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OUD ECHO Medical Co-Morbidities

Endocarditis – Part 2

Indiana University Health

SCHOOL OF MEDICINE
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Disclosures

Clary

- None

Hiles

- None

Today's Agenda

- Management
- Prognosis

Epidemiology

- Annals of Thoracic Surgery, 1996
  - 13% febrile IVDU will have echocardiographic evidence of IE
  - 41% of bacteremic IVDU will have echocardiographic evidence of IE

https://www.annalsthoracicsurgery.org/article/0003-4975(96)00029-X/pdf

Management Guidelines

- Valvular Heart Disease
  - AHA/ACC 2014, focused update 2017
- Infective Endocarditis
  - AHA Scientific Statement
  - Endorsed by the Infectious Diseases Society of America

Management

- Antimicrobials are the cornerstone of therapy
  - Agent and duration guided by susceptibility of organism
- Early surgical intervention often indicated
- Heart team approach
  - Cardiologist
  - Cardiovascular surgeon
  - Infectious disease specialist

JACC Vol. 63, No. 22, 2014
June 10, 2014:e57–185

Management

- Antimicrobials are the cornerstone of therapy
  - Agent and duration guided by susceptibility of organism
- Early surgical intervention often indicated
- Heart team approach
  - Cardiologist
  - Cardiovascular surgeon
  - Infectious disease specialist
  - ***Addiction medicine specialist and team***

JACC Vol. 63, No. 22, 2014
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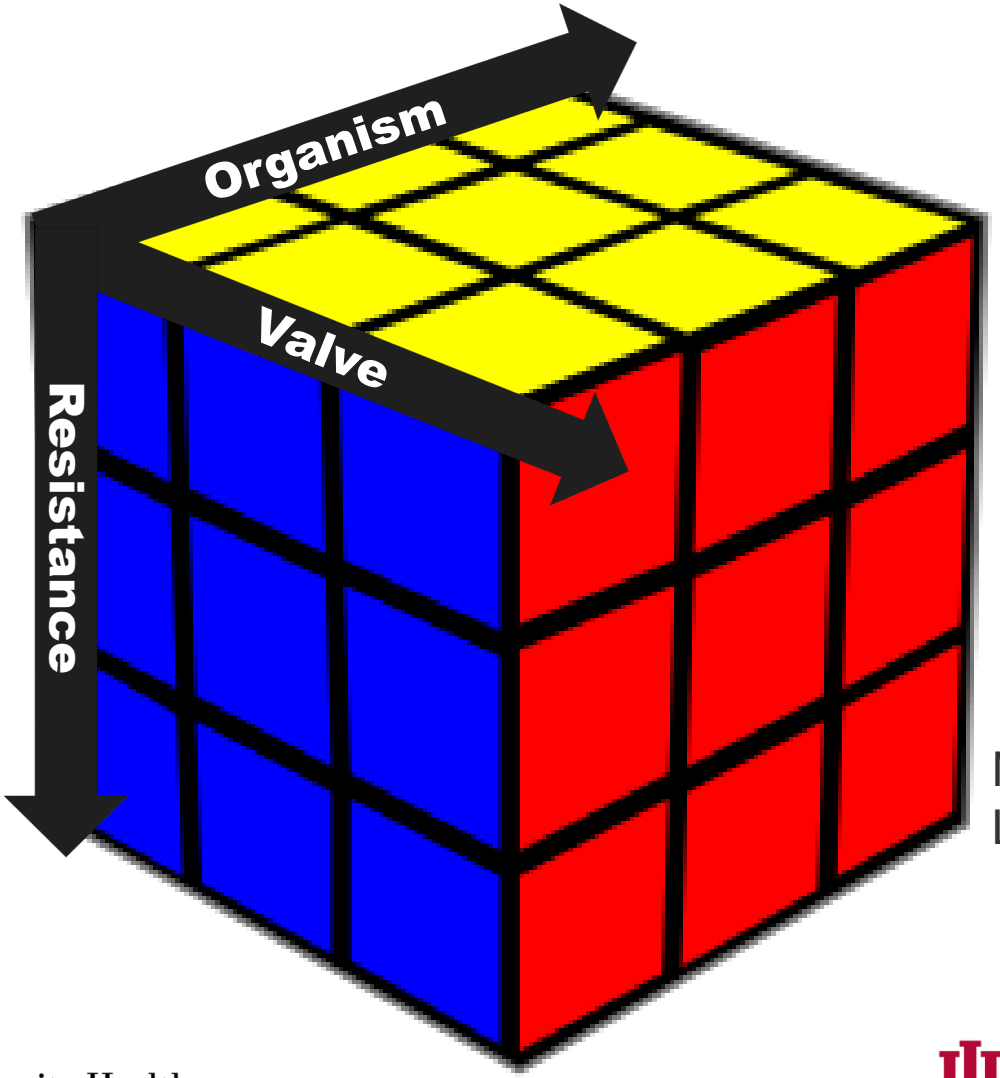
Antimicrobial Management



