Lupus Nephritis Diagnosis, Classification, Treatment and the role of the Pediatrician - Pediatric Grand Rounds-10-10-2025-Meeting Recording

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Kamat, Deepak M 0:48

Good morning. It's 7:30 in Texas and 5:30 in California for Doctor Puni and Doctor Patel. So welcome to Pediatric Grand Rounds. Just a quick reminders that the CME code is in the chat box and we'll keep repeating those.

Every 10-15 minutes, so no need to send us a reminder. It's my great pleasure to introduce today's two speakers we have. First one is Doctor Ruby Patel, who is a clinical assistant professor in the Division of Pediatric Nephrology at Stanford University.

She was a pediatric resident and chief resident from 2018 to 2019 at Kaiser Permanente in Northern California in Oakland, CA. She finished her fellowship training in nephrology at Stanford in 2022 and has remained at Stanford with a clinical focus in general nephrology and.

Transplantation. She's also associate program director for a nephrology fellowship. She has presented on general nephrology topics as well as advanced dialysis in neonatal population and various topics related to transplants such as.

Disparities, adolescent outcomes and normal medications, medication regiments in transplant patients internationally, nationally and regionally. Our second speaker is Doctor Rajdeep Puni, who is a clinical assistant professor.

In the Division of Paediatric Allergy, Immunology and Rheumatology at Stanford University in California, she trained at Kaiser Permanente in Northern California in Oakland, where she was a paediatric resident and the chief resident between 2016 and 2017.

Following residency, she completed her fellowship in pediatric rheumatology and master's degree in health research and policy at Stanford in 2020. In addition to caring for general rheumatology patients, she has special research interest in clinical

informatics and chronic non-bacterial osteomyelitis. So Doctor Patel and Doctor. Puneet, thank you very much for accepting our invitation. The floor is yours.

Ruby Vishnu Patel 2:58
Thank you.

Rajdeep Pooni 2:58
Thank you so much for that kind introduction. Dr. Patel and I are excited to be here today. I don't know if anyone had a chance to glean from the bios. Yes, I have known Dr. Patel's residency and so we have had many mutual patients over the years and and more recently as faculty we shared.
patients with lupus nephritis and we're happy to share our experience.
We have no disclosures.

Ruby Vishnu Patel 3:28
So we'll go over the objectives for our talk today. We will review and and discuss clinical and laboratory features of lupus. We'll review the classification system as well. We'll review the general approach to therapies for the 2024 ACR guidelines and after our talk, we hope that you understand.
some of the potential side effects of these therapies and how to approach the care of an immunocompromised patient. We'll also review how to monitor for certain clinical complications that can be associated with lupus nephritis, and we'll review the role of the pediatrician in the management of these complex patients.
So we'll start with the case. This is actually a recent patient that we cared for in our hospital. She's a 12 year old female. She presented with a one week history of right lower quadrant abdominal pain and with daily emesis and chills. She also had diarrhea about one to two times in the past week. Her emesis.
Is food content. Yellow in color occurs one to two times per day. She was seen by her PCP and appropriately counseled for precautions for appendicitis. And upon further discussion on review of systems, she maybe has had some darker urine for the past three months, which didn't change with hydration.
A picture of her actual urine is in the bottom right of this slide. And then additionally, after starting her period three months ago, she mentions that her first period was really heavy.
Eventually the parents and patient presented to the Ed because of the symptoms. In

the Ed, her vitals were as follows. A heart rate of 58, blood pressure 142 / 86, temperature of 36.9, respiratory rate and saturation normal. They did additional. Work up in the ED, which included an ultrasound because they were concerned for appendicitis. The ultrasound showed a small free fluid collection in the lower quadrant, some prominent dilated small bowel loops, some prominent right lower quadrant lymph nodes as but the appendix wasn't visualized, so they.
Proceeded with the CT. The CT scan also showed this free fluid in the pelvis, but commented on some body wall soft tissue anosarca and moderate pericardial effusion on the imaging. The appendix was normal. Interventions done in the ED included a dose of Tylenol, Zofran.
And a bolus of 20 MLS per kilo and the patient was started on some maintenance IV fluids.
All right, so this was her exam documented in the ED. It was significant for moderate tenderness in the suprapubic epigastric right and left lower quadrants. Her extremities had pitting edema over both feet and legs.
And these were her labs.
So what is abnormal with these labs? We'll kind of go over that.
So as you can see, she had pretty significant pancytopenia. Her serum laboratory results showed a low serum bicarbonate of 14 and an elevated serum creatinine of 3.03. Her urinalysis had protein.
Blood as well as white cells and red blood cells under urine microscopy.

Rajdeep Pooni 7:04
So when this patient was admitted, a few questions, you know, came up, the first of which being which additional labs were testing to obtain. And so given this patient's presentation, I would plan to, you know, repeat and trend the chemistries.
Repeat CBC with smear potentially if there's any indication of precipitous drop in hemoglobin or thrombocytopenia, anything to suggest microangiopathic changes in terms of further work up. At this point the differential would be still broad, but you would consider.
Additional workup for glomerular disease evaluating for post-infectious etiologies, including your post-strep titers, so your ASO, your DNSB complements for immune complex mediated disease, specifically C3 and C4. Think about lupus.
And then you would also think about.
Vasculitis, so incas, so your C inca, your P inca. You'd want to check NANA I think at

