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TRANSCRIPT - GR 04 22 22 Grollman Lecture - "Infective Endocarditis: Why Cardiologists Need to Remain Grounded in Internal Medicine" ***Patrick T. O'Gara, MD,*** **from the Brigham and Women's Hospital**

Medicine Grand Rounds

- 00:27:17Good afternoon, everyone.
- 00:27:20Like to for our distinguished speakers introduced I'd like to introduce the Marjorie and Jake Roman visiting lectureship cardiology.
- 00:27:30Dr J Roman received his MBA from the University of Maryland and trained in Ob gyn at Baltimore city and the University of Nebraska.
- 00:27:38He then undertook basic endocrinology research and collaboration with his brother, Dr Arthur girl minute as Hopkins and subsequently began a private practice in Ob gyn in.
- 00:27:49Washington DC and he was on the staff of the Washington hospital Center after practicing for 45 years he retired to a second career in farming.
- 00:27:57In Gordon's bill Virginia and at that time became a a patient of Dr George belters his wife received her bs degree from the.
- 00:28:07From Maryland in 1941 and became a dietitian and nutritionist of the Union memorial hospital in Baltimore and together they in doubt this.
- 00:28:18Annual growing and building lectureship in cardiology which we had to forego the last couple of years due to the pandemic and we're very fortunate to have Dr Patrick go get right here this year from Brigham and women's in Harvard Medical School and formal introduction will follow.
- 00:28:40Hello everyone, it is our pleasure today to have Dr pat aguero with us he graduated from Yale university with a degree in biophysics and biochemistry even obtained his medical degree at northwestern your city.
- 00:28:56From there he went on to complete his internal medicine residency I had chief residency and his fellowship and cardiology at the Massachusetts general hospital.
- 00:29:06and Dr Guerra joined the Faculty at Harvard Medical School in 1984 as a clinical instructor in since risen to the rank of for professor and, most recently the Watkins family distinguished chair and cardiology at the Brigham and women's hospital.
- 00:29:23doctor okay Ray is a force to be reckoned with and with he has served on a truly staggering number of internal committees and the Harvard Medical School and associated hospitals, as well as external communities through the American college of Cardiology and American heart association.
- 00:29:42among many others in.
- 00:29:46He was the president of the American college of Cardiology Dr Guerra has over 200 peer reviewed publications.
- 00:29:54He serves as the either reviewer associate editor or editorial board member for jack circulation New England Journal of medicine hj and many other journals as well.
- 00:30:08For all of his work within the Harvard Medical School and medical system, he and the greater cardiology community in general.
- 00:30:16He was aware of the Eugene Grunewald clinical teaching award from the Brigham women's hospital in 2021 and that distinguished teaching award from the American college of Cardiology in.
- 00:30:29Given all of that, it is truly an honor to have him with us today to present the.

- 00:30:35Roman lecture series or lecture Dr Guerra, the floor is yours.
- 00:30:54ruthie well thanks very much Sam for that Nice introduction and to my friend and colleague Dr Kramer for this wonderful invitation.
- 00:31:03it's really extraordinary for me to see the list of people who have provided this lecture over the course of the past 30 years or so, beginning and Dr.
- 00:31:11bellows tenure and I'm very proud and humbled to be included on that list you know it's always interesting to sit in an audience and hear a little snapshot of your bio isn't it.
- 00:31:24So what Sam didn't say, as I graduated from college.
- 00:31:31Almost 50 years ago so it's really nice to see such young faces in the audience and you're not sitting in the next zip code which is typical.
- 00:31:40of medical grand rounds and cardiac grand rounds all the young ones you guys like and you look ladies like to sit in the back so maybe we'll have you come up to the front, so I can call on you.
- 00:31:51Would you like that, and he did this is just to try to develop a little interaction, I know that we have some people on zoom as well it's great to be back in person.
- 00:32:01And these kinds of auditoriums are wonderful places to lecture I think that the line of sight is great, and I can see all of your eyes and you can see the top of my bald head.
- 00:32:14So it's extraordinary to me that I actually graduated with a degree in biophysics and biochemistry I can't remember any of that.
- 00:32:24But I do remember my art history course, and I do remember my constitutional law course.
- 00:32:30And you come to a place, like the University of Virginia and I think it instills in you this recognition self recognition that we all need to remain liberally educated don't wait.
- 00:32:39And, especially given the challenging times in which we live.
- 00:32:43In a place, like the University of Virginia that provides you with this kind of curriculum and this kind of opportunity and speaking mostly to the residents and fellows.
- 00:32:51Really extraordinary and I'm sure that you're taking advantage of it, whether you're an undergraduate and medical student and medical resident or fellow and training so keep the fire burning, as they say.
- 00:33:02Now, when I was thinking about what kind of a lecture to give to an internal medicine audience, I thought that it would be.
- 00:33:11worthwhile for us to talk about infective endocarditis because, after all, cardiologists are internists That is our grounding you wouldn't really know it, these days, which.
- 00:33:21because so many of us in cardiology take care of really relatively small areas of Cardiology, so there are people who do ECHO and there are people who do CT and people who do, Mr.
- 00:33:35And some people who do electrophysiology and cardiac cath and then the pie gets sliced and slice but, at the end of the day, we're actually all internist and I do think that people with infectious endocarditis provide us with a lot of clinical as well as research.
- 00:33:51Challenges to try to put things in perspective in a much more holistic way than we are typically used to, especially in the hustle and bustle of the current environment.
- 00:34:01ACS check the box proponent etc and you're on your way so let's just think a little bit more about the holistic approach to effective endocarditis and what some of the.
- 00:34:11challenges are in the bumps along the road and how it is you might approach this problem now Dr Kramer is a history buff.
- 00:34:19Now I don't think that necessarily extends to the history of medicine, but it probably does knowing your intellect.
- 00:34:26This is the most prized possession in my office so, like many of you, I have a little office and I have a computer there, but I have this old bookcase, and this is a textbook that was given to me.
- 00:34:39By the second chief of the cardiac unit at mass general hospital, the first Chief of course his name is written, right here, do you recognize the name Paul Dudley why.

