VHL Family Forum

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Pregnancy and von Hippel-Lindau

By Yasser Y. El-Sayed, M.D., Assistant Professor, Division of Maternal-Fetal Medicine, Dept. of Gynecology and Obstetrics, Stanford University. From his talk at the VHL Conference, Palo Alto, June 2001

When Dr. John Adler first asked me to speak about pregnancy and VHL and I started to research the topic a little bit, the first thing that struck me is how limited the data really was. There are essentially only case reports in the literature, which makes it very difficult to come up with any cohesive message to give to patients. What I have tried to do is to put together some of the highlights in the literature, and to raise some of the important questions.

I found this quote in the *Journal of Maternal-Fetal Medicine*.[1] I start with this because I think it is quite telling of the difficulty of bringing to bear some of the data on this disorder in pregnancy. "As many women start to develop clinical features in their reproductive years, one may wonder why so little is published regarding the association of pregnancy and VHL. It is likely that either most patients remain asymptomatic during their pregnancy, or the close clinical surveillance regimen results in recognition and treatment of tumors before or between pregnancies." The surveillance ameliorates some of the complications. But I think the last line is important: "Any complication of the disorder may present during pregnancy", and frequently does so quite unexpectedly, sometimes as the first diagnosis of the disease.

The case reports focus on four topics:

- Pheochromocytomas,
- CNS hemangioblastomas,
- Anesthesia, especially as it relates to surgery during pregnancy and during delivery, and the
- Mode of delivery, specifically vaginal delivery, forceps, vacuum assistance, cesarean section

Pheochromocytoma. In the general population pheos occur in once in 54,000 people. But pheos occur in about 20% of people with VHL, and they represent a very significant risk for a pregnant woman and her baby.

The classic symptoms of pheo are headache, palpitations, and perspiration. In pregnancy, these can be absent or can be misdiagnosed as a disorder known as preeclampsia, or toxemia of pregnancy. Preeclampsia is a placental disorder that occurs in about 9% of women. It manifests as hypertension, renal damage, liver damage, seizures, and if untreated, death. Because the symptoms of pheo are similar, it is mismanaged as preeclampsia.

Other manifestations of pheochromocytoma include: abdominal pain, postural hypotension[2] (which is a key factor in differentiating it from preeclampsia), visual disturbances, convulsions, adult respiratory distress syndrome (ARDS), collapse, shock, and death. All of these symptoms have been reported with pheochromocytomas in pregnancy.

The consequence of having an undiagnosed pheochromocytoma that is active in pregnancy is really tremendous. In the literature it results in a 40-50% maternal mortality rate[3] — a shocking statistic until you consider what can go wrong. The good news is that with early diagnosis and appropriate management by

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Inside this issue!

Adventures in Pregnancy

Brian T.

by Pat T., Michigan

He's ten, our pheo baby. I was happy when he learned to read, happy when he talked, happier still when we learned he does not have an alteration in the VHL gene. He gets math concepts very well, but I can't help wondering if my pheo contributed to his Attention Deficit Disorder (ADD) and sensory integration problems.

Pheo problems have seemed to run in our family for years. My parents are both hale and healthy, but my brother had pheos on both sides at the age of 11. That was 1962, and at our local hospital they didn't take children's blood pressure. "They're children! Of course it will be high!" But he had bilateral adrenal masses, and he was admitted to the adult unit, so they took his blood pressure before beginning surgery — it was 300. There were no catecholamine blocking drugs in those days. They proceeded with the surgery, and my brother died on the table from a pheo-induced heart attack, one month after his 11th birthday. My parents were told not to worry, that "it never happens twice in the same family."

In 1969, when I was 10, my mother noticed that I was choosing short-sleeved dresses in winter time. This time my parents decided to take me to the University of Michigan in Ann Arbor, the largest teaching hospital three hours from our home. Dr. John Bartlett diagnosed pheos on both sides. But he used a new approach. He used blocking agents to keep my heart rate from soaring. He removed bilateral extra-adrenal pheos at that time — both outside the adrenal glands — and I was able to keep my adrenal glands. I recovered well from the surgery.

In 1975, while in college, I developed some large blind spots in my eye. I went first to the optometrist who suspected an infection and sent me to my regular doctor. He sent me to Ann Arbor, admitting that he had no idea what it was. The doctors looked at my pheo history, and just to rule it out, they sent me off to "do a jug" — a 24-hour urine collection. It came back positive for pheo. They had a hard time locating it, but finally found a pheo on the right ganglia of my spine, again outside the adrenal gland.

While I was in the hospital I met a charming nursing student — not assigned to me, my husband hastens to add! — and we began dating. We married and decided to have only one child because of my health issues. Our David arrived in 1985, following a very uneventful pregnancy. He had a mild abnormality in his heart, pulmonary stenosis, but it was controllable and he is a normal active child, a scholarship student at college with a black belt in Tae Kwan Do.