Streptococcus
Staphylococcus
Enterococcus
HACEK
Other gram negative
Candida

Penicillin R
Methicillin R
Vancomycin R

Native vs Prosthetic
Left vs Right side

Circulation. 2015;132:1435-1486.

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Antimicrobial Management – Native Valve

Organism	Resistance	Drug(s) of Choice	Duration	Issues
Viridans group streptococci	None	**Ceftriaxone** OR **Penicillin**	2* to 4 weeks 2* to 4 weeks	Ceftriaxone once daily and doses can be IM Penicillin is either continuous infusion or 4 to 6 times per day
		*Add **Gentamicin**	2 weeks	Shortens required duration to 2 weeks for ceftriaxone and penicillin. Gentamicin can be once daily
	Relatively Resistant to Penicillin	**High Dose Penicillin** OR **Ampicillin** AND **Gentamicin**	4 weeks 4 weeks 2 weeks	Penicillin is either continuous infusion or 4 to 6 times per day Ampicillin is either usually 4 to 6 times a day and is not stable at room temperature Gentamicin can be once daily
		Vancomycin	4 weeks	Usually 2 times daily in younger patients. Requires monitoring including levels
Staphylococcus (aureus or CoNS)	Methicillin susceptible	**Nafcillin/Oxacillin** OR **Cefazolin**	6** weeks 6** weeks	Nafcillin/Oxacillin is either continuous infusion or 6 times daily Cefazolin can be 3 times daily **2 weeks could be considered with gentamicin in uncomplicated right sided endocarditis in IVDU
	Methicillin resistant	**Vancomycin** OR **Daptomycin**	6 weeks 6 weeks	Daptomycin doses should be higher than product package insert, usually once daily dosing

Circulation. 2015;132:1435-1486.

Antimicrobial Management – Native Valve

Organism	Resistance	Drug(s) of Choice	Duration	Issues
Enterococcus	None	**Ampicillin** AND **Gentamicin**	4* to 6 weeks 4* to 6 weeks	Ampicillin is either usually 4 to 6 times a day and is not stable at room temperature *4 week regimen for patients with symptoms <3 months
	Ampicillin resistant	**Vancomycin** AND **Gentamicin**	6 weeks 6 weeks	Usually 2 times daily in younger patients. Requires monitoring including levels Gentamicin can be once daily
	Vancomycin resistance	**Daptomycin** OR **Linezolid**	>6 weeks >6 weeks	Linezolid can be oral, although daptomycin usually preferred due to tolerability (linezolid can cause bone marrow suppression with long term use)
HACEK	N/A	**Ceftriaxone** OR **Ampicillin**	4 weeks 4 weeks	Ceftriaxone once daily and doses can be IM Ampicillin is either usually 4 to 6 times a day and is not stable at room temperature
Gram Negative	Various	**Beta-Lactams**	6 weeks	Too many scenarios here, pseudomonas is a potential organisms and cefepime 3 to 4 times daily would be option
Candida	Various	**Azoles** AND/OR **Echinocandins** AND/OR **Amphotericin**	>6 weeks >6 weeks >6 weeks	After initial therapy, lifelong oral suppression with fluconazole

Circulation. 2015;132:1435-1486.

