



The National Ichthyosis Foundation

ICHTHYOSIS FOCUS

The National Ichthyosis Foundation
P.O. Box 252
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From a Medical Point of View

SYNTHETIC RETINOIDS FOR SCALING SKIN DISEASES

By Nicholas J. Lowe, M.D., MRCP,
FACP

Dr. Lowe is Associate Professor of Medicine/Dermatology at UCLA School of Medicine and a member of NIF'S Medical Advisory Board.

Vitamin A has been used for many years in the treatment of a number of skin diseases and attempts have been made to use it to treat the various forms of ichthyosis. However, the high oral dosages usually required to produce an improvement in the skin condition frequently produced significant side effects, some of which were potentially severe. Liver damage and central nervous system symptoms, including nausea, vomiting, headache and dizziness, have been reported. A good response in patients at dosages below these toxic levels was usually impossible.

Work over the last few years has focused on the effects of analogues of Vitamin A known as the retinoids. Two major retinoids are presently under study in this country for the treatment of certain skin diseases. 13-cis-retinoic acid, also known as Accutane®, has recently been approved by the Food and Drug Administration for the treatment of severe pustulocystic acne. This drug has also been investigated in different scaling diseases, disorders of keratinization and some forms of ichthyosis. Two types of ichthyosis which seem to respond to 13-cis-retinoic acid are lamellar ichthyosis and epidermolytic hyperkeratosis. A recent report by Baden, et al¹ showed that of 59 patients with these types of ichthyoses, 57 showed significant improvement following treatment over a 16-week period. Some side effects were seen but these were principally related to the skin and mucous membranes and included increased dryness of the lips and nose and some skin fragility. Another problem is occasional epistaxis. It is also important to watch for abnormalities of the lipid levels (levels

of cholesterol and triglycerides in the blood) which can become elevated after chronic long-term use of 13-cis-retinoic acid. Therefore, all patients treated with these drugs should have preliminary blood examinations which must be repeated every four weeks. Long-term 13-cis-retinoic acid use may also affect the skeleton since an overgrowth of bone has been reported in some patients (so-called hyperostosis). The incidence of this effect following 13-cis-retinoic acid is not yet clear and further investigation of this possible side effect continues.

It should be stressed that 13-cis-retinoic acid is not approved by FDA for use in conditions such as ichthyosis, and is used on a purely investigative, experimental basis. The patient should also be aware that when treated with 13-cis-retinoic acid, the ichthyosis will return or relapse within 4 to 6 weeks after this medication is discontinued. Women of child-bearing age need to avoid pregnancy because of teratogenicity or fetal disease.

The longer term side effects of 13-cis-retinoic acid are not as yet known. Hence, the hesitancy at present for approval for this medicine for anything requiring long-term treatment. 13-cis-retinoic acid for the treatment of severe pustulocystic acne is usually needed for up to five months of therapy and has FDA approval.

Another drug now approved in some European countries is aromatic retinoid, also known as Etretinate® or Tigason®. This drug has been evaluated in several skin diseases and seems to be very useful for the treatment of more severe forms of psoriasis^{3,4} and pityriasis rubra pilaris⁵. It has also been evaluated in Europe for the ichthyoses and other scaling skin diseases.

In one report², improvements in ichthyosis vulgaris as well as lamellar and x-linked ichthyosis after etretinate therapy have been claimed. In the

bullous type of ichthyosis-form erythroderma, however, it was reported² that the blisters may persist and increase in size.

While etretinate seems to show a good response in certain scaling skin diseases, it must be used with caution. The same side effects occur with etretinate as occur with accutane, including abnormal infants born to mothers who have been taking etretinate. Drug excretion is more prolonged and the drug persists for longer in the body than does accutane.

In summary, the synthetic retinoids currently being evaluated show significant promise as alternative forms of therapy for the treatment of certain diseases, including the severe forms of ichthyoses that hitherto have been largely untreatable. They do create a significant risk of side effects and must be monitored very carefully by the physician skilled and experienced in their use.

It is possible that newer synthetic retinoids may become available that may have the same therapeutic effects with lesser toxicity. And, it is hoped, research will result in effective topical retinoids that do not have the same irritancy as retinoic acid creams and gels currently available.