Eighteen months later, in 1986, our daughter Kate was born. Again it was an uneventful pregnancy, but she too had pulmonary stenosis, this time much more severe, critically ill from birth. She had corrective heart surgery, but died at the age of 18 months in 1987. We went through some genetic counseling then, since we had had two children with pulmonary stenosis, but were not given any helpful information. They suspected that I might have Multiple Endocrine Neoplasia (MEN), but the heart problem didn't fit the syndrome. My mother had had thyroid cancer, but it was not the type of thyroid cancer typical of MEN, so they were still unsure.

When David was four, my husband was offered a job transfer, and we were pondering the move when David declared that he wanted to move to Grand Rapids, and he wanted a baby brother. Within the next few years we were able to give him both.

When I was 6 weeks pregnant, the normal work-up showed that I had some gestational diabetes, and that my blood pressure was quite high. They "did a jug" and found evidence of a pheo. The first endocrinologist told me that I should abort the child. My obstetrician, who had recently managed a patient through a successful pregnancy with a cancer of the adrenal gland, was concerned but open to discussion: "Clearly we need some advice here in how to manage this tricky situation." So I hunted down Dr. Bartlett, who was then in the navy.

"I'm pregnant," I blurted out. "Congratulations!" he said. "And it looks like I have another pheo." "Oh, dear!" "And I really want to keep the baby."

"Well, of course you can keep the baby!" he said, and proceeded to provide sensible advice for me and my obstetrician.

They blocked me up like crazy, and removed the pheo in the 13th week of my pregnancy. After the pheo was out, the diabetes also went away. Evidently when the catecholamines are high, it can cause the sugar to rise as well.

The remainder of the pregnancy went well, and Brian arrived as scheduled, with a vaginal delivery, weighing ten pounds. We saved amniotic fluid and the umbilical cord for genetic analysis and research.

Later I went to a new endocrinologist, Dr. Tennyson. He read through my history and noted that my brother and I had both had pheos at 10-11 years old. "Your son is now 10 — has he been checked for a pheo?" With all the excitement of Brian's birth, I had forgotten the promise I had made to myself to have

David checked at 10. Dr. Tennyson ordered the tests, and sure enough, David's catecholamines were 20 times the normal levels. They took him off Ritalin, and the levels dropped to 10 times normal. He had a pheo.

Dr. Tennyson suggested that perhaps NIH would like to review our family's history. So off we trooped to NIH for analysis. As my husband and I were talking the night before David was scheduled to have bilateral adrenal tumors removed, we decided to make up 3x5 cards of the messages we would like the doctor to tell us. We wrote them out one by one: "He's fine." "The surgery went well." "Yes, we saved the gland." "I've never seen anybody heal like this!" "Gee this boy has nice parents!" "He can go home soon." It helped to keep us focused on a positive outcome. When we handed the cards to his surgeon, Dr. Walther, he laughed. After surgery, however, he opened his folder and began handing the cards to us one by one. All the good messages had come true.

At NIH they did a full work-up on David and me, and for the first time said "VHL". They found that I had a pancreatic islet cell tumor, so David's surgery was closely followed by my partial pancreatectomy. My parents were also screened for VHL as part of the NIH protocol. My father tested positive for the VHL gene, but still has no tumors, not a single retinal angioma, nothing.

In 1996, the two boys were sleeping together on vacation. When I woke them I noticed that one of the sheets was quite wet. At first I though the younger boy had wet the bed. But instead, David was having a sweating attack -- another pheo at age 13. They immediately put him on blockers, which made him very tired. After the flank-cut surgery, he bounced back quickly and two months later earned his black belt in Tae Kwan Do. Today he is at college, getting A's in Chinese, working up to a belt in Kung Fu. He is an exceptional boy. He did not read well until second grade, but then went through what the Montessori school calls "a reading explosion" and has doing extremely well since then.

My husband attended a medical conference where they were talking about the learning problems of babies who are born addicted to crack. The problem, they said, is the catecholamine surge that babies get during pregnancy. Catecholamine surge? — sounds like what a pheo generates too. It has made us wonder whether Brian's ADD and sensory integration problems might be attributable to the catecholamine surges that he underwent during the early stages of my pregnancy.

We've gone a couple of years now without surgery. For so long I remember VHL defining my life. Now my second son, Brian will be in sixth grade and won't get a pheo. He has been tested for VHL and does not carry the mutation. What will that be like? My fears still come up, and I have to remind myself that I don't have to worry about VHL for this one.

I try not to cripple myself or my son with this condition. I told David when he was 11 that he could go through these VHL episodes and come out the same, or he come out stronger. David still has one adrenal gland. He is very healthy, has a strong spirit, and is in a good spot in his life. He has a good understanding of people and their trials and tribulations, but doesn't wear it like a cloak or use it like a crutch. We try to make NIH visits a vacation, with trips to the Air & Space Museum.

The doctors and hospitals have learned so much about patient care just during the time we have been observing. In 1986 I had to sleep in a recliner chair near my infant daughter. In June 1987, the University of Michigan had created a "Mom-spot" for every bed — they had learned that the patients did better, and it was easier on the nursing staff. Kate and I worked as a team. I was able to ground her and give her comfort, which in turn comforted me.

