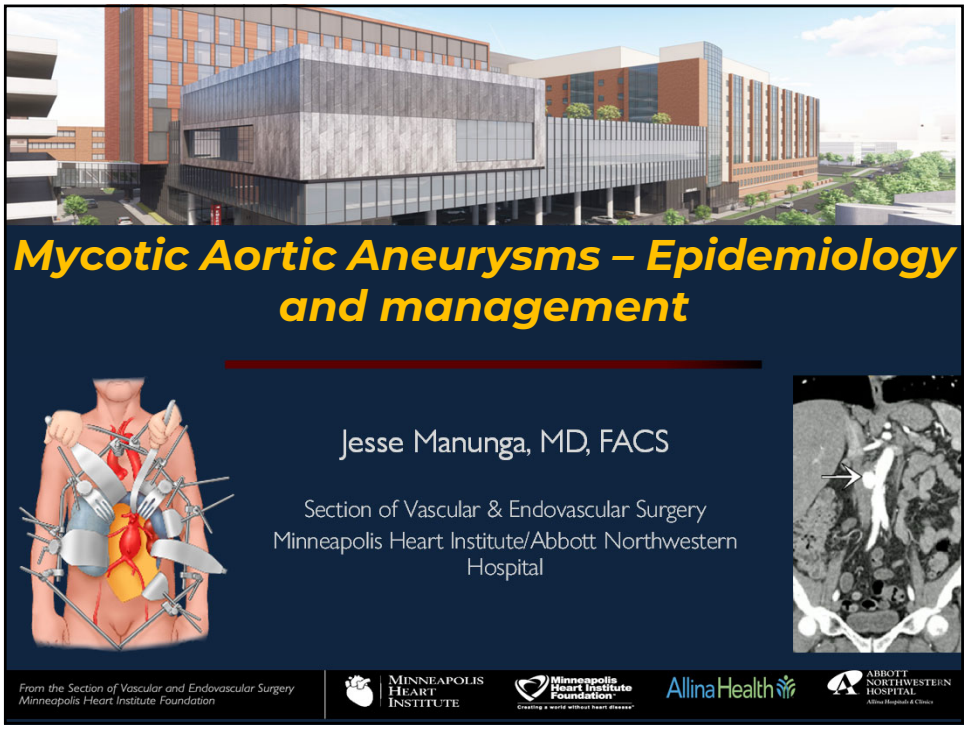


1

FACULTY DISCLOSURE

- Use of Investigational Devices

IDE for physician-modified endografts for treatment of complex aortic aneurysms

- Consulting

Medtronic, Inc.

L.W. Gore

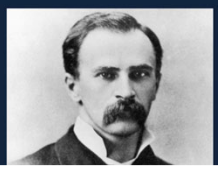
2

Objectives

- Discuss the clinical presentation of infected native mycotic aortic aneurysms and aortic grafts infections
- Review outcomes of medical management alone vs medical + surgical repair
- Discuss the role, *if any*, of endovascular therapy in the management of pts with aortic mycotic aneurysms

3

Historical Perspective



- Described by William Osler – noticed during autopsies of pts who died of endocarditis

March 7, 1885.] THE BRITISH MEDICAL JOURNAL. 467

THE GULSTONIAN LECTURES.

tonsillar crypts, and about the tufts of actino-mycos... Two conditions must be distinguished from the lesions of malignant (mycotic) endocarditis: the atheromatous degeneration in sclerotic valves, which leads to ulceration and extensive destruction of segments, a process which has nothing in common, except in its effects upon the valves, with the acute ulcerative changes above described, but is similar to the atheromatous processes in the aorta. It must not be for-

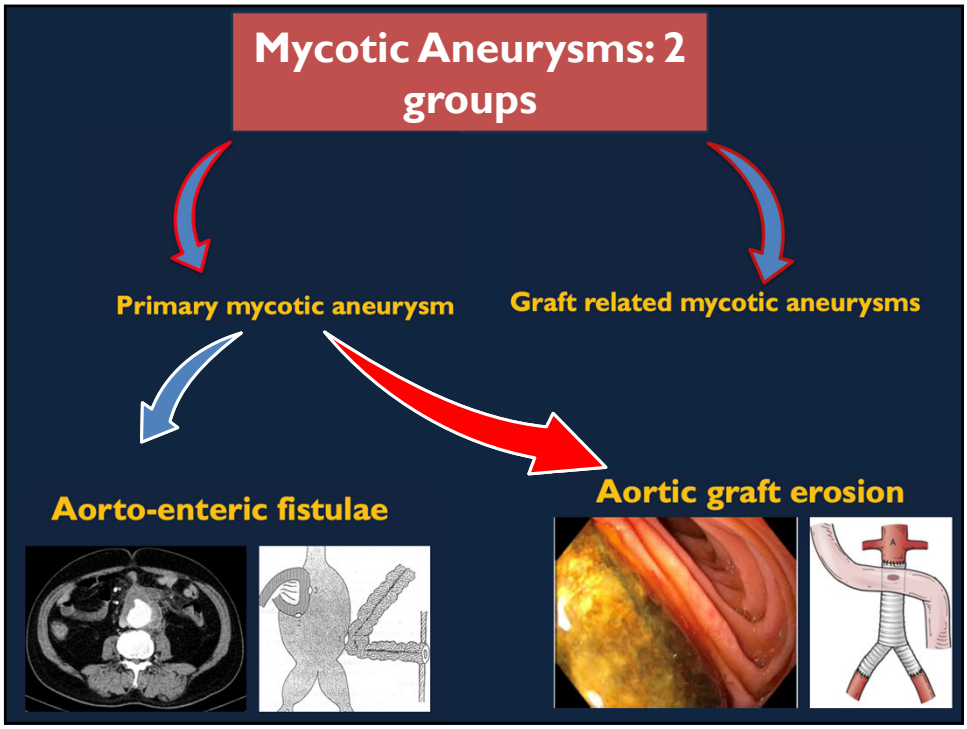
the phenomena of which were first clearly explained by the late Dr. Kirkes, from whose investigations in 1851-52 we date our accurate knowledge of the affection. Some of those who listen to me to-day can doubtless recall, and recall with pleasure, the Gulstonian Lec-

use to describe the grave form, and it expresses well an anatomical feature present in a large proportion of cases: but in others it is very

2, as a secondary affection in connection with many diseases, particularly rheumatic fever, pneumonia, scarlet fever, diphtheria, ague, etc. 3, as an associated condition in septic processes, traumatic or puerperal. We shall discuss first the anatomical characters, then the clinical features, and lastly the etiological and pathological relations.