- 00:34:52And some of you do some of you don't okay so Paul Dudley white practice at the turn of the century, and in the early 19th century, but eventually became Dwight Eisenhower's cardiologist.
- 00:35:04he's the guy who took care of Dwight Eisenhower when he had a myocardial infarction and Denver Colorado and against all tradition, at that time said, I think you should get out of bed and start walking.
- 00:35:15Because prior to that time people with myocardial infarction were admitted to the hospital and forced to bed rest for three weeks and usually died of pulmonary embolism.
- 00:35:24So it was Dr white who established this whole idea about well, maybe there's going to be this thing called cardiac rehabilitation.
- 00:35:31And by the way, I think exercise is important, and you should watch what you eat and you should try to keep your weight down within an ideal range now familiar, so this is actually now about 100 years ago when all of this was starting and Dr lights.
- 00:35:46imagination, have you heard of the white part the wolf Parkinson white syndrome well that's Dr white and so Dr white is actually the person who is.
- 00:35:56accorded the distinction of being the first person in the United States to establish an academic program in cardiology on the bed distinction.
- 00:36:06And he went on to become the president of the American heart association and all all sorts of other things, and he.
- 00:36:13It has been a leading force in the history of Cardiology now for over a century, and he passed the baton on to Dr Edward bland this has nothing to do with anybody here in the audience i'm sure, except Dr bland was a wonderful gentleman from rural Virginia.
- 00:36:30and was one of the first people I met when I started my training and when he decided to retire late into his 80s, he said, I think you might like this book, and so this is actually a 1920 edition of.
- 00:36:45textbook of the principles and practice of medicine.
- 00:36:49Why is this important well, I think, historically generations of internists and cardiologists we're talking about the natural history of endocarditis on the basis of observations that Sir William osler had made.
- 00:37:04Over a career that actually began in Montreal and included pathology.
- 00:37:09And then, of course, extended to Hopkins where he was the ostler professor and everyone else who is followed in his footsteps are usually accorded.
- 00:37:19That extraordinary distinction so isn't it nice to sort of go back in time and recognize that this problem that we face has actually been described in multiple kinds of clinical ways for over 100 years and I'll share a little bit of his text.
- 00:37:36So what he said in 1892 is that it's difficult to give a satisfactory clinical picture of the disease, because the modes of onset are so varied.
- 00:37:46And the symptoms are so diverse and what I take away from this is that if you've seen one case of endocarditis you've seen one case of endocarditis.
- 00:37:55and be careful not to cut corners, or to think that everybody fits in the same box so in the current era we have people who inject drugs.
- 00:38:04But 40 years ago we had endocarditis have a different type we had endocarditis like this lady here in the lower left hand panel of this slide.
- 00:38:13What did this woman present with when I met her in the emergency room she thought that she had developed a complication for missing her doses of thyroid hormone replacement.
- 00:38:25And, of course, the history revealed that she'd had low grade fever for a while and was losing weight, and this is what our life's look like what in the world is this.
- 00:38:35Well, this actually turns out to be performance and this is a flagrant case of Lupo side of classic vasculitis well what's that.

- 00:38:43That actually happens to be an immunologic complication that the card is the kind of endocarditis that hangs around for a long period of time.
- 00:38:51and eventually causes immune reaction with compliment activation and then vasculitis in the small vessels of the skin now certainly had shared.
- 00:39:00Many of a pathologic features is other causes of animal the vasculitis.
- 00:39:05But it's interesting to note that there's a reason for this, and this is the reason for which people with endocarditis a long time ago, used to sometimes present with pulmonary Ilona Freitas red cells in their urine or even read style cast.
- 00:39:19We don't spend the urine doing anymore it's usually sent some place and okay.
- 00:39:26Are you with me alright so back in the day, we used to see people with rheumatic heart disease, even the days well proceeding me and the 1970s, or so patients were younger.
- 00:39:40And they typically had native heartfelt disease related to their romantic disease aortic regurgitation and Michael stenosis in particular.
- 00:39:49And then predominant organism one strength and the kind of strep that is an oral pharyngeal origin.
- 00:39:55And patients presented with a sub acute illness something stretches out over weeks or months associated with things like weight loss.
- 00:40:03or back pain or splinter magaly are the kinds of things that we now worry about are associated with lymphoma or cancer.
- 00:40:11And this was the mode of presentation for the majority of people in that particular area and I’m showing you a little snapshot of vascular complications of endocarditis here in the lower left hand part of this slide.
- 00:40:23So this is a person who turned out not to have positive blood cultures, this is a person who turned out to have pancreatic cancer.
- 00:40:31And this is an example of somebody with non bacterial from bardic endocarditis or Miranda endocarditis or the kind of endocarditis that exists across the spectrum of true so syndrome if that's familiar to you.
- 00:40:49So what are we seeing now well we're seeing a lot of older patients who have degenerative disease of the fibro skeleton of their heart.
- 00:40:55They already felt mitral valve with people with diabetes right a lot of people with end stage renal disease on haemodialysis sometimes even with infected fistula and we're seeing a lot of people who use drugs right.
- 00:41:08And a lot of people as well, who have implanted cardiac devices which can be really nettlesome to take care of in the context of a bacteria or somebody who has a very popular infection.
- 00:41:19And in the current era staff is king, is it not staff or is methadone sensitive or methicillin resistant.
- 00:41:27If you look at the Microbiology data that now populates registry or observational studies of who's coming to the hospital with endocarditis staff is at the top of the list.
- 00:41:36That kind of organism, that is not touched by antibiotic prophylaxis prior to dental procedures there's the row right.
- 00:41:44Okay, and it's an acute illnesses shown here on the bottom right hand side of the slide this actually is a doppler pattern of somebody with the orange.
- 00:41:53regurgitation and this steep green line that i'm showing with my arrow is indicative of a rapid decrease in velocity during the asked to leave because the pressure and the Left ventricle is rising so quickly.
- 00:42:05So this is a patient with acute severe a Nordic regurgitation.
- 00:42:10And here's another wake up call for the current generation of patients, we see with infective endocarditis here's an infection on somebody with a normal aortic valve.

