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

ICHTHYOSIS FOCUS

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FROM THE EDITOR'S DESK

Our last issue quoted part of a letter from F.I.R.S.T. member and attorney ***Jessie Deely****, praising advice offered by Dr. Betts at our conference. Here is the rest of her letter, with her permission:*

". . . Dr. Betts' report to the Conference was right on target as to the importance of the parents' acceptance of their child's ichthyosis. As an only child, born and raised fifty years ago in a small Kentucky town by parents who were both lawyers, I had the benefit of acceptance and my friends' indifference to my skin condition. It was perceived as a problem no different from another child's asthma, hearing loss or any other minor physical problem. I was taught early how to explain the basic facts of my skin condition to strangers while assuring them that it was not painful or physically debilitating.

I have been married almost twenty-seven years and we have three children, 22, 24 and 25, all of whom have normal skin. My law practice is a typical small town practice consisting of real estate, wills, domestic relations, etc. My husband is the President of his family's business, a lime business that was founded over one hundred years ago by his great grandfather. I would be happy to assist in any way I can, and you may feel free to use me as a resource person. It is of utmost importance to reassure young people and their parents that they can, despite their condition, have happy, fulfilling lives with children and close family relationships. Sincerely, Jessie Deely, Attorney." [Mrs. Deely has Lamellar Ichthyosis]

Mrs. Neely provides a wonderful example of the fortitude, optimism, and positive outlook that everyone, patients, parents, and families, should have. How we feel about life and the world depends more on our own attitudes than on external factors. "If life gives you lemons, make lemonade." You can complain that the lemons taste sour, or you can enjoy their tangy, refreshing flavor. It's up to you. It's mainly a question of the attitude you **choose** to have, or have been raised to have. Parents who help their children develop a positive outlook by emphasizing the good side of things and what **can** be done instead of what can't, give their children the greatest gift of all: a view of life's opportunities, not limitations.

Sorry for the delay in getting out this issue of ICHTHYOSIS FOCUS: We are working on a new look and better newsletter for you, but the process is slow. - The Editor

SJOGREN-LARSSON RESEARCH VOLUNTEERS NEEDED

*[**William B. Rizzo, M.D.**, is looking for volunteers to help him with his research into Sjogren-Larsson Syndrome. Dr. Rizzo is Assistant Professor of Pediatrics and Human Genetics at the **Medical College of Virginia**, Richmond, VA, and has prepared the following article about Sjogren-Larsson Syndrome. Dr. Rizzo earned his M.D. from the University of Illinois, and has had further training at Johns Hopkins Hospital and the National Institutes of Health.]*

Sjogren-Larsson Syndrome (SLS) is one of the rare forms of ichthyosis associated with other symptoms. The disease was first described in 1957 by two Swedish physicians, Sjogren and Larsson, who reported on a group of 28 patients from a region in northern Sweden. In addition to ichthyosis, all of these patients had neurological symptoms, especially leg spasticity and mental retardation. The diagnosis of SLS is based on patients showing all three cardinal symptoms (ichthyosis, mental retardation and spasticity).

SLS is inherited in an autosomal recessive fashion, which means that the parents carry the abnormal gene but do not themselves express it. In the region of Sweden where SLS patients were first described, the disease affects one out of 12,000 people. SLS has been seen in all parts of the world, including the United States, at a much lower incidence. The true prevalence of SLS in the US is unknown. Since most inherited disorders show a wide spectrum of clinical variability, it is possible that some SLS patients do not express all of the symptoms. If so, SLS may occur more frequently than presently suspected.

The ichthyosis in SLS is usually apparent at birth or shortly thereafter and varies in severity. It resembles Lamellar Ichthyosis at first glance, although certain features distinguish it from this form of ichthyosis. Patients with SLS typically develop some degree of leg spasticity, resulting in difficulty or an inability to walk, and mental retardation. These neurological symptoms are not apparent at birth, but become evident by two years of age in most known patients. The mental retardation is usually severe, although it may be mild in a minority of patients. About half of all patients have had one or more seizures. Most SLS patients have "glistening white dots" inside their eyes, although their vision is normal. Less commonly, patients have short stature, abnormal tooth enamel and curvature of the spine. In spite of these other medical problems, SLS patients typically live into adulthood.

