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## TRANSCRIPT - GR 01 21 22 *"Striving for the Future of Sarcoidosis: The Science and Challenges Behind Rare, Underserved Disease Guideline Development and Center of Expertise Care"* - Catherine Bonham, MD from the University of Virginia

* 00:13:47Okay, everyone, welcome to grand rounds it start with the introduction and head over to Dr Bonham so.
* 00:13:52Today grand rounds will be delivered by Dr Catherine Bonham from our own division of pulmonary critical care medicine.
* 00:13:58backer bottom of tantra medical degree at the University of Michigan and then completed a combined internal medicine and pediatrics residency at the University of Michigan.
* 00:14:06Following that Dr Bonham included pulmonary critical care medicine fellowship at the university Chicago.
* 00:14:12doctrine Bonham served on the Faculty at the University of Chicago for two years before joining me being in 2018.
* 00:14:18to become an assistant professor and the scientific director, the interstitial lung disease program here at uva.
* 00:14:23And the clinical sphere, Dr Bonham works in our adult medical intensive care unit on pulmonary consoles.
* 00:14:29And in our pulmonary clinic with a specific focus on the care of patients with five brodick pulmonary sarcoidosis.
* 00:14:34And idiopathic pulmonary fibrosis and the research sphere, Dr Bonham is an NIH funded researcher put multiple active grants.
* 00:14:42Dr Bonham 's research interests include T cell activity and IPF T cell responses to search coby to and novel computational approaches to identifying treatments for idiopathic long fibrosis.
* 00:14:53Dr Bonham is a fixture in a pulmonary division, but is also a member of multiple American thoracic society committees and is the Chair of the ETS allergy and analogy inflammation assembly early career working group in.
* 00:15:05 Bonham with the invited subcommittee chair for the ETS clinical practice guidelines for the diagnosis it's our code.
* 00:15:11Given all that and more she certainly an expert in that field and is ready to give us a true toward a for presentation and sarcoidosis including updates on epidemiology management and how to tackle guidelines for a rare and underserved disease with that I’ll hand it over to Dr Bonham.

**Cathy Bonham**

00:15:31Thank you, is he for that kind introduction.