- At the time he used the term "micrococcus" to describe this infection …that was likely due to TB, or syphilis but it is unclear since (in his discourse) he describes the Gramm's technique to stain tissue

4



5

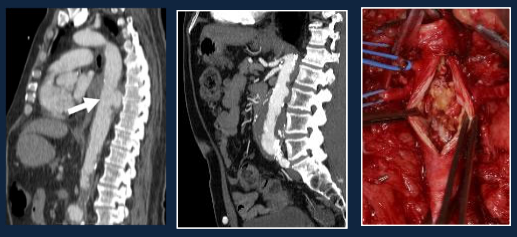
Overview- Aortic graft erosions and fistulae

- Aorto-enteric fistula is *different* from graft erosions
- A "fistula" communicates two cavities – must be blood flowing into the viscus

6

Etiology- Primary Mycotic Aneurysm

- Usually, a result of bacteremia and subsequent "super-infection" of the diseased or irregular aortic surface
  - *Atherosclerotic*
  - *Aortic ulcer*
  - *Aortic aneurysm*



- Forms pseudoaneurysms that are unstable

7

Etiology- Primary Mycotic Aortic Aneurysm

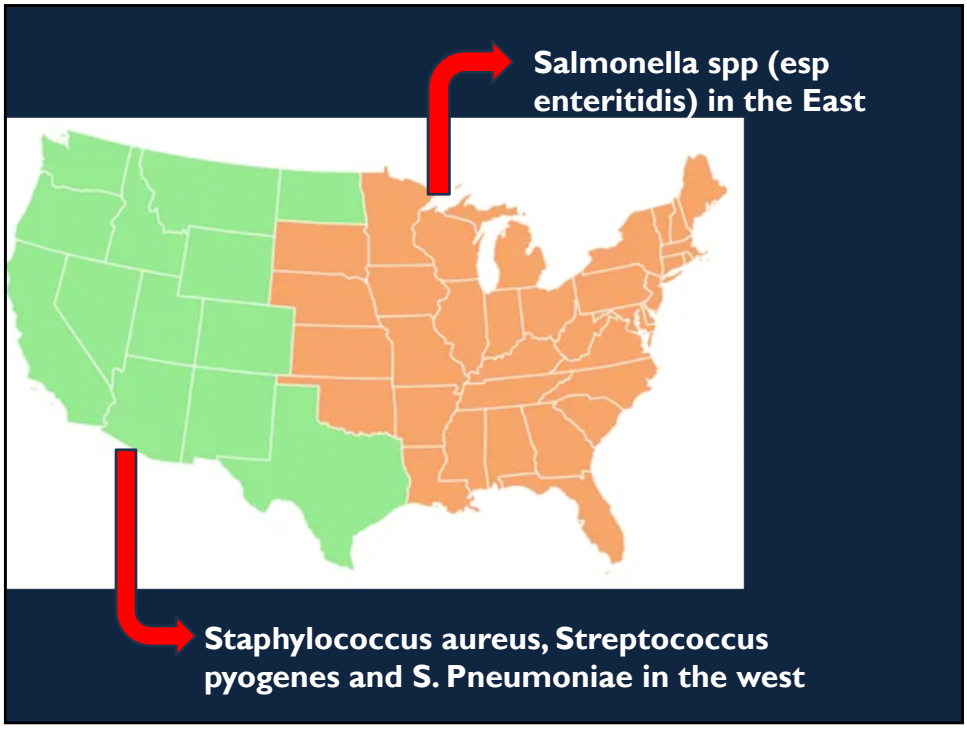
- However, source can also be from extra vascular infection
  - Spine (osteomyelitis)
  - Pyelonephritis
  - UTI
  - Perforated viscus
  - Colonoscopy
  - BCG treatment for bladder cancer
  - Aneurysms/dissection can erode into the esophagus, spine, ureter or bowel
- Can also indolent

8

Overview- Primary Mycotic Aortic Aneurysm

- Very rare condition – 0.65% to 2% of all aortic aneurysms
- Most are saccular and often multifocal
  - Syphilis (Treponema pallidum): historically
- However…..

9



10

MICROBIOLOGY – Mayo Clinic Experience

	n =54	Percent
Culture negative	9	18
Culture positive	41	82
Polymicrobial infections	34	68
Streptococcus viridans	22	44
Candida sp.	19	38
Lactobacillus	13	26

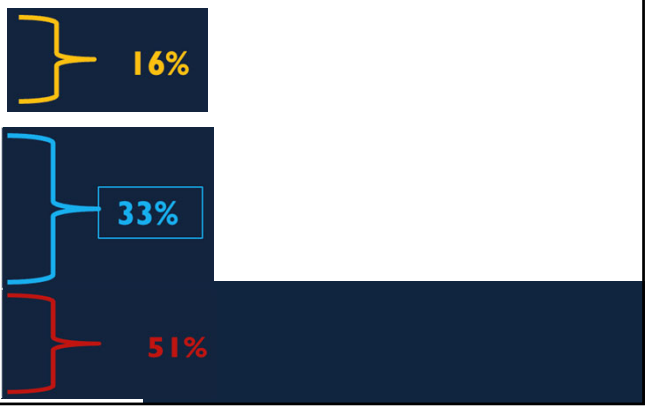
Enterococcus sp.	*E. coli*	*Staph Coag Negative*	*Bacteriodes fragilis*
Klebsiella sp.	*Enterobacter sp.*	*Staph aureus*	*Nocardia sp.*
Prevotella sp.	*Proteus Mirabilis*	*Eikenella corrodens*	*Rothia mucilaginosa*
Pseudomonas sp.	*Peptostreptococcus*	*Corynebacterium sp.*	*Citrobacter sp.*

11

Primary Mycotic Aortic Aneurysm: distribution

Infected aortic aneurysms: Aggressive presentation, complicated early outcome, but durable results

Gustavo S. Oderich, MD,[a] Jean M. Panneton, MD,[a] Thomas C. Bower, MD,[a] Kenneth J. Cherry Jr, MD,[a] Charles M. Rowland, MS,[b] Audra A. Noel, MD,[a] John W. Hallett Jr, MD,[a] and Peter Gloviczki, MD,[a] *Rochester, Minn*



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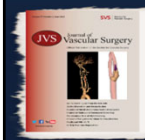
Treatment

- Antibiotics



Selective medical treatment of infected aneurysms of the aorta in high risk patients

Hsu RB et al. J Vasc Surg 2009;49:66-70

Conservative treatment of Aortic Graft Infection

Lawrence, PF. Semin Vasc Surg 2011 24:199-204

- Hospital mortality is 36% to 82%
- A series of 22 "high-risk pts" had a 50% hospital mortality with most pts dying within 2 wks of hospital admission and the rest who made it out died within 2 wks of discharge
- Aneurysm related mortality was 77%
  - Generally considered worse in Salmonella sp (or other G-negative bacteria)

13

Is this the best we can offer?

How about surgery?

14

Surgical approaches

- As in any other instance, wide debridement and removal of infected tissue is better than leaving this tissue in place.
- Question remains, however…..
  - What do you replace it with
    - Prosthetics will get infected
    - Aortic ligation has been attempted in the 20s and 30s but consequences are not acceptable
- And if replaced, can mortality & morbidity in this already vulnerable population be lower than medical management?

15

- Perhaps…. But what conduit?
- How about cadaveric vessels?