1. Baden HP, et al: *Treatment of Ichthyosis with Isotretinoin*. 4 Part 2:716-720, 1982.
2. Orfanos CE: *Oral Retinoids — present status*. Br. J. Derm. 103:473-481, 1980.
3. Lowe NJ, Kaplan RP, Breeding J: *Aromatic Retinoid treatment for Psoriasis inhibits ornithine decarboxylase*. J.A.M. Acad. Dem. 6 (2) 697-698, 1982.
4. Kaplan RP, Russell DH, Lowe NJ: *Etretinate Therapy For Psoriasis*. J. Am. Acad. Derm. 8:95-102, 1983.
5. Goldsmith LA, Weinrich AE, Shupack J: *Pityriasis Rubra Pilaris responses to 13 cis retinoic acid*. J. Am. Acad. Dem 6:710-715, 1982.

State of the Foundation

Dear Friends and NIF Members:

The afternoon session of our First National Conference on December 2, 1983, was spent in discussing the status, needs and goals of the Foundation.

After stressing that the Foundation is still a young, small organization staffed entirely by volunteers and completely dependent on the donations of its members, the conference participants helped set our priorities: self-help, education and research.

The response on how to accomplish these goals with our limited resources was clear. First priority was assigned to **further development of a strong national organization** on all levels — national, regional and local. So far, the national organization is strongest, and local chapter development is weakest. The emphasis in 1984 will be on regional conferences to strengthen the

regions and then local chapters. Local chapters carry the word about ichthyosis fastest and farthest. They best fulfill the critical role of putting patients and families in touch with each other, and they are the grass roots strength that we have to focus the nation's concern on ichthyosis. Your regional representatives need your support in organizing the conferences. Please be in touch with them to offer support and help. In the east, contact Marisa Mandia; south, Betty McMasters; midwest, Dick and Carol DeLoughary; west: Jeannette Jensen.

More research was a close second on the list of priorities. Clearly, support of the new National Institute of Health for Skin Diseases will be an important task for NIF in 1984.

Education was discussed, and remains very important. However, the resources for development of educational materials and for supporting dermatology students who are interested in studying ichthyosis just aren't available now. If you know of a donor for a

special education project, please let us know. We also need an Education Committee Chairperson. Ideas are ready to be acted upon, but we need manpower and funding.

Regarding our office needs, Jeanette Jensen has met with an accountant and our books are now arranged and up-to-date. However, we still need someone to assume the account responsibilities. It's also crucial that we hire a director in the near future. As volunteers, we are not as effective or efficient as we should be. A full-time staff person would ensure that your Newsletter arrives on time and that fundraising gets done. We need contributions to fund the position for at least six months. During that time, enough money could be raised to keep the position going. Other Foundations have done this and it has worked quite well. Our fundraising goal for 1984 is \$20,000 — won't you please help us?

Best regards to all of you,
Charles Eichhorn and Susan Nye

De Haan
Co-Presidents 1984

NATIONAL ISSUES NEWS

Charles Eichhorn, Co-President

This is my first contribution to ICHTHYOSIS FOCUS since the December workshop and Board of Directors Meeting in Chicago. My feet have barely hit the ground since.

As you have already heard, the National Conference was quite a success. It brought together people from all over the country. It was a great opportunity not only for members to meet each other, but also for the Foundation's leadership to communicate directly with our constituency.

The National Conference in Chicago on December 2, 1983, was held in conjunction with the American Academy of Dermatology meetings there at the same time. The Medical Advisory Board turned out in force and we got together for a fast-paced breakfast meeting at one of the major hotels.

Because the newsletter is our main communication link among all those concerned with ichthyosis, ICHTHYOSIS FOCUS was a major topic. The Board give their full support and cooperation to a new concept we want to try in the newsletter: In the past, we asked the doctors to provide us with feature articles about ichthyosis.

Well, beginning with this issue, the Medical Advisory Board will address more specific questions about ichthyosis. Your questions and suggestions, tips and pet peeves about treatments, medicines, diagnoses, kinds of ichthyosis, etc., should be addressed to the **Ask the Doctor** column. Subjects such as retinoids, employment disabilities, diet therapy, etc. are already on the table for discussion in the new column.

The Medical Advisory Board also expressed enthusiastic support for keeping the international ichthyosis computer registry project alive and well. The Board created a special subcommittee to keep the project on track in 1984. All NIF members who have paid their dues will receive a questionnaire asking for basic information, which will then be coordinated to create the broadest database on ichthyosis available for research. The system will initially be developed on an IBM PC with 640K RAM and 2 DD/DS drives. The data will be managed by dBase II, a powerful program by Ashton-Tate, Inc. Eventually, we hope to transfer the data to a larger computer as more

information is available and used by researchers all over the world.

