TRANSCRIPT

S2:E7 CHILDHOOD EXANTHEMS

Dr Blake Mumford: Welcome to season two of the *Spot Diagnosis*, a podcast about all things dermatological brought to you by the Skin Health Institute in Melbourne, Australia. I am Dr. Blake Mumford, Education and Research Fellow at the institute.

Associate Professor Alvin Chong: I'm Associate Professor Alvin Chong, Director of Education and specialist Dermatologist. Blake and I are your co-hosts. Today's episode is on childhood exanthems. This topic has unfortunately become more important than ever with the rise in outbreaks of what are largely preventable infections such as measles. Our guest today is Associate Professor John Su whom you may remember from previous episodes on atopic dermatitis. John Su is both a Dermatologist and Paediatrician and the Head of Dermatology at Eastern Health.

John, welcome back to *Spot Diagnosis*, I'm glad we haven't scared you away.

Professor John Su: Thank you for having me, Alvin and Blake.

Blake: John, since you last joined us, we've introduced a new tradition for Season 2 and that is to ask our guests speakers to share a fun and obscure dermatological fact. Can you tell us anything that comes to mind perhaps theories on how chickenpox got its name?

John: Thank you, Blake. I was just having a search of the Internet, which I know is a bit dangerous given that, pardon the pun, "misinformation" is going a bit viral these days.

John: Looking at the source of the name chickenpox was interesting because there are a number of very credible sites and they all have different theories. One relates to the lesions of chickenpox looking like chickpeas. The second one talks about the scarring looking like pecks from a chicken. What I thought was more interesting was that in the middle English in the 13th to 1500s, there was a term called "Giccan" sometimes "Icchen" which was used to refer to itch. I think that sounded interesting. Probably the one that fascinated me the most was the one that used the word chicken referring to "small" or "minor" and said that chickenpox may have come about because it was a smaller or more minor version of smallpox.

Blake: It sounds like we may never know the truth of how chickenpox got its name. A child presenting with fever and rash can be a diagnostic challenge. The vast majority of children with this presentation will have a benign self-limiting viral infection. In a small minority, a more sinister

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pathology is at play, and separating these two is crucial. Thankfully, there are a few clues which can point us in the right direction which is what John is going to help us with today.

Alvin: John, there's a child in front of you with a fever and a rash. Can you take our listeners through your approach?

John: The thing I think is really important is to get a sense of how well or unwell that child is. Sometimes it is not that straightforward if you've got a child who's got a bit of a fever and is a bit irritable, bit lethargic, bit tired, not quite him or herself. I think really listening closely to the history is important. One of the early lessons my consultants used to teach me was always listen very carefully to the parents, without being gender-biased, particularly to the mother because often they will give you little clues which may not necessarily be present at the time of examination. So, is the child really out of character? Or if they've noticed some small feature, just be very, very wary.

I think the wellness of the child is by far the most important. Of course, when we examine a child, there are features like is the child pale and floppy or listless, or not responsive as you might expect for a child of that age, or if their distress seems to be exaggerated, or there might be other more systemic features, for example, in basic exam, of tachycardia, breathlessness, dehydration, which may be related to the degree of sickness that they have or more specific focal features. Of these in particular, of course, signs like neck stiffness or neurological symptoms or seizures and so on are very, very important. I'm sure no clinician would miss those but sometimes we're in a rush, we might actually skip over some of these features because parents may not necessarily, when they're very distressed, bring them out until we actually specifically ask them.

The second thing is looking at the rash itself. There are some features which generally I think must be taken seriously. For example, if there's bruising or purpura, if there's blistering or bullae, those are not normal things that we see with rashes. We must think about them very carefully, they may be indicating significant infection or other things like infiltrations and systemic disorders. Sometimes if we're better clinicians, we would also look at the subtle signs, for example, hands and feet, acral signs that might suggest systemic disease.

Of course, if the rash as we follow them up is progressing in a “funny way” or not healing persisting, then we do have to think about evolution into something more serious, or complications like superinfection. The third thing is the fever itself. This is sometimes a bit harder to gauge. If you have younger children, you do have to be more cautious. For example, as a rough guide, and this is very rough, if a child is under two and they've got continuing fever for over a day or if they're a bit older and the fever has been persisting for three days, we don't really want to write it off too quickly.