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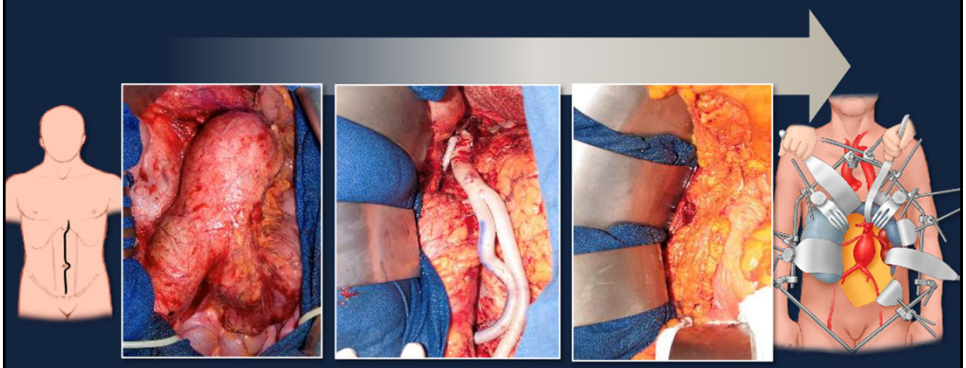
Surgical approaches: Cadaveric Grafts

- Used to replace a carotid artery in 1903
  - First used for the aorta by Gross in 1948 (Coarctation)
  - Dubost in 1952 used it to replace infrarenal aorta
- Remains useful to this date



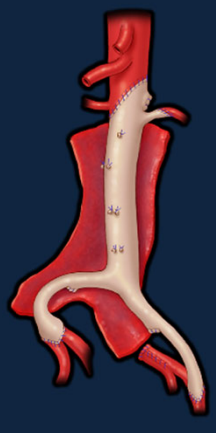
17

Use of Cryopreserved Aortoiliac Allograft for Aortic Reconstruction in the United States

Vascular

LFDC

Low-Frequency Disease Consortium



Harlander-Locke et al J Vasc Surg 2014

18

Cryopreserve arterial Allografts

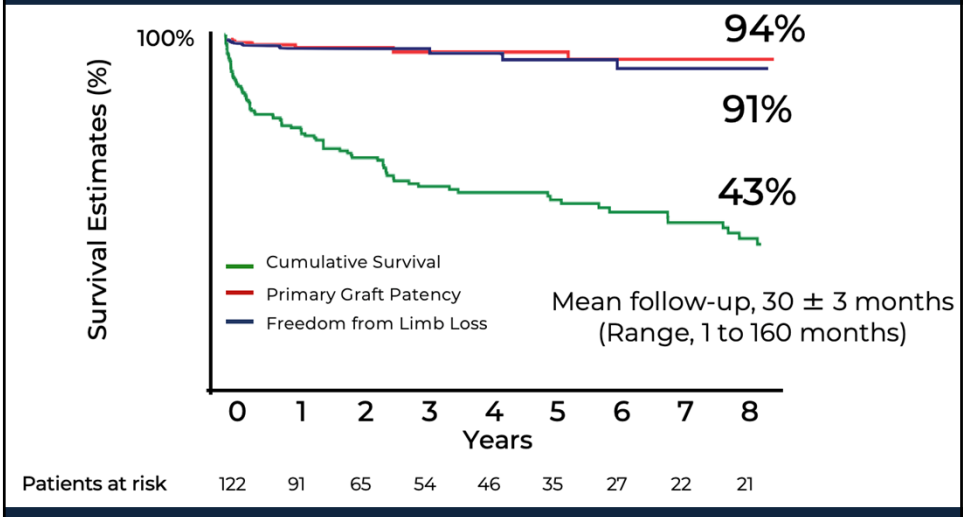
- 220 patients treated at 14 academic centers

	n	%
Initial aortic procedure		
Open reconstruction	209	95
Endovascular	11	5
Indications		
Primary prosthetic graft infection	143	65
Infected aortic aneurysms	44	20
Graft enteric fistula/ erosion	33	15

- 30-day mortality, 9%
- Length of stay, 24 days

19

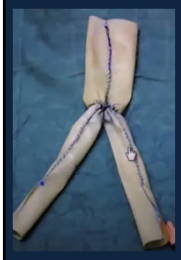
Late Results



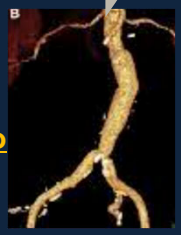
20

Neoaortic reconstruction with Xenografts (Bovine patch)

Due to the high cost of cryopreserved graft, a group in Norfolk, UK evaluated making their own graft and went on to treat 6 patients



- Kept all 6 pts on antibiotics
- 30-day mortality: 0%
- At 13 months, there were NO reinfection AND
- 100% survival rate



Review > Ann Vasc Surg. 2017 Oct:44:419.e1-419.e12. doi: 10.1016/j.avsg.2017.02.021. Epub 2017 Jun 20.

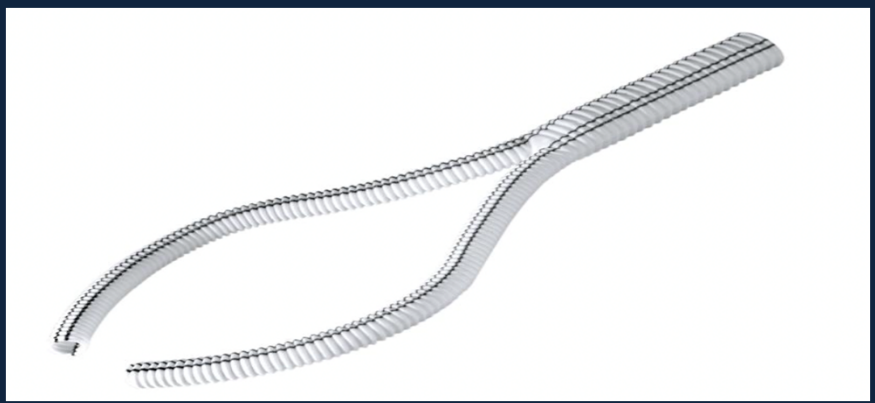
Neoaortic Xenoprosthetic Grafts for Treatment of Mycotic Aneurysms and Infected Aortic Grafts

Chukwudubem Anibueze [1], Visesh Sankaran [1], Umar Sadat [1], Kelvin Tan [2], Yvonne G Wilson [1], Robert E Brightwell [1], Michael S Delbridge [1], Philip W Stather [3]

21

How about using a regular graft?

It will get reinfected.



CAN WE PREVENT GRAFT INFECTION?
This has been tried!

22

Rifampin-soaked Dacron grafts

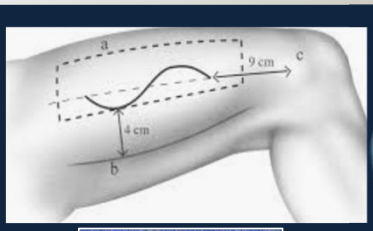
- To mitigate the risk of graft infection, antibiotics were added to Dacron and tested for resistance in the 1980's

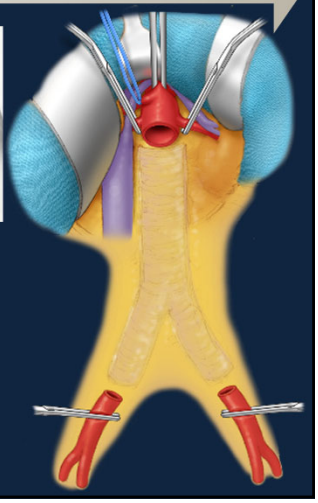
In situ rifampin-soaked grafts with omental coverage and antibiotic suppression are durable with low reinfection rates in patients with aortic graft enteric erosion or fistula

- The best concentration both in-vivo and in-intro is 60 mg/mL as it was found to be 100% resistant to intravascular inoculation of gram + organism (S. aureus) at 7-10 days, 80-100% in 10 days
- Very popular

