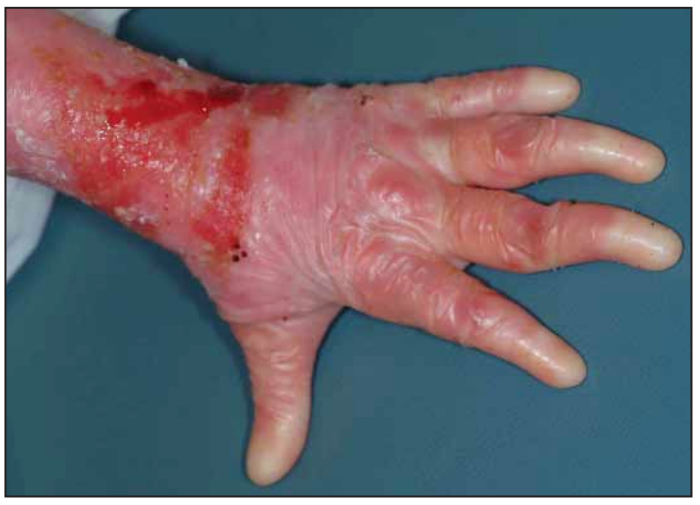
Epidermolysis Bullosa Forms Look Similar, Show Few Clues

BY KATE JOHNSON
Montreal Bureau

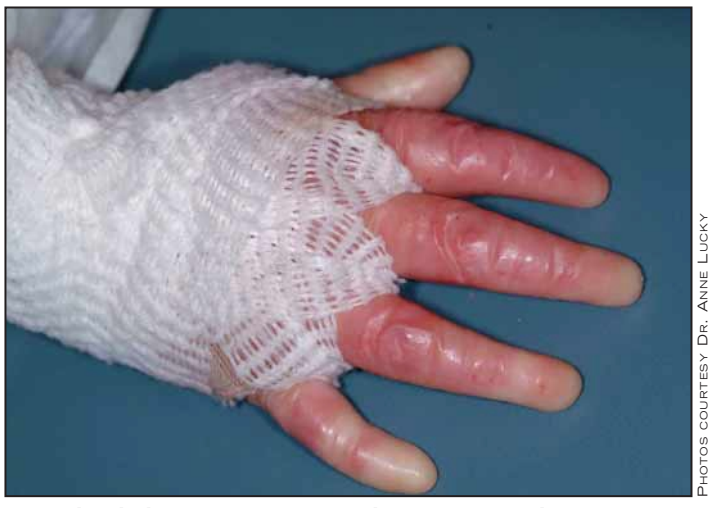
SNOWMASS, COLO. — Physicians diagnosing epidermolysis bullosa in a newborn have few initial clues about which type of the disease their patient has, or the course it will take, until they do electron microscopy and immunofluorescence testing, according to Anne Lucky, M.D.

"At the very beginning the different forms of epidermolysis bullosa (EB) all look virtually the same. We tell parents we don't know if it's going to be a severe or mild form until the testing is done." In other words, the child may have a normal lifespan or may die in the first year of life, she told this newspaper.

Speaking at a clinical dermatology seminar sponsored by Medicis, Dr. Lucky, professor of dermatology and pediatrics at the University of Cincinnati and the Cincinnati Children's Hospital Medical Center said that electron microscopy, immunofluorescence mapping of the basement membrane, and genetic investigation for specific proteins, can help distinguish between epidermolysis bullosasimplex (EBS), junctional epidermolysis bullosa (JEB), and dystrophic epidermolysis bullosa (DEB).



"Pseudosyndactyly" can occur in epidermolysis bullosa. This 4-year-old patient has a moderate case.



PHOTOS COURTESY DR. ANNE LUCKY

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EBS is caused by keratin and plectin mutations, while JEB is caused by mutations of basement membrane proteins, and DEB is caused by mutations of type VII collagen, she explained. Although all forms of EB cause severe blistering and skin erosions, blister formation in EBS is within the epidermis, while it is seen within the basement membrane zone in JEB, and within the upper dermis in DEB.

Correct identification of the type of EB is important for giving parents a realistic outlook about the prognosis, she explained. While all types of EB have variations in severity, certain subtypes of JEB (Herlitz) probably carry the worst prognosis, often associated with pyloric atresia, as well as severe, generalized granulation tissue around the trachea. Forms of DEB can be accompanied by esophageal strictures, as well pseudosyndactyly, and an increased risk for squamous cell carcinoma, among other things, she said.

Wound care plays an essential role in the management of all types of EB.

"Extensive aplasia cutis is usually fatal in the first weeks of life. It is really like handling a burn patient—they are very susceptible to infection," she said, adding that new silicone-based bandages (manufactured by Mölnlycke) have made great improvements because they minimize skin trauma.

"They stick well to the surface of the skin, but with no adhesive—it's more like a suction," said Dr. Lucky, who has no financial association with any company that makes products for treatment of EB.

In addition, biologically active dressings and grafts, such as Apligraf, a semi-permeable living skin graft, not only cover the wound, but promote healing. Wrapping is also important for protection and for avoidance of progressive syndactyly or fusion of digits as a result of extensive erosions.

Although esophageal strictures are common in certain forms of EB, Dr. Lucky says routine investigation for them is not necessary. If symptoms are present, barium swallows must start above the clavicle otherwise the stricture will generally be missed, she added. When indicated, esophageal dilation can be performed with hydrostatic balloon insertion and dilation, and the effects of this procedure can be expected to persist for at least 1 year.