* 00:15:35And Thank you everyone for joining me and what is a really a busy time for all of us and.
* 00:15:40My heart is with everyone on for South and on the words and then all of the ice us where we are taking care of people right now so thanks for taking this time to spend with me on a disease that's outside what is on everyone's minds.
* 00:15:55i'm going to speak a little bit about my experience on the guideline committee but I’d like to kind of take a broader view also on the challenges of developing.
* 00:16:07Science and disease that we haven't always been able to focus on, and as a Center of expertise here at uva we're working now to really try to bring sarcoidosis into the future and that's why I titled this talk striving for the future.
* 00:16:26I do have a single disclosure at the has asked me my opinion on what might make good treatments for sarcoidosis and I’ve given them my opinion that should not impact any of the learning that we have today.
* 00:16:41Objectives specifically would be to address really red flags for alternative diagnoses when we're thinking about sarcoidosis when to biopsy wouldn't treat and then the longitudinal management of sarcoidosis as a disease that occurs across the age spectrum.
* 00:17:00I think another important objective is systemically, what are the sort of advantages and the occasional limitations of guideline development and also Center of expertise based care.
* 00:17:11So kind of going to start it off.
* 00:17:14I I’m not a funny person, a lot of speakers, like to start out with something funny to capture your attention.
* 00:17:22I do like medical history, a lot, and this is actually one of the first reports of sarcoidosis explains the name, which is Greek and oriented comes from the word circle annoyed and that translated, means flesh like.
* 00:17:37it's because circle it, as we know, has skin manifestations, and so it refers to the skin nodules that this Norwegian dermatologist described in 1899.
* 00:17:49And so we have Caesar back to thank us for that funny name, there was a alternative name that was proposed by Dr Hutchinson, who also is setting syphilis at the time and Britain His name was lady mortimer's malady after his patiently mortimer I think sarcoidosis as a better name.
* 00:18:11The report, as you can see here had some beautiful sketches of the histology that was appreciated at the time, also the patient.
* 00:18:20Is pictured here, he was a policeman in Norway, who developed these cutaneous manifestations I think there's some learning points to take out of this early literature even now.
* 00:18:31One is that you know star quick patients are dapper dressers the sky shirt certainly kind of set the standard right.
* 00:18:40The other thing I think that was very precious about this is that you know it was appreciated in a time when really infectious pathogens and the early appreciations of what is cancer malignancy.
* 00:18:55Were we're really on the top of everyone's differential and it was recognized that sorrow quite is neither of these things it's neither an infectious etiology it's not a cancer.
* 00:19:07It is in fact something different it's an immune dysfunction, and so I think we have this early report to the thing for that.
* 00:19:15The final thing I would take away from this that I actually appreciated this morning, as I was reviewing the slides is that.
* 00:19:22Dr Beck looks a lot, like our department chair medicine these guys were separated at birth, so if Dr risers watching it I think I’m glad you are both in medicine, Dr buck and Dr Ross.
* 00:19:38So what is circling and so there's a classic definition that if you read any stark White Paper, this is what they say right.
* 00:19:45it's a granular ominous inflammation of unknown etiology I find this definition is a little bit unsatisfying I think that I think it.
* 00:19:54lends the reader to think that we should still be searching for this etiology that there is something there we just kind of don't know what it is.
* 00:20:04I think it's more constructive to think about it as a persistence of granular ominous inflammation in the absence of a persistent trigger, that is when you have a biopsy.
* 00:20:15you no longer have a detectable antigen or pathogen that you're able to culture, otherwise appreciate, and yet the patient is still producing granulomas inflammation enough to usually be symptomatic.
* 00:20:31Another key point that I discuss it and clinic with patients is that it's not strictly an autoimmune disease, when we think about autoimmunity we think about.
* 00:20:41Be cell mediated disease we think about being able to draw a circle ology and test for auto antibody levels.
* 00:20:48That is not the pathology that's at play here, this is more of a summation of adaptive and innate immunity.
* 00:20:56it's more of an immune dysfunction that's macrophages T cell mediated not be so mediated.
* 00:21:02And so I think it's important to think about this in the context, perhaps, of what many lay people understand is like autoimmunity.
* 00:21:09it's an immune system problem that is now attacking you right but it's not purely an auto antibodies problem.
* 00:21:17And most commonly affects the lungs in 90% of people, but it can cause trouble really in any organ system and that's consistent with the idea that your immune system has to perform surveillance in every part of your body.
* 00:21:30And then finally it's actually important to the diagnosis to recognize that circulate, by definition, is a multi systemic disease.
* 00:21:37And it also requires lifelong surveillance and care because we never really consider a person sure per se of sarcoidosis they still require that you know that suspicion that you could have some solid manifestations that are late in the presentation.
* 00:21:54So what are some of those manifestations so signs and symptoms can vary and they depend on the organ system that are involved in the location of the granular openness inflammation so common examples.
* 00:22:06To pulmonary we think about presentation of cough or this MIA and then imaging abnormalities or pulmonary function tests abnormalities.
* 00:22:15Another common presentation that can be very dramatic as cardiac our code, where you have inflammatory marker data and that can present as a syncope.
* 00:22:24or even heart failure heart block and then some patients ventricular tachycardia and sudden death.
* 00:22:32And one of these patients who survived and episode like this, who was completely asymptomatic until he tried to run across the parking lot and he fainted and was rescued by a bystander but that can be a presentation of of cardiac star quit.
* 00:22:48And the other thing that often can be an issue is constitutional symptoms so they're not specific journal sentence, of course, like the key Malays fever child children sweats and that can be worries of as a mimic for malignancy or infection.
* 00:23:07So let's remember the granuloma you haven't thought about granulomas in a while.
* 00:23:14There is the one key feature of the granular when we think about which is non criticizing insert coin, so the circle granuloma cartoon here would be what I’m showing here on the right hope you can see my pointer.
* 00:23:30Non equity arising granulomas would be the classic star quite granuloma feature in leaks are quick, though they can have just a five brodick granuloma here, which is shown.
* 00:23:42On occasion granulomas install code can have an advertising features, but that's typically a feature that you see more and infection or malignancy.
* 00:23:51soccer granulomas should be sterile if you culture that there is some good basic science, research that's been done in the last decade or so looking at possible triggers for sarcoidosis.
