Ichthyosis Focus

F.I.R.S.T.
Foundation for Ichthyosis and Related Skin Types

Vol. 23, No. 4 | A Quarterly Journal for Friends of F.I.R.S.T. | Winter 2005

Ichthyosiform dermatoses: So many discoveries, so little progress.

By John DiGiovanna, MD

The term ichthyosis comes from the Greek *ichthys*, meaning "fish," and refers to the clinical appearance of scaly skin. Ichthyosis can be present at birth or develop later in life, be limited to the skin, or occur in association with abnormalities of other organ systems. Cutaneous (skin) manifestations span a broad spectrum of severity. For many ichthyosis patients, diagnosis can be uncertain. Without a specific diagnosis, genetic counseling and predictions based on family history and pedigree can be unreliable. Accurate genetic counseling is important. Each child of a person with an autosomal dominant disorder has a 50% risk of inheriting the disorder. However, for an individual affected with an autosomal recessive ichthyosis, unless he or she marries a close relative, the risk of producing a similarly affected child is very low. Mutation identification can permit not only a precise clinical diagnosis, but also reliable genetic counseling and prenatal diagnosis. Once the mutation is identified, testing of the family members can provide accurate information about the risk of transmission.

Discovering the precise genetic cause of one form of ichthyosis tells us not only a great deal about the affected individual, his or her family, and other individuals with the same disorder, but it also teaches us about normal epidermal biology. Furthermore, it helps us to understand the entire spectrum of ichthyosis, not unlike solving a puzzle where fitting one piece helps to clarify the role of all of the other pieces, which have not yet found their place. To date, while a series of discoveries have identified the molecular basis for several ichthyosiform dermatoses, and these have enhanced diagnosis and genetic counseling, little progress has been realized in treatment and ultimate hope for a "cure."

Epidermolytic hyperkeratosis (bullous congenital ichthyosiform erythroderma; EHK) is characterized by hyperkeratosis, often in association with peeling and blistering. While at least six clinical phenotypes (the outward expression of the disease) have been described, all share the same histopathology of hyperkeratosis with epidermal vacuolar degeneration.[1] Most cases have been found to be caused by mutations in KRT1 or KRT10, the genes for the differentiation specific keratins 1 and 10. Mutations in either the KRT1 or KRT10 gene lead to keratinocyte (skin cell) fragility, and the clinical result is hyperkeratosis, or peeling, and easy blistering in the affected layers. Identification of the specific mutation can confirm the diagnosis and enables prenatal and/or preimplantation diagnosis. *Ichthyosis bullosa of Siemens* (IBS) is similar in clinical appearance to EHK, but with a more superficial peeling. As with EHK, the epidermis is fragile, but the fragility is more superficial and confined to the granular layer. IBS is caused by mutations in KRT2e, the gene encoding keratin 2e, a differentiation specific keratin, which is expressed in the more superficial, granular layer of the epidermis. Therefore, the pathophysiology of these two disorders is weakness in the internal structure of the skin cells with subsequent epidermal fragility, and it differs by the location of the keratin whose function is abnormal.

Erythrokeratoderma variabilis (EKV) is characterized by both hyperkeratosis (generalized or localized) and distinctive, sharply demarcated, migratory, red patches. The patches move over short periods of time (10 to 20 minutes) and may be precipitated by trauma or change in temperature. For patients with classic features, the diagnosis is clinically apparent; in others it can be elusive. The discovery of mutations in either GJB3 or GJB4, the genes encoding connexins 31 and 30.3, in patients with EKV enables a definitive diagnosis and implicates defective communication between the epidermis and cutaneous vasculature (the system of blood vessels that supply the skin) as the cause.[1] Structural proteins group to form channels that dock with a neighboring channel in an adjacent cell membrane. The resulting channels allow direct cell-to-cell communication, the transfer of physiologic signals, ions, and small nutrients, and coordination of cellular responses to internal and external stimuli. In addition, the identification of

continued on page 3

Ichthyosis Focus

Vol. 23, No. 4
Winter 2005

Ichthyosis Focus is published quarterly by the Foundation for Ichthyosis & Related Skin Types

Requests to reprint information contained in Ichthyosis Focus should be directed to the editor.

The Foundation for Ichthyosis & Related Skin Types
1601 Valley Forge Road
Lansdale, PA 19446

215.631.1411
800.545.3286
215.631.1413 fax
email — info@scalyskin.org
www.scalyskin.org

The Foundation for Ichthyosis & Related Skin Types is a 501 (c) 3 charitable organization supported by public and private donations. All contributions to the Foundation are tax deductible to the full extent of the law.

The editor invites your correspondence. We welcome your comments, observations and suggestions. Please send your letters to Ichthyosis Focus at the address listed above.

Ichthyosis Focus is provided as a service to members of the Foundation as a medium for the free exchange of information. Neither the Foundation for Ichthyosis & Related Skin Types, its Board of Directors, its Medical Advisory Board, nor the Focus Editors endorse any treatments or products in Ichthyosis Focus. Views and opinions expressed in this publication do not necessarily reflect the views of the Foundation or Foundation officials.

Correspondence Corner

Dear Members of F.I.R.S.T.:

My type of skin condition is called ichthyosis vulgaris, vulgaris meaning "common." I never knew what my skin condition was called until I was well into my forties. I tried to submit my name into the National Institute for Skin Disorders database but was told ichthyosis vulgaris is too common to be considered for the Institute. One person in every 250 people has ichthyosis vulgaris, yet in my fifty-eight years I have only seen one other person with a skin condition similar to mine. I have been to over 37 dermatologists in my lifetime and even went to a teaching hospital in Munster, Germany for this condition. There is no cure, and it is only through trial and error that I can manage it. Since there is no cure, and I have learned to manage it, that leaves the self-conscientiousness of having ichthyosis as my only problem.

This time of the year is the most difficult. Around October 1st of every year, my skin makes a remarkable transformation. The dryness and cracking of the skin becomes even more intense as the weather cools and the heaters come on. My fingers crack when I make a fist, so out come the Band-Aids to wrap the joints until spring comes. My two most favorite products are Eucerin in the one-pound tub and Lac-Hydrin 12% lotion. My HMO used to dispense Lac-Hydrin as a prescription, until they removed it, and now they sell it over-the-counter for $50.00 a bottle. I have a source in Canada now that is far more reasonable. I, like many ichthyosis managers, have a million tubes, creams, and bottles of products to try. Every year at Christmas, I invariably get a bottle of lotion from some well-meaning friend. Don't they know we use lotion by the gallons?

Growing up with eczema and ichthyosis was not difficult for me. By the time I knew of the difficulties of my infancy, my parents had moved our family to Arizona from Georgia where the eczema, the more severe problem, cleared up immediately. As a teen, the style was knee-high socks. That fit my condition perfectly. The positive result is that I did not have acne like many teen-agers. Oily skin was not my problem. To my knowledge, my skin condition never lost me a date. I had one boy tell me that he would like to start dating me and asked if there was anything he should use to prevent him from catching the disease. That did hurt my feelings. I later married a man with great skin (yes, it was a consideration). We have two beautiful blue-eyed boys with normal fair skin.

I have learned not to allow the condition to dictate or play a detrimental part in my life. I keep saying to myself, "My hands may look bad, but there is nothing they cannot do." Both my profession and my hobbies are hard on my skin, particularly my hands. I am a registered architect by day and an old house remodeler by night. For a time, I had my own construction business. All of these endeavors exposed my skin to extremes in weather, water, dust, gypsum board mud, grout, and

continued on page 5

continued from page 1

different mutations in the GJB3 gene in other patients with deafness (with and without skin disease) is an example of how different mutations in one gene can cause overlapping clinical syndromes with abnormalities in one or more organ systems. While these discoveries enhance diagnosis and a general understanding of the pathophysiology, they also highlight our poor understanding of the complexities of cell-to-cell communication and its mediators.