- 00:42:20This is not somebody with a bike custody or the family or a prior history of endocarditis.
- 00:42:25or rheumatic fever, this is a person with a normal tried leaflet a already fell who developed strep bogus endocarditis that's really worrisome isn't it.
- 00:42:35And so strap Bovis it's a little nastier than the certainly the viridian strap that live in our mouths but it's not as nasty as some of the other streptococcal organisms that.
- 00:42:46We might run into and people that have helped confections, for example, and this is really worrisome when is it going to happen to one of us that.
- 00:42:54We have a polycom in our colon or we have died particular disease, and you have strep Bovis bacteria and then you get endocarditis.
- 00:43:02And the other interesting organism that's popped up is the one that causes acting certainly are a lot of folks with acne.
- 00:43:09But propre on a bacterium at basis popping up all over the place, and people were had previously normal bouncy big vegetation, is where the tendency to ambled ization, particularly in young men.
- 00:43:23So here's another set of interesting observation, so how often do you do we encounter effective endocarditis in an academic medical Center like uva.
- 00:43:33So these are data and that are put together by some colleagues of mine who are oral surgeons in the UK and they've been interested in this question about.
- 00:43:42The efficacy of antibiotic prophylaxis prior to dental procedures for prevention of effective endocarditis for a long period of time.
- 00:43:49And they've done these massive epidemiologic studies, using the National Health Service database and here's a nice study looking at what they report as the.
- 00:44:01annual rate of admission for effective endocarditis across the National Health Service in the UK.
- 00:44:07Before and after the National Institute for health and care excellence decided that nobody needed antibiotic prophylaxis and that's about 2007 2008.
- 00:44:18So they took all the categories of potential need for prophylaxis right off the table to the data just don't support it or not going to recommend it for anybody.
- 00:44:29So what they have found interestingly enough in tracking this incident rate of admissions to the hospital with infective endocarditis that the.
- 00:44:38The incidence per million of the population has increased from approximately 27 to 50 maybe a doubling.
- 00:44:46Of course you'd look at this information and say, well, do you have the streptococcal organisms to go with this is everybody coming to the hospital have.
- 00:44:54endocarditis from an oral pharyngeal origin would these have been prevented with antibiotic prophylaxis because what we're seeing here, of course, is all of this is occurring in the opioid epidemic.
- 00:45:06And the scourge of staff and the influx of patients with end stage renal disease and I don't think any talk around it and endocarditis in the current era is complete without recognition of the.
- 00:45:20Extraordinary impact of the opioid epidemic on this particular cardiac confection.
- 00:45:27And I think that we've all been chasing with respect to our awareness of this problem, our ability to treat it effectively our ability to prevent relapse our ability to prevent reinfection.
- 00:45:38And then of course the ethical concerns about multiple cardiac surgical procedures in persons who continue to utilize injection drugs after hospitalization.
- 00:45:50So just to bring up really close today, right here here's something that we discussed it aren't morbidity and mortality rounds and sure you still have those on a monthly basis.
- 00:45:59Okay, all right great so here's a heart looking at it from the outside.
- 00:46:04And this is the gross pathologic appearance of fitness pericarditis the so called bread and butter pericarditis remember that term Probably not.

- 00:46:14Okay, but you can see here this lovely Sheen is, if you put a little virgin olive oil over the top of somebody's heart that appeared to be.
- 00:46:22A little bit irritated inflamed and you can see here in the region of the aorta and you can see the proximal pulmonary artery.
- 00:46:31there's clearly evidence grossly of inflammation and discoloration.
- 00:46:37And this fellow turned out to have a Nordic route endocarditis to beat the band.
- 00:46:43So what you're seeing here is the Left ventricle filleted open, and these are the three cusp of the already found, two of which are completely involved with staff for his infection.
- 00:46:53has turned out to be a 47 year old gentleman who was seen in the emergency room twice over the course of the preceding six days for low back pain.
- 00:47:03And was felt to be a mullingar because of his known history of injection drug use, he was last seen by his neighbors crawling up his front stairs because it's back pain was so severe he couldn't stand up.
- 00:47:16And then he was found the subsequent day by police personnel when they were called to his apartment because he was not responding.
- 00:47:26And this is perhaps one of three cases of this degree of a Nordic rude infection i've seen over the years.
- 00:47:35The other two of which died with pulses electrical activity in the context of usually complete heart block and then inability to mount a blood pressure.
- 00:47:47So a very startling wake up call that not everyone with back pain is necessarily malingering but she wouldn't that be a tough clinical situation to find yourself in.
- 00:47:57Especially if somebody didn't have a fever or something of that of that site.
- 00:48:03So infective endocarditis, of course, has been the King of the roots here for a while among patients.
- 00:48:09Who inject drugs, and these are some epidemiologic data from one State among our 50 Pennsylvania I don't think that any state has been spared the scourge of this particular epidemic huge problem in New England where of course poverty is is not.
- 00:48:26What should we say necessarily quarantined places in Maine and Vermont and new Hampshire really in the top five across those states in the United States West Virginia being at the top of the list.
- 00:48:39And here's a change in the percentage admission of patients with infective endocarditis due to drug use, and you can see, this uptick between 2015 and 2017 and 2020 and then, of course, much of this was made even worse by the COPA pandemic.
- 00:48:55In which we still find ourselves and then this is infected endocarditis from the national readmission database.
- 00:49:02Looking here in the blue line at the trend in opioid related overdose deaths between 2010 and 2015 and in the red line.
- 00:49:11A gradual increase in the number of patients with injection drug use related effective endocarditis admitted and readmitted to the hospital.
- 00:49:21For critical care, and you can see here that the incidence of infective endocarditis due to drug use, increased by about two full over this five year.
- 00:49:30timeframe and folks who do inject drugs are more susceptible to having recurrent episodes of bacteria relapse and readmission following discharged from the hospital, but we do know this here's a really nice example that was published about.
- 00:49:48A week and a half ago in the New England Journal of medicine in their image interest in clinical medicine section, which is kind of fun to look at every once in a while and on your left is.
- 00:49:59A picture taken on day zero when this 43 year old woman presented to the emergency department with fever and.