* 00:24:02And that is ongoing and as possible that there is a fragmented Michael bacteria, or even a P acne is bacteria, this is a vector that's responsible for common acne and force that can be acting, perhaps as an energetic trigger for at least some cases of sarcoma.
* 00:24:21Unfortunately, you know about my Michael bacteria, or even acne everyone's got it so thing you would eradicate that is very difficult.
* 00:24:29And there is a recent trial actually looking at anti micro bacterial therapy it's called clear therapy, which showed no advocacy for several outcomes in circuit so again identifying sort of a PDA logic trigger for ongoing information may still proved not fruitful.
* 00:24:50granulomas are occurring a lymphatic distribution in our code, we look for that, on the chest imaging.
* 00:24:56And then the the basic sciences, that you have a CD for T cell mediated macrophage recruitment and activation.
* 00:25:04And there is T cell repertory restriction in the T cell receptors so this does support that there is a specific antigen in some patients that's driving at least the trigger of the granulomas inflammation all of that may not be a persistent Turner.
* 00:25:27I always like to put the disclaimer to when we talk about granulomas diseases, and this is a theme throughout right.
* 00:25:33Is that granulomas are caused by all kinds of diseases and so that, if you see a non-case eating granuloma when I look at a non-casing and granuloma.
* 00:25:43On a biopsy my next action is to stand on the page and make sure that those cultures and smears to look for alternative diagnoses like infection or there that there's no features or worry for malignancy either.
* 00:25:58So here you've I’ve shown you the cartoon version here's an actual lung biopsy of histology.
* 00:26:06So this is an airway here caught on end, you can see the Nice affiliate lining here's some smooth muscle.
* 00:26:15Musa and then kind of traveling throughout a highly inflammatory knowing us here are multiple non know criticizing granulomas.
* 00:26:25A little bit of antibiotic pigment there, these are well formed kind of typical for sarcoidosis granulomas inflammation in the long of a patient of mine who had circulated pulmonary as well as prominent hypertension involvement.
* 00:26:41Just to show you an alternative histology this is, I know what a net criticizing granuloma would look like right with kizzy ation at the Center.
* 00:26:51there's also quite a bit of with acidic inflammation this was a case of military tuberculosis.
* 00:26:58So just to briefly summarize epidemiology, as we currently understand it for sarcoidosis.
* 00:27:05sarcoidosis considered still by the NIH a rare disease, because the incidence is less than 200,000 per year in the US, but in fact, because people are diagnosed throughout the lifespan.
* 00:27:18Some people, some people in my clinic have lived with sarcoidosis for 60 years, so the lifetime risk for sarcoidosis in the US is just under 1% for wider Caucasian populations in 2.4% for black and African American individuals.
* 00:27:36It is a subject of an entire Conference, I think, and a real gap in our research needs to understand a bit better some other racial disparities in mortality that our President stark would there are also.
* 00:27:52A body of literature that describes racial differences in the presentation, the the age of onset for African Americans is on average 10 years younger.
* 00:28:01And there is some data that suggests that there is some pulmonary hypertension at a higher incidence in African Americans versus Caucasians.
* 00:28:12The genetic underpinnings are partially understood, we have patients that have some familial clustering.
* 00:28:20And that was examined in the access study.
* 00:28:23If we look at specific syndromes like lofgren syndromes for sarcoidosis, which is, I will go through later, but it's a very, very specific clinical presentation they're actually Hla and Yun phenotypes that are linked to offering syndrome in those populations.
* 00:28:40The data and sarcoidosis mortality is shown here, this was actually a really nice study that looked at death certificate data over 10 years is published in 2014.
* 00:28:49This is United States population and what really jumps out of you, when you look at this figure what is that when you do an age adjusted rate.
* 00:28:58per 1 million of mark mortality, obviously the African American population bear is a large bird no mortality in comparison to other racial ethnic groups.
* 00:29:09And I think the other thing that bears witness is that the mortality occurs in patients who are much younger than patients who are identifying as Caucasian.
* 00:29:21And this requires further study to understand, I think, historically we've understood is potentially a issue with biology, I think we need to hang that up in the light and really look at it.
* 00:29:36You know other authors have proposed that part of this is a diagnosis diagnostic biased in that African Americans have a 10 year.
* 00:29:47Earlier diagnosis and then also attributed some of this early mortality to pulmonary hypertension, which is often Center based care right so access to care problems will.
* 00:29:58Impact mortality related to that, but I think of course there's a larger social and economic disparity that we're all.
* 00:30:06Trying to understand now.
* 00:30:11In addition to that, we also can note that sarcoidosis prevalence is higher in women, as well as African Americans, this is a nationally representative data set that was published in 2016.
* 00:30:24So you can see the prevalence rate per 100,000 listed there it is higher and, all in all comers for for women and it's bears out in our regional data so.
* 00:30:34I have been looking at the regional selfie circulate population within five circuit centers that are here, we see, on average, and equal split.
* 00:30:44of racial and ethnic groups for star Quinn, but about 60% of our patients are women, and the reason for this gender difference is not well understood right now.
* 00:30:58We want to look at sort of how sarcoidosis is interacting with the hospital system, and this is an interesting study hospitalization rates specific to the cardiovascular.
* 00:31:12SAR quite phenotype and what those outcomes are like this is a national impatient sample and it was over half a million hospitalizations for star quit that are represented.
* 00:31:22Over a 10-year period, you could see that sarcoidosis hospitalizations were, on average, on the rise, about 26% increase.
* 00:31:32But at the same time, there is a 26% decrease in in hospital mortality so that's a positive thing is that specific to sarcoidosis Probably not.
* 00:31:42There is enhanced public awareness of cardiac arrest and sudden cardiac death and protocols within the hospital and gotten a lot better.
* 00:31:48at managing the most you know feared complications of circling meteor and so forth, and I think we made a lot of strides and guidelines and system based advances in a cardiac arrest care.
* 00:32:01What this means is that patients are getting hospitalized more but they're surviving and higher rates than they used to within the hospital, but we are developing a more complex population that we care for over time.
* 00:32:20Another issue that is important, I think, in the care of star coin, and you know what outcomes, should we be really studying to try to make high impact.
* 00:32:34diagnosis and treatment decisions is you know where does the mortality and circling come from, and it is clear that in pulmonary sarcoidosis.
* 00:32:45mortality is really driven by the pulmonary hypertension and the pulmonary fibrosis phenotype which, in this study is defined by more than 20% scar on the high risk CT.
* 00:32:56And so you can look at these nice kaplan Meier curves but certainly in this sample, this is a large group from university of Cincinnati you can simply see that the incidence of pulmonary hypertension.