***K**eratitis-**I**chthyosis-**D**eafness* (KID) syndrome is characterized by keratitis (inflammation of the cornea), ichthyosiform skin changes, and neurosensory deafness. There are usually discrete, fixed erythematous (reddened) plaques, and there may be generalized hyperkeratosis. Hyperkeratosis of the hair follicles can result in scarring alopecia (baldness), and there may be an increased susceptibility to infection. The discovery that KID syndrome is caused by mutations in GJB2, encoding connexin 26, allows for molecular diagnosis and provides a framework for understanding how this group of clinical findings can be caused by disordered cell-to-cell communication in the skin, eyes, and ears.[1]

The *collodion baby* is born ensheathed in a shiny translucent membrane. This phenomenon can have a spectrum of severity at its presentation and a spectrum of clinical outcomes as the baby develops. These range from the mild "self healing" phenotype to the more severe types including congenital ichthyosiform erythroderma (CIE), lamellar ichthyosis (LI), and Netherton syndrome (NS), with or without the involvement of other organ systems. Some will develop a distinctive clinical phenotype (physical presentation of the disease) of severe LI or CIE. However, there are a spectrum of phenotypes with variable erythema (red skin) and scale that do not fit neatly into these categories. While several genes have been discovered to cause LI and CIE, thereby enabling a precise diagnosis for a few patients, an understanding of the genotype-phenotype correlation (the genetic make-up of the person versus the outward expression of the disease) for this spectrum of disorders has had limited progress. The recent suggestion that specific mutations in TGM1 may correlate with the mild phenotype suggests that some useful predictions may yet be realized.[2]

Lamellar ichthyosis typically presents as a collodion baby. During the newborn period, the skin may be red, but over time it develops large, plate-like scales that appear to be arranged in a mosaic pattern. Tautness can lead to ectropion (flipping out of the eyelids), eclabium (turning out of the lips), and alopecia (baldness). Patients with this phenotype of severe LI often have little to no erythroderma (reddened skin) in adulthood. Mutations in TGM1, the gene encoding transglutaminase-1, were first found to cause LI and probably account for most patients with this severe, classic phenotype. One study showed that the transfer of the TGM1 gene to human LI epidermis temporarily corrected the epidermal deficit, suggesting the potential for therapeutic gene delivery to human skin.[1] However, the engineered keratinocytes did not retain the gene. More recently, mutations in adenosine triphosphate-binding cassette A12 (ABCA12) have been found in a few families with LI from North Africa.[2] ABCA12 is a member of a superfamily of proteins that translocate substrates across membranes and may be important in cellular lipid trafficking in keratinocytes.

Congenital ichthyosiform erythroderma (nonbullous congenital ichthyosiform erythroderma; CIE) usually presents as a collodion newborn, similar to LI. Infants with CIE have skin that remains red, usually with a fine, white scale, and there is a spectrum of involvement with ectropion, eclabium, and alopecia. In a few families with CIE, mutations have been found in one of two lipoxygenase genes (ALOXE3 and ALOX12B).[2] These lipoxygenase enzymes catalyze the oxidation of fatty acids. A few patients with CIE are reported to have mutations in TGM1.

Netherton syndrome (NS) is characterized by ichthyosis, a hair shaft abnormality (trichorrhexis invaginata), and atopy (allergies or hypersensitivities). The typical cutaneous manifestation is ichthyosis linearis circumflexa with red, wavy, scaling plaques marked by characteristic, migratory doubled-edged scale at the margins. Newborns may present with generalized erythroderma or a collodion phenotype, and some may not survive infancy. Atopy may manifest as dermatitis or asthma with marked elevation in IgE. Some patients may have aminoaciduria (excess amino acids in the urine), mild developmental delay, and impaired cellular immunity. NS is caused by mutations in SPINK5, a gene encoding LEKT1, a serine protease inhibitor expressed in epithelial and lymphoid tissues.[1] Before this was known, this diagnosis was often difficult to establish because of indistinct cutaneous findings. In addition to focusing on pathophysiologic abnormalities, this discovery allows accurate molecular diagnosis and permits prenatal and carrier testing.

Ichthyosis can occur with progressive neurologic disease. In *Sjögren-Larsson syndrome,* pruritic (itchy) ichthyosis, in association with the neurologic involvement (spasticity), should prompt an examination for glistening white dots in the retina and testing for fatty aldehyde dehydrogenase activity or for mutations in FALDH, the gene encoding that enzyme. Ichthyosis in association with progressive neurologic degeneration, as seen in *Refsum disease*, a disorder of phytanic acid catabolism, can be identified by measuring phytanic acid levels or identifying mutations in PAHX or PEX7 genes. The constellation of ***P**hotosensitivity, **I**chthyosis, **B**rittle hair, **I**ntellectual impairment, **D**elayed development, and **S**hort stature (PIBIDS)* is one of the clinical phenotypes of trichothiodystrophy and should prompt the light microscopic examination of hair with polarizing lenses to demonstrate the typical tiger-tail banding. Amino acid analysis of hair can confirm low sulfur content, and mutations may be found in

continued on page 6

Everything and Nothing About Ichthyosis

By Laura Phillips

Laura Phillips astride Stan.

From the time I was born with lamellar ichthyosis, my life has been something of a paradox: at once, everything and nothing is about ichthyosis.

Born a collodion baby, my family was fortunate to at least have received a timely and accurate diagnosis of lamellar ichthyosis as the cause of my problems. However, the information my parents received about my ichthyosis in those early days was, at best, incomplete, and often, devastatingly pessimistic in terms of the quality of life I was expected to experience. It's no wonder they had doubts about what life would hold in store for me and decided it would be best not to have any more children, at least until they saw more of how things turned out for me. I didn't know the reasons for my parents' choice until later in life; all I knew growing up was that I thrived as an only child. When I first learned about birth order theory, I considered myself a lucky product of all the beneficial things that birth order theory suggests as hallmarks of only children: an innate sense of independence, strong problem-solving skills, and a tendency toward leadership positions. Even today, I can't imagine growing up (or wanting to) any other way.

My family, especially my parents and my grandmother, embarked on a trial-and-error quest in search of effective treatments for my skin that continues to this day. Early on, two distinct goals for any type of treatment emerged: (1) improve my appearance and (2) improve my physical state. From my perspective, the cosmetic aspects usually took precedence (and usually still do). Above all, I wanted to look normal. How I define "normal" has changed over the years. As a child, "normal" meant being able to go out in public, carry on everyday activities that most people take for granted, and not have all sorts of people stop dead in their tracks, compelled to stare at me. I never had any difficulty responding confidently to people's questions about what was wrong with me. However, every time someone stopped to ask that question, it served as a disappointing confirmation that no matter how close to "normal" I thought I had gotten, I still wasn't.

Often, the cosmetic and the physical objectives intersect. For example, like many people with lamellar ichthyosis, the skin around my head is tight enough that it pulls at my eyelids and causes ectropion. Much to my ophthalmologist's relief, the consistent addition of a nighttime eye lubricant alleviated what was becoming a dangerous drying of my corneas. Much to my delight, this addition lessened the effects of the ectropion, making my eyes appear less red (and more "normal"). But, miss a single night and the difference is immediate --both in comfort and appearance.

Quite apart from anything having to do with ichthyosis, and like so many little girls for generations around the world, I fell in love with horses. My first regular contact with real horses started with weekly lessons when I was eight, and my interest has continued ever since. Therapeutic riding, hippotherapy, has become more commonplace in this country. I can't help but recognize the profound influence I believe horses have had, physically and emotionally, in my life. Besides inspiring in me the same Zen-like awe that millions of people before me have felt, handling horses gave me a sense of accomplishment and empowerment that I know has permeated all aspects of my life.