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Likewise, the height of the fever, if you've got a younger infant under three months with fevers over 38, slightly older infant or toddler degree over 38.5 Celsius or older children above 40 degrees. Again, that may be an indication of seriousness although it's not altogether reliable.

The fourth thing is if there are any clues in the history, for example, if there's been travel or animal exposure that might suggest that they have caught something which is a bit out of the ordinary.

Fifthly, the immunisation status. This works in two ways. If they have been vaccinated, sometimes the rashes and clinical presentations may be milder or modified as in the case, for example, with measles or even varicella. In these instances, they may still be community hazards and at risk of spreading disease even if they themselves are not too sick. There are public health issues that we need to address, notification and so on.

On the other hand, if they're immunocompromised or unvaccinated, we then have to be more careful then make it, more serious disease and there may be other measures that need to be undertaken.

Finally, we have to bear in mind that there are other things that can mimic infective exanthems. These include drug hypersensitivity, toxins, connective tissue disease. I think a thorough history looking at all those possible things as well as the environment and the child are necessary.

Alvin: Thank you, John. That was comprehensive and really excellent. Can you give us an example when you were surprised by what you thought was a typical viral exanthem and actually turned out to be more serious than that?

John: There's one event that happened quite a few years ago because I was a second-year resident. Not too many years, just a few. In the emergency department, it was a very busy night, there was a long waiting list. A child comes up with a runny nose, a fever, and what looks like a viral exanthem on the body, blotchy macules, some vaguely palpable plaques, irregular shapes. Child is distressed. Mother is more worried than I am because any child with a fever often is a bit distressed but she says this is not in character with him. During their time of waiting, on close examination, there were just a couple of small petechiae on the legs.

Our emergency department was very full and we had to decide what do we do? Do we send the child home? We can't observe here or do we admit? In the end, we decided that we would have to do the full workup. We did a workup including blood cultures, lumbar puncture, started antibiotics, sent the child to the ward just to be on the safe side. The next day I was rung by the Consultant to say they had grown meningococcus. Sometimes these things can be insidious but sometimes quite rapid. This evolution is something unfortunately we can never really do properly as an outpatient. We have to always be aware and always be on our toes.

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Blake: I think it's time for the first **skin tip** for this episode. The first step in assessing a child with fever and rash is to determine whether or not the child is well, or unwell. Signs that the child may be unwell include whether or not they are pale, floppy, listless or not responding properly. Neurological symptoms or signs, signs of dehydration, or specific rashes, including purpura, petechiae, and blistering.

Blake: John, what's the difference between an exanthem and an enanthem?

John: An exanthem refers to something on the outside, something visible on the skin. It refers to something breaking out.

Enanthem refers to something affecting the mucus membranes involving the hidden areas. I think it's a really good question because often the enanthem can present fairly early on. If we don't look for them, they can be missed but they can also give a clue to the diagnosis.

Blake: What would you say is a classic example of an enanthem?

John: An enanthem would include Koplik spots that we see in measles or Forchheimer spots that we can also see in measles or rubella or scarlatina.

Blake: There are a group of viral exanthems which have a very distinctive appearance, which in many cases we can readily diagnose based on that. What are these classic viral exanthems?

John: They can be classified in a few ways. I learned them as they were historically described. First disease refers to rubeola or measles. Second disease is Scarlet fever, which is bacterial. Third disease is rubella. Fourth disease, historically, is not too clear. It's called Filatov-Dukes. It possibly refers to Coxsackievirus araco-virus, possibly that's staph scalded skin. Fifth disease, we still use today to refer to Parvovirus B19 infection. Sixth disease, Roseola infantum. There are some other viruses of course which include human herpes virus, herpes simplex, varicella zoster, and others.

Blake: Start with measles first. Can you tell us what it looks like and how does it differ from rubella which is also called German measles?