The Board was excited about the new National Institute of Health that is being created by Congress. This will be the first time a national Institute will really focus on research on skin diseases, such as ichthyosis, in addition to arthritis and other health problems. We are all hoping the leadership of the new Institute recognizes the need for a closer "focus on ichthyosis." One of my jobs in the NIF, of course, is to keep abreast of this legislation, and offer support wherever possible.

Following the MAB meeting, nine members of the Board made presentations at the First National Conference. The audience response was terrific, and it was no surprise. Our Board is comprised of the top dermatologists, educators and researchers in the country, all actively working on ichthyosis. Those in attendance were able to hear the latest news directly from the source. (Those who couldn't make it to the Conference and Workshop will be reading the news in future editions of the newsletter this year.)

Each of the MAB members who

Ask the Doctor



By Lawrence Schachner, M.D. (Dr. Schachner is Professor of Dermatology at the University of Miami School of Medicine. A member of our Medical Advisory Board, he is a prominent researcher in the study of ichthyosis.)

1. Q: Are there any topical creams that could be used to control severe hyperkeratotic conditions on the palms of hands and bottom of feet that would result in decreasing the dosage of 13-cis Retinoic Acid (Accutane)?

A: The goals of topical therapy in hyperkeratotic conditions usually involve two principles: (1) increasing the water content of the epidermis; (2) promoting the loss of scale from the epidermis. Numerous formulations exist that can accomplish either one or both of these goals, and, in doing so, contribute to the management of ichthyosis. The more successful these topical therapies in a given patient, the greater the opportunity to decrease the amount of Accutane, the duration of therapy, and even the necessity of utilizing this potent medication at all.

Among the many formulations that promote scale loss are: (A) salicylic acid; (B) lactic acid; (C) urea; (D) propylene glycol; (E) Vitamin A preparations.

Many practitioners find that in the early evaluation of therapeutic efficacy for each individual patient, it may be useful to try a number of these medications simultaneously. This could be accomplished by having salicylic acid put on one hand, urea on another, Vitamin A on one foot, etc. If the patient continues to treat each extremity with the designated

medication, then, at the end of several weeks time, it becomes clear which of the preparations may be best for this given patient.

The use of lubricants such as petrolatum based products aquaphor, eucerin, etc. improves the moisture content of the epidermis, giving it greater pliability and freedom of motion; again these products may be used in combination with the products that promote scale loss, and can even be compounded together by the pharmacist. The successful use of emollients and keratolytics can obviate the need or decrease the dosage and duration for systemic retinoid use.

2. Q: What is the role of Accutane in X-Linked Ichthyosis?

A: The greatest experiences in ichthyosis vis-a-vis Accutane therapy have been in lamellar ichthyosis, epidermolytic hyperkeratosis and Darier's disease, rather than in x-linked or ichthyosis vulgaris. Most people with these disorders find that Accutane begins to work after several weeks time and an appreciable effect may be noted by four to six weeks. I have not personally used Accutane in x-linked ichthyosis, or in ichthyosis vulgaris, nor do I know of any colleagues who have treated x-linked ichthyosis in large numbers with Accutane. I think that your letter relating the efficacy of the summer months and the salt water in your disease reinforces the benefits of moisturization and humidity. I feel many patients with x-linked ichthyosis can benefit from active use of lubricants and scale promoting agents. In the above letter we have reviewed many of these products and mechanisms by which they may be employed. As for the side effects you asked about with the use of Accutane, some of the list includes: (1) elevation of triglycerides, hence increase in serum fats in some patients; (2) joint and muscle pain and injury in some patients; (3) fetal malformations if used by females in pregnancy; (4) increased pressure on the brain (called pseudo tumor cerebri); (5) eye change (corneal opacities); (6) inflammation of the bowel; (7) chafing and

dryness of the skin, lips and eyes. Certainly many of these side effects represent mild or transient problems, however, the potential for long-standing and severe problems related to the use of this medication exists. It must be reiterated that this is a strong and serious medication that requires good judgment in its use and its monitoring during therapy. I must strongly recommend that patients with ichthyosis and disorders of keratinization utilize the strongest of topical preparations, that may be safe and effective, before starting a trial of Accutane.