I can't say enough about the wonderful people who have helped us through all this: the many outstanding doctors, and the many wonderful friends. Cia Manolatos and Kathy Hurley at NIH are phenomal people. Cards from classmates, phone calls and offers to cook meals, all are much appreciated. And my friend Rosemary Anderson gave me the best gift of all — she hooked me up with the support group of the VHL Family Alliance. As I have spoken since with people with a variety of genetic diseases, they tell me that when they hooked up with a support network, that's when things began to get better. We're really glad we're here.

New Brochure

You will have received copies our new yellow brochure in the mail. This brochure was created by Tim Nielsen and donated by Transamerica Insurance and several of its suppliers. We are very grateful for their help!

This brochure is our first step in brightening up our corporate image and broadening our appeal. We welcome your feedback.

We hope that you will share copies of the brochure with your family and friends, and encourage them to help us meet our goal of funding one more research grant in full next year! Let's cure VHL in this decade!

Write us in on your United Way campaign!

U.S. Federal workers, choose # 1098 in the CFC campaign!

Karen's Story

by Karen H., Pennsylvania

I was six months pregnant with our second child when I started having headaches. They weren't every day, but they did get progressively worse. My gynecologist kept telling me that headaches were common with pregnant women. I told him that I had VHL but that didn't matter. Frankly I don't think he knew what that was.

To make a long story short, I eventually was admitted to the hospital with double vision and in terrific pain. I was transferred to Hershey Medical Center in Pennsylvania where we were told I had about 24 hours to live because the pressure was so great inside my skull.

The neurosurgical team did emergency surgery and put in a shunt into my jugular vein (which I still have 20 years later). Once the shunt was installed the double vision went away. After that, I had no problems and delivered a baby girl at full term.

Three months later, I returned to Hershey and had two tumors removed from the cerebellum. I never had a brain tumor after that, although I am affected in a lot of other areas.

Renée's Story

By Renée S., Ontario, Canada

I was diagnosed with VHL during my first pregnancy. The pregnancy itself went without a hitch. Because I have no adrenal glands, I was referred to a high risk pregnancy unit. When I gave my medical history, the astute obstetrician suggested I see the resident geneticist.

During my first appointment with her, at five months pregnant, she told me that she could give me a clinical diagnosis of VHL based on my medical history, and could send my blood to Philadelphia for the genetic test. I agreed, but I was terrified to learn too much about VHL. So when my oldest was six months, I hurriedly became pregnant again, before I could learn anything that might make me change my mind about having more children. I have always wanted to have a big family.

The second pregnancy, from July of 1998 to March of 1999, was a difficult one for me. I had two spinal tumors, both located between L3 to L5, one about 2 cm and one 3 cm. I did not know prior to the pregnancy that I had these tumors, and in fact, did not find out (for sure) until three months after my son was born that they were there. I was only diagnosed with VHL in 1997, and my doctors knew very little about VHL and I was too frightened to do any research on my own.

But as the pregnancy progressed, I was suffering from an unusual amount of back pain, along with some numbness and weakness in my legs. This prompted me to do a little research which led me to suspect I had a tumor on my spinal cord. There was very little to do about it at that point, and I am quite sure my obstetrician thought me a hypochondriac (even though I did give him the literature on VHL), so I just carried on as best I could. I took Tylenol with codeine for the back pain and tried to vary my position as frequently as possible. I spent about three hours of the night in bed, followed by an hour of pacing around my kitchen waiting for the next pain-killer to kick in, and another three hours in my lazy boy chair. I prayed for the pregnancy to end early, and even asked my obstetrician to induce me at 34 weeks. With a one-year-old at home to care for, I truly felt I could not carry on. He refused, but at 35 weeks my water broke and Michael was delivered on March 30, 1999. He spent almost 3 weeks in the neo-natal intensive care unit, and came home on April 17.

I was not checked before and after my first pregnancy, only after my second, and then only at my insistence. My family doctor (also not familiar with VHL) thought it was "overkill" to have an MRI following the pregnancy, even though I gave him the VHLFA *Handbook* and showed him the part about having an MRI yearly. He told me that I didn't have "that kind of VHL". Good thing I was tired of keeping my head in the sand, and smart enough to realize that doctors might not always be right. I insisted on the MRI. I had surgery to remove the tumors on May 25 of 2000, after putting it off for as long as possible. I didn't feel I could have the surgery until Michael was a year old.

The surgeon removed one tumor. When I woke up he told me that there had only been one tumor, and that it was bent over on itself to make it look like two on the MRI films. So I went about my life and assumed that my lingering leg numbness and weakness were residual to the surgery. I paid very little attention when the numbness crept into more areas, assuming that it had always been like that and I just hadn't noticed. Luckily, in May of 2001, I was invited to the NIH. They, of course, found the remaining tumor and I had surgery to remove it in August of this year. So, although I have been left with numbness, and weakness in my left leg, and bowel and bladder difficulties, I do not like to say that these symptoms were related to or caused by the pregnancy. I think if both tumors had been removed in one fell swoop, I would have had a better outcome. If I do decide to have another child (not very likely at this point) I would certainly be checked before and after the pregnancy.

