Infections and Ichthyosis or Epidermal Differentiation Disorders

CME Series on Epidermal Differentiation Disorders — Presented by Dr. Erin Mathes

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Welcome to Infections and Ichthyosis or Epidermal Differentiation Disorders, Part of First's CME series on EDDs or ichthyosis. Presenting this topic is Dr. Erin Mathes. Dr. Erin Mathes is a professor of dermatology and pediatrics at UCSF. Her clinical focus includes epidermal differentiation disorders and complex pediatric dermatology. She directs UCSF's Disorders of Cornification program.

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It's a pleasure to be talking to you today about infections and ichthyosis and epidermal differentiation disorders. I have no relevant conflicts of interest. Our objective today is to recognize and manage infections in patients with epidermal differentiation disorders using visual pattern recognition.

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Infection is an important thing to consider in epidermal differentiation disorders. Because epidermal differentiation disorders are inherited disorders in which abnormal function or formation of the epidermis produces scaling, erythema, thickening, and fragility, and this abnormal epidermis leads to an impaired barrier which

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leaves the skin vulnerable to infection. So the question for today is how can we recognize, treat and prevent infection in patients with EDDs

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Just as one example you can see here on the left we have a patient with ABCA12 non syndromic epidermal differentiation disorder. And this is the baseline for the patient. And then this is the patient with an infection. So you can see how this can be difficult to discern. But also it is possible to tell when there's an infection.

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And we have to learn which signs to look for.

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So why does infection deserve attention? Well, we already discussed that the skin can look different at baseline. And so change is the signal that you want to pay attention to. First there is barrier disruption with fissures erosions and fragile skin. And this can create portals of entry for infection. Second it can be hard to recognize. And so primary care providers and specialists can struggle to recognize infection in the skin of patients with epidermal differentiation disorders.

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Because the baseline erythema scale and odor can obscure classic signs of infection that we are all trained to recognize. Third, it's important to recognize that some patients have variable risk for infection. So this group of epidermal differentiation disorders is actually quite heterogeneous. And the risk for infection varies by diagnosis, age, severity of disease and also what treatments the patient is taking at baseline.

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So for both primary care doctors and specialists, a pearl to ask is what is different from this person's usual skin?

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So as we've discussed already, infection risk is different in patients with epidermal differentiation disorders because of the fissures and erosions. In addition, the thick scale on some patients with ichthyosis can be a microbial reservoir. Maceration in folds, which is, it can exacerbate infection risk, and some patients with epidermal differentiation disorders have more maceration in their folds than others.

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In addition, the pruritus and scratching that comes with epidermal differentiation disorders can lead to additional barrier injury. And then some people with with EDDs have inflammation and immune dysregulation at baseline that can lead to a higher risk of infection.

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And the risk is not uniform. So it's important

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that there you should have a higher concern for infection in selected

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who have severe barrier disease.

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The risk is not uniform. It's important to remember that you need to have a higher concern for some epidermal differentiation disorders and those with very severe barrier disease. In particular. Think about infection in people with epidermolytic ichthyosis, Netherton syndrome, severe erythroderma - and so that's when a person has head to toe erythema and rash neonates and young infants.

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And then don't assume that all patients are immunocompromised. But knowing and understanding their diagnosis will give you some clues about whether or not their immune system is altered.

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So how do we recognize infection? Well, you look for a change from baseline. In particular, pay attention to new or rapidly worsening erythema, new warmth, swelling or tenderness, pustules, drainage, crusting or erosions, new or worsening malodor, fever, lethargy, and poor oral intake. You can ask the patient or their caregiver, what does a normal day look like for you?

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What changed about your skin and how fast did it change? Is this area more painful than usual? Do you have any fever or systemic symptoms like feeling tired? What has worked for your prior infections?

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And then here on the left we have an infant with lamellar ichthyosis,

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transglutaminase 1 variant who has a yeast infection because of increased maceration in the

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So it's important to note also that bacterial infection is common, but it's also easy to overcall. And that's because there is a high rate of colonization in patients with epidermal differentiation disorders. But that doesn't mean that they always have an infection. So just because you can find a microbe on the skin doesn't mean that there is a clinical infection syndrome.

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So microbes can be present on the skin without invasive disease. And so that's colonization. And it's important to remember that odor or a positive swab alone doesn't prove infection. A clinical infection is signs of infection. So a clinical change and positive testing. And so these are things like impetigo, folliculitis, infected fissures and erosions,

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abscess.