this point and by immunofluorescence given possibility of lupus.
And then you know trending inflammatory markers including ESR and CRP, I think we'd also want to work up the anemia further specifically again if there's any concern for autoimmune hemolytic anemia and we would likely obtain a Coombs haptoglobin LDH and if this patient's not.
Already had imaging at which she has. You could have considered additional imaging such as being on bladder ultrasound in terms of what needs to be monitored acutely. I think at this point we're still concerned about AKI, possibly AKI in the setting of chronic kidney disease, so.
So electrolytes, ins and outs, weight are all going to be critical in the management of this patient. This patient was also interestingly noted to be bradycardic, which is a little unusual given the presumed inflammatory state that she's in. So it would be.
Key to keep this patient on monitors in addition to checking her blood pressure regularly and then given the known edema in this patient with hypoalbuminemia, her clinical exam will also need to be monitored, particularly if there's any concern for new respiratory symptoms as she's at risk for pulmonary edema.
And then lastly, the the cytopenias are of concern. One, we're worried about clotting bleeding risk if we're at all concerned about thrombotic microangiopathy or even worsening thrombocytopenia. But we may also be worried about, again, acute hemolysis given anemia and then.
Kind of like with broader systemic involvement, you might be thinking about things like macrophage activation syndrome, given that all her cell lines are slightly down. So it'll be important to trend her CDC at least initially.
And So what are the emergent issues that could come up for this patient? She's at risk for fluid overload, so monitoring her eyes and nose will be important. You may have to think about restricting her intensibles, monitoring her urine output.
She's also at risk for electrolyte disturbances, specifically hyperkalemia. Again, she's also at risk for bleeding infection. And then in terms of what is the suspected diagnosis, we're worried about AKI.
Acute, acute and chronic. And so you know as a rheumatologist the the things I'm thinking about are lupus and and vasculitis and then who should we consult? So would consult, you know, general pediatrics for admission as the workup is pending. You consult Dr. Patel or your local nephrologist for their recommendations as well, given the AKI and the concern for AKIAKI on CKD and then likely consult rheumatology as well.

Taking a step away from the case just for a minute, I wanted to review both the laboratory and clinical features of systemic lupus. Is this the patient's diagnosis to be determined? And what I'm actually sharing here is the 2019 classification criteria for lupus that was developed.
By the American College of Rheumatology and the European League Against Rheumatism, or UR. Although this criteria was developed with clinical research in mind, we do use this classification criteria to help diagnose lupus. As you can see here, having a positive ANA is an entry criterion and.
There are both then clinical and immunologic domains, and you need both immunologic and clinical criteria to consider a diagnosis of lupus. Clinical criteria can include constitutional symptoms such as fever.
Entologic symptoms, so leukopenia, hemolysis, neuropsychiatric disease, so seizures, psychosis, eukocutaneous symptoms. And this is kind of a number of clinical manifestations, so everything from oral ulcers to rashes.
Is consistent with acute cutaneous, lupus, alopecia, serosal involvement. So that could be having pericardial effusions, acute pericarditis, other signs of serositis, MSK involvement, so arthritis.
Myositis, although that's a little bit more or not as common in lupus and certainly renal involvement. And then for the immunologic criteria, you'll see a whole host of laboratory tests here. Starting from the bottom, there's the lupus specific antibody, so your.
Anti double-stranded DNA antibody or your anti-smith antibody. There's a low complement that would also earn you some points, the low C3 or C4 or having both that are low.
And then the presence of some anti-phospholipid antibodies and specifically your anti-cardiolipin, your anti-beta 2 glycoprotein antibody and your lupus anticoagulant. And so again, it's a combination of clinical factors, laboratory features.
That help us diagnose lupus. One question that sometimes I get is is, you know, there's different types of testing for the ANA, specifically ANA by immunofluorescence versus Eliza. In general, the IFA is better because the negative predictive value.
Is better. The way that that test is done, it's labeled antibody to antigen that's looked at under the microscope. Amy by ELISA is usually automated. It's more cost-effective, but that's looking at antibody to antigen and then that is then enzyme labeled.
To antibody to detect color change. So again, if there is an option, checking ANA by

IFA or immunofluorescence is the better test.
So prior to 2019, there were classification criteria used to define lupus again for research purposes. The reason that they developed the newer criteria in 2019, aside from having kind of a unified international consensus, was to improve upon the sensitivity of the criteria.
from 1997, but sustain its specificity. And then as you can see here, the 2019 ACR-ULAR criteria did just that with a sensitivity of 96.1%, specificity of 93.4% in the validation cohort. Uh
Which demonstrated improved performance compared to the ACR 97 and Flick 2012 criteria. I point this out because you might see different rheumatologists refer to the more recent criteria as well as the prior criteria.
Um. And again, you know, I think um.
Keeping in mind at how to diagnose lupus, you still need clinical and immunologic criteria. For all of these criteria, you still must have a positive ANA. Some of the tests that we order again specifically like the.
Antibodies, whether it's the ANA or the anti DSDNA or Smith antibodies can sometimes take several weeks or several days to a week to come back depending on the lab. So it's important to look at kind of other clinical domains and and have high suspicion based on.
What else might be present?
So this slide here highlights some of the clinical features you may see in patients with lupus. The top left photo shows a child with alopecia. Typically alopecia is non-scarring in lupus. The bottom left photo shows palatal ulceration in a teen patient. And then the top right photos show bailar rash. The one kind of the furthest top right has more significant involvement with some dermatitis and possibly even some vasculitis. And then the bottom right photos here show changes.
Associated with acute cutaneous lupus.
So some common questions that I get regarding the diagnosis of lupus is one, when should I get an ANA or other antibodies? And my answer to this is usually if there are concerns about the history, you know if there's history of chronic unexplained fevers, arthritis.
Rash or concerning laboratory features like leukopenia, anemia, AKI that those might be reasons again to kind of explore a diagnosis of lupus and that's when I would get the ANA by immunofluorescence.
The other question I commonly get is in addition to rheumatology, who else should I

