



Endovascular Infection

16 June 2016

Adhiratha Boonyasiri, MD



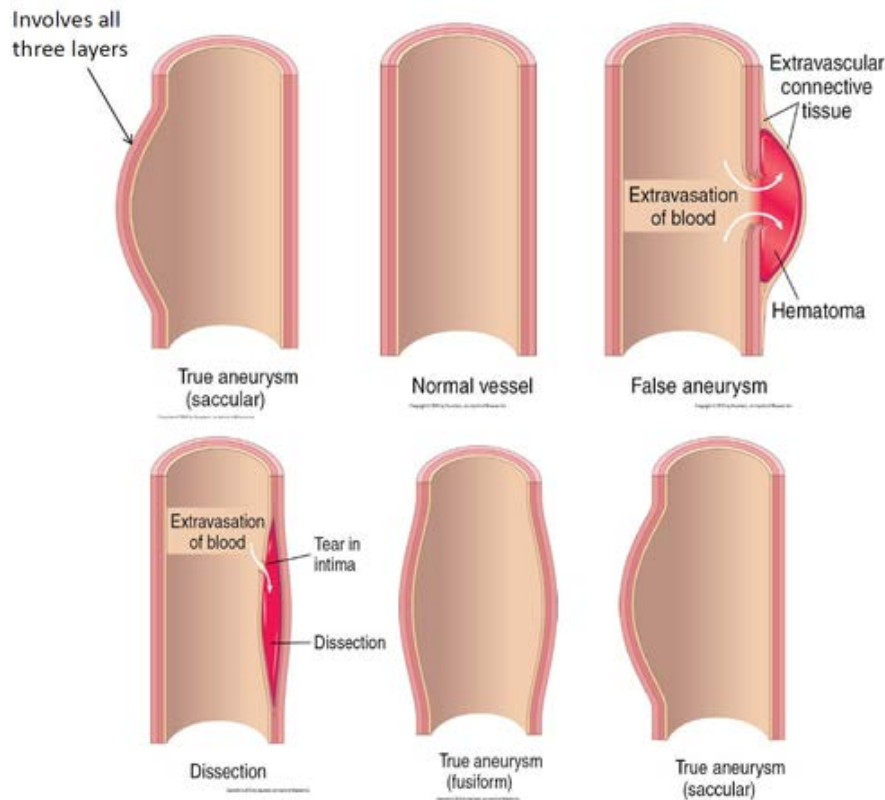
Outline

- **Mycotic aneurysm**
- **Suppurative thrombophlebitis**
 - Definition
 - Epidemiology
 - Risk factor
 - Pathogenesis
 - Microbiology
 - Diagnosis
 - Treatment



Mycotic aneurysm

Definition



- An aneurysm is an abnormal focal arterial dilation
- True aneurysms: arterial dilatation involve all 3 layers of arterial wall (intima, media, adventitia)
- False or pseudo-aneurysm: arterial dilatation with disruption of one or more layers of its walls



Definition

- **Mycotic aneurysm** coined by Osler in 1885 to describe a mushroom- shaped aneurysm
- Mycotic aneurysm still used for all aneurysms of infectious etiology **except for syphilitic aortitis**
- Significant morbidity and mortality
- Preexisting aneurysms can become secondarily infected, but can also be the result of infection



Definition

- **Endarteritis:** inflammation of the arterial wall, occur with or without coexistent aneurysmal dilation
- **Arteries are highly resistant to infection**
 - Deep anatomic location ➡ less prone to trauma
 - Tunica adventitial resists most forms of injury
 - Endothelial cell as a barrier to invasion by organism
 - Rapidly immune and RE systems clearance



Epidemiology

- Incidence figures are unavailable
- 2.6% of aortic aneurysms
- 0.03% in IVDU
- Male:female = 3:1
- Mean age 65 yrs
- Mean age 40 yrs in IE



Risk factor

- **Arterial injury**
 - Pseudoaneurysm is common
 - IVDU, iatrogenic (invasive monitoring, percutaneous access)
- **Antecedent infection**
- **Impaired immunity**
 - Diabetes, alcoholism, chronic glucocorticoid therapy, chemotherapy, and malignancy
- **Atherosclerosis**
- **Preexisting aneurysm**
 - Risk for secondary infection due to bacteremia or spread from a contiguous infection