23

Rifampin-soaked Dacron grafts





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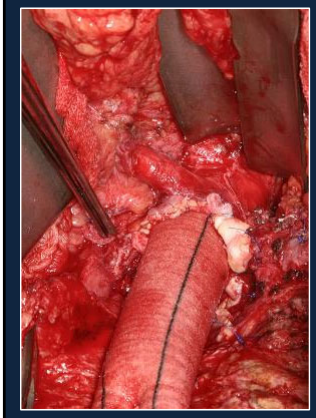
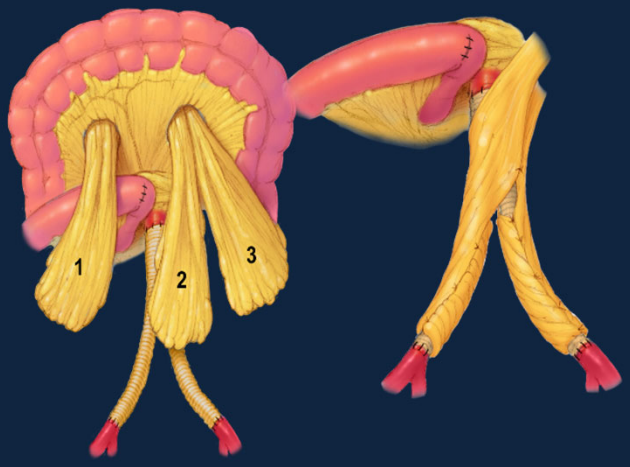
Rifampin-soaked Dacron grafts

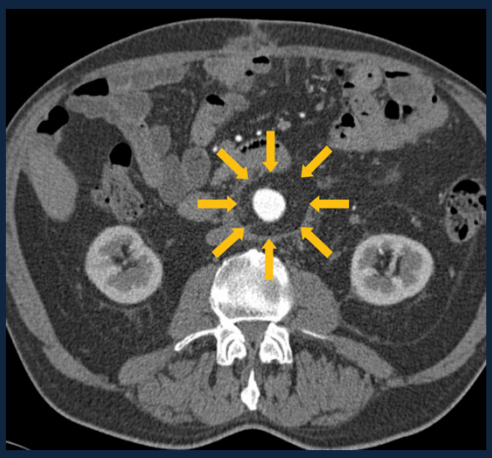




Drawings – courtesy of Gustavo Oderich, MD

25

Rifampin-soaked Dacron grafts



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Rifampin-soaked Dacron grafts

In situ rifampin-soaked grafts with omental coverage and antibiotic suppression are durable with low reinfection rates in patients with aortic graft enteric erosion or fistula

Oderich GS et al. J Vasc Surg. 2011; 53 (1):99-106

- Included 54 pts with aortic graft erosion or fistula
- Presentation
  - GI hemorrhage: 33 pts
  - Fevers: 25 pts
  - Hemorrhagic shock: 10pts
- Operative mortality 2.3% in stable pts and 40% in pts in hemorrhagic shock
- HLOS: 20 ±18 days
- 5-year survival was 59 ± 8%

- No late graft related death
- Two pts (4%) had a graft reinfection

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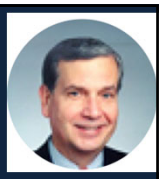
"NAIS" Procedure



- George P. Clagett, MD - UT Southwestern in Dallas, Tx.
- Noted high thrombosis (43% patency at 3 years and 33% amputation rate) and reinfection of prosthetic grafts
- Described the technique of **"NAIS"- neo aorto-iliac system** using femoral vein in 1993

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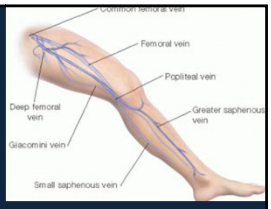
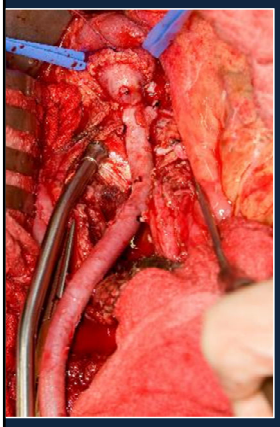
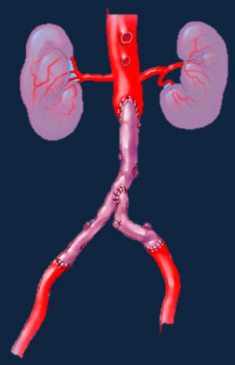
"NAIS" Procedure





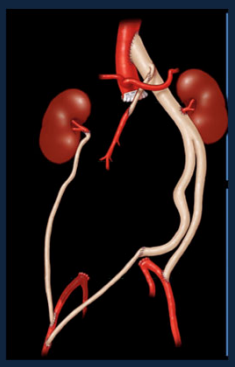


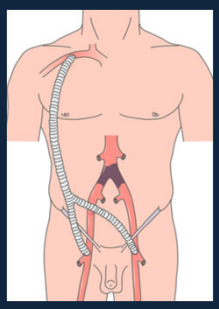
Has Excellent patency and limited risk of infection
Some have advocated "staging" the procedure – same outcomes

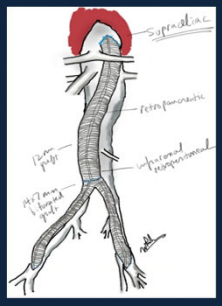
29

Extra-Anatomic bypass

- Aims to revascularize the lower extremities *before* removing the infected aorta in the middle
- Several alternations
  - Axillo-femoral bypass is the most common
  - Ascending or descending aorta to bilateral common femoral arteries







30

Infected aneurysm of the thoracic aorta

Hsu R.B, Lin F.Y. *J Vasc Surg 2008; 47: 270-276*

- Rare cases – experience limited to case series
  - Mortality: 30%-50%
- Largest series was by Hsu et al (25 pts -13 in the arch)
- Medical treatment results in near 100% long-term mortality (57% in hospital mortality)
- Surprisingly, surgical repair had a 12%
- However, *aneurysm-related mortality was 28%* in the surgical group
- Late graft re-infection – 16%

31

Considerations in pts with Thoracic Mycotic Aneurysms

- Does it involve the arch?
  - Pt will need hypothermic arrest
  - This adds to complexity and increased mortality
- Is there an actual fistula to the esophagus/trachea/bronchus
  - Worse outcome
    - Cancer
    - Bleeding
    - Aged pts
- What do you replace it with?

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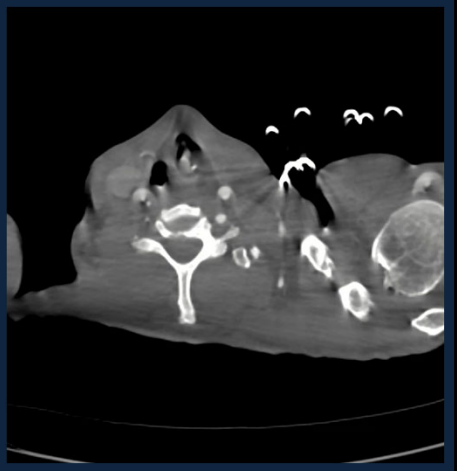
47 y.o. male with Marfan syndrome and Type B AD



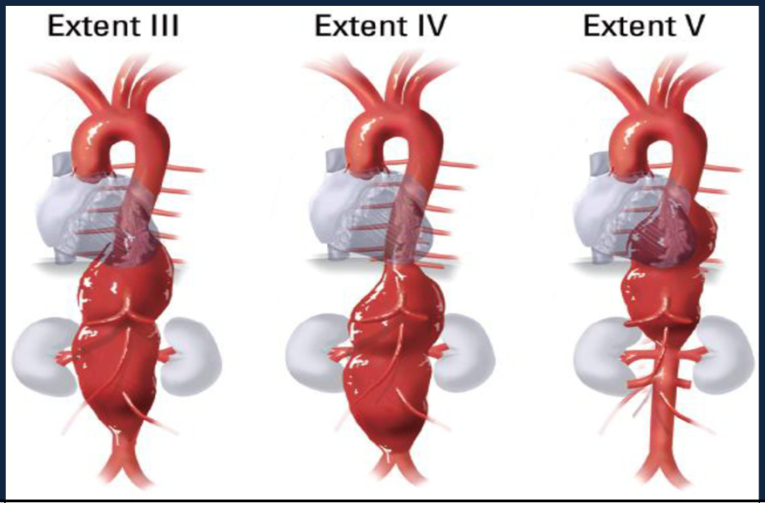
33

47 y.o male with Marfan syndrome and Type B AD

34

35

How do we address patients with infected TAAA?