Esophageal strictures and a gradual reduction in a child's ability to fully open his or her mouth can lead to poor nutrition, osteopenia, and dental problems. For these reasons, feeding gastrostomies should be considered, and prophylactic dental hygiene should be stressed, she said.

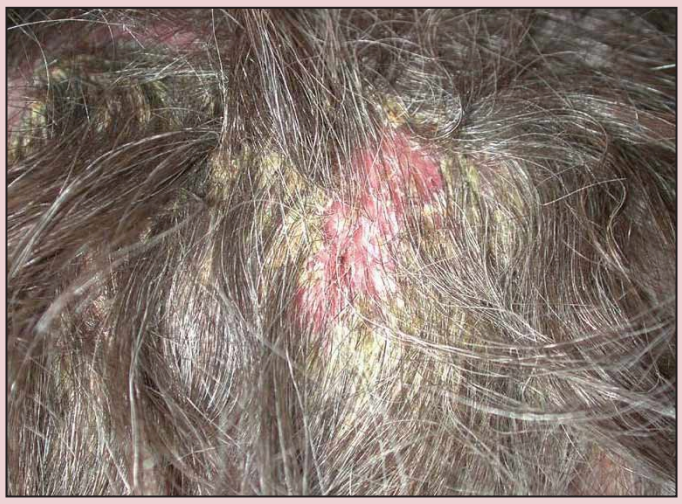
Hand surgery to separate webbed fingers is also an "untapped area," she said. "Some surgeons do it, but with variable success. The future may lie in physical and occupational therapy."

Pain management and psychiatric support are also important—and often go hand-in-hand because of the potential for drug addiction.

Dr. Lucky said many physicians have never heard of EB, and their first encounter may be overwhelming. The Cincinnati Children's Hospital Medical Center has an interdisciplinary EB team offering a full range of resources (www.cincinnatichildrens.org/eb-center), and she says there also are EB centers starting in Chicago, Denver, Miami, and at Stanford University. ■

DERM DX

A 46-year-old white male with a long history of atopic dermatitis was admitted to the hospital for urinary frequency and incontinence considered secondary to his multiple sclerosis. He developed a scalp rash and atopic dermatitis was again diagnosed. The clinical presentation, however, did not improve with a clobetasol and tar shampoo regimen. He again presented with ear pain and a painful rash. What's your diagnosis?



KEY BISCAYNE, FLA. — Laboratory tests indicated the patient had diabetes insipidus. A bone scan was negative. MRI of his head showed pituitary stalk infiltration and plaques typical of multiple sclerosis. A chest CT scan revealed multiple pulmonary nodules. Both biopsies indicated Langerhans cell histiocytosis (LCH). The patient was diagnosed with stage III LCH with skin, lung, and CNS involvement.

Assess hematologic, pulmonary, hepatic, renal, and skeletal systems to determine extent of disease, Paul A. Krusinski, M.D., suggested at the annual meeting of the Noah Worcester Dermatological Society. Treatment is guided by extent of disease and number of systems involved, added Dr. Krusinski, professor of medicine at the University of Vermont in Burlington.

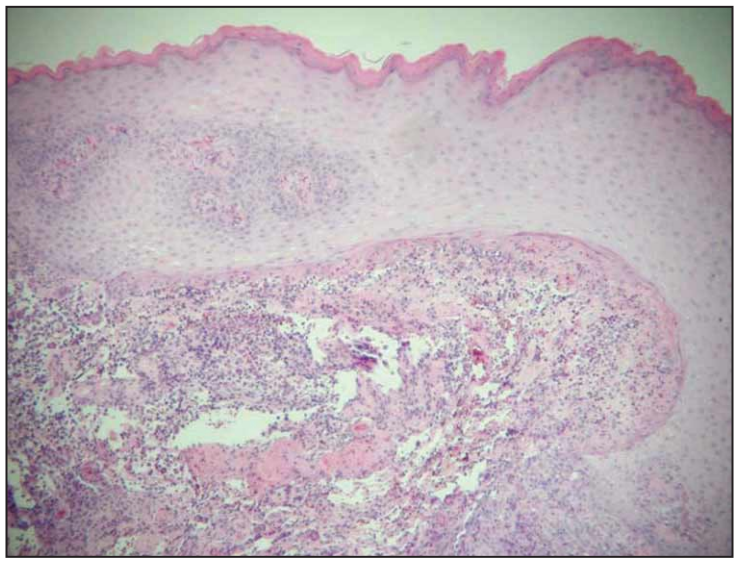
In cases of single-system skin disease, treatment options include topical steroids, psoralen-ultraviolet-light treatment, and topical nitrogen mustard.

With multisystem involvement, combination therapy with vinblastine and a steroid is most common. Vinblastine plus etoposide, prednisone, and mercaptopurine is more effective than monotherapy. A failure to respond to therapy by 6 weeks indicates a poorer prognosis.

The patient was treated with desmopressin acetate for his diabetes insipidus. He also received six monthly cycles of 2-chlorodeoxyadenosine (cladribine) for the histiocytosis. Cladribine destroys resting and dividing lymphocytes and is approved for treatment of hairy cell leukemia. Cladribine trials for LCH are ongoing; it may be effective at blocking the clonal proliferation of Langerhans cells responsible for the disease. Principal toxicity is from myelosuppression, but long-term malignancy effects are unknown. Another potential treatment is imatinib mesylate.

With single-system disease, 5-year survival is 100%. With multisystem involvement, 5-year survival is 92%. If there is lung disease, 5-year survival drops to 87%.

—Damian McNamara



PHOTOS COURTESY DR. PAUL A. KRUSINSKI