So what have I learned from all this? Go to the experts, even if I have to travel to do it. Trust myself; I know my body best. And, educate myself and my doctors. It is in my best interest to be an expert in VHL. After all, I am the one with the vested interest. My life, and my sons' lives, depend on it.

Three Healthy Babies and a Healthy Mom

by Laura H., Massachusetts

I had a brain tumor in 1990 that was successfully treated. They suspected VHL, and a series of retinal lesions confirmed the diagnosis. Nonetheless, no one in my family had anything that looked like VHL.

In 1994, the new availability of prenatal testing seemed to support a decision to become pregnant at age 36. . . The gene had been found in 1993, but they were still doing mostly linkage analysis. They did a sampling of the placenta (CVS) which had some risk both to me and to the baby, but we felt it was important to know, and to know as early in the pregnancy as possible. Fortunately the result came back negative.

After the test there was still a lot of debate about whether to delivery vaginally or not. With my brain tumor history, they were concerned about the increased blood pressure during pushing. My obstetrician is wonderful but of course knew little about VHL. She reviewed the literature. Having attended the VHLFA meeting in Boston, I knew enough to say that the literature was very thin and did not contain all the answers. I did not want to have a scheduled cesarean section if it was not absolutely necessary. I contacted NIH and organized a telephone conference call among researchers and clinicians at NIH, my obstetrician, and the head of anesthesiology at Beth Israel Hospital in Boston. The consensus was that cranial pressure was not an issue because there was no evidence of another hemangioblastoma in the brain. To this day the obstetrician refers to me as her "activist patient." As it turns out, the baby was facing backward and took a long time to deliver. I imagined myself a yuppie supermother in great shape and insisted that I could do it the natural way, but after 3 days of labor my daughter was delivered by cesarean after all.

When my daughter was two, we found out that my mutation is still among those that cannot be identified. This threw the results of the prenatal testing out the window. By this time, charmed by our wonderful daughter, we became more philosophical about VHL, and decided to have a second child. Our desire to have a child, coupled with an optimism about diagnostic and treatment advances outweighed our fear of VHL. My VHL screens continued to be clear, so the risks to me were minimal.

There were no special arrangements during the pregnancy other than the routine things they do for an "older" mother (I was now 40). My VHL mutation had still not been identified. Everything went smoothly, but during delivery they discovered that the cord was wrapped around the baby's neck and they wound up delivering her too by cesarean section.

Last year when I became pregnant with our third child, we checked again with NIH to see if my mutation had at last been identified, but it had not. Prenatal testing was therefore not an option. With new anesthesiologists on board at Beth Israel, we had to review again the question of delivery. They reviewed my last neurological scans and decided, reluctantly, to permit a vaginal delivery. My body decided otherwise, so our little boy was also delivered by C-section.

"Our tranquil bunch:" Harry and Laura H., with Erica, Alexandra, and Gabriel.

I have nursed each of the children for one and a half years. I have delayed my post-natal scanning until after weaning, to make sure the baby is not exposed to radiation. It's funny, but pregnancy, childbirth and nursing seem to supplant all other non-urgent medical activities and make you put off everything else. I feel just fine, but I should do an MRI now just to make sure the scans agree.

My oldest child just had her first retinal exam. It was interesting watching them do a pre-reading visual acuity test. They haven't updated the pictures they ask the child to identify — they showed a phone from the 1940's with a handset and a flared base with a rotary dial. For her, a phone is a rectangular thing with buttons. I couldn't even identify some of the pictures .

We will continue to test the children following the guidelines in the *Handbook*, and do the monitoring. If and when we're able to identify my mutation, we'll test them for that too.

Pronouncements are always dangerous, but it's inconceivable to think that we considered childlessness the only responsible VHL driven step. If any or all of them do end up with VHL, I'm sure we'll feel a terrible responsibility. But our children are so precious and so vital, that we'll manage their health as a part of their unfolding lives.

VHLFA Down Under

by Don Marshall, Mississippi

During a vacation trip to Australia, my wife Peggy and I participated in a meeting of the VHL Family Alliance Australia. We rented a car near Brisbane and drove to Sydney, enjoying the friendly people and beautiful vistas along the way. Each morning we would wake up and watch the sun rise over the Pacific. It challenged my sense of direction. We were introduced to a few foods we were were not accustomed to -- squid, lobster, prawns, octopus, and a delightful treat -- *bugs!* Not insects, but a crustacean tasting somewhat like lobster or shrimp.

In Sydney we were joined by Gay V., co-chair of VHLFA Australia. She and her husband Paul are a loving couple, full of life and spirit. Like most other VHL families they live life to its fullest. They bent over backward to chauffeur us around Sydney and out to the Blue Mountains, 50 miles inland, to see the rugged cliffs and waterfalls and the legendary Three Sisters rock formation. I was walking near Pittwater Bay when I was stopped dead in my tracks as a wallaby stepped out in front of me. We stood facing each other for a moment and then the wallaby hopped off. I sat down on a small bench to get my act together. In a few minutes the rest of the group joined me. As I rose, out from under my bench came a three-foot lizard. It slowly walked (as lizards do) toward me and climbed on the wall I was sitting on. Peggy made a quick exit.