- 00:50:08vascular abnormalities of her fingers and a history of injection drug use and had a routine chest X Ray for the coffin shortness of breath she had and Sam you're going to be a pulmonologist this looks at normal to you.
- 00:50:24But all right, you ready to go.
- 00:50:28Okay, so it looks like there are a lot of these coalescing areas of.
- 00:50:33fluffy infiltrates one would have a high index of suspicion of course in somebody who is an injection drug user that try.
- 00:50:40To develop endocarditis may be right around the corner and she elected to sign out against medical advice, before anything else could be done with regard to her evaluation.
- 00:50:49And then she came back 21 days later, with the extra you see on the right.
- 00:50:54Which is a radiographic natural history study of septic and mobilization to the lungs, in the context of try customer bell endocarditis, this is a real tough problem for us to treat isn't it.
- 00:51:05Usually endocarditis on the right side of the heart, have a higher threshold for surgical intervention, most of these patients get better on their own, most of them are younger, some of them have poly microbial disease.
- 00:51:17And we can usually get through a couple of different septic emmeline but not these kinds of septic envelope right, depending upon what things look like when you take another.
- 00:51:26snapshot of the try custard belt on fl, and this is not a problem confined to the United States is it.
- 00:51:33So this is a lovely registry that's available to all of us it's called the international collaboration on endocarditis and here, looking at reports from all of the continents across the world, with respect to.
- 00:51:46The admission of patients with and without injection drug use, who happened to have infected endocarditis looking at mortality rates and looking at the prevalence that which surgery was performed.
- 00:51:58And here in the United States or North America, I should say let's just focus here and surgery was undertaken and about a third of patients.
- 00:52:06Who inject drugs at the time of their initial hospitalization and I think this reflects the fact that a lot of these folks that try custard valve disease.
- 00:52:14For which we generally have that higher threshold to intervene and hospital based mortality rates here about 10%.
- 00:52:21Of the population of patients that tends to be younger than those with left sided native tell them apart is and actually have fewer comorbidities like diabetes and end stage renal disease.
- 00:52:33The pathogenesis of endocarditis is always fascinated me because I think you could close your eyes and say this looks like something that.
- 00:52:40is very similar to Afro genesis if i'm not mistaken, there has to be a break in the end of valium and then the next thing you know these very smart.
- 00:52:49organism it's called staff or is that look like grapes here Okay, they find their way.
- 00:52:55Through platelet five and from by that have been caused called into the situation in order to seal off the endothelial and then they create a little nest of infection and then they make their way across the.
- 00:53:06Internal elastic basement membrane, as you can see here and then set up a cascade of inflammatory reaction those systemically as well as within the vessel all itself.
- 00:53:16And you get this cytokines activation and you get these ramped up white cells and macrophages and abscess formation and then reintroduction of the staff organism into.
- 00:53:27The circulation very similar to the kind of injury and inflammation that we've been watching we've been made aware of over the course of the last 50 years when it comes to coronary artery disease, for example.

- 00:53:39Just think of this as the exposure here is a micro organism and not oxidized ldl.
- 00:53:46So how are we going to go about managing these patients first, of course, diagnosis is key, you have to have an index of suspicion and it is true that, even though they came from Duke.
- 00:53:57Everybody uses a modified new criteria right to help make this diagnosis and establish whether or not it's highly likely to somebody has the problem or it's not so highly likely.
- 00:54:07And the modified dude criteria been around for decades, and there are a tremendous I think structure that allows us to make clinical decisions in.
- 00:54:17A more rigorous way and blood cultures are key.
- 00:54:19And then we wouldn't be anywhere without multi modality imaging in the 21st century, and certainly when it comes to endocarditis, this is the mechanism by which we verify the diagnosis, and this is also one of the mechanisms by which we assess risk.
- 00:54:36And certainly from a clinical perspective we look for heart failure at time and presentation.
- 00:54:41extracellular extension of infection which you can detect with imaging whether it's an abscess, for example, or a fistula metastatic infection.
- 00:54:50tends to reside in places like the lumbar spine or the spleen or some neat place like that, and your greatest fear.
- 00:54:57Perhaps is to replace a valve that's infected, only to have the infection in a satellite facility continue to provide a source of bacteria and require treatment unto itself embolism complicates the natural history of endocarditis and up to 40% of patients that's almost wanting to.
- 00:55:17Something that we look for less that situationally perhaps then is done in research studies, where everyone goes through MRI studies of their brain or CT scans of their abdomen.
- 00:55:28But certainly embolism is another source by which have satellite infection can be established.
- 00:55:33The immunologic manifestations that I've shown you usually implies that the infection has been around for a few weeks.
- 00:55:39And the presence of prosthetic material which is you know, is a vascular and not likely to be cleared of its infection in the absence of its removal.
- 00:55:48And it's really as simple as that, when it comes to managing patients with prosthetic valve endocarditis or rings after mitral valve repair agent co-morbidities are obviously part of the risk assessment, do you think this person has the tickets to get through open heart surgery.
- 00:56:06Now here's some examples and hopefully they will play.
- 00:56:10If I can get this up fantastic it looks like it's playing, and this is a transit stop the geo echocardiogram you can see that.
- 00:56:20And as you can see here, this is the mitral valve or my pointer is and there's this little thing flicking.
- 00:56:26The posterior leaflet of the mitral valve Can you see that little did so that's an echocardiogram term for a small.
- 00:56:35ECHO I don't know right mobile density it's a default okay.
- 00:56:39And the anterior leaflet looks a little thicken, and this is a 54 year old man with diabetes and important comorbidity came to the.
- 00:56:47Emergency room with fever and he had back pain and was not able to raise his left leg appropriately he turned out to have a SOA abscess from which strep was sample.
- 00:57:02And then two days later, somebody heard a moment and exactly how this sequence of events went along and whereas to see him because he's in the neurosurgical icu with an interim complication i'll show you later.
- 00:57:15So the question of course was here his echocardiogram findings and we're talking about risk stratification.
- 00:57:23And perhaps we're going to talking a few minutes about when do you operate on endocarditis and you can see here on the right hand side, this is a signal of mitral regurgitation.