consult? And I would say it really depends on the clinical manifestations of disease. Obviously if there's concern about like AKI or CKD, then nephrology.
If there are questions about skin changes, then obviously dermatology, it really just depends on on the clinical manifestation. And then the other question I I often get is if there's a family history of autoimmunity, should any pre-emptive testing be done in a in a healthy?
Child and usually the answer to this is no, unless there's concerning symptoms. Lupus is likely both due to genetic and environmental factors, but we only know a small subset of the genes involved, so.
I would not do any pre-emptive testing unless there was some clinical concern. And then last question is, is how childhood lupus differs from adult lupus. And so we'll actually talk about that on the next slide.
And so in terms of childhood versus adult lupus, it's generally worse. We tend to see more pulmonary neurologic, hematologic involvement in childhood lupus. There's a higher prevalence of renal disease in children, usually children present.
With more active disease as well and kind of like with this, you may also see higher medication burden in children certainly at the start, but then also in time and then the related toxicities with those therapies.
About 20% or so of cases of lupus nephritis are diagnosed in childhood, and about 40 to 70% of children with lupus will potentially develop lupus nephritis at some point in time.
Although the the clinical manifestations of childhood lupus and related kind of medication toxicities tend to be worse, we have gotten much better at treating lupus. So as you can see here back in 1945.
The five-year survival of patients with lupus was only 28%, but by the 1990s around 91%. So again, significantly improved in terms of renal prognosis. This has also gotten much better in the 80s or 90s. We were anywhere from 85 to 90% renal survival to.
Mid 90s by the early 2000s, and I'll hand this over back to Doctor Patel to discuss the prognosis of lupus nephritis in a little bit more detail.

RP **Ruby Vishnu Patel** 20:41
Yeah. So this is more about lupus nephritis in our pediatric patients. So lupus nephritis, you know, the numbers are very variable, but it can occur in close to half of patients with systemic lupus. So some of the numbers maybe say 10 to other data

says maybe closer to 32.
To 55% of patients will have lupus nephritis. What's interesting is a majority present within the first couple years of diagnosis. So 88% of patients will present with lupus nephritis within the first year of their systemic lupus diagnosis.
And 94 will present within two years. And of those with lupus nephritis, anywhere from 10 to maybe 22% will go on to develop end stage in their lifetime. Lupus nephritis carries a mortality rate of up to 30% at 10 years.
Like we mentioned earlier, in the 1950s, death was pretty common within two years of having lupus nephritis. So outcomes are better, but it's still guarded. And now the mortality rate on dialysis is about 22% at five years.
And this is pediatric and adult data. So who are the patients who are more at risk of developing this end stage from their lupus nephritis diagnosis? Well, it's the younger children. It's seen more in males and people of certain backgrounds. So African Americans, Hispanics, American Indians, Alaskan Natives.
And Asian, those with Asian ancestry. And in general, we know that this is not limited to just lupus nephritis, but patients who are socially disadvantaged and live in medically underserved areas have worse kidney outcomes as well.
So going back to our case, these were the additional lab work up that was ordered. It showed a low C3, low C4, again pan cytopenia Coombs negative. What was interesting is at the time of.
The time the patient came to the ED, nephrology was actually consulted for admission and we didn't have many of these labs back. So the concern was we have a patient who's presenting with GN. Ultimately, the patient was cared for by general Pediatrics because there was such a high suspicion for lupus.
And then once some of these serological tests resulted in the morning, she was transferred to the rheumatology service. Treatment was started and we planned to do a renal biopsy later in her admission.
All right. I think the next slide, perfect. So in case you were curious, we did get additional labs back. But again, and this took some time, she had a pretty high, she had a positive anti Rho and and positive double-stranded DNA antibodies. Some of her anti-phospholipid antibodies also were positive and we'll talk about the.
In the coming slides, but biopsy showed class 4 lupus nephritis.
So I do want to spend some time discussing when we do a biopsy in patients with suspected lupus nephritis. Of course, your nephrologist will help answer this question, but sometimes, you know, as the general pediatrician or maybe the

hospitalist, you're the first provider that's coming face to face with this patient.
And maybe family has questions about what are next steps. So in general, the guidelines say a biopsy should be performed in any new diagnosis lupus patient with proteinuria and the cutoff is 0.5 grams per gram or if the patient has abnormal renal function, that's other.
Otherwise unexplained. Those are two kind of key reasons to do a biopsy. For patients with known systemic lupus, we consider biopsy in the setting of a nephritis flare if after six months of appropriate treatment, their proteinuria hematuria.
Or renal function is not improving. And then there are certain cases where a biopsy may not be possible. There may be concerns around the procedure, such as maybe the patient's really inflamed and we're concerned about bleeding or if the patient has positive.
Titers that make them at risk for clotting or sometimes these kids present with uncontrolled hypertension and this would make doing a biopsy or anesthesia unsafe.
The guidelines say if a patient mainly has hematuria as part of their presentation.
You choose treatment for class 3 and four lupus nephritis, or if they have features that are more nephrotic, so more heavy proteinuria, you would treat according to class 5 recommendations if you can't do a biopsy.
So what is lupus nephritis? Well, we consider it an immune complex mediated glomerulonephritis. So you have a large amount of autoantibodies that react with self antigen creating these immune complexes which then deposit in the glomerulus.
These deposits result in activation of the classical complement pathway and activates. It activates macrophages, neutrophils, as well as pro-inflammatory and pro-fibrotic cytokines. Basically, all of this results in podocyte injury, mesangial, endocapillary and epithelial hypercellularity.
As well as extracellular matrix deposits and eventually all this will lead to renal injury and impairment. There are other features that you can also see in a kidney biopsy like such as TMA immune complex, tubulo interstitial nephritis, amyloidosis.
Um are all kind of other features as well that we can see as see.
So we'll go back to the next slide and this is kind of going back to medical school where I'm sure we all looked at EM images and pathology. So this is a part of glomer part of the glomerulus where you have the podocyte and the foot processes.