J R Soc Med 1999; 92:255

Am J Cardiol 1997; 79:873

J VascSurg 2001; 34:900



Pathogenesis

- **4 Mechanisms**

- Embolomycotic aneurysms
- Hematogenous seeding
- Extension from a contiguous infected focus
- Direct contamination

- **Mycotic aneurysms**

Intracranial arteries ➡ Visceral arteries ➡ Upper or Lower extremity arteries

- Typically occurring at arterial bifurcations



Pathogenesis

Embolomycotic Aneurysms

- Septic microemboli ➡ **vasa vasorum** of artery or preexisting aneurysm
- Usually occur with active IE
- Often at points of bifurcation of the affected artery
- Estimated embolism occur between 25 - 50 % of IE patients
- Only about 1/5 develop symptomatic mycotic aneurysm



Pathogenesis

Hematogenous seeding

- Most common mechanism
- Bacteremic seeding through an existing intimal injury, atherosclerotic plaque, or preexisting aneurysm
- Primary bacteremia most commonly originates from distal infections in soft tissue, lung, bone, or joint
- Atherosclerosis accounts for ➡ existing intimal injury, preexisting aneurysm
- Aorta is the most common location



Pathogenesis

Extension from a contiguous infected focus

- Direct penetration of the vessel wall
- Circuitously via the lymphatics
- Common mechanism for tuberculous aortitis
- Post operative and non operative
 - Pyogenic vertebral osteomyelitis: present in 1/3 of cases
 - Extension of a postoperative infection described in the setting of appendectomy, cholecystectomy, and following knee or hip replacement surgery



Pathogenesis

Direct contamination

- Injury by self-inflicted, iatrogenic, accidental, or due to assault (gunshot, stab)
- The femoral artery is the most commonly involved arterial site
- > 80% located in the extremities
- More extensive local tissue inflammation



Microbiology

- Blood cultures are positive in 50 to 85 % of cases
- Isolated organisms from aneurysmal tissue up to 76 % of patients
- **Nontyphoid *Salmonella* species** and ***S. aureus***
most common causative organisms
 - *S aureus*: Western countries
 - Non typhoid *Salmonella* species: Asia
- Different organism determined by preexisting or IE associated



Microbiology

- Bacteriology of infected aneurysms in a series of 43 patients treated at the Mayo Clinic 1976-2000

Organism	Total (n = 43)
Culture negative	10 (23%)
<i>S aureus/epidermidis</i>	11 (26%)
<i>E coli</i>	6 (14%)
Streptococcus species	5 (12%)
Salmonella species	4 (9%)
<i>Listeria</i>	1 (2%)
<i>Candida</i>	1 (2%)
Other	5 (12%)



Microbiology

- Mycotic aneurysm in Northeast Thailand: the importance of *Burkholderia pseudomallei* as a causative pathogen
1993-2007 (n=40)

Organisms	Numbers (%)
<i>B. pseudomallei</i>	17 (42.5%)
<i>Nontyphoidal Salmonella</i> species	12 (30%)
<i>E. coli</i>	2
<i>Pseudomonas</i> species	2
<i>S. aureus</i>	1



Microbiology

- **Preexisting atherosclerotic vessel**

- Gram-positive organisms (60%)
 - $> 2/3$ *S. aureus*
 - *Streptococcus* spp. (10%)
 - *Enterococcus* spp.
- Gram-negative bacilli (30-40%)
 - Most common *Salmonella* spp. (20%)
- Polymicrobial cultures (IVDU)

- **Mycotic aneurysm associated IE**

- Before the antibiotic era
 - More virulent organism: GAS
- Now
 - *Streptococci* or *Staphylococci* ($\geq 60\%$ of cases)
 - *Enterococcus* spp.
 - *S. pneumoniae*



Microbiology

- **Geographic areas**

- Tuberculosis aortitis is seen in endemic countries
- Endemic melioidosis
- *B. pseudomallei* was the
- most common pathogen (42.5%)

- **Sites of Infection**

- *Salmonella* :

- 83% Abdominal aorta
- 17% Thoracic aorta

- *B. pseudomallei*:

- 87.5% Abdominal aorta
- Syphilis: Thoracic aorta > Abdomen
- (ascending > arch > descending)
- Tuberculosis:
- 2/3 abdominal aorta
- 1/3 thoracic aorta



Clinical manifestations

- **The classic presentation**

- Painful, Pulsatile, and Enlarging mass with systemic, such as fever
- Found only superficial infected aneurysms (common femoral artery)

- **For deeper sites**

- Depend imaging studies
- Abdominal or back pain
- Fever of unknown origin
- Some remain undiagnosed until rupture



Clinical manifestations

- **In the setting of IE**
- Infected aneurysm of the intracerebral vessels → stroke or subarachnoid haemorrhage
- **Undiagnosed, infected aneurysms**
- Sepsis, thrombosis, or haemorrhage
 - Depend on location (eg. GI Bleeding, Congestive heart failure, Mesenteric ischemia)



Diagnosis

- **Diagnosis is established by**

- Clinical symptoms**
- Aneurysm architecture
- Operative findings
- Positive aneurysm wall, thrombus and/or blood culture

**** Positive tissue cultures in the absence of clinical findings do not confirm mycotic aneurysm**

- Continuing bacteremia despite “appropriate” ATB in elderly (esp. diabetic) pt without signs of IE suggests an infected intravascular site
- CTA definitively diagnoses the aneurysm



Diagnosis

If suspected infected aneurysms

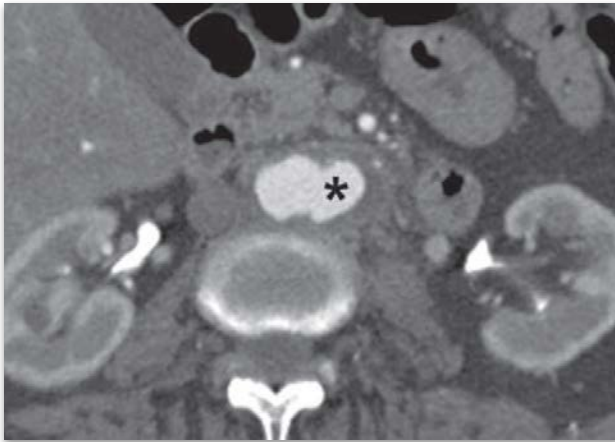
- Blood culture (negative 25-50%)
- Look for primary source of bacteremia
- ESR, CRP
- Imaging
- Intraoperation: G/S, Cultures, Pathology
 - Cultures will confirm the diagnosis/the selection of appropriate antibiotics



Imaging

- **CTA is the most useful for diagnosing** infected aneurysm
(Sensitivity of 92-96% Specificity of 93-100%)
- MRA is an alternatives
- Repeated scan can be performed to evaluate for rapid enlargement or changes to the aneurysm
- Nuclear medicine studies, including FDG-PET, gallium are alternatives

CTA



Characteristics

- Saccular, eccentric aneurysm or multilobulated aneurysm
- Soft tissue inflammation or mass around a vessel
- Aneurysm with intramural air or air collection around the vessel
- Perivascular fluid collection



Infected vs inflammatory

Infected Aneurysm

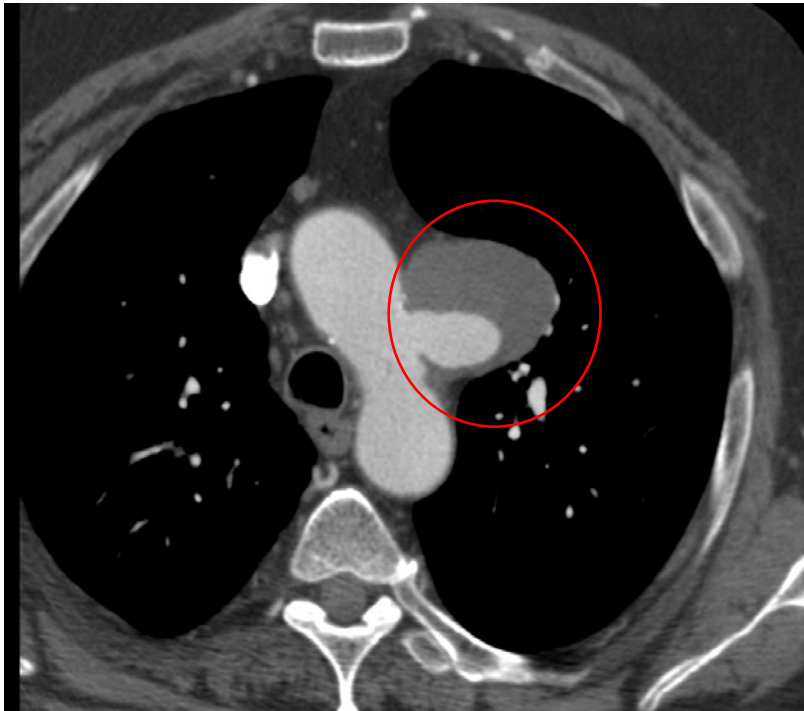
- Saccular, eccentric, or multilobulated AAA
- Soft tissue inflammation surrounding the aorta
- Intramural air, or air collection around the vessel
- Perivascular fluid collection