John: Measles often presents with a prodrome. The prodrome tends to be characterised in the typical case with fever and the so-called “three Cs” of coryza, conjunctivitis, and cough. Then they come to the so-called enanthem phase, the Koplik spots that we see as little bluey, white spots of the buccal mucosa opposite the first and second molars as the typical textbook description goes. We tend to see in the couple of days around the time the rash is about to appear.

Then with the onset of the rash, which is usually around day four give or take, the fever may go up a little bit and then you get a breakout of rash starting from around the head and neck, mastoid area

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that then slowly works its way over a few days cephalocaudally. It's usually a fairly red rash with macules and flat plaques. These can coalesce as time progresses and become quite dark purple, almost bruise-like, and subsequently brown and exfoliate with healing. The cephalocaudal progression is quite characteristic and occasionally you can see other enanthems early on like the Forchheimer spots as well, which are little pink macules of the soft palate.

Rubella is often called three-day measles or German measles and it's a bit milder in most of these features and also a bit more rapid in its progression.

Often the prodromal features are not as severe and they also can go on between one to five days. You can get the so-called Forchheimer spots on the palate but you don't tend to get the Koplik spots. Then the rash tends to progress cephalocaudally very quickly can be within 24 hours and it usually only stays maybe three to five days as opposed to say seven to ten days with measles.

The other thing that rubella's quite famous for is the so-called lymphadenopathy, which we tend to find in the suboccipital area, posterior cervical, retroauricular area**.** Why that is the case is not too clear. Presumably, the virus is taken into the lymph nodes and causes a slightly exaggerated reaction. You can sometimes get accompanying symptoms like arthralgias as well.

Blake: It's time for the next **skin tip**. Measles has a prodrome of cough, coryza, and conjunctivitis (The 3 C's) and an enanthem called Koplik spots, which precedes the exanthem which spreads from the head downwards.

Alvin: John, have you diagnosed much measles?

John: This is a slightly touchy point for me, Alvin. I was a resident when I had the privilege of catching measles. Unfortunately, I don't know who I caught it from. I think it was a baby on ward eight west, but obviously I missed the diagnosis. Then to make things worse, my mother diagnosed my measles when it came out as a rash. I think it is important to recognise that measles today can be modified because most people have been vaccinated. When you've been vaccinated, often it takes a milder form and it's easier to miss and may not have all the textbook features.

Alvin: Can Rubella or measles cause issues in pregnant women?

John: Yes, they can. Rubella is very well-known as you know and there is routine testing. If you're not immune to measles, if you haven't been vaccinated properly or lost immunity, then measles can also be a problem more because it can cause a lot of complications in adults, especially pneumonia. There are many other complications more so than we tend to see in children.

Rubella in particular is known for the birth defects that can result if you were to catch rubella during pregnancy.

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Blake: Just how contagious is measles and what steps can be taken to prevent it to spread?

John: Measles is very contagious. It's probably the most contagious virus we know. I just learned something from Professor Chong recently about a thing called R0 which talks about how much a virus can spread, how many people one case can infect on average when you are in a non-immune population. For measles, that number is 12 to 18 which is very high. Every case can spread it to 12 to 18 and each of those can spread it to another 12 to 18. Before you know it, a whole population is affected.

Compare that with other very infectious conditions like varicella and *pertussis* where the corresponding number is only four to five. Then COVID, still a bit debated, but has been estimated to be closer to the two to three mark.

If you have a child coming into the office with measles and there's a bit of coughing and sneezing, it's an airborne virus, it's known to hang around the air for a couple of hours.

Alvin: It's a very nightmarish type of disease, isn't it, John? Anti-vaxxers would have you believe that measles is not a serious infection but there are some pretty nasty complications that measles can cause. Can you tell me, in children, what complications can measles cause?

John: Measles can still cause various complications in children but it's not at all a benign condition. As mentioned, we can get infections, respiratory infections, it can be ear infections, it can be bronchitis, and pneumonia. Secondary bacterial infection of pneumonia is also an issue. Fatal diarrhea from dehydration is well-described as well as other organs like hepatitis, mesenteric adenitis, pancreatitis can complicate measles. The heart can be affected, so-called myocarditis, pericarditis inflammation of the heart.