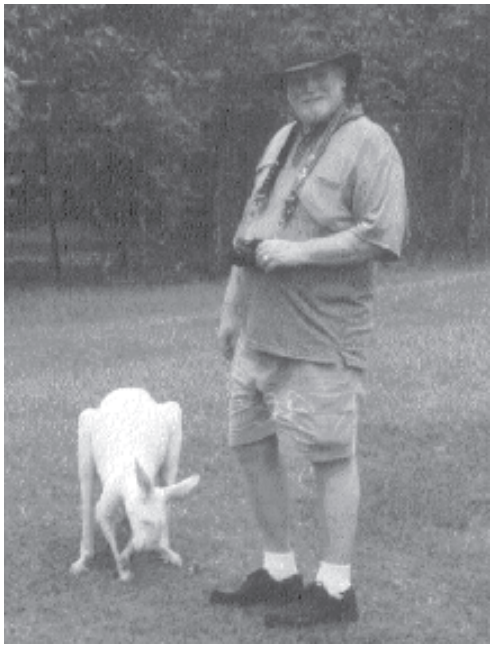
Babs from Victoria; Jon and Val J., VHLFA Chairs from New Zealand; and Jennifer K., Co-Chair from Queensland joined us later in the week. The meeting took place in North Sydney with about 45 attendees. Two guest speakers, Dr. David McKay of the Ophthalmic Genetic Service and Dr. Lesley Andrews of the Hereditary Cancer Clinic at Prince of Wales Hospital provided information about ophthalmology and genetics. Peggy and I had the opportunity to speak with several VHL affected and family members from the east coast of Australia. Basic medical care is nationally funded in Australia, and supplemental insurance is available to complement it. Other than that, they have the very same concerns shared by the rest of us with VHL around the world.

Susan M., North Carolina (Don's sister); Peggy M., Mississippi (Don's wife); and Gay V., New South Wales, VHLFA Co-Chair for Australia.

I would be remiss if I did not related the story of Peggy and the Kangaroos. While at the zoo Peggy had the chance to feed the kangaroos. She picked up a bag of kangaroo feed that looked suspiciously like puffed rice and walked out into the kangaroo enclosure. There were about 50 kangaroos of all sizes lying in wait. As she started to feed a couple of the kangaroos, a crowd began to encircle her. One of the bolder kangaroos started to slap at her arm to get her to drop the food. Peggy thought she could hide the bag behind her back, not knowing she was surrounded. Perplexed, she held tight to the bag and proceeded to give the same lecture that she would give to the children she cares for in her Day Care as to the etiquette of waiting your turn. We all expected her to start teaching them to say, "Please" and "Thank you."

The trip to Australia was a dream come true and we look forward to going down under sometime in the near future. Thank you to all our friends in Australia and New Zealand.

Note: This trip was privately funded. No VHLFA donations were used to fund this trip.



Don with an albino kangaroo

Eva Logan Honored

A Special Directors' Award has been given to Eva Logan for eight years of service as a volunteer on the VHLFA Hotline and chairing the Georgia chapter. Many of you will remember her warm Southern voice, comforting and coaching you through new information and hard realities. Eva, we love you and we thank you for your willingness to share yourself with all of us.

Two Meetings in 2002

There are two large meetings in 2002. We hope you will be able to attend one of them.

Cleveland, July 19-21, 2002

Padua, June 6-8, 2002

The Cleveland meeting, chaired by Dr. Robert Uzzo of the Fox-Chase Cancer Center and Cleveland Clinic, is a continuing medical education conference for primary care physicians and any other family member or medical professional who would like to join us and learn about VHL. The level of language will be suitable for a family physician or a relatively well-informed lay person. People who are attending a conference for the first time are encouraged to attend "VHL 101," a workshop with Joyce Graff on Friday morning, to get to know one another and to introduce the language and concepts that will be heard in the meeting.

The Padua meeting is the Symposium we hold every two years, gathering the medical experts on VHL together to collaborate and move the level of knowledge about VHL significantly forward. This meeting is being chaired by Dr. Giuseppe Opocher. Papers are being accepted now for participation in that meeting. Families are welcome to attend. The level of language will be highly scientific, especially in the early part of the meeting. Events are being planned for European families on Friday and Saturday. VHLFA volunteers, and people who want to help grow VHLFA in their own countries should plan to stay as long as possible on Sunday.

Families should choose the meeting nearest them. We move the meetings around so that at some point it should be within reach. If you want the meeting to be closer to you next time, please volunteer to create a meeting!

Update on VHL:

An Integrated Medical Approach to a Multisystem Disorder

The Cleveland Clinic Foundation and the VHL Family Alliance will sponsor a continuing medical education event for primary care physicians, nurses, and genetic counselors to be held at the Marriott Airport Hotel, July 19-21, 2002. The meeting will be chaired by Dr. Robert Uzzo of the Fox Chase Cancer Center and Dr. Andrew C. Novick of the Cleveland Clinics. Continuing Medical Education credits will be awarded by Cleveland Clinic to physicians and genetic counselors for the sessions they attend.