Inflammatory Aneurysm

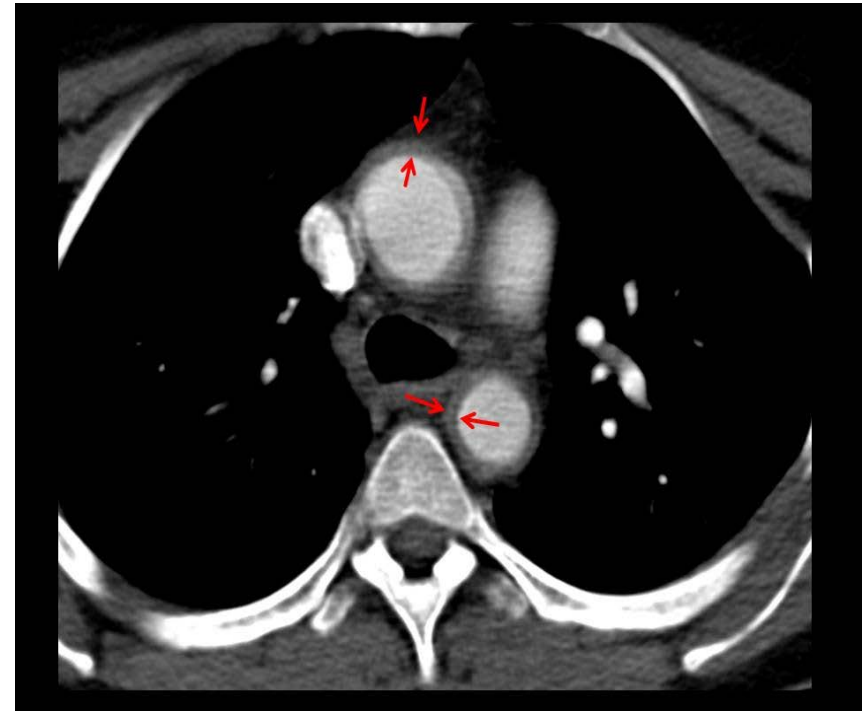
- Thickening of the adventitia (≥ 1 cm of adventitia)
- +/- Periaortic soft tissue density
- Planes between the aorta and retroperitoneum are indistinct
- Fibrosis of the adjacent retroperitoneum

Infected vs inflammatory

Infected Aneurysm



Inflammatory Aneurysm





Management

- No Randomized trials
- 2 modalities

1. Antibiotics

- Antibiotic therapy combined with surgical debridement with or without revascularization

2. Surgery

- Aneurysm excision and ligation without arterial reconstruction
- With reconstruction (immediate and interval)
- Revascularization procedures are performed depending upon status of distal perfusion
- Endovascular techniques are emerging as a treatment alternative for infected aneurysm



Antibiotic therapy

- Initial choice of ATB based upon the clinical circumstances and should be initiated ASAP
- Optimal duration of ATB is uncertain
- **At least six weeks** of parenteral and/or oral antimicrobial therapy is administered
- If surgical drainage is performed, this time period commences from the day of surgery
- A longer duration of treatment in the setting of
 - Antibiotic-resistant organisms
 - Persistently positive cultures
 - And/or inflammatory markers that are slow to normalize