Antimicrobial Management – Prosthetic Valve

Organism	Resistance	Drug(s) of Choice	Duration	Issues
Viridans group streptococci	None	**Ceftriaxone** OR **Penicillin**	6 weeks 6 weeks	Ceftriaxone once daily and doses can be IM Penicillin is either continuous infusion or 4 to 6 times per day
	Relatively Resistant to Penicillin	**High Dose Penicillin** OR **Ceftriaxone** AND **Gentamicin**	6 weeks 6 weeks 6 weeks	Penicillin is either continuous infusion or 4 to 6 times per day Ampicillin is either usually 4 to 6 times a day and is not stable at room temperature Gentamicin can be once daily
		Vancomycin	4 weeks	Usually 2 times daily in younger patients. Requires monitoring including levels
Staphylococcus (aureus or CoNS)	Methicillin susceptible	**Nafcillin/Oxacillin** OR **Cefazolin** AND **Rifampin PO** AND **Gentamicin**	≥6 weeks ≥6 weeks ≥6 weeks 2 weeks	Rifampin is well absorbed, IV usually not required. Does have MANY drug interactions (methadone). Evidence isn't great for having it so may argue for avoiding
	Methicillin Resistant	**Vancomycin** OR **Daptomycin** AND **Rifampin PO** AND **Gentamicin**	≥6 weeks ≥6 weeks ≥6 weeks 2 weeks	

Circulation. 2015;132:1435-1486.

Antimicrobial Management – Prosthetic Valve

Organism	Resistance	Drug(s) of Choice	Duration	Issues
Enterococcus	None	**Ampicillin** AND **Gentamicin**	6 weeks 6 weeks	Ampicillin is either usually 4 to 6 times a day and is not stable at room temperature Gentamicin can be once daily
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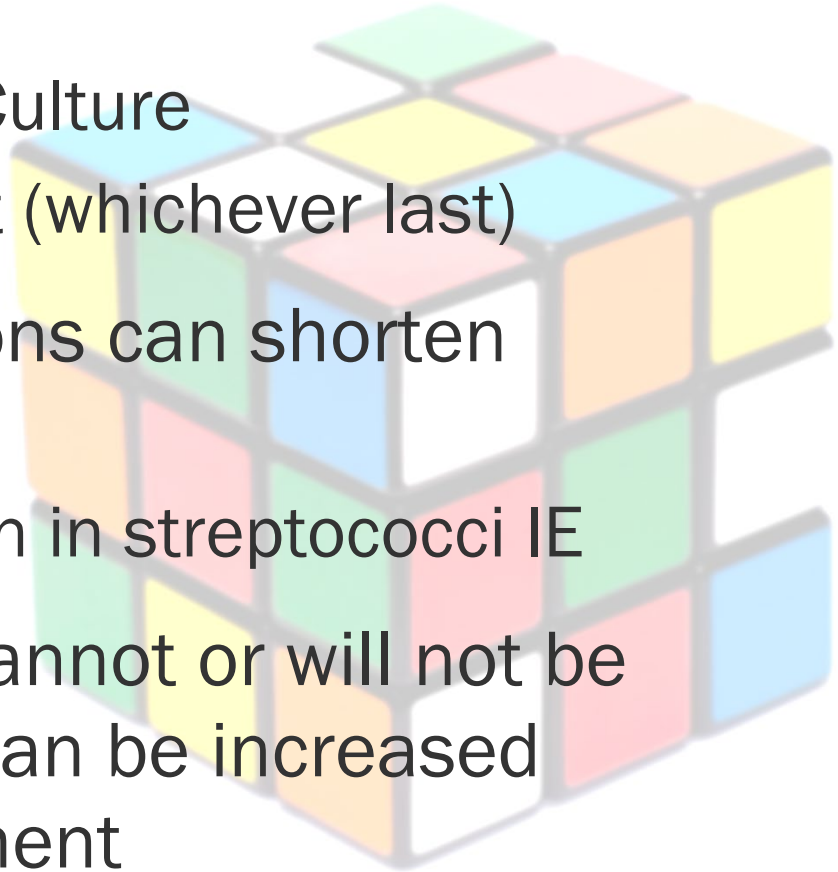
Antimicrobial Management – Duration

- Start time is either:
  - First Negative Blood Culture
  - Surgical Management (whichever last)
- Sometimes combinations can shorten durations
  - Addition of Gentamicin in streptococci IE
- When source control cannot or will not be performed, durations can be increased depending on ID judgment



Antimicrobial Management – Oral Antimicrobials (POET Trial)

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., et al.

