, ovarian involvement has also been reported. In an exceedingly rare case, a female patient presented with a giant pyomyoma suggestive of ovarian neoplasm [109]. The origin of this presentation, however, was traced to *Streptococcus agalactiae* endocarditis and deep vein thrombosis of the right external iliac and femoral veins [109].

6. Extremities and musculoskeletal system

In general terms, extremity involvement in association with IE represents approximately one-third of all cases of SE, with clinical manifestations involving the musculature in approximately 40% cases and bones/joints in >10% of instances [10, 110]. Other than massive embolic events involving acute occlusion of arterial flow to an extremity producing significant ischemia, symptoms tend to be more “nebulous” in terms of clinical presentation, more self-limited in nature, and easily overlooked by clinicians [10, 100]. Pathognomonic signs such as Osler nodes



Figure 4. (A, left) An example of an Osler node in a patient with infective endocarditis (source: Ref. [112], image used in accordance with the terms of the CC BY 4.0 License); (B, right) Janeway lesions (see arrows) in a patient with aortic valve vegetation (source: Ref. [113], image used under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License).

and Janeway lesions are rare (2.7 and 1.6% cases, respectively) but highly suggestive of endocarditis [111]. **Figure 4A** shows an example of an Osler node, while **Figure 4B** demonstrates a Janeway lesion [112, 113].

6.1. Acute extremity ischemia

This potentially devastating presentation has been reported in the setting of more severe cases of IE, often involving valve replacement [114–116], with some patients experience multiple/recurring embolic events [114, 115]. In terms of clinical presentation, patients may exhibit a broad spectrum of complaints including pain, pallor, poikilothermia, and paresthesias with extreme cases threatening the viability of the limb itself [114]. Both surgical and thrombolytic management options have been reported [117, 118]. Prompt recognition of the cardiac source of SE is critical in preventing further embolic events.

6.2. Septic arthritis

Due to their non-specific nature and general commonality, joint-related complaints can be challenging to diagnose and easily misinterpreted. Not infrequently, multiple diagnostic tools must be utilized to successfully identify the cardiac source of the patient's original symptoms (and thus the proximal source of infection) [119]. In one case, it was the complaint of septic arthritis which led to the ultimate diagnosis of streptococcal endocarditis [120]. Similar to other embolic phenomena associated with IE, septic arthritis tends to be a manifestation of multi-focal metastases of infectious material [119, 121].

7. Uncommon neurologic presentations

This section will discuss a heterogeneous group of less common manifestations of SE affecting the CNS, including extracranial involvement. The paucity of published literature in this broad

topic area is likely due to limited awareness and under-recognition of such clinical presentations. Within the microcosm of SE associated with IE, approximately 30–40% of events involve neurological manifestations [10, 122]. Beyond the more commonly seen complaints (e.g., stroke, transient ischemic attack, meningitis, brain abscess) within this subset, less frequently reported clinical manifestations may include visual loss, seizures, acute mononeuropathy, and even spinal cord involvement [122–124]. Septic emboli can migrate to the spinal cord, causing segmental infarction [122, 123]. These exceedingly rare events have the potential to result in severe disability and often accompany additional, simultaneous SE to other anatomic regions [10].

8. Miscellaneous considerations

During the past two decades, significant increases have been noted in the number of valvular repairs, valve replacements, intracardiac devices and hemodialysis catheter placements [125–128]. Collectively, these procedures inherently create a small, but significant risk of IE, especially in patients with chronic comorbid conditions such as renal insufficiency, diabetes and autoimmune diseases [129–131]. Given the potential for major morbidity and mortality associated with IE in the setting of indwelling intravascular/intracardiac devices, the primary focus should be on prevention. Within this context, efforts include more selective device implantation policies and better modulation of known post-implantation risks [132].

In terms of general diagnostic considerations, numerous guidelines and recommendations have been published to date. Although beyond the scope of the current discussion, certain aspects of these recommendations warrant a brief mention [133, 134]. One very important highlight is the emphasis on prompt echocardiography in cases of suspected IE, with TEE recommended if the initial TTE is negative and clinical suspicion remains high [8]. Echocardiographic imaging can then be repeated in 3–5 days if clinical symptoms/suspicion persist [8]. It is also suggested that patients with vegetations >10 mm in size, embolic events while on antibiotic treatment, and patients with >2 embolic events should be evaluated for surgical intervention [8]. One unique diagnostic consideration is the inability to use magnetic resonance imaging (MRI) in patients with certain types of intravascular devices/implants. Amraoui et al. recently described the use of positron emission tomography (PET) as an alternative method of identifying foci of SE in patients with implantable cardiac devices, with limited success [135].

Treatment options start with intravenous antibiotics, however in certain cases prompt surgical treatment is necessary. The American Heart Association developed guidelines to assist with identification of patients who require prompt surgical intervention [136]. Patients with IE who develop decreased left ventricular ejection fraction (LVEF) or a new aortic or mitral valve murmur require prompt surgery [50, 136, 137]. Patients with preserved LVEF that are stable and adequately managed on medical therapy do not need an immediate corrective surgery [138]. However, a recent study demonstrated that surgical intervention in the setting of CHF can reduce mortality from approximately 60–85% to 15–35% when compared to medical therapy alone [139, 140]. Patients who present with valvular vegetations >10 mm in size, or with multiple vegetations on imaging, are likely to benefit from surgery [136]. Another important indication for surgery is lack of improvement after 7 days of appropriate antibiotic

therapy [136]. Any SE to end organs or associated arterial aneurysms also warrant immediate surgical evaluation and prompt intervention. As mentioned earlier in the chapter, emboli to different anatomic regions may require distinct plans and different timing in terms of surgical intervention [50]. The diagnosis of prosthetic valve endocarditis constitutes another major indication for surgical intervention. Patients who present within 60 days of discharge following the placement of a new prosthetic valve with persistent fevers should be evaluated for the presence of IE, and if proven to harbor such infection should undergo operative management. It is important to remember that roughly 25% of prosthetic valve patients may be at risk of IE [136, 141].

9. Conclusions

Despite significant clinical research and advances in clinical management, septic embolism associated with infectious endocarditis continues to be a diagnostic and therapeutic challenge. Given the increasing number of intravascular and intracardiac device implantations, as well as the greater prevalence of chronic comorbid conditions, it is not surprising that the incidence of both infectious endocarditis and septic embolism has followed suit. In this chapter, we outlined general pathophysiologic and anatomic considerations with which all physicians should be familiar. This important knowledge should serve to assist providers in maintaining a high level of clinical suspicion for potential IE and/or SE. Given the continued high rates of associated disability and mortality, more research is needed to better understand and treat these “low-frequency, high-impact” events.

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