- 00:57:33Which is modest will say that on a scale of mild moderate and severe, this is not more than moderate and this man had been scheduled for cardiac surgery.
- 00:57:4412 hours after we were asked to see him everything had been set up, this will just be fine it won't take you very long.
- 00:57:52we've already called cardiac surgery so think about this 54 year old fellow he's got an infection and SOS muscle, he has this degree of micro regurgitation no heart failure and he's scheduled for heart surgery, are you ready to go.
- 00:58:06Remember now your internist and then your cardiologist and you're sort of thinking about whether or not indications are met for surgery.
- 00:58:14And whether or not he would have the tickets to survive surgery okay so we'll go through a couple more examples here's a patient of mine who's 26 years old and 26 weeks pregnant.
- 00:58:27Her husband was a dealer and she thought that she would experiment and then she became unfortunately addicted.
- 00:58:35And she came to the hospital with fever and high grade staff or his factory MIA and this finding.
- 00:58:41Which corroborated the diastolic heart murmur heard on physical examination in the Nordic area, so this is an example of severe a Nordic regurgitation, this is a transit socket to ECHO and what you see here is this very broad blue, yellow.
- 00:59:00streaming jet of a Nordic regurgitation that fills the entire left and trickier alpha track, this is about in severe as it gets so she had heart failure acute severely autistic regurgitation high grade staff or his factory MIA and she's 26 weeks pregnant.
- 00:59:19So the question institution need an indication for surgery, and do you think that she has the tickets to get through surgery.
- 00:59:25Now it takes a bit of a village right to evaluate a patient like this, so now is internists and it's cardiologists and as imagers we're talking with maternal fetal medicine.
- 00:59:36And we're also talking with her family and we're talking with her about what the risks might be to her and to the baby should she require a cardiac operation.
- 00:59:50And then, finally, this gentleman who on the left here also has a Eric regurgitation he'd had a mechanical heart valve replaced.
- 00:59:59Some years ago, and you get a little bit of information here on this trance thoracic study there's a little bit of a signal of a leakage here.
- 01:00:07It seems to violate some of the anatomic boundaries what's going on here Well, this is a reason to get more imaging information, this is the reason for which we have.
- 01:00:17kind of a graded approach imaging wise to the assessment of patients with endocarditis start with a surface ECHO think about a transit stop the geo ECHO better pictures more sensitivity, even better, said.
- 01:00:30specificity in some areas and i'll show you some examples of pet CT so with the transit soccer God prob while ah.
- 01:00:39This is a gentleman who looks like he has a very large clear space between his mitral valve and he is a Nordic route, and this is an abscess into which you can see color flow you see where my.
- 01:00:54hand here, he is with the index finger that is diastolic flow into an abscess what along what we call the mitral a Nordic intro vascular fibrosis and so this is a violation.
- 01:01:09This is not something that responds to antibiotic therapy and hoping for the best, so this is extra valuable or extension of infection with abscess formation as visualized by transits on GEO echocardiography.
- 01:01:25And then, finally, the imaging modalities that we have brought to bear over the course of a shorter period of time, perhaps the last five or six years.

- 01:01:32Is the use of either cardiac see key or the combination of cardiac CT with mtg pet remember mtg pet is going to find macrophages that are all jazz stuff.
- 01:01:43or they're going to find tumor cells or something to that effect and here's a person with a previous aortic valve replacement, you can see the struts of the aortic valve over here, where I have my arrow.
- 01:01:54Okay, and then the plane contrast CT scan itself shows what appears to be a false aneurism and a collection of die outside that normal border of the order and it's also seeing here on this particular image at the bifurcation of the pulmonary artery, and this is a post cheerier.
- 01:02:16False aneurysm of the organic route also something that's not going to respond to antibiotics.
- 01:02:21And what is it well, it shows up like a Christmas tree here, and this is a few image with mtg pet and CT in which you can see unmistakeably.
- 01:02:31The kind of intense metabolic inflammatory activity that's associated with this abscess.
- 01:02:37And the combination of this kind of imaging has really put us into a different stratosphere when it comes to understanding preoperative Lee.
- 01:02:45The extent of the infection and what it is that one might be up against with regard to the challenge of putting this back together.
- 01:02:52So fused image mtg pet is something that is utilized increasingly frequently, especially in patients with a prosthetic device.
- 01:03:00In whom you can't really see if detection is present with echocardiography and it's also used in people in home you maintain a very high index of suspicion for infection, but you haven't seen it with other types of investigations it's really wonderful.
- 01:03:17So let's move on to treatment with respect to this particular disease and, of course, this is why we're all internists right so now we're going to go through 55 pages of antibiotic choices for endocarditis do that.
- 01:03:33So yeah I can't even remember when you're supposed to check 10 of my son level, so we still do that.
- 01:03:40All right.
- 01:03:42not really hard for your tests remember those days, you know so yeah OK, so we had to get the audiology involved, because we were going to give somebody six weeks of gentamicin and nowadays it seems like.
- 01:03:53You probably go to jail, if you wanted to do that I don't know.
- 01:03:56What we have these my antibiotics are obviously some things to which we would defer to our infectious disease consultants and they are rock stars, in the current era.
- 01:04:06are also the best internist in the hospital and this is part they are part of the heart team are they not in helping to make these kinds of treatment and risk stratification decisions.
- 01:04:17And it's wonderful to have that kind of capability, because I do think antibiotic choices can be really complicated renal function to worry about you've got the organism to deal with.
- 01:04:27You got sensitivity patterns that you can't figure out and then you meet me to make a decision about the indications for early surgery, based on the risk stratification.
- 01:04:37And then, finally, whether other therapies might be useful, you could be required, for example, to coil an aneurysm in the brain prior to its rupture.
- 01:04:46You may need a neural radio a radiologist, who is a neuro interventional as I should say or a neurosurgeon who does catheter based intervention to manage things before they become more problem.
- 01:05:00So it, it does expand the nature of the heart team and then issues in follow up have to do with the duration of antibiotics as well as the type of antibiotics for that period of time.
- 01:05:11Whether an indication for late surgery evolves because, after all these patients will have destruction of their heartfelt to a certain extent, and many of them can transition from acute.