The blood system can be affected and you can get bleeding tendencies from loss of platelets and also the so-called disseminated intravascular coagulation where loss of clotting can cause people to bleed almost spontaneously. The eyes can be affected and you can get corneal ulceration leading to blindness. Conjunctivitis we've discussed. The kidneys can be inflamed, leading to renal failure. Very importantly, the brain can be affected, they can get seizures when they've got the fever, they can get encephalitis.

Then there's a scary, fortunately, less common condition called subacute sclerosing panencephalitis which can develop many years later due to persistence of the infection where the brain just slowly deteriorates and that can be fatal. There are many consequences of measles. To not vaccinate against it would be putting the child at great risk and the community.

Blake: That's certainly a long, scary list of potential complications. I think on balance the vaccine seems very, very safe. Prior to the development of a vaccine, primary varicella infection or

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chickenpox occurred in 90% of children by the time they reached 10 years of age. I was one of those children just missing out on the vaccine by a few years but I did score an awesome Batman toy which I can still remember.

Blake: John, can you tell us what causes varicella and how does it present?

John: Varicella is caused by a herpes virus, it's often called herpes virus 3 but we usually know it as varicella. As mentioned, it's got nothing to do with chickens. It was confused in the old days with smallpox but the lesions tended to be polymorphous which we'll mention in a minute and also tended to be relatively central on the body as opposed to smallpox which often was more head and neck and distal limbs.

It is a condition that again tends to affect adults much more potentially seriously. We don't see it as much since the introduction of vaccination thankfully. It often has an incubation period of 10 to 21 days so it's a little bit longer than for measles. It comes up very early. Usually, on the first day of fever, the rash will come up. The rash evolves. It starts with little papules and then becomes vesicles and pustules and then they scab up.

This change can often be seen at the same time on the skin on examination so it's polymorphous. It's where you have papules sitting alongside vesicles and pustules. That is very helpful with the diagnosis. It tends to be centrifugal in spread starting centrally and then spreading to the extremities. Usually, they tend to scab up after maybe four, five days but the extent can vary from person to person.

Alvin: When someone with chickenpox has lesions which are completely scabbed over, they're no longer considered infectious, is that true?

John: Yes, that is true. That can be five days. It can be a little bit more but the actual virus from the vesicle can cause infection. Again, respiratory, inhalation, and infection from that way. One thing I did not mention is that they often can cause “pox marks”, scarring as well.

Alvin: In adults, because the virus actually lives in the dorsal ganglia, they can come out and cause dermatomal rash of shingles. The same virus reactivating at a different stage.

Blake: The history of chickenpox is quite interesting. In fact, it was in 1888 that someone actually recognised that children could get chickenpox from exposure to herpes zoster infection in adults.

Blake: It's time for the next **skin tip** for this episode. Primary varicella infection or chickenpox manifests as a polymorphic rash which means that there are several different lesion morphologies at any given time on the skin.

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Blake: John, what about the complications of chickenpox?

John: Chickenpox is very itchy and children can scratch themselves and get secondary bacterial infections. That can even lead to soft tissue infections and necrotising fasciitis. They can also get respiratory symptoms with pneumonia, asthma flaring. Again, if they're sick and not eating and drinking, that can lead to systemic problems. If they are immunocompromised they are particularly at risk in particular of getting more widespread dissemination and involvement of the CNS and also with thrombocytopenia and purpura.

Sometimes we can still see varicella deformities in children where non-immune pregnant mothers have been exposed. Often in those instances, we see limb reduction and developmental defects as well as the potential to affect CNS, small head, scarring of the babies, spontaneous abortions.

Blake: I suspect I may have suffered the small head complication as a result of my chickenpox infection.

Blake: Can you tell our listeners about erythema infectiosum or 'slapped cheek' disease?

John: Erythema infectiosum or "slapped cheek" is caused by Parvovirus B19 virus. It's an erythrovirus which means that it targets red cells and bone marrow. It also is spread by respiratory spread. The incubation period is give or take about a week. When it comes out, it usually presents with a bright red burning erythema of the cheeks. Then often as this settles, we get the development of a lacy erythema, often a bit urticarial but not migratory, on the limbs. Can be on the torso. Usually, it's symmetrical. This is so called evanescent, which means it can fade but then it can come back. That rhythm can happen over a few weeks, can be four to six weeks, for example.