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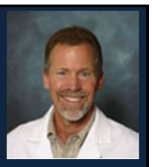
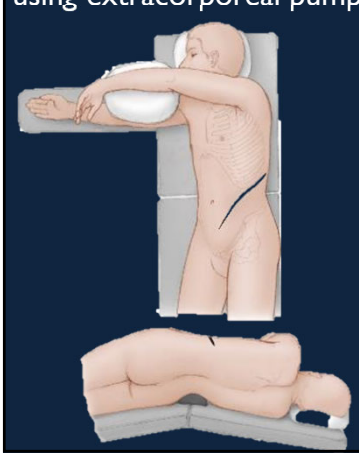
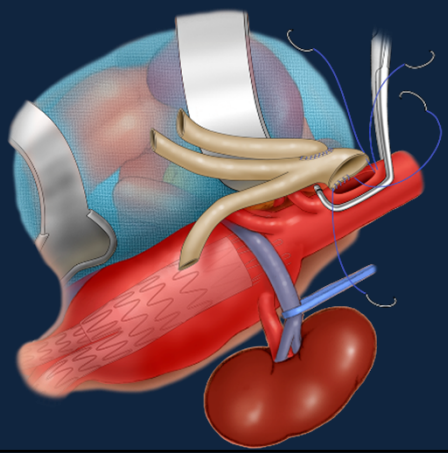
Jeffery L. Ballard, MD



Vascular surgeon from Loma Linda University who was interested in perfusing the intestines while repairing a TAAA (Type III-V) without using extracorporeal pump





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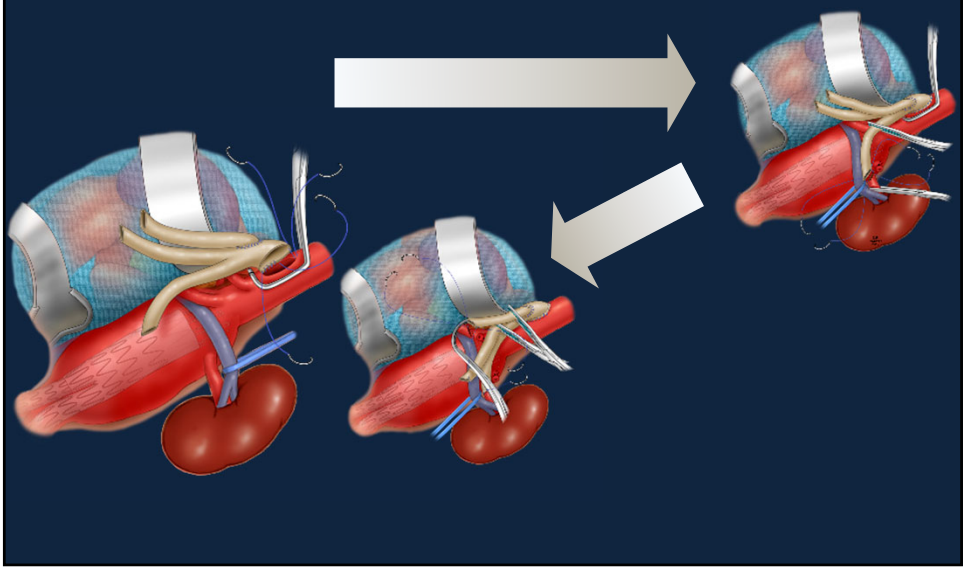
Ballard Technique



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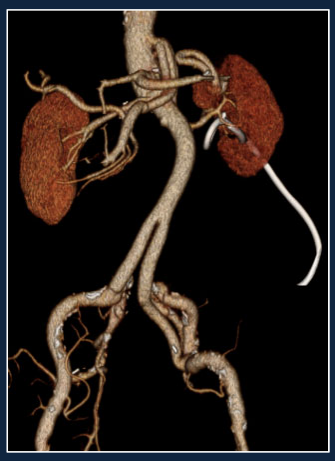
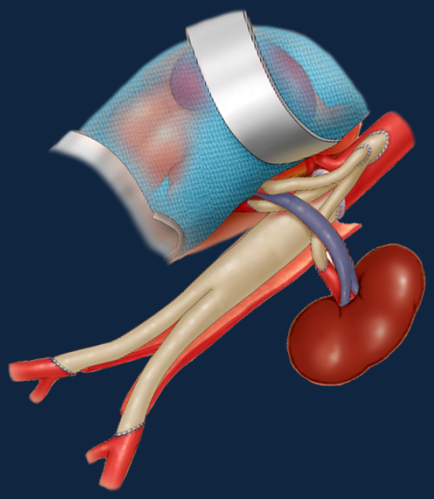
Ballard Technique





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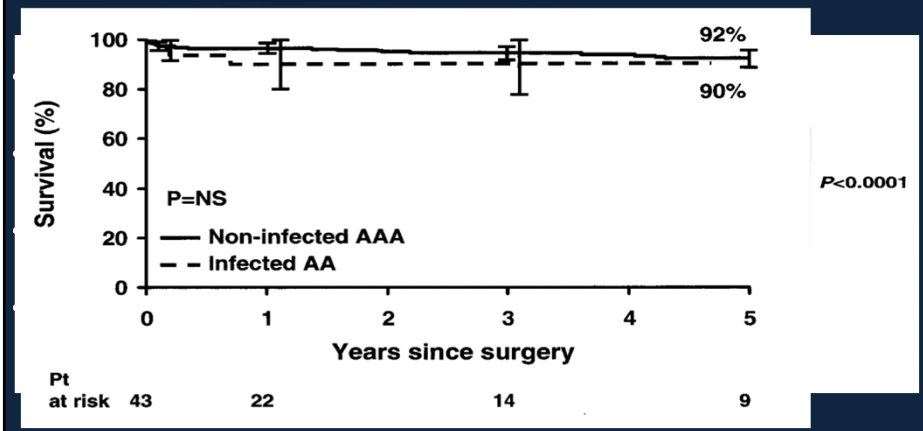
Infected aortic aneurysms: Aggressive presentation, complicated early outcome, but durable results

Oderich et al. J Vasc Surg J Vasc Surg 2001; 34:900-8



- Graft related complications were low and similar to non-infected pts (90% freedom at 5 years

40

Surgical management - Taiwan Experience

- A series of 56 pts treated with open repair from Taiwan
- In-hospital mortality was 23%
- HLOS: 45 days (5-149)
- Death after discharge were all re-infection- related (4/4)
- Late surgical-related complications were low (16%)
- 1 year survival:
  - Infrarenal: 82%
  - Thoracic: 47%

41

CONTEMPORARY RESULTS

	n	% 30-d Mortality	% Graft reinfection	%Primary patency	% Limb salvage
Axillo-femoral bypass					
Yeager (1999)	60	18	10	73	82
Seeger (2000)	36	19	3	64	80
Femoro-popliteal vein					
Clagett (1993)	41	7	0	83	86
Arterial allograft					
Verhelst (2000)	90	22	2	98	100
Kieffer (2004)	179	22	2	NR	99
Harlander (2014)	220	9	4	97	97
Rifampin-soaked					
Oderich (2006)	52	8	12	89	100
Oderich (2011)	54	9	4	92	100

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Clearly outcomes of these open repairs are underwhelming….