Correspondence

A note for the strangers in the street:
I owe you nothing for my existence
raw, coarse questions concerning my
handicaps and my sex life belong to you
not me

I know you at a distance
I know exactly when to walk away and
when I need to run
I am tuned in to you

Know that you have taught me well
Then dare look me eye-to-eye
recognize my differences
and my equality

it **can** happen
just like an eclipse of the sun
can happen

and when it does happen
that is beauty

By Julie Martinez, New Jersey

The annual meeting of the American Academy of Dermatology and the National Ichthyosis Workshop was not only enlightening, but also exhausting—so much to comprehend in too little time.

We were privileged to represent the **National Ichthyosis Foundation**. The Foundation's table was surrounded by elaborate booths and displays of pharmaceutical companies who exhibited at the meeting, which was attended by several thousand physicians. We were able to distribute the Foundation's newsletter and to inform that Chapters do exist, which was of great interest to one physician especially. He took many of the newsletters to show his patients what the Foundation has accomplished.

Many physicians had at least a few patients with Ichthyosis. . . Lamellar

(cont'd on p. 5)

and Epidermolytic Hyperkeratosis were mentioned more than other forms. Questions were asked of us when we mentioned our daughter being afflicted with Ichthyosis (what treatment works best, how severe a case, and if any other conditions existed).

During the Ichthyosis Workshop, we were educated on various treatments and research by the Foundation's Medical Advisory Board. Much of what was discussed, we are already aware of (Typical Treatments, Accutane and its side effects), but it was refreshing to hear what is being done by those who are directly involved.

Susan Nye chaired a discussion on psychological problems. Charles Eichhorn contributed both professionally and personally, as did others with Ichthyosis, parents and grandparents.

Our special thanks to Susan, Charles, and Jeannette for the MANY hours of work for the Foundation. In our opinion, the Workshop was a success; we only wish more could have attended.

Soon, we hope to form a Certified Chapter.

Carol and Dick DeLoughary,
Michigan

January 17, 1984

Dear Susan:

Just wanted to pass along some information on some results I have had due to attending the Ichthyosis Seminar in Chicago in December.

As you remember, Dr. Van Scott of Philadelphia spoke and showed some slides of Ichthyosis. He also spoke of some acid type creams that are showing some results. I made an appointment and went to see Dr. Van Scott on December 19, 1983. He gave me 6 different lotions to try on various parts of my arms. Amazingly, in just 3 days, one of the lotions began to make me peel, a second began to work in 5 days, a third in 8 days and a fourth in 2 weeks. Only one of these is on the market and available for purchase. It is called Aqua Glycolic Lotion and contains 5% of Glycolic acid. This lotion has my legs clearer than they have ever been except for when I have tanned and cleared up from sunshine (sunshine clears my type of ichthyosis "x-linked"). I am now using the lotion on my arms and legs and although this is not a cure and I do have light peeling every few days, the appearance and comfort of the skin is almost normal. The lotion can be purchased direct from

Herald Pharmacatal in Richmond, Va., if it is not available locally. The Ichthyosis Seminar and Dr. Van Scott have done more for my skin problems in the last month that I have been able to do in my 45 years of life.

I told you with my x-linked ichthyosis sunlight clears me so I'm still using a sun booth and I haven't tried the lotion on my body as that is clear but I don't see why it wouldn't work as it's working everywhere else I have applied it.

There is a slight redness of the skin from the Aqua Glycolic Lotion as there was from all the creams I tried that Dr. Van Scott gave me but I now only apply it once a day after an evening shower and in the morning I rub baby oil over my body. I was applying it three times a day to start and cut back as I cleared. Anyone who has any questions can certainly call or write me.

Sincerely,
Joe Galluccio
1408 Williams Dr.
Belmar, New Jersey 07719
201-781-6824

NOTE: If you have a remedy that has worked for you, please pass it along and we'll put in in Ichthyosis Focus.

Helen Tomalesky's Story



Helen Tomalesky with her family: husband, Stan, and daughters Tammy, age 10, Lisa, 4½, and Jennifer, 3.

Forty years ago, I came into the world as a five-pound "cellophane wrapped" baby girl (the doctor's description of my appearance). My skin gradually dried and thickened into scaly layers. My skin was thickest on my scalp, palms and soles. The skin on my scalp was so thick that hair growth was prevented. When I moved, my skin would crack and cut into my joints.