However, the most infective time tends to be before the actual rash comes out. In adults, we tend to see joint involvement with painful swollen joints but we don't tend to see this so much in children. The most problematic part of the virus is the way that it can affect the red cells and cause aplastic crisis. Especially if it affects a non-immune pregnant woman and the fetus is affected, we can get spontaneous abortions, intrauterine death, and so-called "hydrops fetalis", where we get significant edema of the baby related to the red cell effects.

Alvin: Okay. Let's talk about a theoretical scenario, John. There's a pregnant woman at a pre-COVID-19 party. Remember those? A child is running around with slapped cheek disease. Is there anything you can do or should be done for this woman who is pregnant?

John: A good history is really important. Often, we tend to diagnose a child relatively late. We sometimes see it in the body-limb phase and there may not be any slap cheek. In this case, if there is a slap cheek, it would suggest that hopefully, the child is not so infective now that the rash has

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broken out but it's still relatively early on in the illness. Confirming the exposure time is important. Then we can do serology on the mother.

Most adults do tend to be immune with IgG but we still have some adults who are not. If not immune, then it is important that the Obstetrician is informed. Different units have different policies. I think most of the hospitals here and most of the Obstetricians do tend to follow up with more regular, one to two weekly ultrasounds just to make sure they're not missing hydrops, monitoring for 6 to 12 weeks. If there is concern, sometimes they do offer therapies including intrauterine transfusions.

Blake: What is hand, foot and mouth disease? Is that something that cows get?

John: It depends how you define the foot and the hand in a cow. Hand foot and mouth disease is due to enterovirus and it's usually a Coxsackievirus. Coxsackie is actually a town in New York State, I think. I don't know how they pronounce it over there. The traditional form that's been described in textbook is with Coxsackie A16. That tends to have small ulcers in the mouth as well as the hands and the feet particularly the palmoplantar surfaces, where they often appear as ovoid, grayish, small blisters. Sometimes the buttocks can be affected as well.

However, more recently, we have a different strain, Coxsackie A6, which gives a different appearance which often still has accentuation around the acral distal limb areas, but also around the mouth. Sometimes it can look a bit like impetigo, and as it heals, the skin shows these browny scabs or browny scale which is quite characteristic. These cases don't tend to get so much actually in the mouth and the children usually eat and drink quite normally. In itself, it's not particularly sinister.

There is a variant caused by echovirus which can be a bit more severe. The main thing is just to recognise it and appropriate hygiene to minimise spread from body fluids. There is a variation that we see in children with eczema where it can spread in the skin so-called “eczema coxsackium” which is a little bit like what herpes simplex virus can do in eczema herpeticum and those cases are more severe.

Blake: Eczema coxsackium, sounds like someone sneezing? What tests are used for diagnosing these viral exanthems?

John: Apart from a very good clinical examination and history, usually it's by PCR these days. Nasopharyngeal or pharyngeal swabs as the case may be, for example, with herpes simplex or varicella, lesional swabs. It is important to get a good swab from the base. We can do serology as well. Serology looking for IgM, and rising titres of IgG, however, can have limitations as well.

For example, with measles, very early on, you might not actually pick up the IgM. Some tests if they've got super-sensitive to IgG but less to IgM, you might actually not pick up the IgM because of

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the IgG. We have to be aware of that. Of course, the IgM tends to be the first few weeks and then once they have more established immunity, it has to be the IgG. You also get false positives as well. Again, taking measles as an example, for example, with rheumatoid factor or other virus infections like Parvo, you can sometimes get false positives and that can be confusing.

Blake: I read the other day, apparently with mumps, even if you have IgG positive, it doesn't actually mean that you're immune. I found that really interesting. We have covered some of the viral exanthems now. What about some common bacterial infections that affect children and can cause a rash?