The cause of SLS has been unknown. An abnormality in fat metabolism was suspected as the basis for the symptoms, including the ichthyosis, because of improvement in the skin of several patients placed on a low-fat diet supplemented with medium-chain triglyceride oil. Recent research from our laboratory indicates that SLS patients are unable to metabolize a certain type of fat called "fatty alcohol." Normally, fatty alcohol metabolism is important in the skin and brain, where it is used for the synthesis of membrane components. Using cultured skin cells (fibroblasts) from 5 SLS patients, we have found a deficiency of an enzyme, "fatty alcohol:NAD oxidoreductase" (abbreviated FAO). FAO deficiency was also observed in blood cells (leukocytes, or white blood cells) from these patients. Skin fibroblasts from patients with other forms of ichthyosis or neurological disease do not show FAO deficiency, suggesting that this enzyme deficiency is specific for SLS. Furthermore, people who are carriers for SLS have a partial FAO deficiency in their skin cells and leukocytes, an observation that may permit carriers of this disease to be identified.

These initial research findings are important because they provide a "biochemical marker" by which to identify patients who have ichthyosis due to SLS rather than another form of ichthyosis. One of the first applications of this research will be to determine if all patients with FAO deficiency invariably show the three major symptoms of SLS; it is possible that some patients with ichthyosis may lack the mental retardation or spasticity. Furthermore, it should now be able to diagnose SLS at birth by screening babies with ichthyosis for FAO deficiency. Since the skin manifestations of SLS become apparent before the neurological symptoms, a critical question to be answered is whether the mental retardation and spasticity usually seen in patients would be prevented or ameliorated by dietary therapy early in life.
Research on SLS may provide clues to understanding the basis for skin changes in this genetic syndrome and other forms of ichthyosis.

--> HOW MEMBERS OF F.I.R.S.T. CAN HELP WITH SLS:

We are interested in obtaining a blood sample and skin biopsy from patients with ichthyosis, particularly (but not exclusively) those with other neurological symptoms (spasticity, retardation, seizures, tremors, speech disturbances, walking difficulties, etc). If the patient cannot travel to Richmond, VA, the blood samples and skin biopsies may be obtained by his or her dermatologist or other physician, and sent to us for testing. The blood sample (approximately 1-2 teaspoonsful) will be used to measure fatty alcohol levels, which may be elevated in Sjogren-Larsson Syndrome. The skin punch biopsy will be used to establish fibroblast cultures, which will be tested for fatty alcohol:NAD oxidoreductase. Results of all tests will remain confidential, and each patient will be notified of his own results. Those patients with deficiency of fatty alcohol:NAD oxidoreductase will be offered enrollment in another study to test a dietary treatment for this disorder. Patients will not be paid for their participation, but tests will be performed free of charge. A signed consent form must be obtained from each patient before samples are taken. Anyone interested in participating should contact me, Dr. William Rizzo, at 804-786-9618.

CORRESPONDENCE CORNER

Kathleen Gaffney has a five-and-a-half year-old daughter, Megan, who has been diagnosed with K.I.D. Syndrome. She would like to hear from other parents whose children have similar problems. Her address is: Mrs. James Gaffney, 330 Burd Street, Pennington, N.J., 08534.

Thomas Lycett is 19 years old and has Lamellar Ichthyosis. He would like to correspond with others in his age bracket, especially someone of the opposite sex with the same type of ichthyosis. Thomas's address and phone number are: Thomas Lycett, 465 King Road, Forestville, N.Y., 14062; 716-934-2589.

The Jacobsmeyers would like to hear from you, too. Marirose, eight years old, has been diagnosed with **Netherton's Syndrome**, a type of ichthyosis which apparently involves seizures and other problems. Her mother, Kathryn Jacobsmeyer, says, "If anything we have learned that this particular syndrome is not merely skin deep! I am requesting contact, through the newsletter, with anyone who has Netherton's Syndrome -- or family members thereof." And Marirose herself would like to correspond with a girl around her age who has any type of ichthyosis. They can be reached at 6767 Eichelberger, St. Louis, MO 63109.

F.I.R.S.T. ANNUAL CONFERENCE

In our last issue we reported that we hoped to have our annual conference in New England this fall. Well, plans have changed a bit, but it turns out we were on the right track. We do plan to have the conference in New England, hopefully Connecticut where we have quite a few members. The time has changed, though, from Fall 1987 to Spring 1988. We'll keep everyone posted as soon as we have definite times and places, but for now let's just think Spring! . . . in New England!