IS THERE AN ENDOVASCULAR OPTION?

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Endovascular Enthusiasts must have a say…

- **Semba et al.** in 1998:
  - 0% 30-day mortality in 3 pts
- **Patel et al.** – TEVAR in 14 cases of infected thoracic aneurysms:
  - Early survival: 86%
  - 3-year survival: 58%
  - Re-infection: 25%
- Kan et al. (*J Vasc Surg 2007*) - reviewed of 48 pts:
  - 30-day mortality: 11%
  - 20% had persistent infection
  - 3-year survival of 30% with persistent infection
- Why even offer open repair with such great outcomes???

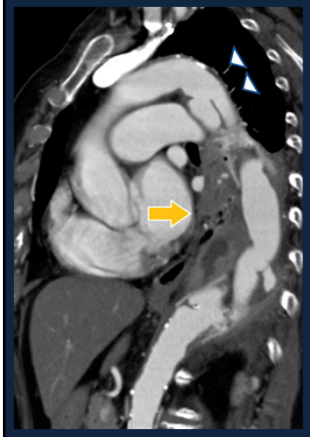
44

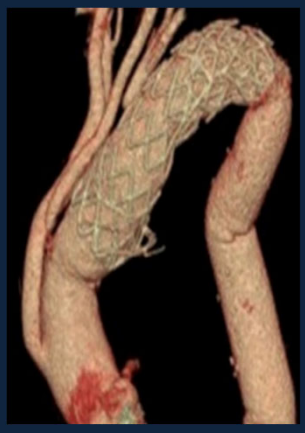
So, Why not use an endograft?

- Well… think about it…
- If you place a prosthesis into an infected aorta, it will ultimately become infected
- This is particularly true if you are not removing all infected material
- Surgical principles dictate that you *HAVE* to immediately repair or exclude the duodenum, esophagus or ureter in the aorto-enteric fistulae and remove all dead tissue to enhance survival

45

52 y.o. male with an aortic dissection and multiple sternotomies presented with an aorto-trachial fistula





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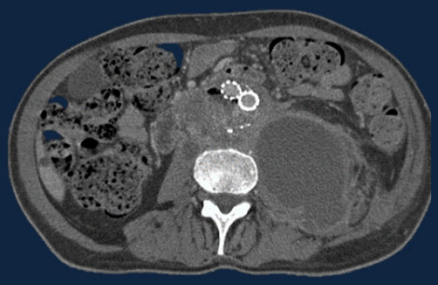
Infected infrarenal endograft

- 60 y.o. male with back pain and infrarenal penetrating aortic ulcer
- underwent EVAR at an OSH
- Returned with fevers, chills and worsening abdominal, worsening abdominal pain and in renal failure
- Started on broad spectrum antibiotics for presumed graft infection and transferred



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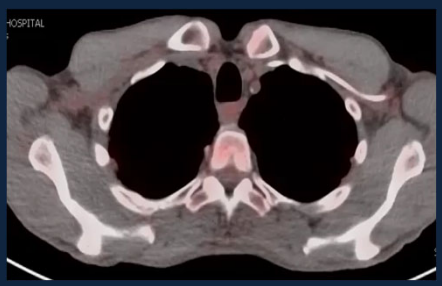

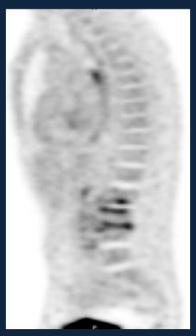

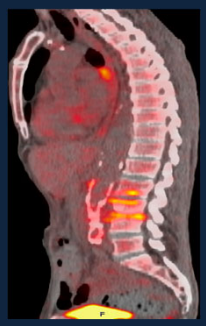

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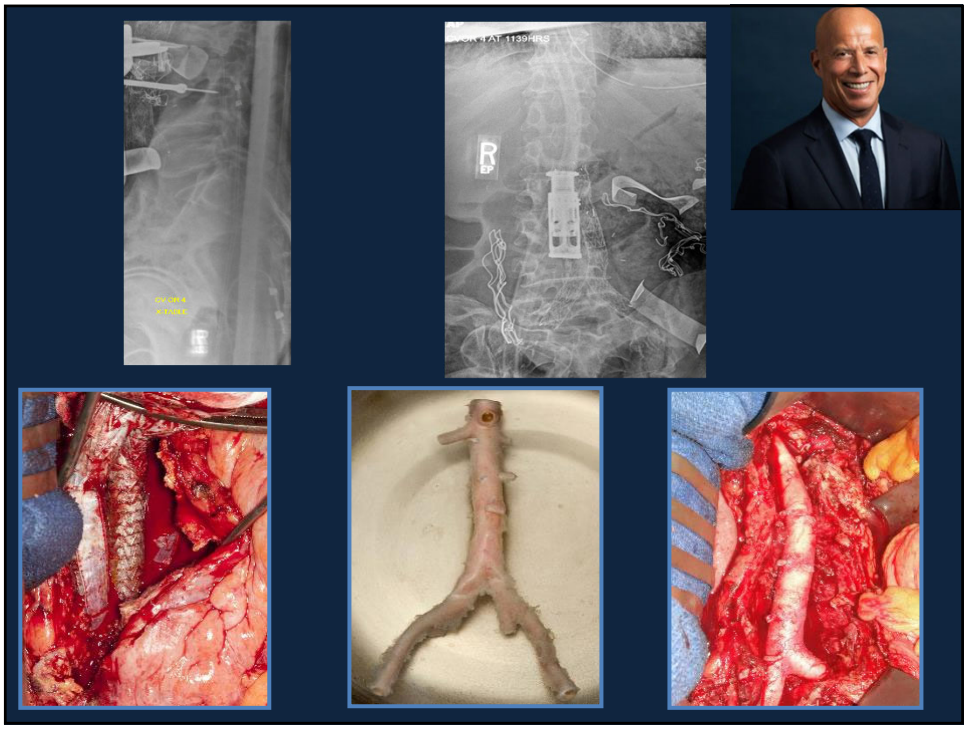