The daily and weekly routine to maintain my skin is labor intensive and involved, a constant trade-off between looking and feeling "good" yet not consuming so much of my life that my world becomes unhealthily dominated by it. The first time I was completely responsible for all aspects of my skin care was when I went away to college. I surprised everyone, most of all myself, by ultimately following my father's footsteps into public accounting; very "public" in fact, as up until recently, I was a practicing auditor with a Big Four public accounting firm. Unlike some people with ichthyosis who struggle to establish themselves professionally (and attribute many of their struggles to others' lack of acceptance of their skin), both my colleagues and my clients were well-educated and gracious. I am not aware of my skin ever adversely affecting my professional aspirations. On the other hand, because so few people in the workplace ever ask anything about my skin, I sometimes find that I've worked with people for years, feeling as though we've come to know each other well, yet never have had a natural opening to discuss what's obviously wrong with my skin.

No one knows more about everything and nothing with my ichthyosis than my husband. Whether it's scales in our bed, rescheduling plans at the last minute to accommodate a desperately needed bath, trying to cool me down when I've overheated (and, as a result, become wickedly cranky), or running out to the drugstore to refresh my supply of precious

continued on page 5

Everything and Nothing About Ichthyosis

continued from page 4

eye ointment (which I'd neglected to remember to replenish until just minutes before bed), he supports my incessant skin-related issues willingly and as though nothing could be more natural. He's also picked up where my parents left off as my most ardent fan and staunchest advocate; he makes sure that I believe I can do anything. For instance, he decided, several years ago, that the world needed a website devoted to ichthyosis. As a network administrator, he handled all the technical aspects and I developed the content; together, we created www.ichthyosis.com.

Even now, my life is a rewarding mix of things related and unrelated to ichthyosis. We've recently moved to Washington, D.C., so that I could accept an appointment to the staff of the Public Company Accounting Oversight Board (more in the public eye than ever). I'm continuing to serve, as I have for several years, as a board member of the Foundation for Ichthyosis and Related Skin Types, a beloved and critically important group with which I'm very privileged to be associated. I'm still trying to find more effective treatments for my skin, still pretending to be "normal." All around, I'm having the time of my life.

Perhaps it's the permanence of living with a severe but as yet incurable disease that forces me to find some conciliatory peace with my situation. But, given the choice, I'd change everything about my situation and yet nothing at all.

Reprinted from the Journal of the American Academy of Dermatology, Volume 51, Laura J. Phillips, "Everything and Nothing About Ichthyosis," pp. s34 s35, 2004, with permission from Elsevier and the American Academy of Dermatology.

Foundation Resources

Jane Bukaty Membership Assistance Fund

The Foundation is now accepting applications to the Jane Bukaty Membership Assistance Fund for the next review cycle, which will end in June. If your application is accepted, you will receive a cash award to help with the treatment of your ichthyosis.

Email a request for an application form to info@scalyskin.org, or call 1-800-545-3286. Completed forms may be mailed to the attention of the Jane Bukaty Membership Assistance Fund, 1601 Valley Forge Road, Lansdale, PA, 19446. **The deadline for applications is June 30, 2005.**

Donations to the Jane Bukaty Membership Assistance Fund are always appreciated and enable the Foundation to make this fund available to more of our members.

New Fact and Resource Sheets

The Foundation has added two new resources to its publications file. A disease fact sheet on Darier Disease is now available, as well as a resource sheet that addresses the issue of chicken pox vaccination and/ or infection in children with ichthyosis. To order the Darier Disease fact sheet or Chicken Pox resource sheet, email the office at info@scalyskin.org, or call 1-800-545-3286.

National Family Conference 2006

Mark Your Calendars!

Start making plans to come to Atlanta, GA. The dates for the 2006 Family Conference are June 30, July 1 and 2. Check this space or Conference Corner in future newsletters for more details.

Correspondence Corner

continued from page 2

chemicals. These are things that I really enjoy doing, so the consequences are worth it to me.

My first foray into the Internet was about ten years ago when I decided I knew the most about my skin condition, as I had lived with it all my life. I thought I would find my own cure. I am convinced that applying lotions to the skin is not the answer. This is when I found F.I.R.S.T. What a wonderful resource. Being exposed to others who combat the day-to-day skin disorder battle, most with conditions worse than mine, makes me realize how fortunate I am to have this newsletter. I only wish my mother could have had access to this information when she was trying to manage her baby.

Janie Thompson
Decatur, GA

Dear Members of F.I.R.S.T.:

I am Javed Yusef. My son, Saad, is a sufferer of ichthyosis vulgaris. He is 12 years old and a very active child. We are writing from a far away region, from Pakistan. We came to know about the large community of F.I.R.S.T. members who interact with each other to solve their skin problems and support themselves in this way.

It is somewhat difficult for us, here in Pakistan, to access experienced help and up-to-date information. We want to seek help and guidance from F.I.R.S.T. members in this regard. I would like F.I.R.S.T. to please publish this letter, and request anyone who wants to correspond and be our friend to do so at my address.

We will always be thankful and friendly to everyone. We appreciate the Ichthyosis Focus, which is a lifeline for us. Thank you F.I.R.S.T. for the tremendous compilation of facts, insight, and research that you make available to us via the Ichthyosis Focus. We would love to hear from others soon.

Best Regards,
Javed Yusef
H. No. 880, Mohallha, Darianwala,
Kushab, Pakistan
Javed710567@hotmail.com
Saadi_7862000@yahoo.com

continued from page 3

the XPD or XPB genes, helicase components of the transcription factor TFIIH.[1]

These stepwise advances in molecular diagnosis are clarifying the relationship between clinical phenotypes and helping to solve the overall ichthyosis puzzle. I was recently consulted by consanguineous (related by blood) parents concerned about their child, who was born with a collodion membrane and, at 2 months old, has the clinical appearance of typical LI. Previously, cosanguineous cousins in their family also had a collodion baby who had a stormy course and did not survive. That baby had the clinical findings of NS, and molecular diagnosis confirmed a paired SPINK5 mutation. Could there be two different genetic diseases with collodion presentation appearing within this one family? Or, do these children have the same genetic disorder with different clinical presentations? A few years ago, we would have probably guessed that the odds favored a single rare skin disorder causing a collodion presentation within one family. Therefore, we would have interpreted this scenario as representing variable expressivity - the genetic characteristic where the clinical phenotype of a disease varies because of other influences, such as modifying genes or environmental factors. Our prognosis for the health of this baby and for future pregnancies would be problematic, because involvement in one baby appears to be confined to the skin, while the other baby died of multisystem disease. However, in this case, genetic testing found the child with clinical LI had a paired mutation in TGM1, providing molecular confirmation of the clinical diagnosis of LI rather than NS. Further analysis showed that the parents did not carry the SPINK5 mutation identified in their cousins who had produced a child with NS. Therefore, this child is not at risk for his cousin's poor outcome, and these parents are not at risk to transmit NS. This confirms segregation of two distinct ichthyoses with a collodion presentation within this one cosanguineous family, and clearly helps to define the clinical spectrum of both disorders. We do not have to infer an incorrect relationship between the clinical phenotypes of LI and NS.

These advances are enhancing our understanding of pathophysiology. The stratum corneum has been called our "outer skin" and the "beauty layer." It is our direct interface with the outside world. How does the epidermis form this tough, resilient, highly functional stratum corneum? These discoveries of the defects underlying the ichthyoses are helping to understand: (1) the specific processes involved in the formation of the stratum corneum, and (2) how the failure of each of these processes can lead to ichthyosis.