* 00:33:08gives you about a 50% survival rate at 10 years versus those that don't have pulmonary hypertension and, similarly, the survival of patients that have fibrosis on higher CT.
* 00:33:23is diminished over time in comparison to those that do not and so those are the groups that I focus on in my studies is patients who am I think we could make big strides in their care.
* 00:33:36As a Center with some expertise and as a Center with multiple people different specialties who can lend their expertise to the care of these patients and that really is the way that we find that.
* 00:33:53We are making a big impact on patients who are coming from the Community, and who are perhaps not able to access care, otherwise in patients in physicians that are seeing larger numbers of patients.
* 00:34:07This is a model that was first pioneered by cystic fibrosis and more recently in the iot community.
* 00:34:15And so I think that our field is moving that way.
* 00:34:21I'll leave out some details here in this slide and simply show you in addition that others have.
* 00:34:30modeled some of the drivers of sarcoidosis mortality.
* 00:34:35Even to make risk scores on fibrosis and pulmonary hypertension and, ultimately, what we find is that about 75% of mortality in our quiz is due to respiratory causes.
* 00:34:46And when we think about clinical algorithms for the outcome prediction the weights for pulmonary hypertension and fibrosis are heavy and so those are the patients, for whom I think a high index of suspicion and close follow up is most important.
* 00:35:04So I promise in my learning objectives, a little bit of.
* 00:35:08Knowledge about how to nail down your diagnosis, perhaps for primary care providers or those who are seeing sarcoidosis patients in the Community.
* 00:35:22When to narrow the differential because I think one of the problems with circuit, is how wide is that differential.
* 00:35:29There is a two page exhaustive table in the diagnostic guidelines that lists the nuances in the differential diagnosis.
* 00:35:37So some of the things that are red flags, this would be things that mean, I think this may be a case that could be a typical not sarcoidosis.
* 00:35:49And more indicative of an alternative diagnosis and may need further workup including biopsy so certainly any be symptoms fever chills weight loss, this could be infection and film history department malignancy smoking history.
* 00:36:05Travel and I include endemic fungal disease here so that can be you know residing in the Ohio river valley for glasto or for histone, for example.
* 00:36:18parasitic disease and tuberculosis or considerations and then occupational hazards so.
* 00:36:24Some occupations, particularly patients who are working in manufacturing mining construction plumbing or farming will have inhalation exposures to things.
* 00:36:34Even like beryllium, which is an excellent mimic for sarcoidosis and so actually a really great occupational history can be very important to help you, with your differential.
* 00:36:45And we often think of things like CV ID common variable immune deficiency is rare, but I think, especially in a tertiary care setting.
* 00:36:55CV CBD is also an excellent mimic for sarcoidosis and we pick up one or two I think every year HIV can also present in a similar fashion.
* 00:37:07And then, I have a fun time always asking my patients about their hobbies you always want to know, because hypersensitivity new unitas and micro bacterial diseases another great and make for star quid, and so I really always want to know if you have a hot tub or, if you have a cockatoo.
* 00:37:26room until logic features on exam can be very important we do see patients who have a quite a bit of overlap and room to logic features so you're looking for joint fusions joint pain morning stiffness.
* 00:37:38and doing the skin exam.
* 00:37:41And then I think that there are some important imaging findings that raise my red flag when I see them as being a typical for start quick.
* 00:37:51So importantly it's are quite should be mostly symmetric pulmonary disease multinational are usually.
* 00:37:59And in both lines, when you have large nodules that are predominantly on one side or limp at an apathy that only occurs on one side.
* 00:38:08or in a fusion that only occurs on one side that is suggestive of a different process and, again, that would be one that I think requires a bit more workup and perhaps biopsied.
* 00:38:19lymph nodes can also have grossly neck-retiring features on imaging and just radiology will sometimes call that on a chest CT where there's coagulation or kz ation inside those lymph nodes and that's usually a feature of a more infected lymph node or sometimes a malignant process.
* 00:38:37The other issue to be worried about is when you have a patient who has a normal chest X Ray you might say, well, this is great normal chest X Ray.
* 00:38:47You just have extra pulmonary sarcoidosis, but I think that's something to where you have to worry because circling really in 90% of people has some pulmonary manifestation inclusive of.
* 00:38:58add an apathy So if you have a normal chested extra with no, no, no, you might have sarcoidosis it's not totally off the list.
* 00:39:08But your index of suspicion for alternative diagnoses, including a missed infection or miss malignancy is higher and so that's another reason to.
* 00:39:16Perhaps pursue additional work up or an additional biopsied confirm that you truly have a multi systemic granulomas disease of other was on noni geology.
* 00:39:29And then finally you'll sometimes see patients in your in your practice, who have already received some high dose imperative steroids say prednisone 20 milligrams or more, for a period of time and if they are not responsive, especially to a high dose regimen.
* 00:39:48That is worrisome SAR quick sentence will typically improve on steroids, especially if a patient gets worse on steroids I’m worried that something else is going on, that we've missed tuberculosis or something else.
* 00:40:06So that is that those are some of the red flag things I really think about again if you want to really dig into the differential there's a great table that we worked hard on and the guideline to reference.
* 00:40:21A big part of the guideline was to think about whether or not biopsied should or should not be recommended.
* 00:40:28And I would distill a very long conversation to these points that we still recommend shared decision making, you have to talk to your patient.
* 00:40:43A biopsy is not universally recommended in sarcoidosis except if you have some of these red flag issues that tell you that you do need to dig further.
* 00:40:55And if you are going to give someone immune suppression, including prednisone which I think sometimes we may perhaps over prescribe.
* 00:41:06you're committing them to the risks of that, and you need to have a firm diagnosis, so in that case do recommend biopsy and then, finally, I do have patients who.
* 00:41:18Are asymptomatic.
* 00:41:21who have minimal or very little test disease but who are simply you know very worried about the possible alternatives here like malignancy and they really want to know, and that case it is okay to proceed with that procedure presuming that they're an adequate risk.
* 00:41:44I feel, you have to mention, there are three clinical syndromes that are so suggestive of start with that they do not require a bio.
* 00:41:53Little this goes back to Medical School but.
* 00:41:56One of them is lofgren syndrome right, this is a triad acute onset with fevers you have ankle swelling and a symmetric polly arthritis.