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We want to be selective in how we culture. And so you want to culture the right spot. And so those the right spot would be a place that is especially purulent. You also want to culture the right people. And so you want to culture patients who have recurrent, severe or treatment resistant disease. And not everybody.

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Another important thing to remember is that you don't want to miss viral infection. So viral infections including HSV, herpes simplex virus, varicella and coxsackievirus may be unusually severe in some patients with epidermal differentiation disorders. HSV is particularly important to recognize, and probably the more common of those three infections HSV presents with painful monomorphic vesicles or erosions, punched out erosions, rapid spread, and fever or systemic illness.

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A primary care or evaluating dermatologist

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should swab a fresh lesion for HSV PCR. This is widely available and is the appropriate test to do when you're concerned about HSV. If you are concerned, highly concerned, about HSV, don't wait for the culture results to come back. You want to treat with antivirals while you wait for the culture results.

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And this is because patients with barrier dysfunction can have their viral skin infection generalized very quickly. And so if you think that's happening then you want to escalate to a higher level of care. So if patients have extensive disease, eye involvement, a very young infant or any signs of systemic illness like fever or hypothermia, low temperature or lethargy,

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then you should treat more quickly and also consider sending the patient to the emergency department or admitting for evaluation and

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Also don't forget about fungus, yeast and scabies. Dermatophytes can be a particular problem in patients with epidermal differentiation disorders. They can be hard to recognize because a tinea infection often presents as a scaly red plaque, and the patient's baseline scale and erythema may mask the tinea infection. In addition, hair loss can be common in patients with epidermal differentiation disorders, which can make it harder to recognize tinea capitis, which often presents as scaly areas of hair loss on the scalp.

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So for dermatophyte you want to always have it in your mind as a possibility and consider culture or doing another confirmatory test like a KOH If you find that there is a focal area that is newly itchy or resistant to treatment, or a new area of hair

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Because tinea capitus can be unrecognized in some patients with epidermal differentiation disorders, they can go on to have scarring, hair loss. And we'd like to avoid that if possible. Next, you don't want to miss candida or yeast infections. And this can be particularly problematic in moist folds with a lot of maceration. And lastly, scabies is something you never want to miss.

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And so think about scabies when there is a sudden increase in itch or household spread. So other people in the house that are itchy, if the infection that you believe is an infection is not behaving as expected, revisit the diagnosis. Often these things are diagnosed first as bacterial infection, and then when people think harder, they realize that it's actually a dermatophyte

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candida or scabies infection.

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Here are some examples. On the left we have a patient with autosomal recessive congenital ichthyosis who has group A strep and the scarlet fever. And you can see how the rash of scarlet fever is combined with her baseline epidermal differentiation disorder. And that can make it harder to recognize. On the right we have a patient with transglutaminase 1 non syndromic epidermal differentiation disorder who has also hand, foot and mouth disease or coxsackievirus infection.

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And you can see how this is both much more widespread than it often is, and then also has a very different appearance that it would in a patient without an epidermal differentiation disorder.

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So a practical approach. First, always think about whether the patient is sick or unstable. And you want to look for things like fever, toxicity, dehydration, rapid spread or severe pain. This assessment

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is second nature for primary care providers. For dermatologists, we may need to remind ourselves to think about this, and focus on the whole patient and not just the skin.

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So always remember, is a patient sick or unstable? That's your first question. Second, think about what changed. Compare with a patient's baseline skin and ask the patient if this is different for them. Next think about the pattern. Do you see purulent areas that are crusted like you might see with a bacterial infection? Do you see vesicular or erosive disease like you might see with a viral infection?

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Do you see annular and intertriginous

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changes that would point you more towards a fungal infection? Next, sample selectively. So do a test when you have a concern for an infection. Bacterial culture is always a good idea if you think that there is a bacterial infection. Be mindful of colonization and always

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remember why you cultured when you are evaluating your bacterial culture results, send an HSV PCR for anything that you are worried about might be a viral infection, and then do a KOH and fungal culture to assess for fungal infections and then treat and reassess.

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You want to treat the syndrome that you think that the patient has. So if you think they have impetigo, treat impetigo with the same antibiotics that you would use for another patient with impetigo. Although keep in mind that some patients with epidermal differentiation disorders have been treated over and over again with antibiotics. And so they may have a different resistance pattern.

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Remember to always preserve and maintain the epidermal barrier as much as possible, and then always follow up. And when you're uncertain, call for help. Either call dermatology or call the emergency department. Make sure that you're getting help because this is tough sometimes.