The process by which keratinocytes form the stratum corneum is complex. A useful model considers corneocytes as protein-rich "bricks" surrounded by a hydrophobic, lipid-enriched, intercellular "mortar"-like matrix. The importance of lipid formation and metabolism (mortar) was known early on, when steroid sulfatase, controlling the hydrolysis of cholesterol sulfate, was found deficient in X-linked ichthyosis. More recently, additional lipid (mortar) abnormalities have been discovered as FALDH in Sjögren-Larsson, lipoxygenases in CIE, and ABCA12 in LI. The importance of the structural integrity of the bricks was first highlighted by finding mutations in keratins leading to the cytoskeleton fragility that causes EHK. In addition, TGM1 as a cause of LI highlights the importance of proper formation of the cornified envelope, a laboratory analog of the "brick." Discovery of connexin mutations in EKV and KID syndrome tells us that failure of the intercellular communication can cause ichthyosis. We can also see ichthyosis with failure of transcription (PIBIDS), peroxisomal enzymes (Refsum disease) and a serine protease inhibitor (NS). Each of these discoveries is defining a piece of the ichthyosis puzzle.

So many discoveries, so little progress. Discovery of the mutations underlying a variety of ichthyosiform dermatoses has revolutionized diagnosis, enabled accurate and reliable genetic counseling and carrier testing, and created opportunity for both prenatal and preimplantation genetic diagnosis. Insights into pathophsyiology have helped to clarify the relationships between the different ichthyosiform dermatoses and establish the foundation for novel approaches to treatment based on mechanisms or genetic engineering. While these exciting discoveries have led to major advances in diagnosis and understanding, they have not yet led to significant advances in treatment or progress towards the ultimate goal of "cure" for our patients. We are beginning to identify the pieces of the ichthyosis puzzle, and some of the pieces are beginning to fit together. We still have a long way to go. So many discoveries, and yet, so little progress.

Resources. For patients, family, and friends, visit the Foundation for Ichthyosis and Related Skin Types web site at www.scalyskin.org. Genetic testing resources for clinicians can be found at www.genetest.org. For clinical information on genetic disorders for health professionals, visit the Online Mendelian Inheritance in Man web site at www.ncbi.nlm.nih.gov/entrez/query.fcg?db=OMIM.

References.

[1] DiGiovanna JJ. Ichthyosiform dermatoses. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. Fitzpatrick's Dermatology in General Medicine. 6th ed. New York: McGraw Hill; 2003. p. 481-505.

[2] National Center for Biotechnology Information. Online Mendelian Inheritance in Man Web site. Available at www.ncbi.nlm.nih.gov. Accessed February 27, 2004.

Reprinted from the Journal of the American Academy of Dermatology, Volume 51, John DiGiovanna, MD, "Ichthyosiform Dermatoses," pp. s31 s34, 2004,with permission from Elsevier and the American Academy of Dermatology.

Spotlight on Hunter Steinitz

Hunter Steinitz and her parents, Patti and Mark, are always working to teach others about ichthyosis. Hunter is ten years old and has Harlequin ichthyosis. This is her latest effort.

Hunter Steinitz

Hunter and her family moved to Key West, Florida from Pittsburgh, Pennsylvania in October of 2003. Beginning in November 2003, Hunter went to every classroom at her new school in Key West and explained her disorder and answered lots of questions. There are about 600 children in her school along with teachers, aides, office personnel, counselors, a school nurse, and supervisors. Hunter's teacher says she has been accepted as "one of the kids" and plans are in the works for her to talk to classes again.

Arrangements were also made, through the school nurse, for Hunter to talk to nursing students at Florida Keys Community College in Key West. Her talk was teleconferenced with a classroom in Marathon, FL to about 35 students total. "The grown-ups think I have such a bad sunburn," Hunter said, before walking into the classroom filled with adult nursing students. "People stare and it makes me sad, but it's okay to be different."

Hunter had to stand on a chair to see over the lectern in the college classroom. But she stood and confidently answered questions from students interested in knowing more about Harlequin ichthyosis and its affect on Hunter's life. Her school nurse, Beth Oropeza, and her mother, Patti, watched from the back of the classroom. "I would prefer that people just come over and ask why Hunter looks different," said Patti. "They usually think she was burned in a fire."

The story of Hunter "teaching" this class was reported in the local newspaper. Her mother, Patti, remarked that there are about 25,000 full time residents and visitors in Key West. "I don't know exactly how many people read this story. But apparently a lot did, because many people came up to us afterward and said hello. This story even made it to Fort Lauderdale. A woman from there called us. She has ichthyosis and has never talked to or seen anyone, outside of her family, with ichthyosis. I told her about F.I.R.S.T. and the conference, and encouraged her to call and join the support network (ISN). We hope to meet her when she visits Key West."

Hunter and Patti also spoke at their church about ichthyosis and their journey. Patti says, "We educate people nearly every time we go out. The locals are getting to know us. Many people from other countries come here to work and some to attain US citizenship. A lot of people here are from Cuba, South America, the Caribbean, etc. Most still have relatives in their native countries. So we are crossing international borders! How exciting!"

What Brown Did for Us!

United Parcel Service (UPS) Donates $50,000

The Foundation is in receipt of a $50,000 grant from the United Parcel Service (UPS) Foundation. This grant was funded as the result of a direct request made by Mike Briggs, a former UPS executive and grandfather to a young boy affected with Epidermolytic Hyperkeratosis (EHK). Thanks to Mike, this grant will be used to support our programs and research efforts combating ichthyosis.

"This grant will have a big impact for our small Foundation. Our five-year strategic plan focuses on improving our programs and services and funding more ichthyosis-related research. These funds from the UPS Foundation will help us to achieve our goals and improve the lives of patients affected by these types of rare diseases. We are extremely grateful for this generous gift," says Jean Pickford, Executive Director.

Established in 1951 and based in Atlanta, GA, the UPS Foundation identifies specific areas where its support will clearly impact social issues. In 2003, The UPS Foundation distributed more than $39.8 million worldwide. Of that amount more than $18 million was awarded through the Corporate Grant Program, $2.6 million was distributed through the Region/District Grant Program, $2.4 million was awarded through the Community Investment Grant Program, $2.45 million was awarded through the Gift Matching Program, and $9.2 million was donated to United Way. Last year, The UPS Foundation distributed $4.7 million in local charitable giving.

"UPS and its employees have always been committed to serving the communities where we live and work. In fact, community service is a key part of our company charter," said Evern Cooper, president of The UPS Foundation and vice president of UPS corporate relations. "We apply both financial and human resources in our support of groups that address the educational and human welfare needs around the world. UPS's support of the Foundation for Ichthyosis & Related Skin Types signifies our shared focus and commitment to improve our communities."

Executive Director's Report

Dear Members and Friends of the Foundation,

I hope this newsletter finds you and your family enjoying the winter months and looking forward to a wonderful warm spring. As we launch a new year at the Foundation, the staff and I are committed to strengthening the Foundation's programs and services and welcoming new members to our unique and extraordinary ichthyosis family.

In December, the Foundation elected five new members to join our already extraordinary Board of Directors. These new members began serving a three-year term this past January. The new board members include: *Michael Briggs*, a former United Parcel Service (UPS) Operations Manager/Vice President and grandfather to a young boy affected with Epidermolytic Hyperkeratosis (EHK); *Terry Melton*, Ph.D., CEO of a forensic DNA testing company and personally affected with Epidermolytic Hyperkeratosis (EHK); the *Honorable Gary Mills*, a district judge serving the people of Virginia and father of two children affected with lamellar ichthyosis; *David Scholl*, president and CEO of the world's largest cell culture provider and grandfather to a baby affected with Congenital Ichthyosiform Erythroderma (CIE) and; *Terrence Tormey*, managing director of a high-quality film and video production company, former pharmaceutical executive, and father of an adult daughter affected with lamellar ichthyosis.