* 00:42:08A bilateral hyler been an opposite and in a docent if you have that triad including a chest X ray of course of it is actually not needed in a biopsy of an ios would not use your granulomas anyway because remember this is a particular item.
* 00:42:26This is, in general, associated with a good prognosis and you treat with incense.
* 00:42:33The other classic syndrome is a UV parotid fever, this is much more rare than loft grands it's also called here for its there's a nice review on it in New England journal from a bit ago.
* 00:42:45This picture kind of summarizes what's going on the woman in the right that's her usual look.
* 00:42:53In frame a she has the product Glenn enlargement, you can also appreciate that are either a little bit read so she has some interior up itis.
* 00:43:01And a facial nerve palsy and that was also appreciable the product environment it's actually quite dramatic here on her skin and the granulomas are present and pains see so that's syndrome to where it's so classic you don't really have to get a biopsy.
* 00:43:22syndrome three lupus printing all which is granulomas inflammation on the ALA of the nodes this one is one to really take seriously if you see it.
* 00:43:35It does associate with more severe star code, and that is because, even if you have a few panels on this location.
* 00:43:44You can actually get granulomas inflammation of the nasal airway and you Cosa and patients will get masses alterations they can develop airway obstruction and including tranquil.
* 00:43:56involvement with the Nazis, and so this really does require I usually get our your nose throat friends involved take a look.
* 00:44:06And you really want to look at those loops when you get a spirometry to make sure that they are not developing obstructive pathology in their airway.
* 00:44:15In general cutaneous are quite 30% of the time does develop systemic involvement and sometimes it takes months, two years later.
* 00:44:22So this is just something to know and surveillance and follow up that you do want to get your baseline testing and we'll talk about that.
* 00:44:29And then you know don't lose your patients and follow up or make sure that they have a good provider in the Community if they're being seen their nose, they have sarcoidosis knows that they need to you know be vigilant.
* 00:44:42So, what then if you're patient is a symptomatic.
* 00:44:47You know, and there it's either X rays classic they have a bilateral highlight at an opposite, can you not see them.
* 00:44:56Yes, you cannot buy it see them, but only if these conditions are met you don't want to have those red flags symptoms if they're having fevers weight loss and chills they're going to need definitive diagnosis right.
* 00:45:14If they have.
* 00:45:17neck criticizing lymph nodes on the on the on the CT scan those lymph nodes are not only in large, but you can see in the Center their neck are.
* 00:45:25They going to new biopsy.
* 00:45:29You don't have to buy up see them if you're not going to treat them either you know.
* 00:45:35And then, finally, I think it is actually perhaps as important is that you have to be able to conduct some follow up to see the patient again because what can happen, I think this happens.
* 00:45:50More often than we'd like is that patients.
* 00:45:54will hear the message that they don't need anything done and they'll be lost for the next year or two and then they'll come back with a new heart block or something.
* 00:46:07So you do have to have a little bit of close follow up and there are some patients, for whom.
* 00:46:12You know in discussion with them, they do not feel that they would be able to their access to care is fragmented for things like that, in which case we say you know, perhaps it is best them to try to get this settled now and then we have a diagnosis.
* 00:46:30So again, this is a patient and provider conversation that I think is individualized, and that is the spirit of what the guideline recommendation is is that you have some wiggle room to have a conversation.
* 00:46:44With your patient.
* 00:46:47Alright, so let's say you have a diagnosis.
* 00:46:51And either a new diagnosis.
* 00:46:55or someone that perhaps you're following for a while, so in new diagnosis patients, there is a little bit more screening that's recommended and patients who are otherwise asymptomatic.
* 00:47:06Everyone should get an ophthalmology referral to screen for asymptomatic UV is or other manifestations are quick everyone gets a screening ekg looking for evidence of.
* 00:47:19You know, especially for evidence of the Tricolor abnormalities tech Korea Korea heart block.
* 00:47:26And if any of those things are abnormal or your patient had already described to you some suspicious symptoms, then you go down the cardiac screening pathway and you're doing an ankle and potentially I’m arise and pets.
* 00:47:42And then you're screening with pretty basic labs I get a CBC.
* 00:47:49renal and liver function, and I look at calcium and vitamin D metabolism, and just to remember that and vitamin D metabolism and SAR quaint you really want to know both your kelsey dial on Council trial.
* 00:48:02Together right, because if you only measure 25 kills a dial levels, it will be low, but you're one alpha hydrox least is converting all of it to 125 so you need to know both to know whether or not there's really a vitamin D deficiency, or maybe even too much vitamin D.
* 00:48:22And then in patients who you're seeing in follow up, I think, actually the most important thing is that review of systems that sark would focus, so you want to know I ask every patient every time.
* 00:48:36hey any new chest symptoms pain palpitations are you having lightheaded episodes or syncope.
* 00:48:45You know, and certainly if they've had Brady tech a party or if they've had any country in the interval done by their PCP and it's different that's important.
* 00:48:57We do more, testing, including urine calcium if they've had renal stones or renal failure, they actually do not have to go to ophthalmology every year if they are asymptomatic.
* 00:49:11They need a baseline screening and then, if there's a change in vision like floaters or blurriness beyond that baseline then they can go back.
* 00:49:22That is actually a new update from the guidelines and it's based on our ophthalmology.
* 00:49:27Colleagues, expertise and that they do not typically see a symptomatic SAR quaid I disease longitudinally and someone who's had a good baseline exam.
* 00:49:38That being said, I would say, practically most of my patients who are following who have seen ophthalmology for their baseline exam they almost always will uncover something that means a follow up exam.
* 00:49:51You know whether it's glaucoma or something and so there'll be softened seeing ophthalmology anyway.
* 00:49:58And then, finally, I always monitor for some disappear that's out of proportion to their known pulmonary disease and that can be pulmonary disease it's flaring but also you also think about pulmonary hypertension or cardiac disease.
* 00:50:12So we're to biopsy and when to refer, so this is this goes down kind of a first do no harm pathway.
* 00:50:19You want to buy of see the easiest site that is acceptable for your patient that gives them the lowest risk profile.
* 00:50:27So, certainly if they have cutaneous sarcoidosis go for a Punch biopsy if it's in a spot where the patient is okay with that.
* 00:50:35The other thing that is easy, as a purple enlarged lymph node and axillary lymph node is a great spot to biopsy if it isn't large, and so I always am feeling.
* 00:50:44People for that when we're thinking about going down more invasive routes and then a big change since the last set of diagnostic guidelines, which was actually over 20 years ago.