PH **pat herndon** 26:57
Oh.

Ruby Vishnu Patel 27:04

There's also a mesangial cell, which is marked with a black arrow, and the capillary loop is what kind of what we're zoomed in on. The red dot is where you would see mesangial hypercellularity, so more cells in the mesangium.

The darker blue is where you would see sub endothelial deposits and the light blue is where you would see sub epithelial deposits. So just to kind of get an idea of what we will be looking at.

So this is a quick table describing the International Society of Nephrology and the Renal Pathology Society classifications of the various classes of lupus nephritis. So this was developed in 2004 and there have been revisions.

Done in 2018. So it's probably not as applicable to know each type or each class of lupus, but it's it's interesting to kind of note the column on the right which gives us an idea of how these patients may clinically present. So you have class one and Class 2 lupus nephritis which.

These patients will have mesangial hypercellularity and the differentiating factor between one versus 2 is how many cells are present in a three micron thick histological section. So if there are three cells or less, it's classified as class one. If it's four cells or more, it's Class 2.

And clinically, these patients have mild symptoms, maybe some hematuria, maybe some mild proteinuria and overall they'll present with normal kidney function. Then we have class 3 and 4 lupus nephritis. This is defined as having glomeruli that have hypercellularity cellularity.

In the capillaries. So this is due to like an influx of inflammatory cells. You may have heard the term endocapillary proliferation, which is kind of a misnomer. It's more endocapillary hypercellularity or too many inflammatory cells.

In the capillary. So if less than half the glomeruli show changes, it's class 3. If more than half of the glomeruli biopsied shows changes, it's considered class 4. And these patients have a little more AKI on presentation. Perhaps they also have hematuria. And mild to moderate proteinuria and this is kind of like our patient is membranous lupus nephritis where there are protein deposits in the sub endothelial space and what's characteristic of these patients is they have heavy proteinuria, so often nephrotic range.

And if they have isolated class 5, they may present with normal kidney function, but it can decline over time if not treated. And then there is this entity called class 6

lupus nephritis. It still exists, although maybe future nomenclature may do away with it, but.
It's really a biopsy sample with very advanced sclerosis, so almost like an advanced CKD kidney or or end stage kidney.
So again, this is a drawing differentiating the various classes of lupus nephritis where and where the deposits are. I won't spend too much time on this, but it shows kind of what we talked about on the previous slide and if you ever want to look at this for reference, the colors.
Uh, in the box on the the left, kind of indicate what we're looking at in the image images on the right.
So there are still other things you can see on biopsy for a patient with lupus. Just beyond the deposits, you can see crescents there. There can be fibrous crescents. You can have epithelial proliferation and.
The cellular crescents will have a lot of different types of white blood cells in them. This picture here shows a fibrocellular Crescent and the arrow shows where the Crescent is. You can also describe a glomerulus as having global or segmental. Which means partial necrosis in the setting of having a Crescent. And then sometimes with a Crescent you can get fibrinoid necrosis, which is basically like a rupture of the glomerular basement membrane. And sometimes you see these types of lesions also in ENCA disease as well.
And then there are some other definitions like karyorexis, which is basically fragmented apoptotic cells in the kidney.
It's important to review and be familiar with some of these pathological findings because it's how we assign scores to the biopsy. So there is a modified NIH activity index used for lupus nephritis.
And the activity score essentially is given based on characteristics that show inflammation. So specifically this is inflammation that can be treated and is reversible. This activity index also has a a separate chronicity score and these are assigned based on.
Findings like global glomerulosclerosis, fibrous crescents, or basically changes that show irreversible damage or lesions that are scars, and this will not respond to therapy.
So we'll go back to our patient's case. This is actually our patient's biopsy stain. The image on the left is a normal pink H&E stain, and the picture on the left or on the right is her is three of her glomeruli. And as you can see, these three glomeruli look

very pink.
Compared to the normal one, which probably indicates mesangial expansion. And there's just a lot of cells, a lot of little blue purplish dots, which we call increased cellularity in each glomeruli.
We can go to the next slide. Thank you. And so this is her PAS stain. The mesangial expansion looks magenta on PAS. And again, these are the same 3 glomeruli we saw in the previous slide and there's increased cellularity as well.

pat herndon 33:18
Thanks.
It.