- Mulitcenter, randomized, unblended, noninferiority trial performed in Denmark
- IV for 10 days
- Almost all left sided IE
  - ALMOST NO IVDU
- A large proportion of patients had streptococcus (duration 2 weeks potentially)
- More evidence needed for IVDU

		IV (199)	IV to PO (201)	
Streptococcus Enterococcus S. aureus Coag Neg Staph		52% 23% 20% 5%	45% 25% 23% 6%	
Left Sided Prosthetic Valve		99% 27%	100% 27%	
Amoxicillin Rifampin Moxifloxacin Linezolid Dicloxacillin Fusidic acid Other	Combo Therapy	N/A	66% 51% 29% 29% 9% 6% 4%	98%
Mortality		6.5%	3.5%	
Relapse		2.5%	2.5%	

NEJM. 2019;380:415-424.

Antimicrobial Management – New Agents

	Vancomycin	Telavancin	Dalbavancin	Oritavancin
$T_{1/2}$	8 hrs	8 hrs	204 hrs	245 hrs
Vd	0.7 L/kg	0.13 L/kg	0.22 L/kg	1.25 L/kg
%Protein Bound	55%	90%	93%	85%
Dose	15-20 mg/kg every 12 hrs	10 mg/kg every 24 hrs	1500mg x1	1200 mg x 1
Dose Adjustments	Renal Drug Levels	Renal	Renal	Severe Renal Disease
Side Effects	Redman's Renal?	Taste Nausea Foamy Urine Renal?	None	LFTs

T1/2, Half-life; Vd, Volume of Distribution; LFT, Liver Function Tests

Diagnostic Microbiology and Infectious Disease. 2015. 81:275-279.
Antimicrobial Agents and Chemotherapy. 2009. 53(3):1260-1263.

Antimicrobial Management – New Agents

	Vancomycin	Telavancin	Dalbavancin	Oritavancin
MIC 50/90				
MSSA	1/1	0.03/0.06	0.06/0.06	0.03/0.06
MRSA	1/1	0.03/0.06	0.06/0.06	0.03/0.06
VRSA	-	0.06/0.06	-	-
VRE	-	-	>4/>4	0.03/0.12
FDA Indications	SSSI Infective Endocarditis LRTI Staph Enterocolitis MRSA	SSSI Nosocomial Pneumonia	SSSI	SSSI
Cost per Dose	$2.60	$337.34	$2812.52	$2737.02
Cost per Day	$5.21	$337.34	$401.79	$391.00

Diagnostic Microbiology and Infectious Disease. 2015. 81:275-279.
Antimicrobial Agents and Chemotherapy. 2009. 53(3):1260-1263.

Antimicrobial Management – New Agents

- Long acting glycopeptides studied in IE

Study	Drug/Dose	Population	Outcomes
Bryson-Cahn et al. 2019	Dalbavancin var. doses weekly	Deep seated Staphylococcus aureus infections in patients were IV not possible in Montana	4/32 (13%) clinical failure 0/9 IE clinical failure
Wunsch et al. 2019	Dalbavancin var. doses weekly	Gram positive infections requiring long duration of therapy in Austria	5/94 (5%) clinical failure 1/24 (4%) IE failure
Tobudic et al. 2018	Dalbavancin 500 mg weekly	Gram positive endocarditis in Vienna	2/27 (7%) clinical failure
Schulz et al. 2018	Oritavancin var. doses weekly	Gram positive infections requiring long duration of therapy in Wisconsin	0/17 clinical failure
Stewart et al. 2017	Oritavancin var. doses weekly	Deep seated Staphylococcus aureus infections in patients were IV not possible in North Carolina	2/10 (20%) clinical failure
Johnson et al. 2015	Oritavancin 1200 q48h x 3 then weekly x 6	VRE prosthetic valve IE	Case report of success

Surgical Management

- Valve dysfunction results in heart failure
- L-sided IE with virulent/resistant organisms
- Complicated by heart block, abscess, or penetrating lesions

JACC Vol. 63, No. 22, 2014
June 10, 2014:e57–185

OUD ECHO Case Presentation 10.2.2019 / Case ID #: OUD MC 003 **Presenter: Matthew Miles, MD**