Because VHL crosses so very many medical specialties, it is a challenge for any health care professional to follow a patient with VHL. Without the cooperation and close collaboration of the patient and the family, it is practically impossible. For this reason we always work to engender a partnership between the families and their health care professionals.

The agenda includes a survey of the medical issues in VHL, diagnostic techniques and treatments, including legal and insurance issues and stress management.

Families are welcome to attend this meeting. If you have not previously attended a VHLFA conference, you are encouraged to attend "VHL 101", an introductory session with Joyce Graff on Friday morning before the formal start of the conference. You will have an opportunity to meet other attendees and VHLFA Board members, and gain an understanding of terms and concepts that may be new to you, in other parts of the body with which you have not dealt before.

For registration information, see http://www.vhl.org/conf2002 For hotel reservations, call Marriott at 1-800-228-9290 or (216) 252-5333

Padua Call for Papers

Physicians and Scientists are invited to submit papers for presentation at the 5th International Symposium on VHL, Padova, Italy, 6-8 June 2002.

Provisional list of topics:

- New insight into the VHL protein functions
- Genotype phenotype alignment
- Early discovery of new VHL patients
- Expanding possibilities for accurate assessment
- News from VHL clinical care centers
- VHL in children
- Organ transplantation in VHL patients
- Therapeutic progress, from old and new drugs to gene therapy

Please send proposals to Dr. Opocher, with a copy to editor@vhl.org:

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Travel to Italy

Though our world is in turmoil, we must try to do as the experts and our leaders recommend -- we must proceed with positive intentions. People touched with VHL seem to have heard that too often. As we look for positive events in our lives, let's use Padua as a goal!

There are several lovely (spa) villages close to Padua; Abana and Montegrotto for example; both easily reached by bus. If you decide on a vacation in Italy, your options could be endless! -- *Jacki Hunsberger, Odyssey Travel*

Tel: +1 (610) 222-0550 or (US/Canada) 800-972-3178
Fax: +1 (610) 222-0520

Celebrating 50 Years of Brain Research

New Discoveries, New Hope

by Deborah C., Michigan

On October 9-10, 2001, on the campus of The National Institutes of Health (NIH) was held a wonderful celebration of the last 50 years in brain research. The group that assembled for this symposium was primarily neuroscientists, clinicians, and researchers. Much of the ongoing research being done by these groups was funded through the National Institute of Neurological Diseases and Stroke (NINDS) or the National Institute of Mental Health (NIMH). They gathered to celebrate the wonders of what has been achieved so far and what great things lie on the near horizon.

The remaining people who gathered to listen in had various interests, hoping to learn any new bits of information that might apply to their individual needs. Thus, I found myself amongst learn'ed company, representing the VHL Family Alliance. I'd like to share with you pieces of my experience that clearly apply to each of us…

On arriving, I was struck by the theme of the symposium- "New Discoveries, New Hope". There was that word, "Hope", just like our own, "Hope for a Cure".

It became increasingly clear over the course of the next two days that new discoveries truly are happening all the time, and with each there is yet another stride forward in the journey toward understanding and curing a myriad of diseases. Real Hope!!

Especially significant were the advances in research and learning in respect to Parkinson's, Huntington's and ALS (Lou Gehrig's disease). These diseases seem remarkably similar to VHL (in a genome sort of way). As the human genome has now nicely been "unraveled," progress toward real understanding of how to repair those genes with altered proteins (which cause so much chaos in our bodies!) is progressing at a remarkable rate. One speaker went so far as to say that she felt it was not overly optimistic to hope for a cure for Huntington's by 2010! Human drug trials begin in 2002.

That is good news for us! For as researcher after researcher explained their projects, it was easy to see remarkable similarity between all diseases in the brain and VHL. The diseases that were most discussed were; Alzheimers, Parkinsons, Huntingtons, ALS, Schizophrenia, Depression, and Manic or Bi-Polar Syndromes.

Brain research in all of those areas employs the reductionist approach; this simply means that each of them is studied at the smallest level possible-their molecular and cellular functioning. At this level the workings (or not!) of the cells becomes dramatically clear. In order to change the course of diseases, manipulation, both chemically and physically, is being experimented with**.** It is so much simpler to find treatments and cures when the problems are so basically understood. Neurons, our basic nerve cells, are now being successfully generated (Hooray for stem cells!) for use in diseases where healthy neurons are in short supply, like Parkinsons or Alzheimers.

The good news is that whatever is valuable and useful for these "neurological" diseases, is also valuable and useful for the VHL community. The world is watching expectantly (especially us!) as the medical community makes huge strides in the direction of cures for debilitating diseases.

The Center for the Study of Neurological Injury is spending a great deal of time learning all it can about spinal cord injury and stroke, respectively. Research varies from injection of stem cells to recover function in the spinal cord, to fighting the battle to keep cells alive after oxygen deprivation due to stroke. All of these approaches have relevance to those who deal with the various symptoms of VHL.

I know that, personally, I was pleased to learn more about "brain plasticity"- The amazing ability of the human brain to continue to learn and adapt. It was both wonderful and reassuring to know that our brains are *not* static, but are creating new neural pathways always. (After 9 brain procedures, and more to come, that was a decided relief to me!) As this researcher noted, "the brain is a continuously functioning organizing machine. It handles 10s of 1000s of bits of information in a reliable and retrievable way." What an awesome entity!