Ruby Vishnu Patel 33:37
This slide here is a trichrome stain on the left and the blue shows fibrosis and then on the right it's a separate glomerulus, but this is a Jones silver stain and these Lacy like black lines are the preserved glomerular basement membrane.
And you can see towards the top is where we have a fibrocellular Crescent.
This is our patient's immunofluorescence slides. So what was really interesting about this case is she actually had a lot of crescents, almost like a patient with Anka disease rather than lupus. So her her immune deposits actually weren't that impressive.
She had positive staining for IgGC3 and C1Q, which are all shown here. And there also are some lupus cases where you don't get the classic full house staining, but just kind of these three stains come back positive. We can go to the next slide.
And this is not our patient, but this is the textbook, you know, full house IF staining that you would see with C1QC3 IGG, IGM and IGA.
And again, going back to our patient slide, this is an electron microscopy slide of the glomerulus. You can see the Gray deposits which are highlighted by the red arrows showing sub endothelial deposits within this capillary loop.
And then again, another electron microscopy image. The red arrows kind of more to the top of the slide show sub endothelial deposits. Some of them are rather rather quite large. And then the arrows on the bottom right corner show some mesangial deposits.
So just to summarize, the pathology report diagnosed class 4 lupus nephritis with crescents. So 74% of her 35 glomeruli showed some type of involvement, whether it was necrosis or crescents. The activity index was very high, it was 18 out of 24 and

the chronic.
Index was 3 out of 12.

Rajdeep Pooni 36:03
All right. So now big question that now that we've established that this patient has lupus and lupus nephritis is how do we treat these patients? So in paediatric rheumatology, we have a research body called Cara and Cara has developed consensus.
Treatment plans or CTPS for various conditions including childhood lupus nephritis. And so this is from the CARA CTP for lupus nephritis and you can see here that. There's there's a few different treatment arms, but the the main non. So there's steroids and then there's non-steroidal agents. And so for the non-steroidal agents, you're using either cyclophosphamide or mycophenolate and then.
For the steroid component, it can be either oral steroids, a combination of mixed oral and IV steroids with a long taper for the the oral steroids.
However, last year the at the American College of Rheumatology, new guidance for the treatment of lupus nephritis in terms of medication approach and disease monitoring were presented.
We don't have to go into significant detail for the various treatment arms, but I wanted to make you aware that compared to prior and you know what differs from the the care of CTP is, is that there's actually a shift towards triple therapy or slightly more medication.
At presentation of disease. So typically the immunosuppressives that we use include mycophenolate, calcineurin inhibitors, so that's voclosporin in adults or tacrolimus in children. Belimumab, which is a monoclonal antibody that inhibits B cell activation.
Eating factor or bath and and cyclophosphamide. The mycophenolate based regimens are still are conditionally recommended over cyclophosphamide based regimens in patients with class 3 or 4 lupus nephritis due to.
Some of the toxicity associated with cyclophosphamide, but if cyclophosphamide is to be considered, then they actually recommend a lower dose protocol. Other recommendations that are not specifically highlighted in this table.
Have to do with updates for recommendations regarding when to consider kidney biopsy. The new guidelines suggest that repeat kidney biopsy is conditionally recommended in patients who previously were diagnosed with lupus nephritis and remission who then present.

With suspected flare. Kidney biopsy is also recommended for patients who've had the appropriate treatment but have ongoing signs of disease such as ongoing significant proteinuria or hematuria or or decreased kidney function.
So in terms of the the therapies, there's kind of like a main commonality between, you know, steroids, mycophenolate, cyclophosphamide and then some of the B cell agents and calcinerin inhibitors, the top one being infection, so patients who.
Are undergoing induction therapy for lupus nephritis certainly are immunocompromised and at increased risk for infection. So that should always be top of mind. With regards to steroids, they continue to be a manstay of treatment for the disease and although.
As a rheumatologist, I love them. I also kind of hate them at the same time, and that's because there's lots of potential adverse side effects, especially in a growing child. So some of the side effects that we can see include hypertension, which again, as you can imagine that someone who already has AKI.
Or a renal disease is already at increased risk and then you add steroids on top of it. Metabolic effects. So you can see hyperglycemia or even diabetes in these patients on high dose steroids. There are potentially psychiatric effects I would say.
The most common are mood changes, irritability, sleep disturbance, but can be as severe as psychosis. And then with regards to bone health, chronic steroids increase your risk for osteoporosis.
Again, can impact growth in children as well. With regards to mycophenolate, this is a very consolidated list, but in addition to infection, it's tragogenic, so someone who. Is trying to conceive or is pregnant should should not be on this therapy. And then with regards to GI side effects, it's not uncommon when starting mycophenolate that people will have.
Some cramping or even like diarrhea at the start. So oftentimes we'll start at a lower dose and dose escalate over several weeks. In terms of cyclophosphamide, we typically use.
Doses lower than some of our oncology colleagues use in in the treatment of cancer, but there are still risks. So there could still be GI side effects, including, you know, nausea, vomiting.
Obviously reproductive side effects. Aside from teratogenicity, we think about effects on fertility, which is dependent on cumulative dosing and and where kids are in terms of their pubertal growth.
We also worry about secondary malignancy and then lastly we think about

hemorrhagic cystitis, which basically happen or can happen as a consequence of how the medications metabolized and.
With the the the toxic metabolite hanging out in the bladder and so these patients who received cyclophosphamide also received essentially super hydration to clear potentially clear that out and they also received meds to bind the creolan.
In terms of B cell agents and calcinarin inhibitors, just kind of again, very broad. We unfortunately don't have time to go into detail for all these therapies, but we think about everything from allergic reactions with our B cell agents.
Um to Uh AKI and hypertension with their calcineurin inhibitors and then a whole host of other things.
One thing I I will mention before we go on to the next slide is, is that again patients are immunocompromised when they're on these agents and so.
When thinking about how to protect these patients, certainly vaccines are something that come come up and and something that we're really all for except for live vaccines in these patients, those we would typically avoid.

