



International PC Consortium

Pachyonychia Congenita Project

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HAPPY VALENTINE'S DAY. You definitely are sweethearts and we love you dearly. Have you ever wondered why our logo for Pachyonychia Congenita Project (a skin disorder) is a heart? Well, it's because our project is all about LOVE. There's no other reason for anyone to give time, talent and funds to this effort. So every February, as gifts and candy and flowers are exchanged between loved ones, we think of you. The history of Valentine's Day -- and its patron saint -- is shrouded in mystery. But it is no mystery why you are so special. Thank You—With Love, Mary

IPCRR 2004 to 2007

The International PC Research Registry (IPCRR) received IRB approval in May 2004. At that time, we knew of 4 PC patients. In this Newsletter, we are sharing data from the registry that has been gathered in these months. In addition, we asked Dr. Sancy Leachman to write a personal report of her experiences in meeting or speaking with 125 PC patients. We hope this will be of interest and benefit to the IPCC members.

PC Patients: A Physicians Perspective

Sancy Leachman, MD, PhD

On this third year anniversary of the IPCRR, I thought I would share some very informal thoughts about what I have learned about Pachyonychia Congenita. First, I must acknowledge that I have been taught a lot by PC patients! Over the past three years, I have held telephone consultations with 125 PC patients (who have submitted an extensive 44-page questionnaire and photos). Of these patients, I have met personally with approximately 60, and have had close interactions on a regular basis with 10 PC patients. This experience has not only humbled me (to begin to appreciate the hurdles these patients face on a daily basis), but has also enriched my understanding of the disease manifestations and social issues associated with PC.

Many PC patients have “given up”

on doctors and the medical system. They have been to many physicians, often many dermatologists, without finding a strong advocate. They have attended grand rounds, with great hope and expectation that the “best minds” in the region would be able to offer better advice, not realizing that often, the primary reason for the visit is education of the physicians and residents on a rare disorder. Many times, the patients do not receive a follow-up call to let them know the consensus from the grand rounds conference. Their experience is one of great disappointment, and eventually one of hopelessness that the medical community will ever be able to help.

Most patients have been given numerous prescriptions for different medications (again, with hope that *this* medicine will work) only to find that the drugs have little or no effect and frequently sting or burn—or have unacceptable side-effects.

One patient traveled from out of the country to be seen at one of our country's premier medical institutions to be told that perhaps she should attempt skin grafting of her feet. This was done, but the PC persisted. The patient continues to have disabling plantar pain.

Several patients have had a very difficult time convincing their physicians or care giver that their condition is not fungal. Once persuaded that the condition is genetic and non-infectious, then when I speak with the physician, I have found it is frequently difficult to convince them that a secondary infection might be occurring.

Of course, these stories are also accompanied by tales of health care providers that have gone more than an extra mile for these patients. Some who are willing to be available at any time for the patient with an infection, others that have arranged for incredi-

UPCOMING IPCC MEETING Wednesday May 9, 2007

Los Angeles, CA. The IPCC Annual Meeting will be held on Wednesday, May 9 as an ancillary meeting with the SID.

IPCC Focus Group June 15-16, 2007

Park City, UT. The IPCC and PC Project MSAB have identified a need to have a three-year follow up symposium to assess progress and set the next objectives for the IPCC and PC Project. NOTE: The IPCC Focus Group meeting will follow the PC Patient Support Meeting which will be June 12-14 in Park City, Utah. For those able to participate, PC Project is sponsoring a ‘western adventure’ trip to Southern Utah and the Grand Canyon following the Focus Group meeting. If you would like to participate in these meetings, please contact Mary.Schwartz@pachyonychia.org or phone at 877-628-7300. All are welcome to participate but reservations made in advance with PC Project will be most helpful. Thanks.

ble home health care.

However, the most common situation is that PC patients, often struggling to keep their heads above water with family and work obligations, end up surviving by being self-sufficient. They learn to do their own grooming, learn how to incise and drain their own cysts and blisters, learn which physicians will call in a prescription for an antibiotic without requiring an office visit, and frequently acknowledge self-medication with alcohol or prescription medications to be able to function effectively with their pain.

Many do not have a primary caregiver that they rely upon. Although it is quite easy to see how and why providing care to these patients is difficult in our medical system, it offers little solace to the needy patient. We need to do better in caring for patients with rare disorders. It has been moving for me to see how the PC patients involved with PC project have been empowered and have blossomed through the nurturing hand of the organization.

Because of the chronic, disabling nature of PC, many PC patients cope with their lives through denial. It is not infrequent for patients to say, PC is “only impacting my life at a level of 1 on a scale of 1-10” or that they “have no limitations because of PC.” But in the next few minutes they go on to detail how they have lost jobs because of their inability to do the walking required, have been on antidepressants because of their PC, or even have undergone elective sterilization because “they couldn’t bear to bring another person into the world who would have to suffer as they did.”