- 01:05:23valve disease to chronic valve disease, the natural history of which can be followed longer term and then of course the nature of addiction medicine.
- 01:05:32And I think this underscores the need for a heartfelt team in the 21st century So these are some interesting data around which I think are infectious disease program is still quite worried.
- 01:05:44So this is the so called poet study, which is easy to remember and this study looked at whether or not after, at least 10 days of intravenous antibiotics, you could transition to oral antibiotics, if you were stable.
- 01:05:57And if you had cereal T studies that said you didn't develop extra valuable extension of infection.
- 01:06:04And randomized half the group to oral antibiotics to complete a four or six week course or the other half of the group to consider to continue the usual protocol intravenous antibiotics and as it turned out with their initial.
- 01:06:18report published in the New England Journal of medicine and.
- 01:06:22There were no difference and outcomes, the primary endpoint that included all cause mortality, the need for unplanned operation embolism and things of that nature.
- 01:06:31and hear their data that they just published in a letter form to the New England Journal of medicine, no short time ago.
- 01:06:38Looking at outcomes between patients allocated intravenous treatment to those who are transition to oral treatment after at least 10 days, which is kind of cool fair and, as it turns out.
- 01:06:51The they could not perform statistical significance assessment, because the study itself was not powered for clinical endpoints at five or 10 years.
- 01:07:02But it does look like In both instances, for example, the composite endpoint here on the left and death from any cause on the right that oral treatment.
- 01:07:12seemed at least numerically to do better than intravenous treatment in this selected group of patients with endocarditis so relatively low risk group, but perhaps this could be applied at such a way as to reduce the need.
- 01:07:26For all of the kind of monitoring and intervention when needs when providing intravenous antibiotics to these patients who do not have an indication for surgery.
- 01:07:35Okay well let's get to the indications for early intervention and on the top of the list of course with the heart failure, like the 26 year old woman, I showed you with acute severely autistic regurgitation she needs to have an operation.
- 01:07:48need to take care of the mother and then we'll take care of the baby secondarily, we have to save the life of mother she did have surgery she came through just fine and she delivered a normal.
- 01:08:00But unfortunately opioid addicted infant at nine months, and she had a little heart failure postpartum, but I think that was due to.
- 01:08:10So called postpartum preeclampsia which is kind of an oxymoronic term.
- 01:08:15In any case, when heart failure intervenes because of destruction of the bell or when patients have extra value or extension of infection, they need surgery.
- 01:08:24Usually within the acute phase that is while they're hospitalized during the index admission.
- 01:08:29And then I don't want you to forget the issue of a cardiac implanted electronic device infection, this is a situation in which you have to call.
- 01:08:38Dr mason and her electrophysiology colleagues at her device expertise and say, I have a patient with staph bacteria gram positive bacteria, I have a patient with vascular endocarditis who also has a device or I think the device might be infected.
- 01:08:56Under all of those circumstances, you could make a strong argument to take the whole thing out.
- 01:09:02And to reimplanted device after a period of time when antibiotics have been given, and there is no issue with infection.

- 01:09:09So, certainly in a situation in which the generator or the leads are involved and that can be very difficult to ascertain clinically and with imaging.
- 01:09:19Sometimes you get a hint with this with ECHO sometimes you get a hint with it with mtg pet not all the time.
- 01:09:26But when patients are lingering they're not making clinical progress they've been on antibiotics for a long period of time you think you're treating enterococcus bacteria what's wrong with this equation, they should be better take the device out.
- 01:09:40And then ask questions later unless it's life threatening to take the device out, and I think under Dr mason's direction that situation could be appropriately ascertained by her with her expertise and then, of course.
- 01:09:57The issue about whether the valve alone is infected that constitutes need to get the generator and the leads out.
- 01:10:04And then, as I said before, even in the context of bacteria think very hard about it, these are foreign surfaces.
- 01:10:11And boy did those organisms love to live somewhere along the length of the lead that's placed in the heart and it's real tough to find it.
- 01:10:19there's a biofilm that's created typically by staff and they just hide and all of that so Nikki I and all of those things that entrap the right side of leads that are placed in the heart is really tough to find.
- 01:10:32When patients are smoldering think about the device being infected so early surgery seems to have some merit, these are some observational studies.
- 01:10:41On the X axis is the percent of patients who underwent early surgery, and on the y axis is in hospital mortality.
- 01:10:48And this implies that the increasing proportion of surgery done early during hospitalization is associated with a reduced mortality in the context of infective endocarditis.
- 01:11:00Now we do have one randomized study i'm sure you're familiar with this, and this is a very clever study I think if you work for the nhl bi you would ask yourself why can't we do a study like this.
- 01:11:12Less than 80 patients less than 80 patients, this is a practice changing study that was published, I think, maybe close to eight or nine years ago 78 patients mean age 47, and these are from for surgical centers in Seoul South Korea.
- 01:11:31These are the same search and, by the way, who brought forward the notion that it's right to operate at patients with asymptomatic very severely or excelsis same group unbelievable okay anyway, half of them.
- 01:11:46had an belie on admission so they're already kind of a self selected pretty sick group of people.
- 01:11:53Then the third of them had vegetation that exceeded one and a half centimeters so they're already into a kind of range where your intuition, is telling you that maybe they had surgical indications.
- 01:12:05Right from the start 60% of them were infected with strap and the primary endpoint of this randomized study was a six week incidence of either hospital death or involved events.
- 01:12:17And if you look over to the right hand side of the slide you can see that early surgery and red beet conventional treatment in blue with respect to a composite outcome of death or in a hospitalization or amble ization.
- 01:12:32And this endpoint was driven by a reduction in the risk of embolism not much difference here and all cause mortality small data set, but this particular information.
- 01:12:44has resulted in a clear change in practice and embrace across cardiology and cardiac surgery for the potential benefits of early surgery to prevent amble ization and these kinds of at risk, patients.
- 01:12:59They have to be careful because surgery itself is associated with some risk of mo ization you have to choose your patients carefully.