RP **Ruby Vishnu Patel** 43:46
So this slide briefly lists common complications related with lupus nephritis, and these are important to be aware of. So when you see a patient with lupus nephritis, it's very important to review their recent creatinine. This will give you an idea of what their GFR is.
And the renal function is, or if you notice that their creatinine is much higher from previous measurements, this could lead to a acutely a lower GFR. Maybe you're concerned in that moment for AKI or a lupus flare on top of the patient's baseline.
Potential CKD hypertension can also be an active issue. It can be a consequence of the lupus nephritis, or even a consequence of the steroid treatment that the patient's on. If a patient with systemic lupus has hypertension, we often refer them to nephrology for management of the blood pressure.
Pressure, even if they don't have lupus nephritis at that time, or if the blood pressure is dangerously high, I use a cutoff of the 95th percentile plus 30 millimeters of mercury. That's kind of my indicator of should this patient go to the Ed for dangerously high blood pressures.
Again, if the patient doesn't have as high of the measurements but has symptoms of hypertensive urgency, another reason to call nephrology or refer to the Uh, there's always a risk of more commonly like fluid overload, so always trending the patient's

weight.
Especially with active lupus nephritis, just to get an idea of fluid balance, blood pressure may also be elevated if the patient is fluid overloaded. Many times ongoing fluid overload. These patients will be on daily diuretics for management, which can also be a.
Adjusted if they have worsening fluid overload. And sometimes many of my patients go to their pediatrician more often than they're seeing me. And so I do have a lot of active discussion with their primary provider on how to adjust some of these diuretics as things are getting better or worse.
Lupus nephritis patients, especially depending on what class of lupus nephritis, may have proteinuria, low serum albumin. They're always at risk with heavy proteinuria for fluid shifts, hypogamma globulinemia, infection and bleeding and clotting.
And of course also related to renal function and also maybe medication side effects, patients can have abnormal electrolytes. So just looking at potassium for example, especially if there's an AKI from their lupus nephritis and then also related to lupus nephritis.
But also impacted by what antibodies the patient has. For example, if a patient has a positive lupus anticoagulant or antiphospholipid antibody or is very inflamed or proteinuric, could there be a risk for bleeding or clotting?

RP **Rajdeep Pooni** 46:49
So in terms of managing these patients outpatient, we really try to partner with our general Pediatrics colleagues. And so the schematic is actually from Boston Children's and their model when it comes to how specialists and pediatricians can work together to deliver.
Care to medically complex children and also, you know, children with chronic disease and including those with lupus. As you can see here, the majority of children in primary care is are are healthy and that's where.
The medical home is is really with the primary care team. However, once someone's diagnosed with a chronic condition, it is really a matter of the primary care team collaborating with specialists and the and the family and then for those children who have both medically complex and chronic disease.
Their model suggests that either the primary care team or specialty care team can serve as a medical home, but collaboration as well as having support team members such as the coordinator, social worker, a nurse are are really key.

I'm not sure what your current model looks like at your institution, but I think what works best for our rheumatology group is really serving as the medical home for these complex patients. However, really relying on our general Pediatrics colleagues for ongoing support with general preventive care, including vaccination.
Well visits and then urgent sick visits for routine illnesses.
So that actually brings me to this slide, which gives a very broad overview of vaccine recommendations for rheumatology patients in general. And so this is actually family and and patient facing guidance that was put together by one of our former and and recently graduated fellows, Amanda.
Who worked on this internally with considerations from rheumatology as well as our immunocompromised ID group. We don't have to go into this in detail, but I wanted to share some general principles. In general, we know that many of our patients are again at increased risk of infection.
I.
Due to weakened dysregulated immune systems, vaccination may be key in preventing some illnesses. In general, patients with weakened immune systems should not receive live vaccines, but may benefit from additional vaccinations, including pneumococcal, shingles, hepatitis.
B vaccines. And So what I would encourage is that if there isn't already guidance between pediatric and specialty groups at your institution, it might be worth considering, you know, coming up with a plan so that these patients can be screened and receive the appropriate vaccination.
And.
And so in terms of the the role of the pediatrician in long-term care, we've already touched on some of this, but in general as specialists, we really rely again on our pediatrics colleagues for helping to support our patients certainly with lupus or other chronic conditions to evaluate for acute illness.
And anticipate preventive care. Many of our patients don't live within close proximity to our clinics, nor do we always have availability to do sick or urgent visits. So in these cases, our pediatric colleagues are able to support these patients for the initial assessment and determination.
For whether additional workup or admission may be needed, I think again in general for these patients who are immunocompromised, having a low threshold for, you know, workup for infectious illness is is really key.
You you might think about also opportunistic infections, fungal infections, atypical

things. So I would again also encourage not just reaching out to like your local emergency room if if needed and colleagues there and sending the patient there potentially, but also reaching out to the ped spot, the Substat.
Specialist if there's questions and we're generally only a page away. And again, we're usually very happy to partner with our general Pediatrics colleagues to help provide the best care for our patients. For our shared nephrology patients, Dr. Patel already kind of went into this, but.
They're at risk for fluid overload, hypertension. They need to be seen regularly for blood pressure monitoring and other general care. And then for vaccinations, again, in addition to ensuring that these patients are appropriately vaccinated.
We also have to keep in mind that these patients are at risk for more serious sequela from certain infections and may need post exposure treatment. So if there's ever any question of exposure to things like measles, varicella in addition to connecting with the primary rheumatologist or.
Potentially nephrologist discussing with your infectious disease colleagues may be required because there may be some coordination needed for for some of those therapies.

