EDD Treatments from Basic to Advanced

CME Series on Epidermal Differentiation Disorders — Presented by Dr. Cheryl Bayart

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00:02

Welcome to EDD Treatments from Basic to Advanced, part of First's CME series on epidermal differentiation disorders or ichthyosis. Presenting this topic is Dr. Cheryl Bayart. Dr. Bayart is a pediatric dermatologist at Cincinnati Children's Hospital Medical Center and vice chair of First's Medical and Scientific Advisory Board. Her clinical and research focus includes ichthyosis and rare genetic skin conditions, and she helped develop a validated system for assessing ichthyosis severity.

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So today I'd like to talk about evidence based topical and systemic treatment approaches appropriate to EDD subtype and severity. And I will be quite candid with you that there is not a lot of data on this topic, and there are no FDA approved treatments for EDDs or ichthyosis. Thus, I will also be sharing a good deal of expert opinion, anecdotal evidence, and tips and tricks from patients who are living with EDDs

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I have no relevant disclosures.

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I think this article provides an excellent framework for the basic principles of EDD ichthyosis management, and I highly recommend it as a resource. In short, the foundation of EDD treatment remains daily skincare. Medications play a role for some patients, particularly retinoids. There is emerging evidence for the use of targeted therapies, but a lot of this is preliminary.

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So when thinking about EDD treatments, I think it's helpful to think about the functional consequences of having an EDD, namely,

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What happens if the epidermal barrier does not function optimally? When that happens, instead of having a nice solid sort of brick wall as your epidermal barrier, you have a crumbly brick wall, so to speak.

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This leads to scaling, thickening, and redness of the skin. It increases fluid and calorie needs, as there's transepidermal water loss and increased energy needs to rebuild the epidermis constantly. There's impaired sweating, which can lead to hyperthermia, increased risk of infection due to the compromised skin barrier, and risk of toxicity from topical medications. So really, the goal of daily skincare is to reinforce and normalize epidermal function so you can get as close as possible to that fortified brick wall as opposed to the crumbly brick wall.

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And this typically includes three cornerstones bathing, exfoliating, and moisturizing. Daily routines are highly individualized from person to person, and change over time depending on exposures like weather, natural evolution of the condition, and patient's treatment goals.

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It's important to keep in mind that it is expensive and extremely labor and time intensive for patients with EDDs to take care of their skin in a way that allows them to function every day. Anecdotal data from First suggests that on average, patients with EDDs use at least 1 pound of emollients per week.

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This recent study looked at 144 EDD ichthyosis patients in Germany and found that, on average, they spent about 40 minutes daily in the bath, which means that about half of patients spent longer every single day in the tub. Many of them had out of pocket costs for their topical treatments. And this is in Germany, which has a socialized health care system.

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So I think we can just begin to touch the tip of the iceberg of what this number probably looks like for patients living in the United States. 80% of patients reported significant pruritus that interfered with their daily function. So really having an EDD can markedly impact quality of life.

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So the first cornerstone of daily skincare is bathing, which softens scale and hydrates the skin. Typically, these are longer baths than people without ichthyosis are taking, and some patients choose to upgrade them with add ins such as baking soda, Epsom salts, and oils, such as coconut oil. It's really important to warn patients that adding to baths will make the tub extremely slippery, and they need to be really careful to avoid falls.

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Baking soda may be particularly helpful. Two handfuls of baking soda will bring the page of a water bath from 5.5 to 8.1, which significantly decreases any burning sensation from water coming into contact with open skin and really enhances softening of this scale. Easing removal.

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So exfoliation can be done before or after bathing, and removing excess scale is really a key component of ichthyosis or EDD skin care. These means listed here are all means that EDD patients use to remove scale from their skin. And you'll notice that a lot of the supplies needed for these are found at the local hardware store, rather than the pharmacy.

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Dremel rotary tools used with sandpaper are particularly popular for hands and feet, where scale can get particularly thick. Overly aggressive removal of scale can result in skin injury and increase infection risk, so patients should be cautioned to be conservative when using these methods for the first time. Some less aggressive methods to start include exfoliating shower mitts and homemade scrubs made with table salt and oils.

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As we discussed previously, patients with EDDs require a large daily volume of emollients to keep their skin hydrated. These are applied after bathing and exfoliation and throughout the day. For each individual patient, it's important to consider whether they prefer occlusive or non-occlusive emollients.

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Children like thick occlusive ointments because they're most effective at reducing itch and keeping them comfortable. However, the downside of occlusive emollients is that they tend to feel sticky and greasy and get all over clothing and washing machines. They can also inhibit sweating in patients who have some ability to do so.

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So some EDD patients continue occlusive into adulthood, especially those with harlequin ichthyosis phenotype. But many do transition during the adolescent years to less occlusive emollients that they feel soak into the skin more so than sitting on the surface of their skin. Individuals with EDDs often make their own emollient mixes based on their personal preferences, which may include whipping ingredients like shea butter with oils as we can see here.

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Given the volume of emollients that patients with EDDs need to use each day. Most commercially available creams are not affordable. Most patients use an inexpensive base emollient that they can buy in bulk, like vegetable glycerin, petrolatum, plus or minus lanolin and coconut oil, and then add additional ingredients as needed. They often need to be creative if they're traveling for a long period of time, because it's not practical to bring large quantities of these on an airplane.

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This is a really helpful tip for any patient with skin condition affecting the palms and souls, and that's gluing together painful fissures to allow the wound to heal from the bottom up.