In addition to the extreme keratin build-up and constant shedding, my skin was continuously red with inflammation. Dealing with heat was a major task because I could not sweat. As a child, I viewed my skin as suit of armor that I could not remove and held me prisoner against my every attempt to get free. I escaped social ostracism by withdrawal. My elementary teachers

called my escape day-dreaming. Fortunately, I was born with a talent for music which I used to reduce stress. I expressed all my anger, frustration, and happiness through my music. My music was like a living friend to me who understood and allowed me to gain emotional release.

My life was punctuated by numerous visits to numerous doctors. When I was 7, I was treated at Jersey City Medical Center for a period of 7 weeks with a wonder drug of the time called ACTH. Cortisone injections were also used. I was discharged with some improvement, a prescription for cortisone pills and a recommendation to use Vitamin A&D ointment. I kept this treatment up until my teenage years, when I started to use a variety of prescription creams and oil baths.

At age 21, with plans for marriage, I visited Dr. David Bloom of N.Y.C. with my fiancé for genetic counseling. After an examination and an interview with my fiancé and myself, we were told that, since my fiancé was normal and his family is free of any such anomaly, there was little chance that any of our offspring would be affected. Although our children would be normal, they would be carriers of the trait.

In retrospect, of all the topical creams I have used, the one I found most effective was prescribed by Dr. H. Rosenbaum of Waterbury, CT. The cream consisted of 5% glycolic acid in a eucerin base. Until this time, no other preparation created elasticity in my skin

and retarded the drying-out process. Dr. Rosenbaum not only provided the best treatment I had experienced to date, he also told me about the Accutane — Lamellar Ichthyosis study headed by Dr. J. McGuire at Yale University's School of Medicine. Since I no longer wished to increase our family, I started taking the Accutane treatment in December 1981. The total effect of this drug on my problem was astounding. Accutane treatment was a turning point in my life.

With three energetic young children and a husband that travels, time is very important. Accutane saves me a substantial amount of time. Instead of a daily oil bath followed by a shower and frequent expensive cream applications, I now need only a daily shower and vasoline or eucerin. Accutane saves me at least one hour of the time I used to spend trying to keep my skin soft and comfortable.

My favorable response to Accutane does not require high doses. I take 80 mg./day and experience minimal side effects. As far as the risk/benefit ratio is concerned, the benefits far outweigh the risks, from my point of view.

I've come a long way from that cellophane-wrapped, pathetic baby girl of 40 years ago and hope that by sharing my thoughts and medical experience, I may help someone else.

Sincerely,
Helen M. Tomalesky,
Plantsville, CT

shared their time and knowledge so generously has received a Certificate of Appreciation from the Foundation, but a piece of paper can never express our respect and gratitude for the true gift we all received that day.

The afternoon of the Conference gave Susan Nye and me a chance to share ideas and suggestions with NIF members as conference participants from all over the country. (See "State of NIF" article.)

On Monday, December 5, 1983, representatives from most of the major skin disease foundations (including yours truly) attended the inaugural meeting of the Patient Advocate Group in Chicago. Before I report on the meeting, here's a little background.

Non-profit organizations like NIF cannot become too involved in politics, or they may lose their tax exempt status. That doesn't mean a limited proportion of our time and resources cannot be

used for lobbying, etc., however.

The Patient Advocate Group has been created to make the most of the limited political efforts IRS allows the skin disease organizations in the U.S. By coordinating our efforts, we can have a louder voice.

The first meeting was quite a success. We agreed to work together, and reviewed the status of the new Institute. Most of the group will meet again in Washington, D.C., around April.

The First National Conference December 1983 — Chicago, Illinois



Charles Eichhorn smiles for the camera.



Jeannette Jensen and Betty McMasters get the materials together.



Lowell Goldsmith, M.D., Chairman NIF Medical Advisory Board, and Charles Eichhorn listen intently.

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Thanks.

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The National Ichthyosis Foundation is a charitable organization. All the money collected by it will be used for charitable purposes, such as education, counseling, and ichthyosis research. The organization's major expenses are mailing its newsletter and printing educational material. Articles of incorporation as a non-profit organization have been approved by the California Secretary of State and its Tax Exempt Status has been approved by the California State Franchise Tax Board. All contributions to the organization are deemed tax-deductible under both California and Federal Law.

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