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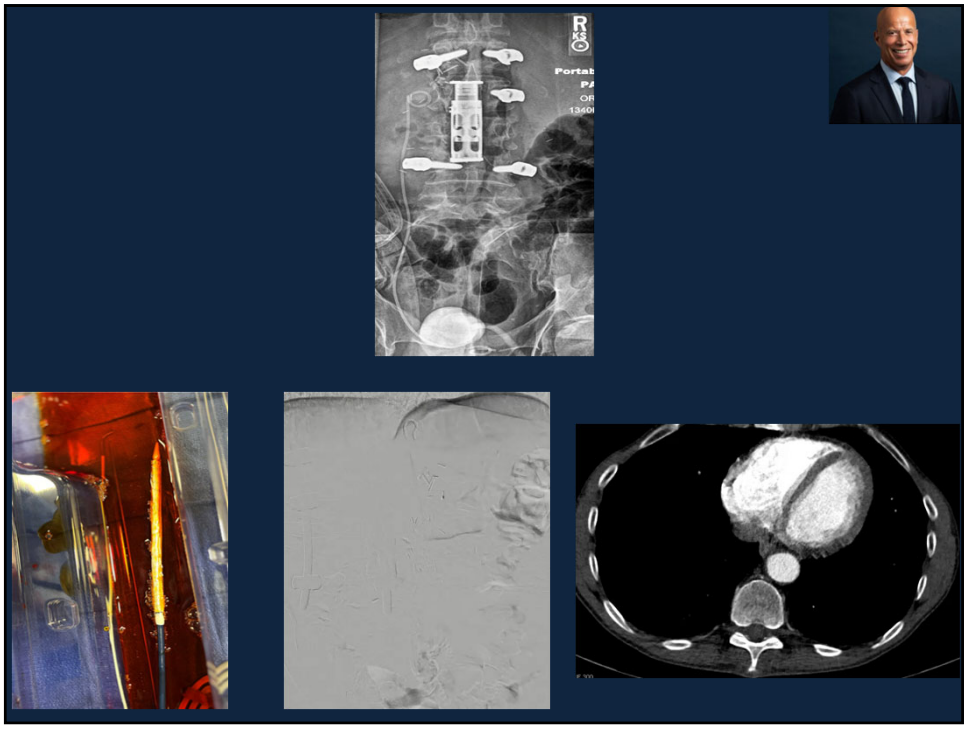

50

Endovascular - outcomes

- Endovascular management is considered as a "temporizing" measure
- Recently, there's been new/resurrected enthusiasm about endovascular repair

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National Study of Treatment of Mycotic Abdominal Aortic Aneurysms Comparing Open and Endovascular Repair

Sorelius et al. Circulation 2016

- 132 patients (mean age, 70±9) treated in Sweden for infected AAA

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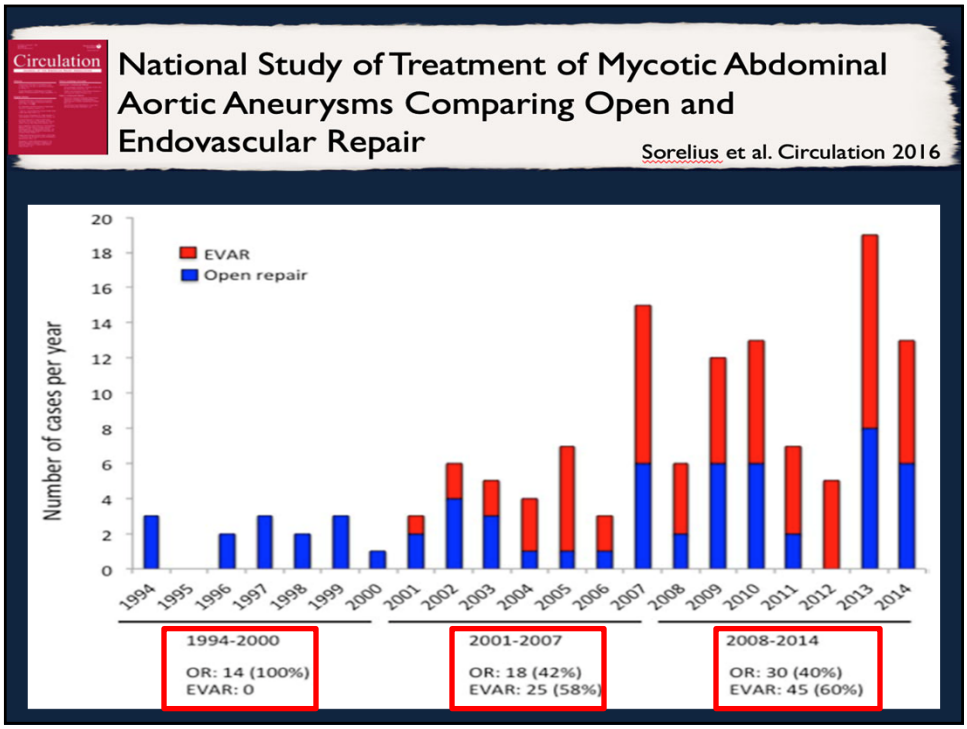
Circulation
National Study of Treatment of Mycotic Abdominal Aortic Aneurysms Comparing Open and Endovascular Repair
Sorelius et al. Circulation 2016
EVAR
Open repair
Number of cases per year
1994-2000
OR: 14 (100%)
EVAR: 0
2001-2007
OR: 18 (42%)
EVAR: 25 (58%)
2008-2014
OR: 30 (40%)
EVAR: 45 (60%)

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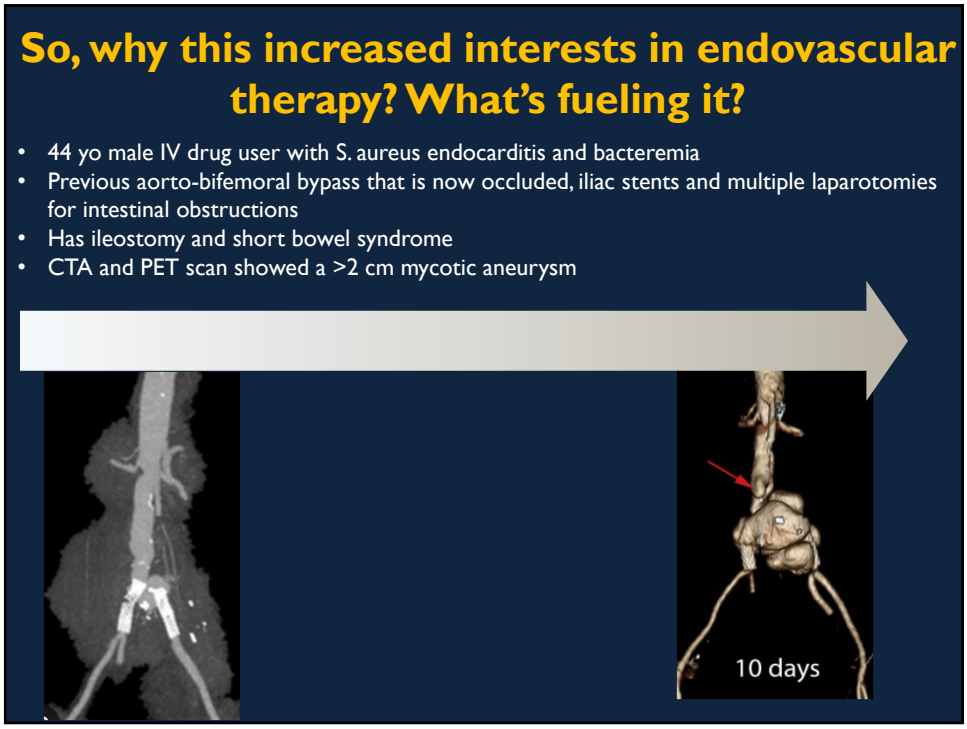
So, why this increased interests in endovascular therapy? What's fueling it?
• 44 yo male IV drug user with S. aureus endocarditis and bacteremia
• Previous aorto-bifemoral bypass that is now occluded, iliac stents and multiple laparotomies for intestinal obstructions
• Has ileostomy and short bowel syndrome
• CTA and PET scan showed a >2 cm mycotic aneurysm
10 days

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Obviously, you have to fix this

- Tried open repair but couldn't
- The idea of an endograft becomes more appealing
- He added:
  - 3 amps of 60 mg/dL Rifampin
  - 30 cc sterile water