As medical science continues to seek out the whys and wherefores of behavior and disease, we all benefit. In the most recent *AARP Bulletin* was an article on Parkinson's and Politics in which the major role of research in the hunt for a cure was discussed. Its author has a spouse who is suffering the debilitating effects of the disease. He has become very involved in making certain that funding remains high for research to cure the disease. The article reiterates what I heard myself, and that is that funding remains at a very high level (at least at the NIH, etc.) and there no expectation of budget cuts. So, have no fear. It seems that funding will remain at an all time high; especially as it is recognized that so many cures may be "just around the corner".

Christopher Reeve -- best known for his role as "Superman" -- spoke to the assembly on Tuesday afternoon. Since an accident in 1995 he has been a voice for all paralyzed Americans. Mr. Reeve spoke

Carrying the Olympic Torch

Larry Bennett has been chosen to carry the Olympic torch through Olympia, Washington, on its way to Salt Lake City. His segment will take place in mid-January. Larry is being acknowledged for his marathon run with VHL. He was nominated by his wife, Debbie, but this award comes from his entire community. Congratulations to Larry and his family!

briefly and poignantly, likening his situation to the building of the Transcontinental Railroad. Imagining himself as the group of railroad workers that started building toward the west, and the medical community as the group that made its way east to meet them, he gave shape to the idea that health care responsibility lies in the hands of the patient *and* the provider. He said, "I am doing my part by fighting against things like muscle atrophy, osteoporosis, and other things that I call chair-caused damage. But you (the doctors) must do your part. Remember that the National Institutes of Health are *not* "The National Institutes of Research"… basic research should lead to therapy." He concluded by saying, pointedly, "I'll meet you in the middle."

As a person who lives with VHL, I know that I too have learned the lesson of "active waiting." I am careful to try and choose a healthy lifestyle and do those things which challenge me to be the best that I can be. Who among us does not live daily a life that alternates between happiness, terror, wonder, disappointment, relief, and waiting? Hard work. We are doing our part … rest assured that our scientists and researchers are doing theirs.

Authors' P.S.- I think of the collective experiences of all members of the VHL Family Alliance as a **V**olume of **H**eroic **L**iving. (I work at a library.)

DNA Testing

DNA Testing in **England** is being handled by a large clinical laboratory where most mutations should be found within 2-3 weeks, and rare ones within two months. If your testing is taking longer, please inquire through your physician. If needed, feel free to escalate to Dan Whitmore (uk@vhl.org) or to Dr. Maher for assistance.

We are pleased to announce that there is a geneticist in **Hungary** who is familiar with VHL who can assist Hungarians with genetic counseling and is prepared to do DNA testing for VHL. Dr. Pfliegler has translated our *Family Tree* brochure into Hungarian.

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There are now four labs in the world who are providing **very highly reliable testing** and who can find even very rare mutations. For people with no clear clinical diagnosis who are the first in their family, it is preferable to go to one of these testing labs:

Europe:
Dr. Alessandra Murgia, Pediatrics
University of Padua
Via Giustiniani 3, Padova 35128 Italy
Tel: +39 (49) 821-3512
Fax: +39 (49) 821-3502
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Pregnancy, continued from page 1

the medical team, the mortality rate can be reduced to 0-11%.[4] It is critically important to communicate fully with the doctor and make it known that you have a diagnosis of VHL, or that there is VHL in the family, even if you have no previous symptoms or no clear diagnosis of VHL. This information can make the difference between life and death for mother and child.

The high blood pressure created by the pheo not only affects the mother, but it can compromise the mother's ability to maintain sufficient blood flow across the placenta to nourish the fetus.

In the setting of a pheo, a number of normal effects of pregnancy can cause a hypertensive crisis: the pressure of the growing uterus on the blood vessels, changes in the body catecholamine levels, uterine contractions, fetal movements, the pain of labor, and the expulsive forces during labor.

The fetal compromise that we worry about most obviously is fetal death, and it is felt to be associated with constriction of the blood vessels in the placenta caused by the elevated levels of circulating catecholamines. With severe hypertension you also see something called placental abruption, where the placenta prematurely separates from the uterus, and that of course disrupts the surface area for nutrition and oxygenation to the baby, and frequently results in massive maternal hemorrhage. Severe, uncontrolled hypertension may result in placental insufficiency leading to reduced amniotic fluid volume, cord compression and fetal jeopardy.

Early diagnosis and appropriate management are key. If the pheo manifests itself in the third trimester and the mother is treated with alpha blockade and the fetus is monitored carefully, you cut the risk of fetal compromise from 42% to nearly zero.[5] If the pheo manifests itself in the early stages of pregnancy, when there is still a long way to go, management is more difficult, but the risk still drops from 75% without treatment to about 17% with treatment.[5] So early diagnosis, aggressive intervention, can really alter the course of this disease in pregnancy. Meticulous monitoring of the fetus is essential, with ultrasounds, and something called a nonstress test which is an indirect measure of fetal central nervous system oxygenation by looking at the heart rate tracing of the baby.