Antibiotic therapy

- If surgery is not emergent
- **Course of ATB for 2 - 4 weeks prior to surgery is recommended**
- To improve local surgical conditions, associated with better outcome
- Suppressive oral antibiotics following prosthetic graft material during active infection
- Serial imaging in case of unruptured aneurysm



Surgery

- Removal of all necrotic and infected tissue and management of any ensuing ischemia
- Vascular reconstruction
 - Patient's underlying vascular status
 - Anatomic site of the aneurysm
 - Availability of autologous graft material

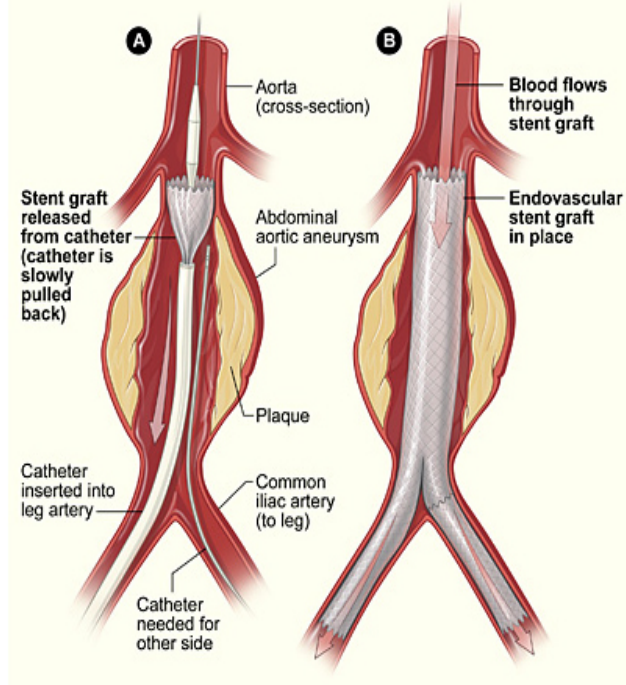


Surgery

- **Aneurysm excision and ligation without arterial reconstruction**
- **Excision with immediate reconstruction**
 - Patients who are likely to develop acute ischemia
 - Potential for recurrent infection
 - Autogenous superficial vein < prosthetic grafts
- **Excision with interval reconstruction**
 - Only mild to moderate limb ischemia
 - Interval with ATB IV 2-4 weeks

Endovascular Aneurysm Repair (EVAR)

Endovascular Aortic Repair (EVAR)



- Suitable for high-risk patients for open surgery
- Beneficial for temporizing measure
- Additional surgical therapy is indicated after acute problem
- Should not be considered permanent therapy



Endovascular Aneurysm Repair (EVAR)

- From September 2005 to May 2010
- 21 patients, 17 abdominal and 4 thoracic infected aortic aneurysms were treated with an endovascular stent graft at Songklanagarind Hospital
- Overall in-hospital mortality was 19% (4/21):
- 60% (3/5) in the fistula group and only 6% (1/16) in the nonfistula group
- Endovascular therapy, as a definite treatment for infected aortic aneurysms, provided excellent results in patients without fistula complications



Summary

- Mycotic aneurysm causes development of a **new aneurysm** or when a preexisting aneurysm becomes **secondarily infected**
- The organisms with the greatest affinity for the arterial wall are ***Staphylococcus spp* and *Salmonella***
- The diagnosis of an infected aneurysm is based upon **clinical and imaging**
- **Surgical excision** of the aneurysm and wide debridement of infected tissues is the treatment of choice with or without revascularization
- **Endovascular techniques** may be useful as a palliative measure for patients who refuse surgery, those with a prohibitive risk for surgery



Suppurative thrombophlebitis



Definition

- **Venous thrombosis associated with inflammation in the setting of bacteremia**
- Histologic findings consist of inflammation and suppuration within the vein wall
- Thrombus with or without pus may be seen within the vein lumen, with evidence of perivascular inflammation



Definition

- **Persistent bacteremia after 72 hours of appropriate ATB (esp. intravascular catheter)**
- Diagnosis
 - Culture
 - Radiographic evidence of thrombosis
- Treatment
 - Removing the focus of infection (eg, intravenous catheter)
 - Prompt administration of IV ATB
 - Surgical intervention
 - Anticoagulation