* 00:50:57Is that our technology for by obscene media steinem news is so much better than it used to be, you have to get the media synopsis up or a blind biopsy was the Needle, and that is no longer the standard of care.
* 00:51:13The standard of care that's very well supported by a large body of literature now.
* 00:51:17Is if you are going for a hyler media cycle lymph node biopsy to do it by bronchoscopy and to do it within the bronco ultrasound.
* 00:51:26to minimize risk to the patient and to increase your yield and the best way to do it, which is the way that's done.
* 00:51:33With most centers and actually most academic places is to have an onsite pathologist who's with you, reading the slides and we do the biopsy in the bronchoscopy suite.
* 00:51:43And he tells you whether or not you have granulomas when you do those ultrasound guided passes of the lymph nodes.
* 00:51:49And one really cleverly titled editorials said that that pathologist is what keeps the Trans bronco biopsy away right because.
* 00:52:00Transparent do biopsies, these are the ones where you go out with a forceps and you take a piece of the lung itself.
* 00:52:06are higher risk for bleeding and higher risk for new, more thorax then ultrasound guided by ups, these are the lymph nodes and so, if you can, if you're doing a star coin focused.
* 00:52:18diagnostic bronk the order of business is really to get those biopsies done of the lymph nodes first and if you're pathologist gives you the thumbs up and says, look at those beautiful granulomas it doesn't look like cancer.
* 00:52:33that's great, then the most from cosmic this can actually stop there, and not go ahead and do additional biopsies of the lungs and that saves your patients and risk.
* 00:52:46alright.
* 00:52:49So I’ve been talking a lot about biopsy I did want to give you a little view into what the decision making is around biopsy you know, because this was probably the most.
* 00:53:00Controversial recommendation was whether or not to recommend really biopsy for most people when there's a sarcoidosis diagnosis being considered and the person is asymptomatic so I, this was the first guideline that I had participated in and I, it was a learning experience for me.
* 00:53:21It really.
* 00:53:24was some of the takeaway points that I got is that, first of all, when you write a guideline it's not like writing an expert consensus document anymore it's not like writing a textbook chapter.
* 00:53:37Which is what I think guidelines in the past, were much more like they were like a really a big review and everyone just said, this is what you should do, because we think this is the best.
* 00:53:46It is now very literature focused, we read guidelines, of course, you know you have to construct a question.
* 00:53:55We used a Pico format question and you have to grade your evidence, and so this was the question that we constructed, which we constructed, based also on what the question that we were able to answer given the literature that's out there right.
* 00:54:08And this is whether or not live not sampling should be performed in a patient who presents with an asymptomatic hyler at an apathy which we would call a stage once our quick right.
* 00:54:20And really there when you do a little sampling procedure and you're suspecting SAR quid there's kind of three outcomes, when you get a diagnosis star code to an alternative diagnosis and then sometimes you get non diagnostic specimens where you just got lymphocytes that no.
* 00:54:35Other pathology.
* 00:54:38The committee and, if you read like them if you dig into a supplement and a guideline you'll see we.
* 00:54:43You know it's a really it's a really large review 2000 articles and then you do you Whittle that down to text reviews and then finally sort of studies that go into the final analysis, so that is what we did, and in the literature what you can see is that ultimately.
* 00:55:03At the top table you're looking at the diagnostic algorithms this is for when you go in with a bronco scope or an end of bronco ultrasound.
* 00:55:12To do a biopsy for sarcoidosis and you are confirming a diagnosis of star code in the pooled analysis 85% of the time 3% of the time there is an alternative diagnosis, some of these diagnoses are scary things.
* 00:55:28Tuberculosis lymphoma non-tuberculosis micro bacterial and one person actually got diagnosed with P, which is interesting and then 10% of the time, this is something that you have to tell your patients, of course, you can set them as though we're not going to find anything.
* 00:55:44I would comment you know, in the specifics of reviewing some of this literature that we are limited by what is out there in the literature and there are biases in the literature, one of them is that.
* 00:55:58Only one of the 17 studies that we were able to review to answer this question was actually Community based and in the Community based.
* 00:56:09paper, the incidence of an alternative important diagnosis like tuberculosis, tuberculosis and lymphoma was over 10%.
* 00:56:18So this was something that we sort of hotly debated is you know, are we really getting literature that's actually reflective of practice.
* 00:56:26And also, I mean we are the American thoracic society, so you know we're trying to make a guideline that that applies to the US, but also as a leader in the world, so you know, is this literature even reflective perhaps if you were to take.
* 00:56:42Your bronchoscopy and biopsy a number of patients let's say in India for TB is endemic right and so that couch is your recommendation, so I think this couch is our recommendation to say you know.
* 00:56:56You must still consider the pretest likelihood of the alternative diagnosis in this.
* 00:57:04Right, and that is that diagnosis of alternative like TV or lymphoma is high, and we have some of those red flags symptoms, for example, that I talked about, then that does push you to to be more invasive in your in your biopsy.
* 00:57:19I would say the one of the things that I thought was quite reassuring was the lack of adverse outcomes that was noted in this pool analysis really we had.
* 00:57:31No.
* 00:57:33Significant there was no mortality, there was no major bleeding or new mythology one person got me a sinus infection from an us that was done, but that also confirmed our clinical impression that these procedures are safely done.
* 00:57:47The question is whether they should be done from most or all patients.
* 00:57:53So I told you a little bit of my thoughts on the clinical practice guidelines, I think that the rigor and the evidence.
* 00:57:58base for this continues to grow and the and therefore the writing of the guidelines is inherently impacted by that.
* 00:58:06And the conclusions and the questions that we are actually able to ask when you write a guideline are actually limited by existing literature.
* 00:58:13And that's out there and I think this is sort of a call to arms for us to answer these questions that are out there, and that is actually how the circle a guideline is written.
* 00:58:22For every question that's answered, there is also a future research, and you know the gaps in knowledge that are identified and in the end, you know I think the other thing is, is that this is still reviewed by a.
* 00:58:37Consensus of experts right, so the data is there, but it is still interpreted by a committee, who has their own biases.
* 00:58:45I think, though, that it is an opportunity for dialogue and that's really important.
* 00:58:50And so I will quickly move a bit through treatment decisions and immune suppression choices attending this rounds is not meant to make you an expert in sarcoma treatment.
* 00:59:04But merely to recognize some of the challenges that we have the immune suppression for sarcoidosis really guided by two main things one is quality of life.