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So we'll talk a little bit about treatment principles. You want to avoid a one size fits all antibiotic recipe. So think carefully about matching the therapy to the syndrome that you see. In general, topical antibiotics are useful for very small areas, maybe for fissures that are beginning to become more inflamed or potentially infected. But if you have more widespread disease or multiple areas on the skin that are affected, then you really do need to do systemic therapy.

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Remember to use your local resistance patterns. So follow local guidance and prior cultures. If you know that you are

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practicing in an area that has a high rate of MRSA or a high rate of clindamycin resistance, then choose your antibiotics appropriately. Always look at the patient's prior cultures to see what they were resistant to, and how many different strains they had.

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Don't treat colonization alone, so you want to avoid antibiotics. If there isn't a suspicion for an infection, keep the barrier supported. So continue gentle cleansing and appropriate emollients and then set a reassessment point. Reassess early if high risk or worsening. So how do we

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prevent infections and protect the barrier? Well first our patients with ichthyosis and epidermal differentiation disorders are expert in maintaining their barrier function. But for those with young infants or those who need guidance, be sure to encourage them to continue to use their daily emollients. Petrolatum supports barrier function and should be continued, and many of our patients use that and then treat fissures, erosions, and itch early.

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So if you have a small localized area, Be careful with that. Either apply extra petrolatum or a little bit of antibiotic ointment to that area to limit spread. And then additionally, you can limit microbial overgrowth when needed by doing dilute bleach baths. And so this is something that many of our patients do where they use a small amount of plain household bleach in a full bath tub of water and soak in that once or several times a week, basically to keep colonization down and to a manageable level, and prevent infection.

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There are other antiseptic washes that can be helpful as well, but you want to be careful because some of these can be irritating to those with impaired barriers. We also do use antifungal washes for shampoo and then also as a body wash, especially for patients that have recurrent fungal or yeast infections.

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If you have a patient who has a recurrent infection, look upstream. So before doing another course of empiric antibiotics, ask yourself is there a persistent colonization? Should I be doing one of those prevention strategies that we just talked about? Or do I have a resistant organism like MRSA? Are there fissures, erosions or scratching that are uncontrolled? Is there chronic maceration that I could help with?

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Are there household members who have recurrent staff infections? And then is the diagnosis one that has a higher risk of infection. So below we have a patient with an ABCA12 non syndromic epidermal differentiation disorder otherwise known as Harlequin ichthyosis with a MRSA, or methicillin resistant staff aureus infection. And people with Harlequin ichthyosis are at higher risk for infection just because of the severity of their barrier dysfunction.

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So consider specialist input for people with repeated or severe infections. Those who need help with decolonization.

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People in whom you culture unusual organisms. If you're uncertain about the diagnosis or if you think there might be possible immune dysfunction. And good specialties to involve are dermatology, definitely, and then infectious disease and immunology are other possible options.

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So before we close, I'd like to remind you of red flags. So these are all situations in which you would want to escalate urgently. So a neonate or a young infant with extensive barrier disease, fever, toxicity, lethargy or poor oral intake, rapidly spreading erythema or severe pain, extensive erosions, blistering or suspected HSV, dehydration or temperature instability. So sometimes patients with epidermal differentiation disorders can actually, especially neonates, can have low temperatures.

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Failure of appropriate outpatient therapy. When the patient looks sick, manage the illness, the acute illness first, and it's important to remember that the underlying skin diagnosis does not lower the urgency. In fact, if anything, it should increase the urgency.

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So briefly we'll look at one case together. So this is a nine year old with an epidermal differentiation disorder who presents with 24 hours of increased discomfort. Her parent says her skin looks more angry than usual. Today when you look at her on exam, she has focal warmth

and tenderness of her neck and back, new yellow crusting, full body erythema and scale, which is at her baseline and she does not have a fever and she's eating and drinking normally.

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Which of these things makes you most worried for infection? Well, it's C - her change from baseline and focal inflammatory signs of warmth and tenderness and crusting. Baseline erythema does not raise flags because that's how she is. Positive skin culture will help you confirm infection, but could also be colonization. And her EDD subtype alone does not determine whether or not she has an infection. It can play into the

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severity of the infection and risk for infection. But when you're faced with somebody with signs of infection, that's the most important thing to focus on. So five take home messages for infection and EDD. Change from baseline is the key signal. Colonization is not the same as infection. Look for signs of infection. Think about bacterial, viral and fungal etiologies.

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Painful erosions and systemic symptoms should make you think HSV and act promptly, and then treat infection while still supporting the skin barrier. Here are some select resources

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and references. In addition, please take a look at our module on vulvar health and that includes a section on infections.

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And thank you very much. Here is the link to the first Foundation

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