SOME HEARTFELT THANK YOU'S

A special thank-you to the children of the Faith United Church of Christ Vacation Bible School of Ridgeway, PA, for their donation to F.I.R.S.T. in honor of Ms. Bailey Jones. We'd once again like to thank all of you who responded to our Renew-Your-Membership campaign. A special thank you to Audrey Henderson, Mr. and Mrs. Bernard Lange, Joe Galluccio, Jr., Mr. and Mrs. Carl Anderson, Helene Tomalesky, Margaret Jacobsen, Rita Koenig, Emily Latour, and Pauline Suter. Thanks very much to Sue Tiffany and her employer, Pfizer Corporation of Groton, CT, which matched her generous donation! Perhaps your company has a matching donation plan? Double your contributing power!

Do you donate to the United Way at work? Ask if you can designate F.I.R.S.T. as the specific recipient of all or part of your contributions! Many members have chosen this easy way to help us and themselves! But you have to ASK!

SPRING S.I.D. MEETING ICHTHYOSIS TOPICS

--> X-LINKED ICHTHYOSIS

*Dr. Peter Elias, M.D., vice-chairman of the Department of Dermatology at the **University of California at San Francisco** and a member of F.I.R.S.T.'s **Medical Advisory Board**, reports here on an abstract presented at the meeting of the **Society of Investigative Dermatology (S.I.D.)** this spring.*

One of the great mysteries of epidermal function is the molecular mechanism whereby individual stratum corneum (the outermost layers of the skin) cells are shed invisibly, one by one, from the surface of normal skin. Because prior work has shown that lipids (fats) are restricted to the intracellular spaces (i.e., the spaces between the cells), in the stratum corneum, and also has shown that the lipids are arranged in an organized or membrane structure, it is generally assumed that it is these membrane structures that control the shedding process.

In Recessive X-Linked Ichthyosis (RXLI) there is an increased amount of cholesterol sulfate in these lipid membranes, and it is presumed that the cholesterol sulfate is responsible for the abnormal shedding that occurs in this type of ichthyosis. Jerry Rehfeld, an engineer who works in the laboratories of Dr. Peter Elias and Dr. Mary Williams at the VA Medical Center in San Francisco, CA., and Dr. William Plachy, Chairman, Department of Biochemistry at San Francisco State University, have studied how cholesterol sulfate might produce the abnormal scaling in RXLI using a variety of physical chemical techniques. Their work, which was presented at the S.I.D. meeting in San Diego, shows that cholesterol sulfate is unable to form normal molecular bonds with other lipid molecules in the intercellular membranes, and for the first time we have some idea why patients with X-Linked Ichthyosis might demonstrate abnormal scaling. This study also provides an idea of the mechanisms that may underlie normal shedding, as well.

In future studies they will extend this work to other forms of ichthyosis, particularly Congenital Ichthyosiform Erythroderma, in which another lipid, n-alkanes, accumulates. Obviously, once more is known about the molecular mechanisms involved in normal and pathological skin shedding, it should be possible to devise new methods of therapy, as well.

--> HARLEQUIN ICHTHYOSIS

*Beverly A. Dale, Ph.D., Research Professor, Departments of Periodontics, Oral Biology and Medicine (Dermatology), **University of Washington**, Seattle, WA, shares here the report on Variable Expression of Biochemical and Morphologic Markers in Harlequin Ichthyosis Biopsies and Cultured Keratinocytes presented at the S.I.D. by **Dr. Dale** and **Drs. K. Holbrook, P. Fleckman**, and **V. P. Sybert** of the University of Washington.*

Harlequin Ichthyosis is a rare, severe form of ichthyosis which is usually fatal within the first few days or weeks of life. It is inherited as a recessive disorder; parents are completely normal. The skin of the infant has large, thick scales because the cells of the epidermis stick together. The epidermis is the outer layer of the skin which provides a barrier to environmental stresses. The whole body is affected. The underlying biochemical cause of this disorder is not known.

We studied biopsy samples from five cases of Harlequin Ichthyosis to identify abnormal tissue and cell structure and alterations in epidermal proteins. Microscopic examination of the different cases showed several abnormal features, including: thickened epidermis and scale, abnormal keratohyalin granules, absence of lamellar granules (these are two typical components of epidermal cells), a decrease in the number of keratin filaments, and an increase in abnormal lipid droplets in the scale. These abnormalities and changes varied between the cases.