The Foundation's 18-member Board of Directors is a committed group of leaders dedicated to making a difference for individuals and families affected by ichthyosis. Board members live and work in many different parts of the country, but the Board meets regularly on teleconference calls and face-to-face meeting retreats. The full Board of Directors will be meeting for its biennial retreat in November of this year.

Our recent holiday mailing fundraiser has been very successful. Donations from this campaign continue to arrive daily, and I am confident we will surpass our goal of $16,000. Thank you to everyone who contributes to our direct mail fundraisers. Without the constant support from our members and friends, the Foundation could not survive. Unfortunately, you cannot see the day-to-day operations, but please know that you are making a difference through your donation. The lives you touch include parents of a newborn, an affected adult who has just now discovered the Foundation, school personnel who are working with an affected student, and health professionals looking for more information, just to name a few.

This month, I will be traveling to New Orleans to participate in the annual American Academy of Dermatology (AAD) convention. Along with other leaders from skin disease organizations, I will be promoting ichthyosis awareness and education to thousands of dermatologists and health care professionals from all around the world. I will also be volunteering at the Dermatology Nurses Association convention a few days prior to the AAD meeting. Nurses are an integral part of the caring community for patients with ichthyosis, and I look forward to sharing our information and resources with them.

While attending the AAD convention, I plan to tour the exhibit hall looking for new products that can be beneficial to ichthyosis patients. Hundreds of pharmaceutical companies exhibit at this event, and it is a prime opportunity to engage new sponsors and products for the ichthyosis community.

Our Medical & Scientific Advisory Board (MSAB) will be holding its annual meeting this month in New Orleans. Currently, the MSAB consists of 23 renowned experts on ichthyosis. It is always an enlightening experience to be among these great leaders and to listen to their progress and future plans for ichthyosis research.

As you know, there has been a major effort to raise more money for ichthyosis-related research over the past several years. Our Fundraising Committee has been working hard over the past few months, but we need more volunteers to assist with a few projects. Our "Adopt a Non Profit" campaign involves compiling a list of 50 or more small to mid-sized companies in your local area and identifying their community relations managers. The second project involves contacting other Foundation members to participate in a letter writing campaign. If you are interested in helping us raise funds for the Foundation, please contact me at your earliest convenience.

The Foundation continues to support the Ichthyosis Registry. By now, you know that the funding from the National Institutes of Health (NIH) has expired. The Registry is no longer enrolling new patients, but, is, instead maintaining the already existing data and promoting its use among the skin disease research community. The Foundation is a proud supporter of the Registry and has contributed $8500 this year to help continue the maintenance phase.

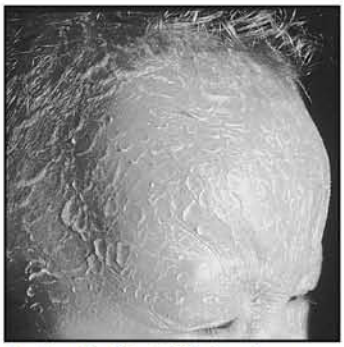
Please know that if you would like to contact me for any reason (share some good news, make a suggestion, etc.), I am always available to our members. I look forward to hearing from you.

Sincerely yours,

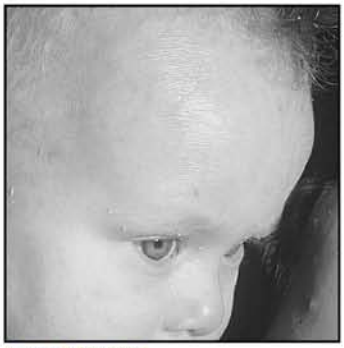
Jean

Jean Pickford
Executive Director

When Timothy* grows up, his parents want him to be ordinary. Just ordinary.



Problem Dry Skin (PDS) Symptoms of Lamellar Ichthyosis
BEFORE



AFTER 4 WEEKS

PDS Symptoms of Lamellar Ichthyosis

BEFORE

AFTER 4 WEEKS
(outer, lower leg)

THE NEOSTRATA COMPANY

Now, thanks to *NeoStrata*, he can be so much more.

Whether a child, or an adult you can choose from the new NeoCeuticals™ **P**roblem **D**ry **S**kin Treatment Products that are right for you. They are brought to you by NeoStrata, the company founded by Drs. Van Scott and Yu, long recognized leaders and patent holders in AHA and Poly Hydroxyacid technology. These new products formulated to aid in controlling the severe dryness and scaling symptoms associated with xerosis, ichthyosis and hyperkeratosis, are a culmination of nearly 30 years of dedicated research by Drs. Van Scott and Yu.

NeoCeuticals™ **P**roblem **D**ry **S**kin Treatment Products contain an optimum blend of Alpha and Poly Hydroxyacids in our exclusive NeoHydroxy™ Complex, combined with other skin conditioning agents. These non-prescription products include the *Extra Strength* and *Regular Strength* Creams and Scalp Solution.

This is a revolution in the treatment of **P**roblem **D**ry **S**kin, and a new quality of life for one afflicted. Discover THE breakthrough in treatments for **P**roblem **D**ry **S**kin.

For more information call 1-800-225-9411 or visit www.neostrata.com

* Ficticious name. Consult a physician before using on children.

Teen Talk

A New Program for Teenagers with Ichthyosis

Calling all teenagers!! The Foundation is launching a brand new program exclusively for you. Thanks to Operation Good Neighbor (OGN), an organization founded by Senator Rick Santorum of Pennsylvania, the Foundation will be providing the opportunity for affected teens to network and share with one another over the next year.

Michael Dunleavy, former board member and president of F.I.R.S.T., and uncle to two affected teens, was responsible for making this program a reality. Mike approached the office staff and said, "I think I found a way to help our teens. Let's write a grant and submit it to Operation Good Neighbor to provide money for a program just for these kids. Affected teens are an underserved population, and they need a way to communicate and learn from one another. A teen networking program matches OGN's giving philosophy, and I think we stand a good chance of receiving some funds." The grant was written, submitted, and funded in two months.

Operation Good Neighbor's philosophy states, "America was founded on some astoundingly simple but profound principles. We are all equal in our Creator's eyes. We each have a God-given right to an opportunity to succeed to the best of our ability. We have a responsibility to individual liberty, as well as a responsibility to see to it that we treat others in the manner that we expect to be treated."

What It's All About

The grant provides the Foundation with $15,000 for one year for four specific teen areas:

1. Monthly Teen Talk Conference Calls. One evening per month for the next year (dates have not yet been determined), a dedicated toll-free conferencing telephone call will be available to any teen wishing to participate. The call will be moderated by a healthcare professional and will focus on different topics each month.
2. Teen Talk Bulletin Board. Teens who wish to post and communicate on an online bulletin board will register for password information at the national office. Once activated, the teen will be able to post questions, send replies, or simply read what others are talking about.
3. Enhanced Teen Program at 2006 Family Conference in Atlanta. A portion of the grant will provide money to make the teen program at our next family conference a more rewarding experience.
4. DVD for Teens. Production has begun on a brand-new DVD, which will address teen-related issues and ichthyosis.

How Can I Get Involved?

You can become a member of the Teen Talk Network by completing the form on the next page and sending it back to the national office. Please note: You or your family must be registered as a member in good standing at the Foundation office to be eligible to participate. Members in good standing are those who have supported the Foundation over the past year. If you are not sure if you or your family are members, please contact the Foundation via email or phone. If your membership has lapsed or you never officially joined, you may complete the online "Become a Member" form on the Foundation's website, www.scalyskin.org, or call the office directly at 1-800-545-3286.

Does the FDA Need Reform?