Pathogenesis

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• Intravenous catheter or PICC• 7 % of intravenous catheter sepsis• Risk factors<ul style="list-style-type: none">• Burns• Steroids• Injection drug use	<ul style="list-style-type: none">• Lemierre's syndrome, postanginal sepsis• Preceded by pharyngitis, dental infection• Infectious involvement of the carotid sheath vessels + bacteremia• Oropharynx to the parapharyngeal or lateral pharyngeal space• Intravenous catheter	<ul style="list-style-type: none">• Setting of a central venous catheter



Microbiology

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• <i>S. aureus</i> (most common)• Streptococci• Enterobacteriaceae• Burn patients may have polymicrobial infection	<ul style="list-style-type: none">• Normal oropharyngeal flora (most common)• <i>Fusobacterium necrophorum</i>• other <i>Fusobacterium</i> species (eg, <i>F. nucleatum</i>)• <i>Eikenella corrodens</i>• Catheter associated jugular vein: skin flora and nosocomial pathogens	<ul style="list-style-type: none">• Nosocomial organisms including <i>S. aureus</i> and <i>Enterobacteriaceae</i>• Fungi are more common• <i>Candida</i> spp.



Clinical manifestations

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• Fever, erythema, tenderness, and purulent drainage at the site of the involved vessel• Septic pulmonary emboli and secondary pneumonia	<ul style="list-style-type: none">• Fever ($>39^{\circ}\text{C}$) and rigors, respiratory distress• Most patients have localized neck and/or throat pain• Oropharynx: ulceration, a pseudomembrane, or erythema• Tenderness, swelling, at jugular vein, over angle of the jaw or sternocleidomastoid muscle	<ul style="list-style-type: none">• Systemic symptoms (fever, rigors and hypotension)• Localized findings are not common



Diagnosis

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• An ultrasound may not be needed• Baseline ultrasound may be useful if subsequent repeat evaluation is needed to evaluate for extension of thrombus	<ul style="list-style-type: none">• CT scan with contrast• It may demonstrate filling defects or thrombus, with or without soft tissue swelling	<ul style="list-style-type: none">• CT scan with contrast• It may demonstrate filling defects or thrombus, with or without soft tissue swelling



Antibiotic therapy

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• Empiric therapy: activity against <i>Staphylococci</i> such as vancomycin• Duration of ATB is at minimum of 2 weeks	<ul style="list-style-type: none">• Ampicillin-sulbactam for <i>Fusobacterium necrophorum</i>• Empirical treatment cover MRSA for catheter associated jugular vein• Duration of ATB is at least 4 weeks, including a minimum of 2 weeks intravenous therapy followed by oral therapy	<ul style="list-style-type: none">• Empirical treatment cover MRSA, <i>Enterobacteriaceae</i>• Duration of ATB is up to 4 to 6 weeks

Surgery

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none"> • Not responded appropriately to antimicrobial therapy • Incision and drainage and, potentially, excision of the affected vein and its tributaries may be needed 	<ul style="list-style-type: none"> • Ligation or excision of the internal jugular vein • Adjacent peritonsillar or other neck abscess in the vicinity of a catheter should prompt surgical incision and drainage as well as catheter removal 	<ul style="list-style-type: none"> • Surgical excision or ligation is not possible for vena cava • Resection of the infected thrombus may be warranted if proximal thrombus propagation occurs • Transabdominal and transfemoral venous thrombectomy (IVC)



Anticoagulation

Peripheral vein	Jugular vein	Vena cava
<ul style="list-style-type: none">• Uncertain• Favor anticoagulation only if there is evidence for extension of thrombus	<ul style="list-style-type: none">• Controversial• Favor anticoagulation only if there is evidence for extension of thrombus	<ul style="list-style-type: none">• Most favor anticoagulation• No controlled studies



Summary

- Persistent bacteremia after 72 hours of appropriate ATB
- Fever, erythema, tenderness and purulent drainage at the site of the involved vessel
- Culture data and radiographic evidence of thrombosis
- Removing the focus of infection (eg, intravenous catheter)
- Prompt administration of IV ATB
- Consideration regarding surgical intervention and/or anticoagulation



Thank You
