

THE USA IP SUPPORT GROUP

Anne K. Ryan

Please allow me to introduce myself and invite you to join my newly founded USA IP Support Group based out of upstate New York.

First, let me tell you about me and why I had to take on this labor of love. My name is Anne Ryan and simply stated, I am a mom. I have a wonderful husband, a beautiful 2-year-old daughter Willow, and a blessing of another daughter, 9 month old, Kateri. Kateri was born in August, 2002. She was diagnosed with IP within one week of birth. I can still feel the fear and hear the words as the doctor read me pages off the Internet on what *incontinentia pigmenti* was. I have never in my life felt so alone. There was no one to sympathize with the grief my entire family was feeling and I knew that someday I had to do something to help.

My background before being a full time mom was in the medical field as an Office Manager/Lung Transplant Coordinator for a pulmonary practice. My husband works two, yes two, full-time jobs to enable me to be home with the girls. He is a Youth Division Aide at a Maximum Secure Facility for Juveniles, and a Personal Fitness Trainer. We are short on time with one another, short on money, but rich with love. Our children are our life, and outside of them, nothing else matters to us. I am also a professional singer and actress, and hope to be cutting a demo CD this summer.



Anne K. Ryan and Kateri (continued on page 2 col. 1)

INCONTINENTIA PIGMENTI: A

NATURAL HISTORY STUDY

COMPILED FROM PATIENT

REPORTS

Ashley Badgwell, MS and

Judith P. Willner, MD

For the past year, a research project to

better document the natural history (symptoms and clinical course) of IP has been underway at the Mount Sinai School of Medicine. Because the types of symptoms and their severity vary greatly among affected individuals, even within the same family, the prognosis is difficult to predict. The last large-scale clinical study of IP was in 1976. As familiarly with this disorder has increased among physicians, milder cases of IP have been described. Based on the cases seen in our practice, we suspected that the more severe cases might be over-represented in the literature. We felt a revised natural history of IP was called for. This is particularly timely since, with the recent DNA-based testing allows confirmation of diagnosis in milder cases.

Dr. Judith Willner, Director of Clinical Genetics at Mt. Sinai, and I, then a graduate student in Genetic Counseling, proposed to compile a natural history of IP based on patient and physician reports. We developed a six-page questionnaire, consisting of questions regarding patients' family histories and medical histories relevant to IP. It was translated into four languages. With the assistance of Susanne Emmerich of IP!F, it was sent to all members of IP!F and posted on the IP!F website. We had received 152 completed surveys by March when the initial analysis was performed. Completed questionnaires have continued to arrive, and we plan to update the analysis continually. We are very grateful to all those who participated.

Because the report on our findings is almost 30 pages long, it is not possible (continued on page 2, col. 2)

LETTER FROM THE EXECUTIVE

DIRECTOR

In each of the previous newsletters I have made an effort to include articles on subjects that are likely to be among the most important issues facing people with IP. Presently one of the most eagerly awaited is the result of the questionnaire that was sent out on the natural history of IP. This tried to determine the frequency of specific symptoms experienced by those with IP. A subject that is always uppermost in the minds of women with IP who are contemplating having children, and of women who are wondering what the consequences will be for the children of their daughters with IP.

Although you will read that 700 questionnaires were mailed out, please keep in mind that many went to families with several members with IP, and to physicians who have many patients. The questionnaire is also posted on the web site and was read and filled out by many more individuals (exactly how many we have no way of knowing). Therefore the number 700 really represents many more people. As the identification of patients was coded, we don't know how many people actually (continued on page 2 col. 1)

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Letter from Executive Director

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responded from each of the categories. The most important fact to keep in mind when reading the article is that it represents a very small sampling of patients with IP, and was answered only by people who have been diagnosed with IP. There is no way to determine how many have extremely mild symptoms, and have never been diagnosed but it can safely be assumed the number is in the thousands. Although the awareness of IP has been heightened by the identification of the gene, there are a great many babies born who are misdiagnosed. This still occurs frequently in many very advanced medical facilities in major cities around the world.

For the results to be truly meaningful it is necessary for us to continue to send out the form, and continue to record the results for many years to come. I would urge everyone who did not return the questionnaire to please do so. As a result of the identification of the gene causing IP, many women who have IP now have reproductive options that were unavailable previously. This newsletter includes articles describing some of these.