Their denial is very effective. Because everything is “really all right,” they get out of bed in the morning with pain, they make it to their job and function with humor, they divert suspicious looks from strangers with all types of imaginative stories, they shop in stores that are smaller or have convenient parking, and they often collapse in the evening without completing all the tasks on their list because

they just can’t walk any further.

There are many commonalities between PC patients that I have seen over the last three years. For example, secondary infection is a major problem for PC patients. Sometimes, sterile blisters form on the feet or around the nails that only require drainage to provide relief, but secondary infection often occurs.

When an adult PC patient schedules an appointment with a physician, there is something unusual going on — a PC patient would rarely have time, energy, or reason to see a Dr. unless something above and beyond their normal pain was going on.

I’ve learned the tip-offs for secondary infection, increased pain, worsening callosities, especially with the keratoderma crawling up onto the dorsal aspect of the foot or between the toes. Frequently patients have red lymphatic streaks, fever, chills, etc. Often the infection seems to be polymicrobial, frequently both bacterial and fungal. A few careful physicians will perform a culture or start a combination bacterial/fungal regimen without the patient having to return several times and without the patient reaching a point where hospitalization is needed. Some physicians have had great success with a combination topical regimen of anti-fungal, antibiotic, and low potency steroid.

Another commonality is the need for some level of social help or proof of disability for PC patients. Disability is a difficult concept for many PC patients; they are very independent and do not want to admit the need for help, but getting appropriate help is essential. Some patients only need a handicapped parking sticker, others need some workplace accommodations, and others require full disability because of the severity of their PC. Getting disability is much easier because of the genetic testing we have provided to these patients. It has been very rewarding to work with PC patients to help them get what they need to make them productive.

Finally, the spectrum of disease, even within patients with a known mutation is dramatic. I have learned that the statement that we “can tell by clinical phenotype which patients are PC1 and PC2” is not always true.

Most PC1 patients who are “not supposed to have cysts” do have cysts, and some are very dramatic, requiring multiple surgical procedures under general anesthesia. Conversely, some PC2 patients do not have cysts. The keratoderma in PC patients varies from confluent to almost non-existent, and many PC patients do not have involvement of all of their nails. Many PC patients experience a “deep itch” that has never been reported in the literature to my knowledge – and they frequently go to great lengths to find something to “scratch that itch!”

With the help of PC-Project, we have developed an incredible clinical resource – one that both patients and health care providers can utilize. For instance, parents love the “Back to School” brochure that tells their children’s teachers that the condition is not contagious, and helps teach the teachers how to advocate for PC children. Dermatology residents who need help with assessing their patients and arranging genetic testing have used us as a resource. Home health care providers who have no idea what to do for a homebound PC patient have received free consultations.

Overall, we have a long way to go before PC patient care is everything we want it to be, but we are on our way. Because of PC Project and the IPCC, the last three years have seen a trend for the better, at least in the few lives we have been able to touch.

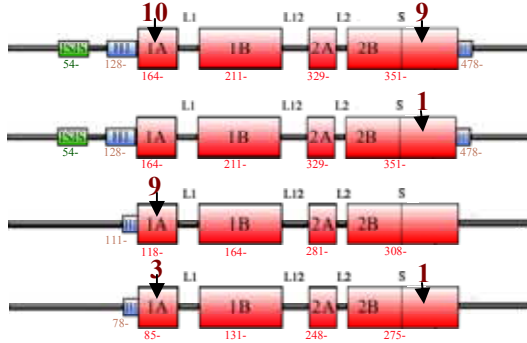
Thank you, every IPCC member, for your selfless efforts on behalf of these admirable and struggling patients.

News Flash—the pre-IND meeting request has been filed with the FDA to begin the drug approval process for our first siRNA.



IPCRR has genetic test results for 116 individuals in 56 families with 33 unique genetic mutations

International PC Research Registry Statistics as of 31 January 2007



K6a	57%
K6b	3%
K16	29%
K17	11%

Since May 2004, we have identified **389** PCers located in **27** countries around the world. We have current contact information for **377**. **133** individuals have joined the registry and we have created a database with all of the information from the questionnaires and from the consultations Sancy has conducted with each patient. We are preparing this to share with you.

Some of the **116** PCers with known mutations have not yet provided the valuable questionnaire data or participated in the clinical consultation. Of the **133** in the Registry, there are **75** PCers in **54** families who have (1) a confirmed genetic mutation in K6a, K6b, K16 or K17 (2) completed a questionnaire (3) had a physician consultation. These 75 patients provide the most reliable information on pachyonychia congenita, on the effects of PC on their life, their style of care, and the signs prevalent for them. We've updated the JID tables with data from these 75 PCers.