By The National Organization for Rare Disorders

The mission of the U.S. Food and Drug Administration (FDA) is to enhance and protect the public's health, yet the Agency is now being intensely scrutinized by the U.S. Congress in the wake of several recent public health scandals. Although the FDA's responsibility is to police the nation's pharmaceuticals, biologics, medical devices, veterinary medicines, foods and cosmetics, which account for nearly one quarter of every dollar spent by American consumers, to ensure that they are safe and effective, it is perceived by many that the FDA is beholden only to industry interests.

Last year, controversy arose when a clinical trial testing Vioxx® as a possible treatment to inhibit the growth of polyps at risk for colorectal cancer uncovered the fact that patients taking the drug experienced a higher rate of heart attack and stroke when compared to placebo. Vioxx®, an anti-inflammatory to treat arthritis pain, is one of the heavily marketed group of drugs known as "Cox-2 inhibitors." These blockbusters, with sales of several billions of dollars annually, were advertised as being safer and more effective than the older anti-inflammatory drugs because they were, according to the pharmaceutical industry, easier on the stomach.

After uncovering the fact that the drug might cause increased rates of heart attacks and/or stroke, Vioxx®'s manufacturer, Merck, voluntarily withdrew the drug from the market, yet other Cox-2 inhibitors such as Celebrex® and Bextra® remained on pharmacy shelves. The manufacturer of those drugs, Pfizer, insisted that their drugs were safe even with mounting evidence about cardiovascular risks. According to news reports, sales of Celebrex declined 47 percent in the week following news reports about possible stroke and heart problems associated with that drug.

Before the Cox-2 problem was publicized, news reports surfaced about problems associated with anti-depressant drugs prescribed for children and teens. The British government had seen evidence indicating anti-depressant

continued on page 11

Teen Talk Registration Form

Name: _____

Age*: _____ Date of Birth: _____
*Eligible participants must be between 13 and 19 years old; no exceptions

Address: _____

City, State, Zip: _____

Phone: _____ Cell: _____ Email: _____

I am interested in (please check all that apply):

- ☐ Participating on the monthly teleconference calls.
- ☐ Participating on the online bulletin board.
- ☐ Attending the Family Conference in Atlanta, GA on June 30, and July 1 and 2, 2006 (see page 5).
- ☐ Purchasing a copy of the new DVD when it is completed.

I give permission for my child to participate or receive information in the checked area(s) above. I understand and agree that participation in this program is voluntary and that (a) neither the Foundation nor its staff, board and/or members is responsible for any comments or discussions that may take place within the Teen Talk Program, and (b) the Foundation's staff and volunteers will make every effort to monitor and minimize any negative or inappropriate comments that may arise. If, in the sole discretion of the Foundation or its representative, my child becomes a disruption, you may remove him/her from participation in the Teen Talk Program. If an issue or subject arises that the Foundation feels may, in some way, be harmful to my child, I authorize the Foundation to contact me.

I hereby release, discharge, covenant not to sue, and agree to indemnify and save and hold harmless, the Foundation for Ichthyosis and Related Skin Types, its officers, agents, volunteers, and employees from all liability, claims, demands, losses or damages on the minor's account caused or alleged to be caused, in whole or in part, by the negligence of the Foundation for Ichthyosis and Related Skin Types relating to the Teen Talk Program.

_____ _____
Signature Date

_____ _____ _____
Print Name Phone Email

This form must be signed by a parent or guardian if you are less than 18 years old. Without a completed form on file at the office, you will not eligible to participate.

Does the FDA Need Reform?

continued from page 10

drugs might cause agitation, aggressiveness, and suicides when prescribed to young depressed patients. Interestingly, the evidence came from clinical studies that had been kept secret because manufacturers didn't want negative information to be published. Those tests also indicated that most antidepressants are not effective in children, even though they are widely prescribed for children.

Based on the mounting evidence against the use of anti-depressants in children, the British government decided that children should no longer use the drugs, but the FDA had not made the same recommendation to American physicians. Instead, the FDA told manufacturers of these drugs to add a warning to the drugs' labels about the higher risk of suicide when compared to depressed children taking placeboes.

Also of concern last year was the critical flu vaccine shortage. In this case, an American company, Chiron, manufactured the vaccine in a British factory. The factory had been inspected by the FDA more than one year before and had failed the inspection, but the company did not fix the problems and continued to make contaminated vaccine. A year later, the British counterpart to the FDA inspected the factory, and finding that the serious manufacturing problems existed, closed the factory down. This resulted in the loss of 50 percent of the annual flu vaccine required in the United States.

These problems, which arose in 2004, followed many other highly-publicized drug tragedies in recent years, such as the Fen-phen diet drug scandal that caused serious heart problems, including deaths, and the 2001 withdrawal of the cholesterol drug Baycol®, after 30 people died from a breakdown of skeletal muscle fibers caused by the drug. As investigative reporters revealed each scandal, and as the stories unraveled in court cases, it was discovered that, in some cases, clinical trials indicating serious problems with these drugs had never been published and were purposely kept secret. In other cases, the studies presented to FDA for approval of the drugs were short-term studies on the healthiest people. After a drug reaches the market, it is used by a larger number of people who have other medical problems and are taking other drugs, so adverse effects arise unexpectedly.

Consumers who have counted on the FDA to police the nation's medicines are bewildered and frustrated. "If you can't trust the FDA, who can you trust?" said one confused consumer.

When the FDA allows a new drug to come to the American market, consumers should be confident that it has been

continued on page 12

continued from page 11

proven to be safe and effective. But after Vioxx® was removed from the market, a Congressional hearing was held. An FDA whistle blower testified that at least six other drugs have come to market in recent years despite intense safety concerns of some FDA scientists. There is evidence of a serious ongoing scientific debate within the FDA between safety officials and the FDA administrators who approve new drugs. Apparently, the safety officials are losing these arguments.

Now there is an intense public debate about FDA's competency. Is the Agency protecting and enhancing the public's health? Is it regulating pharmaceutical manufacturers appropriately? Is it protecting consumers from unsafe and ineffective medicines? The answers are not simple:

FDA Commissioner

The person responsible for managing the FDA is the FDA commissioner. However, in the past four years the Agency has been without a commissioner for more than two years. The President nominates a person to the post, and the Senate holds hearings and votes on the nomination. The post was vacant for a long time after President Bush was first elected, and finally he nominated Dr. Mark McClellan who served about 1½ years. When Congress passed the Medicare Modernization Act in the summer of 2004, the President decided that Dr. McClellan, who is a physician and economist, should be the new administrator for the Center for Medicare and Medicaid Services (CMS). As a result, Dr. McClellan left the FDA in the summer of 2004, and the commissioner's office has been vacant since that time.

The vacant office gives the impression that the FDA is not a high priority for the federal government. Although there is a temporary acting commissioner, many of the top managerial positions at the Agency are also vacant, and an acting commissioner usually does not fill such positions because a new permanent commissioner would be expected to appoint his or her own managerial team. The first goal should be to get a managerial team under a permanent commissioner so that everyone knows where the buck stops at the FDA.

Appropriations

The FDA has had very serious funding problems under the administrations of both political parties. According to a recent article in *Forbes,* the FDA offices that review new drugs received an appropriation of $423 million in 2004, with an additional $220 million coming in from user fees. Congress has apparently felt that FDA is not a high priority in terms of tax dollars. One problem is that, although the FDA is part of the Department of Health and Human Services (DHHS), the Congressional committees that fund health programs do not fund the Agency. Instead, Congressional agriculture committees appropriate funds to the FDA because, when the Agency originally started more than 100 years ago, its primary mission was to ensure the safety of the U.S. food supply.

Therefore, the FDA, which is responsible for regulating so many medical products, has to compete for its annual budget with the milk and crop subsidies, veterinary health and plants, fish farming subsidies, etc. Experts suggest this funding process is long overdue for change, but Congressional committees do not easily cede their realm of authority.