John: The commonest bacteria that cause rashes in children are *Staphylococcus aureus* and cutaneous *Strep*, which is *Streptococcus pyogenes* or group A *strep*. Prevalence varies according to the population. In urban areas, *Staph aureus* is by far the most common. We tend to see a number of infections in particular impetigo or school sores. We can get bullous impetigo, folliculitis, impetiginisation of other diseases like eczema. *Strep* can be an early feature, an invader in the skin. Especially in rural communities with indigenous groups, we often see a lot of *Strep* and that also lays the ground for more severe disease and infiltration with staph.

Blake: *Strep* is like the battering ram and then *Staph* runs in with all the soldiers?

John: It seems so. More severe we can get cellulitis and soft tissue infection and bacteremia and septicemia.

Alvin: How about taking us through the clinical features of Scarlet fever, which is caused by *Strep*?

John: Scarlet fever is caused by Strep and it releases a toxin. This toxin gives the so-called scarlatina or scarlatiniform eruption where characteristically we see a bright red face often with perioral sparing and then a “sandpaper” rough eruption on the upper body, chest upper back that can progress distally and also bright red palms or palmar erythema related from the toxin. It is worth noting that *Staph* sometimes can mimic this as well and we can get *Staph scarlatina* just as we did with *Strep.*

Alvin: John, can you tell us about school sores, please?

John: School sores are generally caused by *Staphylococcus aureus*. Sometimes there can be some *Strep pyogenes*. It causes erosions, flaccid blistering sometimes. Can be on the context of underlying atopic eczema. The lesions often are exuding with a yellow, slightly purulent exudate that often then scabs and you get this honey-colored crust hence the term “aureus”. It can spread by both direct contact and also through fomite spread, where something is contaminated such as a soft toy or some other clothing article for example. Then it can be transmitted to another person or the person can reinfect themselves later on.

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The treatment should really address both the skin aspect and the underlying bug aspect. To reduce them, the environment that fosters infection requires removing the scab, and that usually involves, for example, compressing with saline or in the old days we used to use diluted Burrow's solution, which also helped as an astringent to reduce the exudate. We often nowadays use diluted bleach baths as appropriate and that does tend to reduce the *Staph* on the skin and particularly in the setting of eczema.

We generally treat with antibiotics and aware that the incidence of community resistance *Staph aureus* is increasing so swabs are worthwhile. Often, we would start with something like Cephalexin and be dictated by progress and swab results. It is important that we do use an adequate duration of treatment and have follow-up and also an appropriate dose.

Blake: Why is it so infectious in children? Is it something about the *Staph* or is it the children's immune system that's not so good? Why are they more prone to this contagious spread of *Staph*?

John: Very good question. I think in practice primarily it's because children do a lot more touching and in play and also in other environments. They're exploring constantly. In terms of the skin barrier, it is true there are some differences between children's skin and adult skin. There may be some differences, for example, in antimicrobial peptides as well as the structure. There may be some other environmental and personal factors involved as well. It's a very interesting question that does deserve some more exploration.

Blake: It's time for another **skin tip**. Impetigo or school sores is caused by *Staphylococcus aureus* so-called because infection of the skin results in a purulent exudate that when dry forms honey-colored or golden crust. It is best managed by a combination of topical measures and oral antibiotics such as Cephalexin.

Blake: That concludes our episode on childhood exanthems and enanthems. We hope it brought you infectious joy to be spread virally among your friends and colleagues.

Alvin: We'd like to thank our guest, Associate Professor John Su, for once again giving up his time and knowledge. Thank you, John.

Blake: We'd also like to thank Joanne Coughlin and Peter Monaghan at the Skin Health Institute.

Alvin: We hope you've enjoyed this episode of *Spot Diagnosis*. Remember, these podcasts are not meant to replace medical advice. If you have a skin condition that requires attention, we strongly encourage you to see your medical practitioner.

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Blake: For listeners who want more information on this subject, a transcript of this episode and links to other resources can be found on our website, spotdiagnosis.org.au. That's spotdiagnosis.org.au.

Alvin: For Australian GPs listening, you can receive RACGP CPD Activity points for listening to *Spot Diagnosis,* further information is available on our website at spotdiagnosis.org.au.

Alvin: Please share *Spot Diagnosis* with your friends and colleagues, rate and review us. Let us know what you think. We really appreciate your feedback and any suggestions. This was recorded on Zoom.

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