General Information

- 35 year old Caucasian heterosexual female
- 173 lbs., 5" 6"
- Medicaid HIP
- Role in patient's care: Physician

Medical Diagnosis

- Severe Opioid Use Disorder

Psychiatric Diagnosis

- MDD with anxious features

Opioid Use History

- Recreational use of illicit Rx opioids during teenage years
- Believes "addiction" began 4-5 years ago
- At that time taking up to 200 mg/day of oxycodone (mother's Rx)
- Pills became too expensive, transitioned to heroin by husband
- Initially snorting but transitioned to IV within last 6 months, due to nasal congestion
- Reports sharing needles, does not practice safe syringe hygiene

Other Substance Use History

- History of cannabis use, 2012 "court ordered" MD eval from possession charge
- Tobacco use; 1-2 ppd
- EtOH use: approx. daily since age 27
- Cocaine: experimented at age 19

Co-Infections

- Hepatitis A, B, C: Immune
- HIV Naïve

Labs:

- UPT: Negative
- WBC: 17.4 / Hgb 12.0 / Plt 196
- Na: 135 / K 3.4 / Cl 100 / CO2 23 / BUN 11 / Cr 0.69 / Glu 98
- AST 25 / ALT 29 / AlkP 97 / Bil 0.7 / Pro 6.7 / Alb 2/1
- UDS: Opiate positive, cannab
  Amphetamine negative, barbi
  benzodiazepine negative, coc
  PCP negative
- Blood cultures: 3/4 (2 aerobic,
  MSSA

Medications and/or Behavioral Interv

- None currently
- Paroxetine and citalopram tria
  ago
- Trazodone trialed 7-8 years ago

Additional Information Relevant to

- Patient admitted to h ne month of fever, chills, nausea miting
- Active heroin use lea up to admission
- A transesophageal ECHO two days later reveals a "vegetation on the tricuspid valve with leaflet perforation and moderate regurgitation

Social History:

- Mother agrees to support patient if she seeks treatment for addiction but does not believe addiction is a disease
- Previous husband in jail related to possession charges
- Son, currently 10 years ago
- History of DCS incidents in the past, often related to drug charges
- Reports prior rape at age 18 and then again recently

situation

- Completed 8th grade; literate
- Currently unemployed but previous work at auto warehouse part time

Main Questions for this Patient Case:

- How would you best approach the ongoing management of this patient?
- How would you answer her question with regards to her being restricted to her room?
- Help with non-medication treatment

A transesophageal ECHO two days later reveals a "vegetation on the tricuspid valve with leaflet perforation and moderate regurgitation

Surgical Management

- Valve dysfunction results in heart failure
- L-sided IE with virulent/resistant organisms
- Complicated by heart block, abscess, or penetrating lesions
- Persistent infection (>5-7 days of fever or bacteremia despite appropriate abx)
- Relapsing infection without other source/portal
- Recurrent emboli* or persistent vegetation
- Mobile vegetation > 1cm*

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Surgical Management

- "Because many of the patients with right-sided IE develop infection as a result of IVD, the general approach is to treat these patients medically and to avoid placement of valve prostheses because of the subsequent risk of device infection with continued IDU."
- "It is reasonable to avoid surgery when possible in patients who are IDUs"

Circulation. 2015;132:1435-1486. DOI: 10.1161/CIR.0000000000000296.