There is news about support groups as well as other topics of interest. If you have any suggestions as to what you would like me to include in subsequent issues, please let me know.

IP Support Group
(continued from page 1)
In January, 2003, I began a website telling of my story, and creating a forum for families to get in touch with one another. We have a chatroom, a message board and a photo gallery. The website is a free one that I maintain myself, so it is bare bones, but serves the purpose. My mission is to connect families with other families via email, snail mail or phone. I ask all families to "register" with me by filling out a simple form asking questions about their experience with IP. I enter them on to a spreadsheet with a brief summary of their loved one who has IP. This way, when someone asks to be connected to a similar family situation, I can easily do so. Most of my announcements etc. will be posted either on the website or published in the IP Newsletter, since I will work in conjunction with the IP International Foundation. My goal is to support, not advise.

My response up until this point has been very small simply due to the lack of exposure to IP families. My hope is that, after this newsletter, I will receive more interest and be able to better grow

Demographics of Participants

The participants were from different backgrounds, as IP is a condition that affects all races. While the majority of responses were received from within the United States, responses were also received from 14 other countries. Almost half of the participants were Caucasian. Other ethnic groups represented were Asian, Hispanic, Middle Eastern and Native American. All but one of our participants was female. One case of a male affected with IP surviving to term, but dying after 7 days, was reported. The age range of the participants in the study was large. The oldest person represented was 77 years old at the time of survey completion, and the youngest girl was 10 months old. There was a fair distribution across the age groups. 43% of patients surveyed reported at least one other family member with IP. Questionnaires were received from multiple members of 18 families.

Although the average age at diagnosis was calculated as 3.4 years, the range for age at diagnosis was large. The majority (68%) were diagnosed by 3 months of age (20% "at birth"), but some were not contacting IPIF.

The frequency of red or grey colored patches consisting of skin was found to be 79%, compared with 96%-98% which was previously reported. Age was taken into account: 37% of patients, over the age of 10 reported that this discoloration is still present, and of those who no longer have discolored areas, the average age of disappearance was 13.5 years. Recurrences were rare. 79% experienced these pigmented areas on their arms and legs, but other areas of the body were also affected.

68% of patients surveyed reported the fourth stage. In this stage, light colored areas of skin and hairlessness occur. 49% of the patients over the age of 10 reported that these light spots are still present, and of those who no longer have light spots, the average age of disappearance was 21.5 years. Recurrences were rare. The majority (81%) experienced light areas on their extremities. Only 20% of patients reported having a Wood's lamp exam to observe subtle depigmentation.

Skin Involvement

Of the participants, 95% reported having experienced the first stage of the newborn rash, consisting of small red bumps and blisters. The average age that the first stage disappeared was found to be 17 months. The average number of outbreaks is two. 94% of patients experiencing this stage reported that the rash was on their arms and legs, and 54% also reported the initial rash on their stomach, groin and scalp.

Of the participants, 65% said they experienced the second stage of the rash, consisting of dry, rough wart-like sores. The average age of disappearance is 21 months. For patients who experienced a recurrent rash, the average number of recurrences is two, but this number may be misleading as 20% of patients reported "several" recurrences.

81% experienced this stage on their arms and legs. Other body parts were also affected, but in smaller percentages. The frequency of the third stage, consisting of red or grey colored patches of skin, was found to be 79%, compared with 96%-98% which was previously reported. Age was taken into account: 37% of patients, over the age of 10 reported that this discoloration is still present, and of those who no longer have discolored areas, the average age of disappearance was 13.5 years. Recurrences were rare. 79% experienced these pigmented areas on their arms and legs, but other areas of the body were also affected.

66% of patients surveyed reported having bald spots. Of those who reported (continued on page 3 column 1)

Scalp/Hair Symptoms

between brain abnormalities seen on CT and MRI brain function.

Genetic Test Results

Chromosome analysis was performed on 21% of patients. All reported normal female chromosomes (46,XX). Of those who had undergone DNA mutation testing and knew the result of the test (32% of total surveyed), 84% had tested positive for the common NEMO mutation, and 16% had tested negative for the common mutation. Of the 4% who had participated in linkage studies, linkage was informative in 63% of breast growth. Four (2%) patients described breast asymmetry.