Ruby Vishnu Patel 52:19
And this is a nice summary table for practice guidelines for adjuvant therapies for patients with lupus nephritis. It goes through diet additional medications for proteinuria, which those will probably be managed by nephrology as well as.
Managing blood pressure, bone health. But a focus for a primary physician would be not only vaccinations, but also discussing and aiding in reproductive health as you may deal with, you know, contraception and certain considerations.
Usually in these patients we do recommend using methods without high dose estrogen, so just a nice summary table to reference.
I think that might be all of our slides, yeah.

Rajdeep Pooni 53:02
I think that concludes our talk.
Do we want to oh, I will not share the questions because I think.
Maybe the answers are highlighted, it looks like.

Kamat, Deepak M 53:18
We don't see the highlights, so.

Rajdeep Pooni 53:19
Uh, in the coming slides. Oh, if I click further, they will be highlighted. Uh, so my apologies, but uh, let me see if I can jump to our references slide.

Kamat, Deepak M 53:22
Yeah.

Rajdeep Pooni 53:30
After your references, thank you everyone for your time and for listening to our our talk.

Kamat, Deepak M 53:38
Thank you Doctor Punya and Doctor Patel for updating us on lupus and lupus nephritis. Let's see if anybody has any questions or comments. You can always put your questions in the chat box or.
There's a hand and you can ask the question directly to our wonderful speakers. Doctor Williams, go ahead and ask your question, please.

Williams, Janet F (Dr.) 54:08
Good morning. Thank you. Those were both the speakers were wonderful. Thank you for that information. One just a side comment that's weird, but you know, quite a while ago.
I saw the roof of the mouth ulcer like that related to a patient we diagnosed with scurvy. So just saying to put it in your differential. Of course it's unusual, but it happens.

Rajdeep Pooni 54:33
Oh.

Kamat, Deepak M 54:34
Mm.

Williams, Janet F (Dr.) 54:40
On the other hand, I wondered if you, and if I missed this, I'm sorry, relate more her, her. Is there a relationship, do you think, to her menstrual cycle, the the menarche, that type of part of her presentation?
To what you found, you know that Anna Sarka or any of the other symptoms, what was there a relationship or just it's just happened to be within three months? Yeah.

Rajdeep Pooni 55:10
Like coincidental, I think like at least with lupus and some of our other autoimmune conditions in general, it's not uncommon for STC patients in their early teenage years, kind of in the context of all these hormonal and pubertal changes.
So I think kind of from that standpoint, um.
Could there again be a relationship? I I I think it's possible, but I think in terms of the patient's presentation, I think.
Not, not anything specifically except that maybe again kind of like family perception or or or you know if it can be confusing to patients, you know if they're seeing blood in their urine and again like there's.
Potentially menarche around the same time, but in this case patient had hematuria, so I think it just could have muddied the picture kind of maybe initially for what the family was thinking or maybe what their primary care doctor was thinking just because there are other factors.

Williams, Janet F (Dr.) 56:09
Right.
Yeah.
Sure. OK. Uh, thank you so much.

Perlman, Jeremy S 56:23
Yeah.

Ruby Vishnu Patel 56:27
And Doctor Williams, I wonder if your patient was scurvy, were they like autistic or had certain eating behaviors? I just diagnosed A scurvy patient yesterday, so it's we're seeing it a lot.

Rajdeep Pooni 56:27
Of course, and you bring up a.


Williams, Janet F (Dr.) 56:39
Actually they weren't was amazing. It was a dietary issue and the child got into a vicious cycle and the where the parents only you know that the child would only eat like 3 things.

Ruby Vishnu Patel 56:40
Oh.
Hmm.


Williams, Janet F (Dr.) 56:58
Bean tacos, nothing that had any kind of vegetable vitamin C, any kind of vitamins. I forgot what it bean tacos. There were three things they would eat and and they were so happy that the child would eat anything that that's all they would give him. It was just this vicious cycle.

Ruby Vishnu Patel 57:04
Wow.
Yeah.
But.
Oh.


Williams, Janet F (Dr.) 57:18
It's hard to believe, but yeah, no, we did follow them for some learning issues, but I became a Linus Pauling, you know, follower because the minute we gave them vitamin CI mean, you could see it change from this crabby.

Ruby Vishnu Patel 57:26
Really.
Yeah.


Williams, Janet F (Dr.) 57:39

Kid and and couldn't really walk and and just to like becoming human. So it was pretty amazing.

Ruby Vishnu Patel 57:39
Yeah.

Rajdeep Pooni 57:41
Yeah.
That's incredible. And by so I I do some research in chronic non-bacterial osteomyelitis or CNO or CRMO definitely on the differential. And so I know this patient presented with like.

Williams, Janet F (Dr.) 57:58
Mhm.

Rajdeep Pooni 58:06
You know the oral issues, but it sounds like they also had some bone pain. So when you're thinking about like arthralgias or or limb pain, definitely I I've diagnosed patients with vitamin C deficiency as well. So check their vitamin C level.

Williams, Janet F (Dr.) 58:15
Yeah, yeah.
Check her vitamin C Yeah, check her vitamin C, right. Yeah. Well, thank you. Thank you so much. Yeah, that's a funny little segue, but really, it's important. So thank you.

Ruby Vishnu Patel 58:23
Yeah.

Rajdeep Pooni 58:25
It's magic.

Kamat, Deepak M 58:33
Any other questions or comments for Doctor Patel and Doctor Puni?
Can you quickly comment on use of biologics in lupus pediatrics? What is the what are the indications and what is the current status?

Rajdeep Pooni 59:01

Yeah. So there is this kind of, again, shift towards triple therapy, at least with lupus, lupus nephritis. And so it depends on, you know, the, the, the.