Several years ago, Congress realized that FDA was being short-changed. But, instead of appropriating enough money for the Agency to do its job, Congress instituted a new system called "user fees." Since the mid-1990s, companies are required to pay fees to the Agency when they submit new drug applications, when a factory is inspected, and to register their products each year.

User fees amount to tens of thousands of dollars for each product each year, and they are required under law to be used only to speed new drug approvals. Therefore, if the Agency needs more money, for example, to monitor the safety of a medicine after it is on the market, FDA is not allowed to use user fee revenues on such tasks.

FDA depends on user fees for nearly 70 percent of its annual revenues. Some experts believe this represents a serious conflict-of-interest because it is perceived that companies, rather than the American public, are its customers. With so many resources going to new drug reviews, and with the Agency's performance measured on the speed of those reviews, it sets the stage for rushing products through the approval process possibly without careful review of safety and effectiveness data. Even if this perception is unfounded, something must be done to change this view. Moreover, user fee costs are inevitably passed on to consumers, so we end up paying higher prices for our medicines.

Limitations of FDC Laws

The Food, Drug and Cosmetics Act (FD&CA) does not provide the FDA with enforcement powers and cannot set reasonable penalties when companies or individuals violate the law. For example, if the Agency speeds a breakthrough drug through the approval process (expedited approval), FDA can require the company to do additional Phase IV studies after the drug is on the market when scientific questions remain. Although most companies agree to do the studies as a condition of marketing approval, the directive is usually ignored. The Agency's last resort is to take the drug off the market to the detriment of patients who rely on the drug.

continued on page 13

continued from page 12

Political Pressures

The FDA receives intense pressure from medical industries for the Agency to approve products more quickly, and from patient groups to either move quicker or slower. People with serious and life-threatening diseases want access to treatments quickly, and they may be willing to accept higher risks, but they don't want to spend their money on drugs that don't work. Consumer groups representing healthy people usually want firm guarantees that new drugs are absolutely safe before they reach the market.

FDA has never been able to gracefully negotiate the balance between these two disparate points of view. The question for all consumers is, if you know the risks associated with each drug, would you weigh the risks against the possible benefits and determine how much risk you are willing to take?

All drugs have risks. For example, some people can die from aspirin. Most healthy people do not want to take any risks if they can avoid them, but cancer patients are often willing to take high-risk drugs with serious side effects. It would be a tragedy if FDA refused to allow a cancer chemotherapy drug to come to market because it had serious side effects.

On the other hand, a patient with a cold or flu would not be willing to experience the same degree of side effects as a cancer patient. Therefore, we expect the FDA to look out for us to a certain extent, but ultimately we have to make our own informed decisions. Many people decided to take Cox-2 inhibitors because they claimed to be safer on the stomach than older anti-inflammatory drugs, but unpublished studies indicated they caused as many stomach ulcers as the older drugs when taken over long periods of time. With Cox-2 inhibitors, consumers were not adequately informed, and that has led to public outrage.

Understandable Information

In order to understand the potential problems associated with any medicine, consumers need accurate and understandable information. Over-the-counter drugs have this type of information, but not prescription drugs. Consumers are not usually privy to drug "labeling," and even if we were, we would probably not understand its medical language.

For at least 30 years, laws have been introduced in Congress that would require understandable information for patients to receive with prescription drugs. The pharmaceutical, medical, and pharmacy industries have prevented these laws from being enacted. They say they will educate patients "voluntarily," and many chain drug stores provide leaflets with prescription drugs. FDA is permitted to require patient leaflets for certain medications, but so far it has mandated this for only about 30 prescription drugs. Without government oversight, some of the patient leaflets distributed by pharmacies have been deemed inaccurate and misleading, but they continue to be distributed.

Consumers ought to demand understandable and accurate information for prescription drugs so we will be able to weigh risks against potential benefits and make informed decisions. But if the public doesn't demand this, we will never get it.

Better Safety Monitoring

The part of the FDA that is responsible for monitoring safety of pharmaceuticals and biologics reports to the divisions of FDA that approve new drugs. Therefore, if the safety monitors tell their bosses that a marketed drug is so dangerous that it should be removed from the market, it's like telling their boss that he or she did a bad job. These bosses award raises and decide promotions of the people below them in the safety department.

This supervisory structure sets the stage for internal friction at the Agency and has led to a debate about whether the safety monitors should be in an independent drug safety Agency that does not answer to other FDA divisions and departments. Congress has held hearings on this issue, and legislation will likely be introduced this year.

Post-Marketing Surveillance

After FDA approves a drug for marketing in the United States, we do not have a good system of safety surveillance to determine whether new warnings should be issued, or whether the drug is so dangerous it should be removed from the market.

Doctors are expected to notify the drug's manufacturer and/or the FDA's voluntary "MedWatch" system of serious adverse events (AEs), but only a small percentage of adverse events are ever reported. Also, doctors may not suspect that a person's illness is a side effect of a drug (e.g., a heart attack). Controlled clinical trials are usually needed to detect whether a drug truly causes an adverse event (e.g., comparing people on a medicine to a group of people taking a placebo).

Adverse Event Reports (AER) are put into a database, but there are no dedicated staff to monitor the reports and detect patterns of AEs.

This has triggered a debate about whether adverse event reporting ought to be mandatory. But more importantly, that would not be helpful if FDA does not have enough expert staff to review and analyze all of the reports. Thus, the issue returns to the question of whether Congress is willing to fund the Agency adequately so it can do the job that American citizens expect it to do.

continued on page 14

continued from page 13

Drug Advertising

In the past few years, FDA has allowed Direct-To-Consumer (DTC) advertising of prescription drugs, and companies have spent billions of dollars on radio, TV, and print ads to convince consumers to ask doctors for prescriptions for those drugs. Obviously, the ads are successful, and that is why pharmaceutical companies advertise so much. Vioxx® and Celebrex® were two of the most heavily advertised drugs on TV, but on the heels of the current controversy, Pfizer has stopped advertising Celebrex®.

Under current law, drug companies develop an advertisement and can broadcast and print it before FDA reviews it. By the time FDA decides that an ad is misleading and orders the company to withdraw it, millions of Americans have seen and been influenced by the advertisement.

There is intense public debate about whether the FDA should allow prescription drug advertising to continue and, if so, whether FDA should be empowered to review and approve the ads before they are printed or broadcast. Additionally, print ads for drugs are required to re-print the labeling for each drug, which can take up an additional page in very tiny type, written in medical language that consumers do not understand. Many consumer groups are demanding understandable information written in type that consumers can easily read.

Seniors Speaking

Dear Friends:

I am 59 years old and have X-linked ichthyosis. I have been using Lacticare Lotion for more than 30 years, but the scales return the beginning of each winter season; very embarrassing.

I went to a dermatologist in September; she said she has a patient with ichthyosis and this person takes three fish oil pills a day. She has seen a dramatic difference in the condition of her skin. I now use LacHydrin 12%, Cetaphil soap, and take 3 fish oil pills every morning before breakfast. As a result, my arms do not have any signs of scales, nor do the areas of my legs that are exposed to the weather from wearing shorts. I have some scaly areas, but most of my legs are as smooth as someone who does not have this skin condition. I am extremely pleased with the results up to this point. The winter temps will be the telling sign, but, if this is any indication, my wife will really like not cleaning up scales in the spring.

I just wanted to pass this information along. I don't know if it is a result of the combination of soap, lotion, and pills, or just the pills, but whatever the case, I will continue to use this combination. "If it ain't broke, don't fix it."

If anyone has any questions, please feel free to email me.