Breast Symptoms

Breast abnormalities have been associated with IP. Extra nipples were reported in 3.4% of patients. Four patients reported having one extra nipple, and one patient reported having two extra. Two patients described lack of breast growth. Four (2%) patients described breast asymmetry.

CNS Involvement

Central Nervous System disorders present the greatest threat to a normal life for IP patients. CNS involvement can range from spastic quadriplegia and mental retardation to seizures. Altogether, 43 patients, (28%) reported CNS involvement. This is comparable to the frequency (30%) suggested by previous studies. However, this number may be misleading as 85% of patients surveyed have normal development, with the frequency of each CNS disorder is as follows; learning disabilities were reported by 12.8%, a brain abnormality detected by CT scan or MRI was reported by 11.2%, newborn seizures were reported by 9.3%, mental retardation was reported by 7.6%, an IQ less than 70 was reported by 7%, cognitive delays were reported by 6.8%, spastic paralysis was reported by 4.6%, microcephalus (abnormally small head) was reported by 4.5%, motor delays were reported by 3.8%, hemiparesis (paralysis on one side) was reported by 2.7%, and hearing loss was reported by 1.3%. Some patients experienced more than one CNS disorder.

It has been suggested that IP patients who experience newborn seizures are likely to have a poor prognosis. However, in this study, only slightly over 50% of patients who experienced seizures reported another CNS disorder. Of the 15 subjects who reported a brain abnormality detected by CT scan or MRI, 10 (67%) reported experiencing mental/motor delays or retardation and 9 of the subjects (60%) ophthalmologic problems including strabismus, retinal detachment, cataracts and blindness. Only 2 of the 15 with a radiologically detected brain abnormality did not have ophthalmologic problems or neurologic impairment. The average age of diagnosis of a brain abnormality was 6 years. The types of brain abnormalities observed included abnormal myelination and mild left cerebral hemispheric atrophy. Larger numbers of patients are needed to understand the association

with regard to family history and pregnancy loss, it was interesting that 9% of unaffected mothers of daughters with IP reported multiple miscarriages. 55% percent of the miscarriages reported were by mothers whose IP status was unknown or reportedly negative. A third of these women had more than one daughter with IP. It is possible that these mothers unknowingly have very mild IP, or they have a mixture of IP and non-IP cells. Clearly, DNA mutation testing of mothers of IP girls would resolve this question and provide more accurate risk assessment for genetic counseling.

Conclusions

There are limitations to a patient-reported study, but we were able to obtain (continued on page 4 column 1)

IP Natural History

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these hairless patches, 94% had a bald area at the crown of the head. It is likely that the hairless spots follow the rash and are associated with scarring. 38% reported wiry patches of hair on the scalp.

Nail Symptoms

51% reported ridged or otherwise misshapen nails. Additionally, 9% reported experiencing tumors under their nails.

Dental Symptoms

Dental involvement was reported in 95% of our patients. Of the patients over the age of 14 years, 29% reported the continued presence of baby teeth. 56% of patients reported that their baby teeth were late coming in, and 53% of patients reported their permanent teeth were late coming in. 60% had baby teeth that never came in and 78% had permanent teeth that never came in. The average number of missing baby teeth is four and the average number of missing permanent teeth is five. About 66% of patients had baby and/or permanent teeth shaped like pegs or cones, and 18% had an abnormal amount of decay.

Eye Problems.

In order to analyze the ocular findings, it is necessary to compare the occurrence of eye problems in IP with that in the general population. In this survey, 12% of IP patients reported strabismus "cross eyes" or "lazy eyes". This is 3 times greater than that observed in the general population (4%). Bilateral blindness was also reported in 4% of our patients, almost 6 times greater than that seen in the general population (0.7%). Congenital cataracts were seen 30 times more in our patients (6%) than in the general population (0.2%), and retinal detachment was seen 27 times more in the general population (8%) than in the general population (0.3%). For other eye abnormalities associated with IP such as problems with the veins of the eye, no general population risk could be found. Based on our findings, IP patients are not more likely than the general population to suffer from astigmatism, myopia, amblyopia or obstructed tear ducts.

Skeletal Symptoms

Skeletal abnormalities found in previous studies were thought to be coincidental, not likely to be associated with IP. In this study, patients were asked to write in any skeletal problems. Altogether, skeletal anomalies were reported by 15% of patients. Nine patients (6%) reported scoliosis (curvature of the spine) but did not mention if intervention was required.