- 01:13:07So this is what we're trying to avoid this is all too common and the more you look for it, the more you'll find it.
- 01:13:12This is a gentleman with endocarditis at perforated his aortic out here's the perforation this big blue line and here's the vegetation almost looks like a wart doesn't it.
- 01:13:23it's really quite something away some of these might appear and its associated with this, which looks to me like it's probably an infarct.
- 01:13:32And the question is, if this person has a surgical indication for early intervention.
- 01:13:38perforated leaflet probably had severe aortic regurgitation heart failure in this particular situation and now has an ischemic stroke Is it safe to operate under those circumstances.
- 01:13:50So as a data free zone in which we don't have the benefit of randomization.
- 01:13:55But I think suffice it to say there's increasing comfort with taking patients, just like this to the operating room and placing them on cardiopulmonary bypass and getting them through without further neurologic.
- 01:14:07To that detriment, and when people are studied either with say.
- 01:14:13Mental tasks before and after surgery or does not appear to be an increase in delirium as well, so for a small ischemic stroke, in which there is a strong indication for cardiac surgery we typically do not delay, as we did before.
- 01:14:28But on the other hand, of the spectrum I'll show you somebody else.
- 01:14:31Now this, I think, is that probably the most gnarly area of consultation that you're going to be involved in as medicine.
- 01:14:39And cardiology and infectious disease experts, etc, and that is what should we operate for the presence of vegetation, a law, so you have a patient.
- 01:14:50she or he does not have heart failure, she or he does not have severe vascular destruction, but she or he has the vegetation of 1.2 centimeter side on the mitral valve is that enough for an operation a preemptive operation something to prevent stroke.
- 01:15:08In the hopes that you will avoid that kind of complication so what's the calculus that goes into that.
- 01:15:14Well, generally speaking, if evolution has occurred, more than once and vegetation remains, it would make sense to get rid of what is left right, but if.
- 01:15:24emulation has not occurred and you're just dealing with a relatively large vegetation and isolation it's not clear that that person require surgery.
- 01:15:34And also depends on the nature of your relationship with cardiac surgery, and the degree of expertise that's available to you.
- 01:15:41So this is a much more contentious area and not all patients would simply a large vegetation should be referred for early surgery, they can be followed safely here's an example of somebody who could not be followed safe.
- 01:15:55And this is a physician colleague who had staff blood analysis.
- 01:16:01Which is kind of a long name for something I think that comprises about 10% of staph infections and patients with endocarditis tends to form very bulky vegetation with an early propensity for ambles ation and he had presented with.
- 01:16:19interpreting them all hemorrhage in the brain as a complication of this and was not a candidate for surgery just didn't get to the diagnosis early enough now it's interesting if you're thinking about preemptive surgery.
- 01:16:33so as to prevent stroke and somebody who has an isolated cetacean probably ought to do so, sooner rather than later.
- 01:16:41it's these are some very nice data from the international collaboration of endocarditis that completely recapitulate something that was known as long ago as the 60s and 70s.
- 01:16:52And that is the sooner you start antibiotics that are directed to the sensitivity of the organism.

- 01:16:59The sooner the risk of envelope ization falls over the next five to seven days so as you can see here, strokes per thousand patients with infective endocarditis incidences highest.
- 01:17:11The day before the day of, and the day after presentation fever and then it falls off like this and it falls off most rapidly between one week.
- 01:17:20Excuse me, between days in a row and day seven if you started the right kind of antibiotic and it becomes low enough.
- 01:17:26That it's not clear that preemptive surgery performed at three weeks with necessarily provide incremental benefit that you're looking for with respect to stroke production.
- 01:17:36But here's a complication, and this is a ruptured my coffee cancerous right, so this is another vast it or complication of endocarditis that is associated with terrible outcomes.
- 01:17:5085% of these folks even today will either die or have fixed neurological deficits following discharged from the hospital and this gentleman.
- 01:18:01Is the fellow I showed you who had a small detail on the mitral valve and moderate Mitchell regurgitation.
- 01:18:08So it doesn't take a lot of into part is invalid destruction to cause horrible vascular complications.
- 01:18:15He had a ruptured my conduct aneurysm, as you can see here, and this is a ventricular drain this place for intracranial hypertension and, unfortunately.
- 01:18:26The interventions that are driving itself became infected and then needed to be removed in a second neuro surgical procedure, but this fellow walked out of the hospital.
- 01:18:36which was quite a testimony I think to his Youth at 54 years of age, so here's a snapshot now the people that I'm sure you have involved in the care of patients who.
- 01:18:48Have endocarditis related to drug use, ranging from addiction medicine to cardiac surgery social work, the primary team nursing infectious disease and others.
- 01:18:59And this is the kind of picture that I couldn't imagine having shown now 15 years ago, or so until we came to our senses about how much help we need and caring for these patients and the complexities involved both medical surgical as well as social.
- 01:19:16So how are we doing well we're not doing great I think it's perhaps.
- 01:19:20somewhat similar in some respects to the fact that we're not doing great with coronary disease, either because we have this thing called diabetes and.
- 01:19:27Obesity that continues to stay ahead of us we're not doing really good with endocarditis because we have this thing called injection drug use that I think is.
- 01:19:35out ahead of us, six months mortality rates currently in the range of about 20% one in five that's about as high as having an acute a sending aortic dissection.
- 01:19:46And secondly, that surgery is now performed in more than half of the patients admitted to the hospital, which is a real testimony to the rapid.
- 01:19:55Acceptance of empirical care.
- 01:19:58pathways that have developed over the course of the last 20 or 30 years.
- 01:20:02Certainly, in the 1970s, there was no way a patient would get operated on early in the context of endocarditis they would marinate on antibiotics and if they live, they might have surgery.
- 01:20:14So it's Nice that we're in a different spot perioperative mortality rates are not cheap.
- 01:20:1910% that's really high what's the perioperative mortality rate for isolating yourself replacement it's less than 1%.
- 01:20:28This is tenfold tire it's interesting that the prosthesis one implants in the acute phase of endocarditis very rarely gets infected.
- 01:20:35And that's, I think, also a testimony to our infectious disease consultants who say, well, this is the best type of anti microbial therapy and take care of everything.