* 00:59:15or patients who have critical danger to life for organ function and to me that means having active cardiac are quitting Eurostar quite active.
* 00:59:26pulmonary circuit usually with pulmonary function deficits and symptomatic.
* 00:59:30And sarcoidosis of the eye that's not responding to tropicals I do have patients probably half the clinic that do not have necessarily these very acute and.
* 00:59:41You know act now indications, but who have significant fatigue joint symptoms mile just can't get out of bed brain fog and those are actually also reasons to treat but in these cases the patients that are disease experts and I, we do have that conversation.
* 00:59:58And I’m going to skip This is just me mainly to say that there are many treatment patterns first are quoted and about one in four patients are treated and about half of providers will pick steroids, as they should, first and after that they are often reaching for methotrexate.
* 01:00:17It is appropriate to consider steroids as first line treatment for many patients.
* 01:00:23There is literature that supports between 20 and 40 milligrams equivalent daily, it would be appropriate dosing I consider 20 milligrams adequate and there is some basic science data that supports that.
* 01:00:37And the goal is to taper to the lowest possible Sarah dose that is still effective for the patient after three to six months, that means that you are excluding them to present his own.
* 01:00:4820 milligrams and sometimes more but usually at least 20 milligrams for about three months at the outset and then you're reassessing and if they have good response you may be able to step down on that.
* 01:01:00And that's a strong recommendation and the reason European treatment guideline was a low quality evidence.
* 01:01:09steroid advocacy.
* 01:01:11There is through placebo controlled trials that have examine that and they do show radiographic improvement with steroids, and a lower prevalence of significant deterioration with involvement for pulmonary function, improving for people that had already abnormal.
* 01:01:28The, the question is the long-term effects of treatment, including Sarah, in other words, so we can show short-term effects.
* 01:01:35In shortness of breath in they're improving your X Ray and their lung function test, but what does that really do for long term outcomes.
* 01:01:43Are you actually affecting the evolution of the circuit itself in the lungs, are you controlling symptoms, the evidence, for that is not there, but I would say that.
* 01:01:52In general, the experts in sark would do believe that if you control inflammation when it is robust, you will be controlling the downstream scarring.
* 01:02:03For patients, because we observed that, when patients who have robust inflammatory changes, particularly I’m talking about pulmonary changes that left untreated those patients can develop scar that then becomes a permanent issue of time.
* 01:02:21And that is actually a big focus of some of the research that I’ve been working on.
* 01:02:29inhaled therapy, sometimes we try to temporary as a cough within hill to Google quarter codes.
* 01:02:35There is now three double blind trials looking at that, and there is no significant benefit regarding lung function testing or symptoms in patients who have a very mild cloth a trial could be.
* 01:02:51A trial of inhaled corticosteroid like flow vent might be considered as a step prior to committing to oral steroids, because that treatment is generally thought of as very low risk, and in some patients, it can be effective, particularly if they have like a reactive airway disease component.
* 01:03:13A big issue.
* 01:03:16And steroids side effect risk management, which is, in itself, its own lecture but certainly patients who are on especially more than three to six months of steroids do need bone density monitoring.
* 01:03:29Their impact on their blood glucose and blood pressure is sometimes a limiting factor for giving them steroids.
* 01:03:35And I generally follow the American college of rheumatology guidelines for prophylaxis fortnam assistance, which is to say that if they're on 20 milligrams or more pregnant zone per day, or if they're on steroids plus an additional immune suppression agent I do prophylaxis them.
* 01:03:52When to think about Sarah experienced agents.
* 01:03:56Generally, these are patients, where we are starting something like methotrexate or self select.
* 01:04:01And those are the patients who are intolerant of high to moderate dose steroids, who cannot reduce to less than 10 milligrams of predators on a day after six months or in patients who have some evidence of progression on steroids.
* 01:04:15And then finally importantly I think for patients who have life Oregon threatening disease, and this is particularly true for patients with neurologic involvement with.
* 01:04:25cardiac involvement really have any shade of my card itis yeah for patients with a lot of with significant pulmonary disease, where their lung function tests are impaired will typically.
* 01:04:37accept that they will be needing some immune suppression regimen for longer than a year, and that means that we should start a spirit agent up front and there is literature in cardiac around for doing that, with methotrexate.
* 01:04:54And there is a trial ongoing for this in pulmonary as well and we're waiting, the results of that.
* 01:05:00I just talked about this a little bit.
* 01:05:03Just to define more precisely what I mean about severe pulmonary disease, when I think about starting a stair experience agent early or a front for pulmonary disease what that means to me is that.
* 01:05:14They have a reduced FTC or deal CEO and they have moderate to severe pulmonary fibrosis more than 20% or if they have a pre capillary pulmonary hypertension.
* 01:05:26All right.
* 01:05:28These are some of the medications we use selection of which is usually driven by the organ system that's affected.
* 01:05:35And their previous exposures I keep a close list of what they've had before, because you always want to know why they failed if they have tried, other things before and I encourage you to do the same and your documentation.
* 01:05:45you'll save yourself some heartache and potentially other providers in the future, some Arctic as well.
* 01:05:52And then finally sort of steps for really if they're failing other things is injectable or and i've been infused in medications, and these are typically tnf inhibitors the two most common use their these infliximab and it'll map, also known as humira.
* 01:06:08And you know, failing that we can try B cell depletion with three toxin that.
* 01:06:16One plug additionally besides pharmacotherapy you know, I think it is very important to consider the physiological effects of pulmonary rehab.
* 01:06:26And that is proven in sarcoidosis it has been proven in many diseases to be very helpful, this was a very nice rigorous study from Germany that showed.
* 01:06:36In almost 300 patients after three weeks, they significantly improved on all of these factors, quality of life shortness of breath they walk actually more than 130 feet, which is better than most pulmonary hypertension medications and pulmonary hypertension patient.
* 01:06:49And so I think it's not to be underestimated, both the mental and physical effects of getting movement.
* 01:06:56And just one more plug there's actually been three new guidelines out for sarcoidosis.
* 01:07:02In the last two years, perhaps overshadowed a bit by coven but there's such good progress in the field, and I think it's such a exciting time to be a person that sees sarcoidosis patients.
* 01:07:13Please reach out to me if you have any questions or concerns I’m always happy to see referrals or to discuss patients, and I believe that is all I have.