Surgical Management for R-sided IE

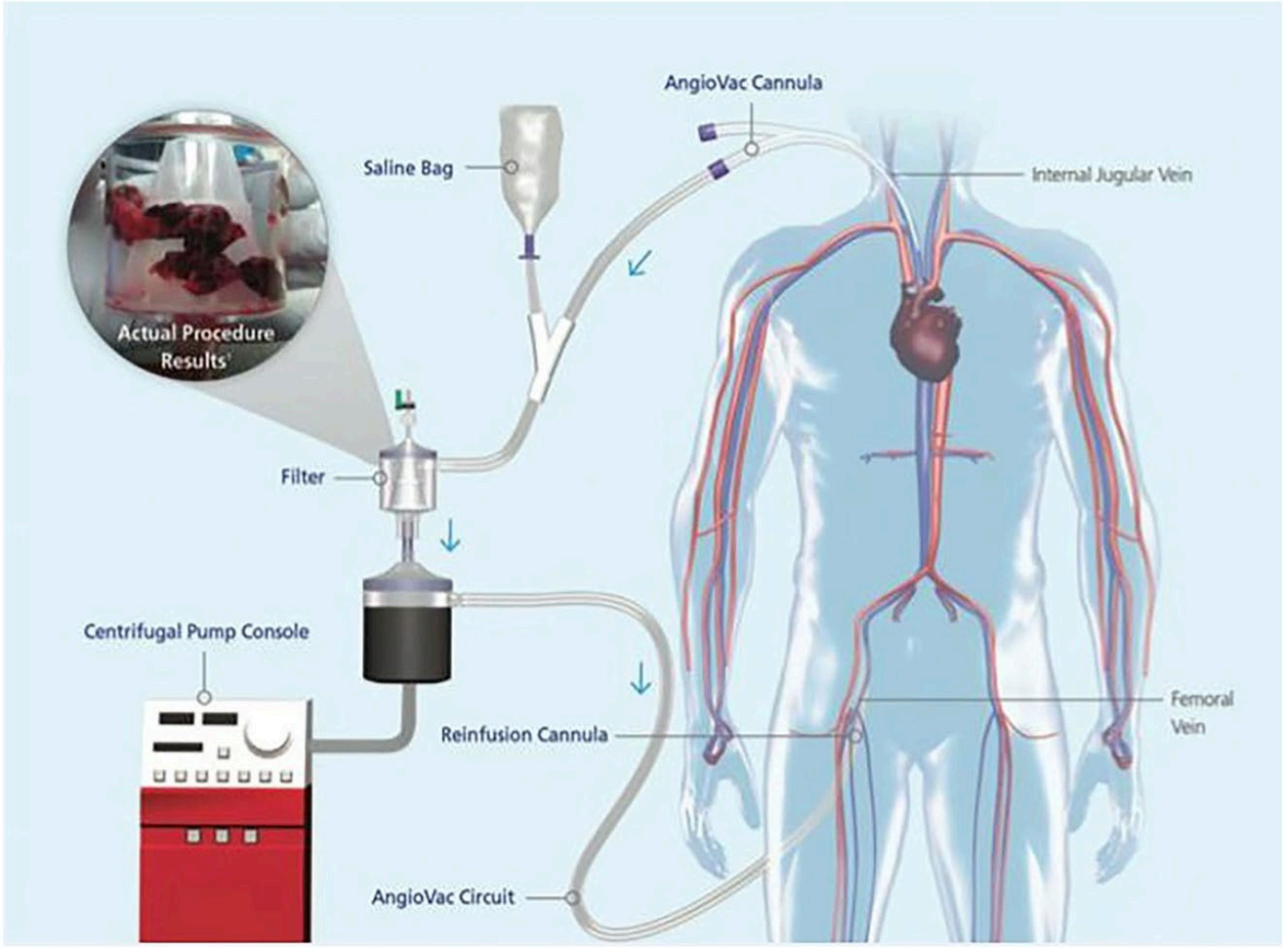
- Right heart failure 2/2 severe tricuspid regurgitation *unresponsive* to medical therapy
- Sustained infection caused by virulent/resistant organisms
- Lack of response to antimicrobial therapy
- Vegetation >2 cm and recurrent pulmonary emboli despite antimicrobial therapy
- Repair favored over replacement

[*Circulation*. 2015;132:1435-1486. DOI: 10.1161/CIR.0000000000000296.]

Management

- So if not surgery, what?
- AngioVac!

AngioVac


AngioVac Cannula
Saline Bag
Internal Jugular Vein
Actual Procedure Results
Filter
Centrifugal Pump Console
Reinfusion Cannula
Femoral Vein
AngioVac Circuit