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VIDEO: “Yes, you can use superglue on your winter cracks first, get something to protect your work surface and your glue. There's a lot of different formulas and brands. Loctite makes this gel one that doesn't run. Crazy Glue has one with a paintbrush, sort of like nail polish, I love it. Some brands will burn. I find the most expensive ones don't burn.

09:11
Hardware stores have the best selection. “ END VIDEO

09:15
Dermabond also works really well, but superglue is definitely more accessible and less expensive for most people.

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So keratolytics are an option for chemical exfoliation, which can be used in addition to the physical exfoliation that we discussed previously. It's really important to educate patients that these are medications with potential side effects, even though many are over-the-counter and they are not daily driver emollients. They have potential side effects. They can be drying and irritating, particularly prescription retinoids, which are the most potent keratolytics.

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It is essential to be very specific about recommended quantities for use. For children, I often recommend starting with a small amount of keratolytic mixed with their daily driver moisturizer. Ammonium lactate is one of the mildest options and a good starting point. Urea is stronger, but not as strong or as drying as retinoids. Keratolytics should typically not be used in infants or toddlers because they have a large body surface area compared to their body volume, and can have significant systemic absorption of these medications.

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Keep in mind there is increased absorption of topical medications in some EDDs such as Netherton syndrome. So these patients also need to be really careful. For these patients, though, it can be safe to use a small amount of keratolytic focally, for example on the eyelids to alleviate entropion.

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Infections are often an important issue for patients with EDDs, especially early in life. Frequent topical and oral antibiotic use will place them at significant risk for resistant infections later in life, so it's preferable to use antisepsis rather than antibiotics where possible. Dilute bleach baths and chlorhexidine are helpful in decreasing incidence of bacterial infections and can be used regularly.

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Dilute vinegar soaps are a great tool for patients with recurrent yeast or fungal infections. Infections often become less of an issue over time, as the immune system learns to recognize more pathogens, and patients learn how to prevent infections and treat them early on. Women with EDDs may be at increased risk for vulva vaginal yeast infections, which are typically responsive to over-the-counter clotrimazole.

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If you are not asking patients about these, you will likely not hear about them, so it's important to ask the questions.

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In terms of systemic treatments. Retinoids have the longest track record and are helpful in some, but not all, types of ichthyosis. Isotretinoin is logistically easier to use, but female patients should be transitioned off of it three years prior to starting puberty. Female patients with reproductive potential should always be treated with isotretinoin. Prescribing prescriptions need to have a candid discussion with patients and families regarding potential treatment risks, and help them weigh risks and benefits.

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So what is the immune profile of EDDs? We know these patients are red. They are itchy. There is certainly an inflammatory component to these conditions. This study used immunohistochemistry and reverse transcriptase PCR to determine the immune profile of common ichthyosis.

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Their study population included 21 patients with genetic diagnoses of EDDs and compared their skin biopsies with specimens from healthy control subjects, patients with atopic dermatitis, and patients with psoriasis. It was found that IL-17 and L-23 are overexpressed in ichthyosis just like they are in psoriasis, raising the question of whether biologic medications used for psoriasis that target these pathways may be effective in patients with ichthyosis.

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So a real world study looking at IL-17A, inhibition with Secukinumab found that it is safe but not necessarily efficacious across the spectrum of adult EDDs So this was a randomized control trial of 50 patients with moderate to severe EDDs.

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Found that unfortunately IL-17A inhibition with Secukinumab did not significantly reduce severity of erythema or scale. On the flip side, it did not increase infection risk either. Only of five of the total 50 patients who were in this study requested drug continuation into the open label phase of the study, which really attests to the fact that it probably was not terribly helpful for most.

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Study looked more broadly at EDD patients treated with biologics and found that in patients with Netherton syndrome and congenital ichthyosiform erythrodermal phenotypes, that IL-12/23 inhibitors and IL-4R inhibitors may be more promising options.

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So Dupilumab is a very promising option for decreasing pruritus. Mostly, but also in some cases, erythema and scale in multiple forms of ichthyosis. This is a recent case series showing significant response into patients with harlequin ichthyosis. In my clinical experience, Dupilumab can be very helpful for any pruritic skin condition, and so it's definitely worth consideration for many patients with EDDs.

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What I think is most exciting and the wave of the future are pathogenesis based therapies, such as the one that Amy Paller and her colleagues discovered for treatment of patients with congenital hemidysplasia with ichthyosiform erythroderma and limb defects, also known as CHILD syndrome. This is an excellent dominant disorder of distal cholesterol metabolism. On the basis of the pathogenic role of both pathway product deficiency of cholesterol and accumulation of toxic metabolic intermediates, they found that topical treatment with lovastatin and cholesterol, but not cholesterol alone, virtually cleared skin lesions after three months of use.

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This was accompanied by histological and ultra structural normalization of epidermal structure and lipid secretion, so these findings validate pathogenesis based therapy that provides the deficient end product and prevents accumulation of toxic metabolites, and this is potentially an approach that can be used for other syndromic lipid metabolic disorders that are associated with EDDs. And I do have one patient with this condition.

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And this treatment has truly been life saving for her. And it is very affordable. So in summary, I think there is much reason for hope going forward in terms of pathway directed treatments, targeted biologicals and gene therapies. There are 87 interventional trials currently listed for EDDs on ClinicalTrials.gov. So, going forward, there is movement not only toward repurposing existing treatments for EDDs but also creating new targeted therapies.

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Thank you.