Location	#	Location	#
ARGENTINA	1	USA-CT	3
AUSTRALIA	13	USA-FL	3
BRAZIL	4	USA-GA	1
CANADA	21	USA-IA	2
CHINA	1	USA-ID	1
DENMARK	1	USA-IL	7
ENGLAND	27	USA-IN	1
FINLAND	2	USA-KS	2
FRANCE	12	USA-LA	1
GERMANY	2	USA-MA	3
GUATEMALA	1	USA-MD	6
HONDURAS	1	USA-MI	1
INDIA	1	USA-MN	8
INDONESIA	1	USA-MO	3
IRELAND	6	USA-MS	1
ISRAEL	1	USA-NJ	5
ITALY	1	USA-NY	26
MEXICO	2	USA-OH	15
NORWAY	1	USA-OK	9
PAKISTAN	1	USA-OR	7
SAUDI ARABIA	1	USA-PA	7
SCOTLAND	5	USA-SC	10
SOUTH KOREA	1	USA-SD	1
SPAIN	9	USA-TN	9
SWEDEN	7	USA-TX	15
NETHERLANDS	15	USA-UT	12
USA-	37	USA-VA	9
USA-AR	1	USA-WA	11
USA-AZ	4	USA-WV	1
USA-CA	25	WALES	1
USA-CO	1	TOTAL	389



IPCRR¹ With Known Genotype N = 75 by Gene

	K6a N = 42	K16 N = 18	K6b N = 9	K17 N = 6
Phenotype				
Toenails (any)	42 of 42 (100)	17 of 42 (40)	9 of 9 (100)	6 of 6 (100)
Fingernails (any)	42 of 42 (100)	16 of 42 (38)	3 of 9 (33)	5 of 6 (83)
Plantar Pain	39 of 42 (93)	17 of 42 (40)	9 of 9 (100)	5 of 6 (83)
Plantar keratoderma	40 of 42 (95)	18 of 42 (43)	9 of 9 (100)	6 of 6 (100)
Oral Leukokeratosis	41 of 42 (98)	13 of 42 (31)	1 of 9 (11)	3 of 6 (50)
Palmar keratoderma	22 of 42 (52)	15 of 42 (36)	3 of 9 (33)	4 of 6 (66)
Follicular keratoses	37 of 42 (88)	3 of 42 (7)	4 of 9 (44)	4 of 6 (66)
Cysts (any type)¹	38 of 42 (90)	5 of 42 (12)	6 of 9 (66)	6 of 6 (100)
Larynx (hoarseness)	20 of 42 (48)	0 of 42 (0)	2 of 9 (22)	1 of 6 (16)
Hyperhidrosis	32 of 42 (76)	16 of 42 (38)	9 of 9 (100)	3 of 6 (50)
Hair abnormalities	9 of 42 (21)	6 of 42 (14)	1 of 9 (11)	4 of 6 (66)
Natal/prenatal teeth	0 of 42 (0)	0 of 42 (0)	0 of 9 (0)	2 of 6 (33)

¹ One registry finding is the prevalence of cysts in PC I patients (K6a and K16 mutations) and that not all PC II patients have cysts.

IPCRR with known genotype N=75 by Mutation Site

Phenotype	1AHIMb (N= 50)	2BHTMb (N= 25)
Toenails (any)	49 of 50 (98)	25 of 25 (100)
Fingernails (any)	48 of 50 (96)	18 of 25 (72)
Plantar Pain	46 of 50 (92)	24 of 25 (96)
Plantar Keratoderma	49 of 50 (98)	24 of 25 (96)
Oral Leukokeratosis	42 of 50 (84)	16 of 25 (64)
Palmar Keratoderma	27 of 50 (54)	17 of 25 (68)
Follicular Keratoses	31 of 50 (62)	17 of 25 (68)
Cysts (any type)	34 of 50 (68)	21 of 25 (84)
Larynx (hoarseness)	10 of 50 (20)	13 of 25 (52)
Hyperhidrosis	39 of 50 (78)	21 of 25 (84)
Hair abnormalities	14 of 50 (28)	6 of 25 (24)
Natal/prenatal teeth	1 of 50 (2)	1 of 25 (4)

Percent of patients with phenotypic symptoms

Phenotype	IPCRR (N=75)
Toenails (any)	74 of 75 (99%)
Fingernails (any)	66 of 75 (88%)
Plantar Pain	70 of 75 (93%)
Plantar keratoderma	73 of 75 (97%)
Oral Leukokeratosis	58 of 75 (77%)
Palmar keratoderma	44 of 75 (59%)
Follicular keratoses	48 of 75 (64%)
Cysts (any type)	55 of 75 (73%)
Larynx (hoarseness)	23 of 75 (31%)
Hyperhidrosis	60 of 75 (80%)
Hair abnormalities	20 of 75 (27%)
Natal/prenatal teeth	2 of 75 (3%)

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