- 01:20:45In the process, including a sonic access or osteomyelitis of the spine and i'll end with this we're still trying to prove that.
- 01:20:54There could be some role for antibiotic prophylaxis proud dental procedures and patients at risk for streptococcal endocarditis, and these are my same colleagues from the UK Sheffield university.
- 01:21:07Who actually were able to document among 7 million patients in this particular database, this is a.
- 01:21:15Extraordinary database that included both Medicare and commercial dental visits in the United States and, as you can see here.
- 01:21:24You can't really quite see the legend, but this is the incidence per million dental procedures of endocarditis among patients who underwent extraction or required oral surgery.
- 01:21:35Really tall blue bars really high incidence of infective endocarditis in the context of invasive dental procedures in high risk patients were these patients, these are patients with a history of endocarditis.
- 01:21:50Patients with a history of previous valve replacement.
- 01:21:55or patients with a history of congenital heart disease that leaves them blue or its own been partially repair, so that is the American heart association definition of a high risk patient.
- 01:22:07And then, interestingly, in the same database what we found was that for those high risk patients who received antibiotic prophylaxis prior to these procedures, there was a marked reduction.
- 01:22:19In the incidence of endocarditis requiring hospitalization look at the height of the red and blue bars here at the far right hand side of the screen.
- 01:22:27So people have been struggling since the 1950s, to try to show that makes a difference to give folks locks on before they go to the dentist, and this is about as close as we are, and it took 7 million patients, I think, to get here, but the editors if he had been have yet to be convinced.
- 01:22:44Alright, so what I hope I shared with you is that effective endocarditis provides variable modes of presentation, the diagnosis and risk assessment are really key right off the BAT think about multi modality imaging think about the.
- 01:22:58Multi disciplinary heart team that is involved in decision making recertification and treatment and think well about prophylaxis, especially for those two conditions I showed you in high risk patients.
- 01:23:10So I do think that reliance on skills that emerged in internal medicine training remain very ratings, very important for all of us.
- 01:23:17And I think that it's a cardiologists are still grounded in this era, and in this particular area and we need to be reminded of that in order to give the best care to our patients, so I want to thank Dr Kramer and certainly the Department of medicine here at uva.
- 01:23:35for giving me this wonderful opportunity to visit with you great to be back in person, thanks, very much for your attention.
- 01:23:50hey Sam I have another chest X Ray, for you know.
- 01:23:56Visa any questions.

Unknown Speaker

01:24:00Do you have anything.

Medicine Grand Rounds

01:24:03I want to see if anyone pops up on the chat here but also open to the room, obviously.

- 01:24:09Chris yeah so one of the issues we talk to our surgical colleagues is around timing of operation because.

- 01:24:19You know they are worried about reinfection yeah so they want you know some time in the antibiotics whizzing around to.
- 01:24:27lower the risk of being infected where you show the data it's a lie it's all in the first couple days a week.
- 01:24:34And so there's this back and forth with our surgical colleagues as to exactly when, where is your take yeah well, I think it is true, they do hold those cards we they.
- 01:24:44they're the ones that we need to rely on to schedule the surgery and habit, I think this isn't one area and cardiac surgery, for which they deserve the.
- 01:24:56The accord that they're given this is a really difficult to patients to operate and it's like they already to section, so I always have some respect that I'm asking somebody to do.
- 01:25:06A procedure that is already at high risk right from the get go and, but I think its persistence on our part saying.
- 01:25:15To to make sure that everyone understands, there are no data to support the notion that a certain number of days needs to go by, for antibiotics in order to be effective, at the time of removal of the primary infection.
- 01:25:28And the risk of reinfection is actually very low, and I think the problem we get into the internal medicine side of things, and the cardiologists side of things.
- 01:25:37The patients Okay, but we're watching everything deteriorate over three or four days before they get to surgery, then they have altered renal function, they could have a little delirium that has been.
- 01:25:48misdiagnosed or not diagnosed, or they could have micro generalization that makes things very difficult post operative but.
- 01:25:55So I try to hammer and with those kinds of observations and, at the end of the day, it still is their decision and it still can be very frustrating, but I think we're better than when we used to be yeah.
- 01:26:08And questions oh here i'm going to leave this open for you and, if anything else, through you can answer it and then all okay.
- 01:26:17So this is a really easy question to answer, I appreciate it on the chat, but I think that the way our team approaches, this is basically through.
- 01:26:30A consultation with our hospital based ethics committee and the recognition that we need help.
- 01:26:38In discussing this very thorny issue with the patient, and if there are any family members, my own personal experience there tend not to be family members that can be brought.
- 01:26:50into the conversation, and I think that this requires time it requires dedication, it requires the kind of skill set that the average cardiology clinician may not have.
- 01:27:06social workers emphasis and people who can look at things from a distance, are very important, I think, in this kind of decision making it's extremely rare that we do not give somebody another chance.
- 01:27:21But it's less rare that if they have gone through this twice that we would think perhaps the third time it's not in their best interest their decision to make.
- 01:27:32So we give everybody I think it's fair to say, everybody gets one chance if they come back which they do is you know and sometimes incentives two months or three months post operative way, and they have a different organism, or they have poly micro organisms.
- 01:27:49We have we have the ethics team come in and help us make a decision and we've operated on some of our patients four times and we've operated on other of our patients only twice.
- 01:28:00I don't think there's one size fits all and I don't really pretend to have the right answer in all circumstances, but it's a it's a bigger problem I think then us good question hey deanna somber note.
- 01:28:15Valentine another.

- 01:28:18person oh okay yeah thanks Mike I think that for the timing of surgery, if you had blood in your brain then typically it's a four to six week wait.
- 01:28:30In the hopes that the blood brain barrier work he'll, to the extent that you don't worse than the insult one place on cardiac coronary bypass and that four to six.
- 01:28:39time frame over which to wait has generally been derived by from consensus at large cardiac surgical centers including say Cleveland clinic and pan Mayo clinic and other places like that so four to six weeks Mike, thank you for the question.
- 01:28:58for everyone for playing a little.
- 01:29:03it's a really good question like, so it should you should we do an MRI or CT scan of the head on every patient that comes in, and we have not adopted that we have been driven by.
- 01:29:14The presence of neurological symptoms, even as a nonspecific as a headache for example, I have a low threshold if.
- 01:29:24A history suggests that there's something not right then do it, but I think to do it and all.
- 01:29:31is not something that we've adopted and the same is true of abdominal CT scanning or taking a look at the spine, it may depend on the patient, the context the organism and other things that might.
- 01:29:43raise your index of suspicion, but not as a routine visit in the context of any patient you put.
- 01:29:53In all the ways.

Unknown Speaker

01:29:57That we can define.

Unknown Speaker

01:30:00Define your highest patient.

Medicine Grand Rounds

01:30:04yeah I think if you if you have them both ization and you have recurrent civilization and you have a persistent vegetation high risk get it done now do not think that antibiotics will calm the situation and don't give aspirin.

- 01:30:22aspirin makes each vegetation work, so we don't have prophylaxis against demobilisation on the medical side of things heparin would be disastrous, for example, you know.
- 01:30:36Great Thank you very much thank you.