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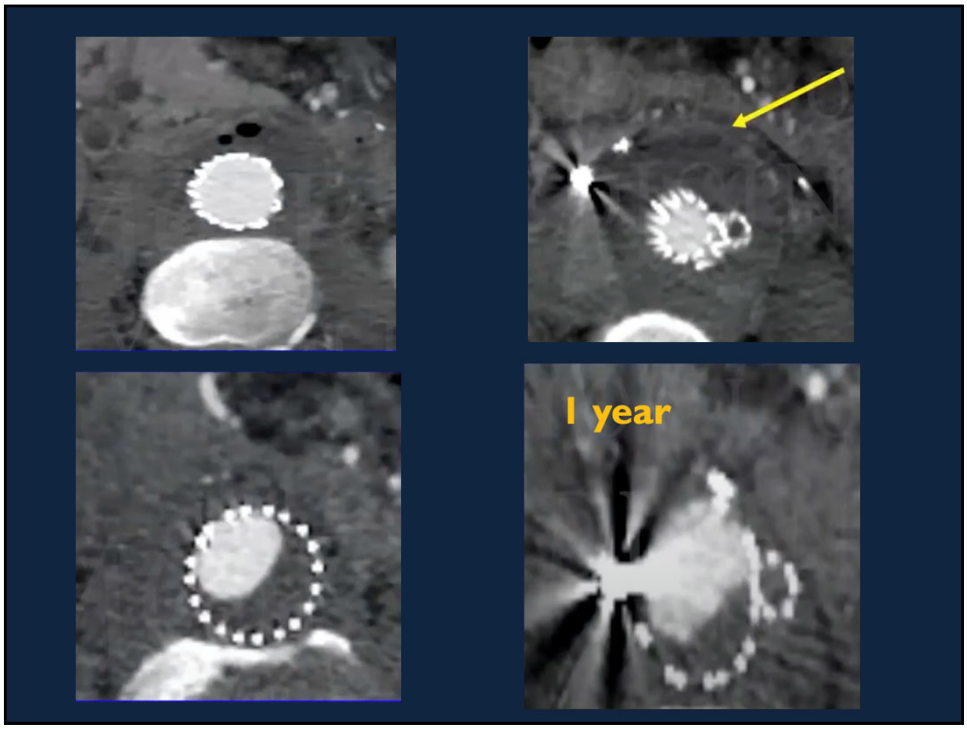

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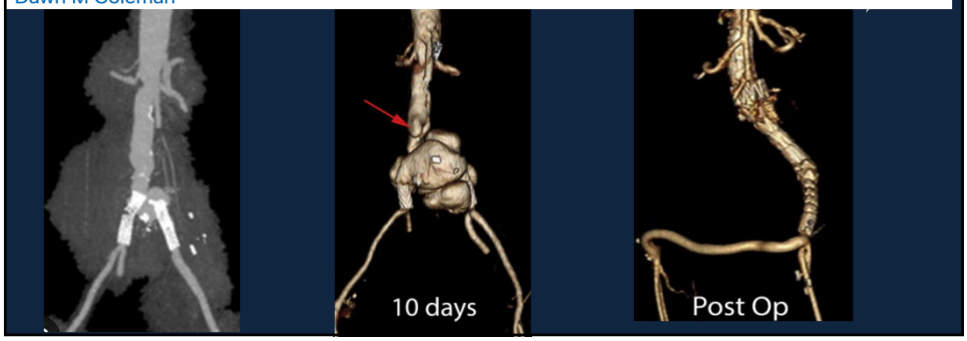
So, if you can't do this, what do you do in a case when the patient's too sick or you just can't get in???

- 44 yo male IV drug user with S. aureus endocarditis and bacteremia
- Previous aorto-bifemoral bypass that is now occluded, iliac stents and multiple laparotomies

Rifampin soaking dacron–based endografts for implantation in infected aortic aneurysms––new application of a time–tested principle

Guillermo A Escobar [1], Jonathan L Eliason [2], Justin Hurie [3], Shipra Arya [4], John E Rectenwald [2], Dawn M Coleman [2]

Ann Vasc Surg. 2014; 28(3): 744-8



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Mortality after endograft for infection

- Most recurrences appear to happen at 1-2 years
- After 2 years, chance of long-term survival is good, much better than open repair
- **So, how do we get pts to this 2 year mark?**

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Optimizing the chance of success of endovascular therapy

- What if we can drain the abscess after endografts for pts who are not candidate for open surgery?
- Described by Belair in 1998
- Literature review of 29 pts with infected endografts
- Hospital mortality was 21% (6 pts)
- Another 7 died within a year so 45% 1-year mortality
- Only 41% of pts got antibiotics and the rest had a drain placed
- Mortality was 50% in drained or not, especially if there was a fistula

Belair M et al. AJR Am J Roentgenol. 1998 Jul; 171:119-24
Moulakakis KG et al. J Endovasc Ther 2014; 21:448-455

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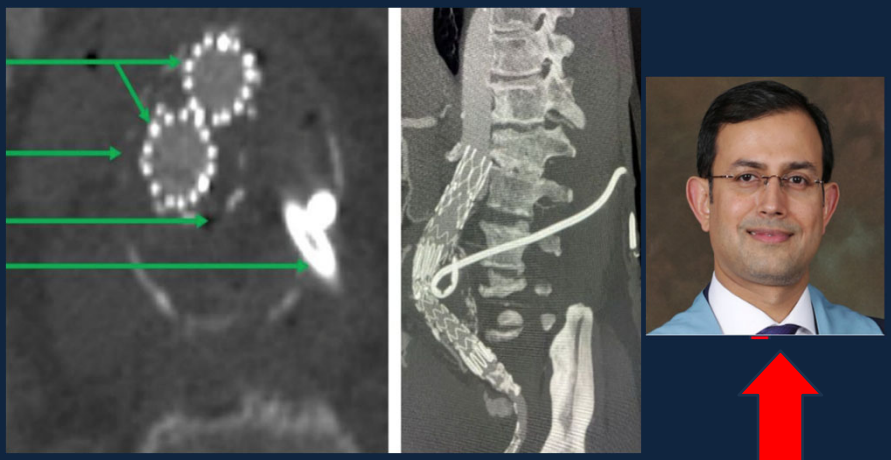
So…. Drains don't work



NOT SO FAST!!!!

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What if we add antibiotics to drain/lavage?

- 10 pts with graft infection treated with drainage and irrigation
- Using a solution of Gentamycin, Penn G and Metronidazole
- Irrigated until sterile culture – how long?
- Only 2 were known to reinfect – 80% survival
- **Even on VRE**
- **Drain placed in the aortic sac and irrigated with linezolid for 28 days**
- At 7 months show resolution clinically and on CT

Akhtar M et al. Int J Angiol 2016; 25: e118-e120
Morris GE et al. J Vasc Surg 1994; 20: 88-95

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Conclusions

- Mycotic aortic aneurysms are rare but deadly
- Medical management *ALONE* results in nearly 100% mortality
- Open surgical repair is better than conservative management, but still carries a high mortality (>20%) and morbidity (up to 50%)
- Endovascular treatment is gaining popularity for *primary* infected aneurysms in pts *without enteric contamination*
- It ***may be used as a "bridge" to open surgery*** in pts with massive hemorrhage, or as a definitive treatment in conjunction with antibiotics in high-risk pts with no evidence of enteric erosion

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