AngioVac

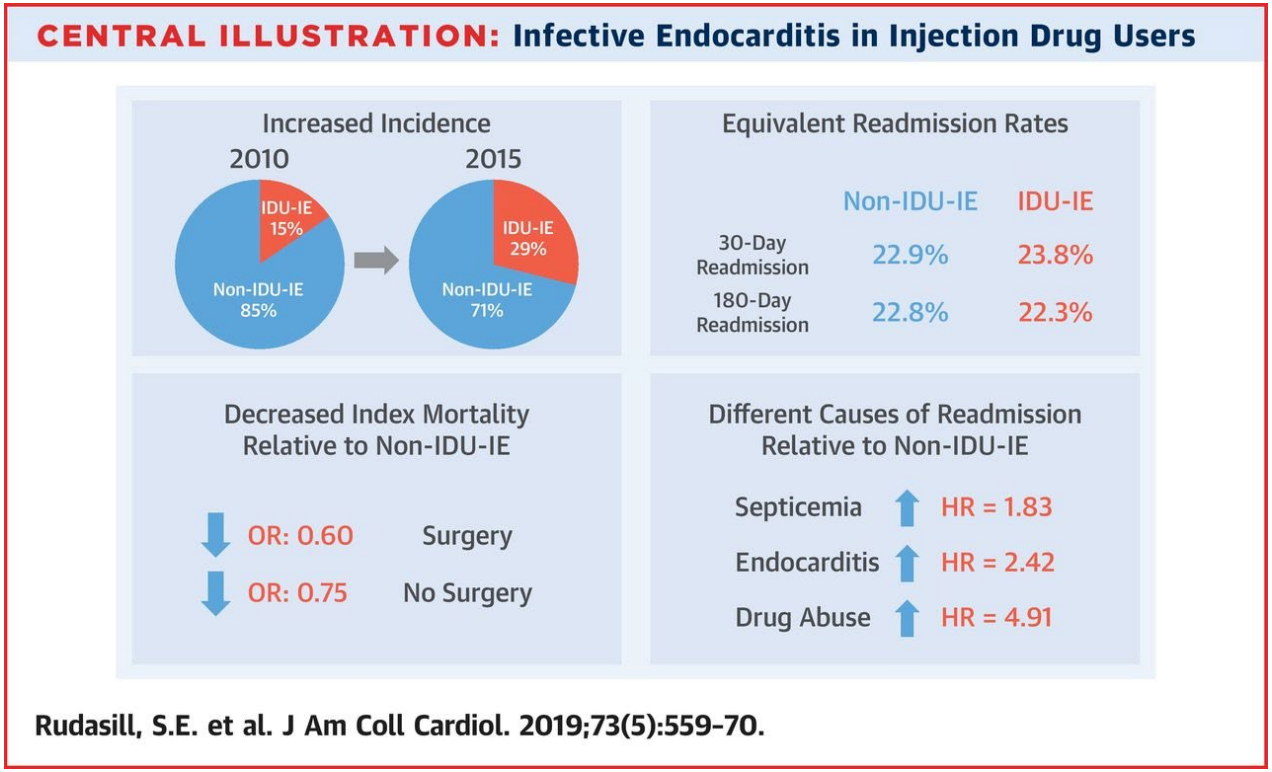
- FDA approved in 2013 for removal of soft fresh thrombi or emboli
- First case report in 2013
  - Used as bridge to surgery in a 17 year old with IE
- Paucity of data for use in endocarditis
  - Largest study by George et al in 2017
    - 33 patients
    - Decrease in vegetation from 2.1 cm to 0.82 cm
    - Debulking may help clear infection

AngioVac

- Concerns
  - Paucity of data
  - Worsening of TR
  - Bleeding
  - Pulmonary emboli

Prognosis

- National Readmissions Database (NRD)
  - IE cases between Jan 2010 and Sept 2015



Prognosis

- Prospective study from 2006-2016 of IVDU hospitalized with infections
  - 105 episodes of IE in 92 IVDU (71% male)
  - 112 episodes of other infections in 107 IVDU
- 30 day survival for IE 85%
- 30 day survival following surgery for IE 96%
- 47% had surgery

Clinical Infectious Diseases, ciz869, https://doi.org/10.1093/cid/ciz869

Prognosis

	IE group	Other infection group
1 year survival	74%	91%
3 year survival	63%	86%
5 year survival	58%	84%
10 year survival	44%	70%

- Cause of Death known in 38 patients
  - 21 IE
  - 6 drug overdose
  - 4 other infections
  - 2 cardiac failure
  - 1 uncertain

Clinical Infectious Diseases, ciz869, https://doi.org/10.1093/cid/ciz869

QUESTIONS?