Two types of structural proteins were studied: keratins (a family of proteins) and filaggrin. In normal epidermis, the keratin proteins form filaments within the cells, and filaggrin causes these filaments to aggregate in the mature cell layers of epidermis. In the Harlequin Ichthyosis cases, keratins that are found in normal epidermis were present, but some cases also contained extra keratins that are only seen in disorders with rapid cell division. The protein filaggrin was absent in all

cases; only its biochemical precursor form was present. We hope to identify the cause of the lack of conversion of the filaggrin precursor, and determine its role in the abnormal epidermis.

Epidermal cells from several cases were grown in culture. The cells were normal. However, the cells do not mature as completely in culture as in the skin. Our results suggest that Harlequin Ichthyosis is a heterogeneous group of disorders in which a single gene defect alters the tissue structure and synthesis of keratin and filaggrin proteins late in the maturation of the epidermal cell.

This information will improve prenatal diagnosis of Harlequin Ichthyosis in affected families, and may aid in designing suitable treatment.

TELL ME, DOCTOR

Two doctors, both members of F.I.R.S.T.'s Medical Advisory Board, are responding to our **Tell Me, Doctor**, question this month. They are **Arthur L. Norins, M.D.**, Professor and Chairman, Department of Dermatology, School of Medicine, Indiana University, Indianapolis, Indiana, and **Nicholas J. Lowe, M.D.**, FRCP, FACP, Professor of Medicine/Dermatology, Division of Dermatology, UCLA School of Medicine, Los Angeles, CA.

Q. I have the EH form of ichthyosis and find that infections are a continuing and recurring problem. They aren't nearly as bad as they were when I was a child, but even now, as an adult, I get occasional blisters for no apparent reason. These infections leave me feeling tired and drained, with my lymph nodes hard and swollen. I've heard other people with EH mention the same problem. I'm also susceptible to fungal infections like athletes foot, and my doctor says it's related to my ichthyosis. Does this happen only with EH or are other forms of ichthyosis susceptible to infections, also? How can people with ichthyosis deal with and hopefully minimize this painful infection problem?

A. (Dr. Norins) In EH there is a break in the natural protective barrier of the skin to the outside. The top layers of the epidermis are not completely sealed together. This frequently allows microorganisms to gain hold and develop an infection.

I have patients attempt to minimize the thickness of the scale/crust and then use routine cleaning. Recently I have been using **LacHydrin** [from Westwood Pharmaceutical Co., Buffalo, NY] to help desquamate the area. This is applied daily. I also have the patient shower two days in a row each week using **Hibiclens** skin cleanser. The patient wets himself in the shower, turns it off, lathers from the neck down (do not get in ears) with the **Hibiclens**, then rinses off completely. Towel drying is important. Intertriginous areas should be dried quite well. I prefer the use of cotton clothing; it tends to be less occlusive.

If a fungus infection is proven, then it is often helpful to treat with an oral antifungal medication.

A. (Dr. Lowe) I am sorry that you are having recurrent skin infections. Patients with epidermolytic hyperkeratosis (EH) in particular appear to be prone to recurring skin infections. These may take the form of infected blisters, and if they become severe then the regional lymph nodes can become enlarged and painful.

It is often advisable with some patients to be treated with long-term antibiotics plus frequent culturing of the skin infections to determine any changing antibiotic sensitivity. In addition, it may be possible to take baths in special solutions such as dilute Domeboro solution to try to reduce the risks of these infections. The formation of infected blisters in patients with epidermolytic hyperkeratosis may be partly the result of the thickened and abnormal horny layer of the skin that leads to increases in the number of bacteria in the skin. The blisters form possibly because of the type of changes seen in the upper skin of patients with EH.

MONEY MAKES THE WORLD GO 'ROUND . . . .

Just a Reminder -- ICHTHYOSIS FOCUS is sent out six times a year to members of F.I.R.S.T. The annual membership fees, due in May, are: $15 - Individual Regular membership; $25 - Contributing membership; $50 - Sustaining membership; 75 - Sponsor; $100 Patron.

Did you remember to contribute this year? At this time the Foundation does not send out annual bills, but we do request you mail in dues during May, "Renew Your Membership Month." Meanwhile, if you can't afford to contribute at this time, you need not worry that the newsletter will stop coming to your home -- it won't stop coming. As yet, no one has been turned away from any of the services of F.I.R.S.T. due to lack of funds. We ask you to contribute an annual membership fee, but if you just can't right now, we understand, and trust you to help us as much as you can as soon as you can.

And, of course, you can make a contribution at any time! The Foundation needs continuing financial support in order to maintain its programs, like this newsletter and our annual ichthyosis research grants. All donations, both large and small, are needed and appreciated; all are tax deductible as allowed by law.

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