**Izzy Budnick**

01:07:24Thanks so much rock bottom we give folks a moment to have their questions, going to filter and then folks can also ask them you to you and.

* 01:07:34Ask your question directly.
* 01:07:45While folks.
* 01:07:47For my three questions I guess i'll just ask sort of the obligatory, how did you know code effect blank disease, but just yeah kind of curious what you've seen, especially with these folks.
* 01:07:57In terms of you know it looks like big part of their care as long term follow up you mentioned specifically like.
* 01:08:04Some folks could differ biopsy as long as you knew they could follow up to that sort of change your practice and then these folks are on pretty significant immune suppressing regiments they end up getting treated to they end up having more severe outcomes.

**Cathy Bonham**

01:08:18yeah, so there is a multinational study of the club star coven the manuscript is being written.

* 01:08:27Where the circuits vendors have pooled their data on the effects of coven and start with patients, I would say the effects are mixed in my own clinical practice, and you know we have certainly seen coven do it's worse in patients who have.
* 01:08:45been on immune suppression for circling and at the same time, I think we've had some very reassuring outcomes in, especially in people who we were able to treat early and effectively.
* 01:08:58and bring them into the hospital when they had symptoms and new oxygen requirements, I think the important thing is again.
* 01:09:05just making sure that your patients know how to reach out, are you know good stewards of their care and partners with you is the most important thing, there was a lot of consternation about the immune suppression effects and how to.
* 01:09:23You know balance that, with the risk of getting cove it.
* 01:09:28And I did have some patients who chose not to receive immune suppression.
* 01:09:35because of concerns for being high risk and exposed to you know, children and family members who are vaccinated I think we have yet to know kind of how that has impacted the field long term.
* 01:09:47But thanks for that question see.

**Izzy Budnick**

01:09:51Another question from the Venerable Dr Andrew wolf as a primary care Doc I’m a little uncomfortable the concept of not by obtaining a symptomatic disease, especially within the Community, setting up to 10% or lymphoma TV how comfortable, are you with the guideline recommendation.

**Cathy Bonham**

01:10:08yeah as I kind of alluded to, I think this is that was the most hotly debated question and the guideline, but I think the balance of it is, is that.

* 01:10:19biopsy can be something that is risky and it depends, too, on your access to safe and effective methods of biopsy, so I think we're really fortunate to have great access.
* 01:10:33To interventionists who can do this if necessary and patients that you know have that have that Center based care, but if you're out there in the Community, and perhaps your only option would be to send to your surgery colleagues for a media staff up in a patient who's otherwise asymptomatic.
* 01:10:59And doesn't have any high risk features, then close follow up, perhaps with repeat imaging and clinical surveillance after three to six months could be appropriate.
* 01:11:11I do think that.
* 01:11:14You know, I wonder if, in five to 10 years with more data, whether or not we will move towards saying that biopsy is.
* 01:11:24warranted in most people, I think the thing that gave me the most pause was that single study from the community that said they were much more alternative diagnoses, then we appreciate.
* 01:11:35It as opposed to the tertiary care setting where I think we have a little bias and saying suspect it's our code and we're kind of winnowed out some of those other people a little more closely so.
* 01:11:47I think anytime you are worried and your patient is worried if they're asymptomatic and you have access to a biopsy method that is has a reasonable risk profile I don't think that biopsies wrong.

**Izzy Budnick**

01:12:07Right and then got another question from Dr Harris to wrap things up, do you think in 20 years we're going to identify have identified more environmental triggers of circle that have not yet been recognized.

* 01:12:19For example, brilliant any thoughts on what we were missing in our histories in that regard.

**Cathy Bonham**

01:12:24oh dear, this is a good question, so I think the literature and brilliant is fascinating so I didn't touch on a lot of brilliant but brilliance of metal that.

* 01:12:35You know, it came to the attention and beryllium factory workers who have who clinically appeared exactly likes our quick patients who have granulomas that look exactly like circling.
* 01:12:46But, for whom because they were working in a brilliant factor in the impact of brilliant was study carefully and they have brilliant.
* 01:12:55Where the brilliant.
* 01:12:57molecule is just fitting elegantly into this T cell pocket and develops a granular ominous reaction, so there is actually.
* 01:13:08A chest article that I thought made me pause in the last year, where they looked at individuals they had a cluster of patients who worked and lived around a concrete refinery these are, or they were recycling concrete.
* 01:13:23And so there was a lot of dust in neighborhood because of this factory and there was a cluster of brilliant cases and they determined that the brilliant source was coming from the recycling of concrete from old buildings.
* 01:13:37And so it is quite possible that we don't always in our environmental occupational history pick up all of these cases.
* 01:13:47I, in general, the treatment for Berlioz since are quite is overlapping and the same the compensation for workers is different.
* 01:13:58So there are some differences there, but to answer most distinctly I, I think that we do miss some of the time we're not perfect.

**Izzy Budnick**

01:14:11awesome thanks so much Dr bottom it's more of five.

* 01:14:15So thanks for coming to grand rounds and.
* 01:14:19And I hope everyone has a great weekend.

**Cathy Bonham**

01:14:21Everybody.