Class of disease for the patient, but if we're thinking about like class 3 or or more commonly kind of class 4 lupus nephritis, then we're thinking about hydrosteroids and and mycophenolate, which is similar prior, but we're also thinking about things like belimumab.

Or if there is a severe or fractal disease, things like rituximab, obinetuzumab. So those are, you know, kind of like B cell or B cell depleting agents in kind of different ways that we're thinking about.

For kind of more of the Class 5 disease, we're we're still thinking more about Casineurin inhibitors, but certainly we have patients with overlap of class four and five lupus nephritis. So again B cell depleting agents might be considered for both.

OK.

And then also you know again this is has been primarily a lupus nephritis focused talk, but sometimes we use B cell depleting agents also for kind of other clinical manifestations of disease.

Whether like severe hematologic kind of refractory disease, sometimes even.

pat herndon 1:00:28

Hello.

Rajdeep Pooni 1:00:33

Kind of the presence of other factors.

Like if we're thinking about like anti-phospholipid antibodies, you know, syndrome in conjunction with lupus, if we're thinking about just other clinical features in general, you know, severe rashes, you see cutaneous findings. So we are using biologics.

Fairly frequently I I would say again bilimumab being amongst the most common and it's kind of more recently approved for the treatment of lupus nephritis and even in children which when I was in fellowship was not the case and then some of our anti CD20 agents.

1:01:06

Yeah.

Kamat, Deepak M 1:01:11

Yeah.

Yeah. Thank you. Doctor Handan, please go and ask your question. Go ahead and ask your question, please.

PH **pat herndon** 1:01:20

Yeah, I was curious about the the general overall epidemiology. For example, I noticed that a lot of these young women.

Passed menarche and then they got involved in sports, sports that relied, that relied on a lot of stress and exposure to heat and, you know, elevated body temperature.

And the other thing I was concerned about.

Since I treated a lot of adult patients is male, male cases of SLE and about they have if you noticed any changes there or any revelations.

RP **Rajdeep Pooni** 1:02:07

Yeah, I think um.

You know, autoimmune disease in general has kind of the increasing prevalence. It's probably due to a whole host of factors, some of which are, as you're alluding to, you know, potentially environmental.

Um. But I I I think that at least um.

With regards to kind of when these patients present, again, it's not uncommon for you to see patients with lupus kind of in their teenage years or kind of entering or or or just having entered puberty.

PH **pat herndon** 1:02:45

OK.

RP **Rajdeep Pooni** 1:02:47

It is far less common still to see really young patients with lupus. I mean, do I have, have I seen it in, you know, a 7 or 8 year old? Yes, but I would say that would be kind of like the exception.

And then certainly we still, you know, the predominance is still female, but we do have a fair number of patients who are male with lupus.

With with uh, renal disease. Um.

Yeah, I don't know that I it's say just anecdotally, but there's increasing frequency in the male population in general. But again I think that we're we're seeing more lupus, more of like general autoimmune disease in general. So I wouldn't be surprised if there there has kind of been an increase.
As well by gender.

Ruby Vishnu Patel 1:03:45
Yeah, I feel like.

pat herndon 1:03:46
I I just got used to. I got used to the idea that males presented with CNS symptoms, behavioral symptoms, pulmonary manifestation and perfectly good kidneys and things like that. Just getting a really, you know, an entirely different constitution. of presentations.

Rajdeep Pooni 1:04:11
Yeah, I think it's, I mean we feel like the whole, the whole host of presentations. I mean we have the saying in rheumatology that if you've seen one patient with lupus, you've seen one patient with lupus. And I can't, I really can't think of like 2 patients that are alike, but I I agree with you that like you know still.

pat herndon 1:04:22
Yeah, exactly.

Rajdeep Pooni 1:04:31
Have a higher suspicion and kind of like our teenage female patients, again higher suspicion for renal disease. But but I do have some male patients who also have renal involvement. So yeah, it just, it just depends.

Ruby Vishnu Patel 1:04:47
I feel like the male patients that I've taken care of with renal involvement usually have a strong family history of lupus, like a parent with lupus, something like that almost always, but again.

pat herndon 1:04:56

Um.
OK. Thank you.

Ruby Vishnu Patel 1:05:01
Who else?

Kamat, Deepak M 1:05:01
Doctor Brooks quick Lee.

Brooks, Edward G 1:05:04
Yeah, it's more of a comment that as an immunologist, I find it helpful to do an initial flow cytometry for team B cell subsets at diagnosis. And and part of the reason is the predisposing factor can become a variable immune deficiency and it can. Symptoms at teenage years can be quite subtle and later with immunosuppression we do see patients with you know T cell deficiencies etc. And you wonder if it's chicken or the egg. Is it the mycophen. I have seen patients with suppression with high doses of mycophenolate and have to back off those doses and see this the.

Ruby Vishnu Patel 1:05:37
Yeah.

Brooks, Edward G 1:05:43
CD4 T cell counts increase after that. So just just a quick comment of a sort of from an immunology standpoint.

Rajdeep Pooni 1:05:50
Thank you for that that learning point. No, definitely it's definitely something to think about.

Kamat, Deepak M 1:05:58
Thank you, Doctor Puni. Thank you Doctor Patel for that wonderful presentation. Thank you all for attending this morning's presentation. I'm going to conclude this morning's grand round. Thank you all. Have a wonderful Friday, wonderful weekend and we'll see you next Friday. Thank you.

Rajdeep Pooni 1:06:13
Thank you all.

Ruby Vishnu Patel 1:06:14
Thank you.

Kamat, Deepak M stopped transcription