Take care,

Bob Craig
Louisville, KY
Rcraig@aegonusa.com

Additionally, we have to question whether the billions of dollars the pharmaceutical industry spends each year on direct-to-consumer advertising would not be better spent on research and development of new treatments that patients desperately need.

Expedited Reviews for New Drugs

Before the AIDS epidemic, FDA took a year or more to review all the data submitted by manufacturers for marketing approval of a new drug. During the 1980s, AIDS advocates demanded quicker reviews, so FDA created a new process of "expedited reviews" for new treatments for "serious and life-threatening" diseases. Thus, drugs for AIDS, cancer, and other very serious diseases could be approved in six months if FDA categorized the product as a "priority" drug. Other "standard" drugs continued to be reviewed in the one-year time frame.

This process worked very well until user fees were instituted. FDA's performance under the user fee law would henceforth be measured by the speed of new drug approvals. Under the new system, expedited reviews were no longer reserved for serious and life-threatening diseases. Vioxx® and Celebrex® for arthritis pain, and even Viagra® for erectile dysfunction (a "life-style" drug), were reviewed and approved within the six-month time frame.

Many consumer groups feel that expedited approvals should be reserved only for serious and life-threatening diseases where time is of the essence. Drugs for conditions such as arthritis should not be rushed through the approval process because they will be prescribed to people who are generally healthy and have many other treatment options.

Experts suggest that the first rule of medicine is "do no harm," so standard drugs should be more carefully analyzed and their risk/benefit ratio should be determined before they reach the market.

Transparency and Public Access to Information

The FDA is one of the most secretive government bodies, and it is not consumer-friendly. Virtually all of the information that companies submit to the Agency about a product is considered a proprietary "trade secret." So, if a consumer tries to find something out about a drug or device, FDA will generally not answer questions and will refer him or her to the product's manufacturer.

Most consumer groups are demanding greater transparency for the FDA. How are decisions made? What scientific debates occur among FDA staff? How are outside experts selected, etc.? Consumers should not have to file a "Freedom of Information" request to obtain simple answers to simple questions about a drug or medical device. For example, if a person calls FDA to find out how to get access to an experimental drug, the FDA says to call

continued on page 16

Camp Discovery Dates

Dates are set for the 2005 Camp Discovery programs.

- Camp Discovery, for children ages 10 to 13, will meet at Camp Knutson in Crosslake, Minnesota, July 16 to 22, 2005.
- Camp Horizon, for children ages 9 to 13, will meet at Camp Victory in Millville, Pennsylvania, August 13 to 19, 2005.
- Camp Discovery Teen Camp, for ages 14 to 16, will meet at Camp Knutson in Crosslake, Minnesota, July 9 to 15, 2005.

Go to the American Academy of Dermatology website, www.aad.org, for more information and online applications for campers and volunteers. Or call the Academy at 847-330-8907. Dermatologists must recommend children with skin diseases for the camp program.

Third Annual Patient Art Exhibit

The Society for Investigative Dermatology (SID) is hosting the third annual patient art exhibit at its 2005 Annual Meeting in St. Louis, Missouri. The meeting will take place May 4 through 7, 2005, at the America's Center in St. Louis.

The art exhibit is an excellent opportunity for patients to present the impact of skin disease in a personal and creative manner to the researchers committed to finding treatment and cures.

Submissions are being accepted through March 18, 2005. An exhibit release form must be filled out for each submission. The SID will pay all shipping charges and insure the piece for up to $200.00. Please contact Becky Minnillo if you need additional information, 216-579-9300, or Minnillo@sidnet.org.

Society for Investigative Dermatology Memo, 1/3/05. Please contact Maureen in the Foundation office for a copy of the Exhibitor Release Form, 1-800-545-3286, or info@scalyskin.org. Be sure to include your name and mailing address if you leave an email or voice mail message.

New Column in Dermatology Nursing Shows Patient Perspective

Health care professionals strive to understand what patients go through with their dermatological diseases, but they may not ask the patient, "What is it like living with this condition?" *Dermatology Nursing* Journal addresses this question with its new series, "Patient Perspectives: Living With …"

Debuting in the October issue of the journal, the series offers a patient's perspective on living with a specific skin disease. It gives insight into how the disease affects the patient's life and relationships with others. Patients submit answers to questions such as:

- How has your condition affected your life, physically and emotionally?
- What would you like health care providers to know about treating people with your condition?
- What do you wish society knew about your condition?
- What would you tell other people who are newly diagnosed with this condition?

"With all the studies looking at quality of life issues for patients with skin disease, maybe it's time we heard the patient's perspective," said Marcia J. Hill, MSN, RN, editor. "I believe these valuable insights will provide important information to help dermatology nurses better care for their patients."

Patients interested in sharing their experiences with the dermatology nursing community can contact Lori Ann Tornatore, Editorial Assistant, at tornatol@ajj.com, for a complete list of questions and submission details. If you do not have access to email, you may call Lori Ann at 856-256-2300, extension 2344, or write to her at:

Lori Ann Tornatore
Editorial Assistant
Anthony J. Janetti, Inc.
East Holly Avenue, Box 56
Pitman, NJ 08071-0056

Reprinted from Dermatology Nursing *press release, November 3, 2004.*

continued from page 14

the manufacturer of the drug. The manufacturers tell people to call the FDA. Consumers find themselves in a never-ending wild goose chase because no one takes responsibility, and FDA operates under a perpetual gag order. Its staff members cannot answer consumers' questions unless the manufacturer gives them specific permission to do so.

Some consumer organizations feel that the public and healthcare professionals should also have access to adverse event reports (without names and addresses of patients), so they can find out how many reports have been filed about problems associated with specific treatments. For example, how many pacemakers malfunctioned within the first two years of implantation? Which nutritional supplements had the most reports of adverse events? How many reports of allergic reactions were filed for blood pressure or cholesterol medicines, and which characteristics did those patients have in common? Even if a medicine is not approved for pregnant women, what happened to babies born after their mothers took the drug?

What Will Happen Now?

In summary, the recent spate of highly publicized health calamities has led to an intense re-examination of the FDA's performance. Some people fear that the current scrutiny may lead to increased regulation of the drug industry, leading to slower approvals of new drugs and devices. Others feel that the current criticism of the Agency is long overdue, and regulation of pharmaceutical and device companies, as well as funding for FDA, needs to be increased. All parties agree that FDA needs a new commissioner as soon as possible, signaling a higher government priority for public health.

Which of these interests will win the public debate? Can the public's anger at the pharmaceutical industry be contained in the face of continuous revelations and scandals? One thing consumers must recognize is that we cannot manufacture new drugs ourselves. We need the pharmaceutical industry to continue research and development of new treatments.

Nevertheless, everyone recognizes that changes are critically needed at the FDA. The Agency cannot protect and enhance public health when its performance is measured on speed and not on scientific excellence. Every major change to the Food, Drug and Cosmetic Act arose because of a scandal not unlike the current Cox-2 problem (e.g., the thalidomide tragedy during the 1960s). Perhaps it is time to bring the law up to the realities of the 21st Century and to remind Congress that it has a responsibility to put its money where its mouth is.

The vast majority of decent law-abiding drug companies will inevitably have to recognize that their industry cannot police itself, and a scandal at one company has consequences for all companies. The fact that some companies will not allow research to be published if the results of the study show their drug is not safe or not effective is shameful in an industry that claims it is dedicated to improving the health of patients. We must all work together to improve the FDA because our lives depend on safe and effective medicines. The future of the pharmaceutical industry also relies on regaining the public's trust.

Have you moved recently or are planning on moving soon? Please let us know your change of address so you can continue to receive the Focus. Postage for the newsletter does not include forwarding.

F.I.R.S.T.
Foundation for Ichthyosis and Related Skin Types

F.I.R.S.T.
1601 Valley Forge Road
Lansdale, PA 19446