In one of the reported cases,[6] a 20-year-old healthy woman was admitted at 26 weeks with bleeding and a blood pressure of 160/100. I can tell you this happens 3-4 times a day on a high risk labor and delivery unit, and the first diagnosis that is going to come to any obstetrician's mind is preeclampsia with possible placental abruption causing the bleeding. She had an obstetrical ultrasound that looked at the baby and incidentally they noted bilateral maternal adrenal masses. An MRI and 24-hour urine confirmed pheochromocytomas. They controlled her blood pressure with phenoxybenzamine, propranolol, and benadine.

At 30 weeks gestation she required a cesarean section for fetal distress and intrauterine growth restriction. Again, the concern with elevated catecholamines is the constriction of the blood vessels that can impair fetal growth and result in fetal distress. In this case they did combined cesarean section and removal of the adrenal tumors, which is frequently what has been reported in terms of the timing of removal of these tumors, and we'll talk a little more about that. Both mother and baby did well.

Again, pre-conception counseling is ideal. Make the diagnosis prior to pregnancy, do the workup prior to pregnancy with urinary levels of catecholamines, CT scans and MRI. If the condition is diagnosed and the pheos removed before the pregnancy, the risks are considerably diminished.

The timing of the delivery can also be a critical element. It can be very complicated. It requires a real team approach.

The optimal timing for surgery is also debatable with pheochromocytomas in pregnancy. Delaying surgery until fetal maturity, is the ideal case scenario — so you are not delivering a profoundly premature baby

"It is critically important to communicate fully with the doctor . . . even if you have no previous symptoms or no clear diagnosis of VHL. This information can make the difference between life and death for mother and child."

that suffers all the consequences of prematurity. You have to balance that against the risks of continuing with an active pheochromocytoma long-term.

Each woman's situation will have to be evaluated carefully. That said, the general recommendation would be that if you are in the first or early second trimester, you institute alpha blockade, and if you are that far away from fetal maturity the general recommendation would be to go ahead and surgically treat the patient. However no definitive recommendations can be made. In general if you have a viable baby (greater than 24 weeks gestation) and you have a reassuring maternal-fetal status – the mother is responding to treatment – you can try and delay resection until cesarean section at the time of fetal maturity. Again it requires a lot of monitoring, and possibly a long-term hospitalization.

If you look at the existing case reports, they generally time tumor resection in the third trimester with cesarean section -- a combined procedure. That can be very tricky. The vessels are hugely engorged, and there is a risk of hemorrhage and other complica-

tions to the mother. Increasingly people are doing laparoscopic resection. Obviously with a gravid uterus in the third trimester that is very very difficult to do. Delaying resection until postpartum in order to do it laparoscopically has been suggested, but is also extremely controversial.

During surgery in pregnancy, one obviously has to do intensive monitoring of both the mother and the fetus, measuring arterial pressures, perhaps using a Swan-Ganz catheter to help assess the volume of blood in the blood vessels, and cardiac function.

> "The patient, family, and medical team need to work closely together. It's a tricky situation that calls for counseling, consent, and understanding of the ambiguities that are likely to arise."

CNS hemangioblastomas. Hemangioblastomas of the retina, brain, and spine are another area that has been frequently discussed in the literature. The spinal cord and cerebellum are the main sites that have been reported. Growth in pregnancy is a concern. It is controversial, but there is some indication of progesterone receptor proteins that may contribute to growth of these tumors in pregnancy. In addition, the issue of increased maternal blood volume, increased cardiac output, all may predispose to growth of these tumors in pregnancy.

- Increased maternal blood volume
- Maternal cardiac output increased by 20%

If a tumor in these sensitive areas should hemorrhage, or grow to the point of needing surgery, the consequences can be severe: hemorrhage, intracranial pressure, hydrocephalus, paraplegia, and herniation of the cerebellum, all of which can be life-threatening.

There is a case report[7] in which a 26-year-old woman with known VHL came in 7 weeks pregnant with headache and paraplegia that had been going on for two weeks. She had multiple cerebellar hemangioblastomas and obstructive hydrocephalus, an obstruction of the flow of spinal fluid through the brain, causing increasing pressure in her skull. The therapy was to place a shunt to divert the fluid buildup, which improved the symptoms and she continued the pregnancy. She was delivered by cesarean section at 33 weeks. After the baby was born they noted a decrease in the size of the cerebellar lesions. So there was apparently some growth or engorgement of these lesions during the pregnancy.

Another case study,[1] describes a 30-year-old woman with VHL at 30 weeks gestation who had symptomatic cerebellar hemangioblastomas. They performed a craniotomy for complete removal of the tumor. The remainder of the pregnancy was uneventful, and she had a vaginal delivery at term under epidural anesthesia.

In another case report,[8] a pregnant woman, age 23, with a family history of VHL, came in at 35 weeks gestation with paraplegia. She was noted to have an acute intramedullary hemorrhage of the spinal hemangioma at the thoracic 4-5 level. A T3-6 laminectomy resulted in improvements. She developed pre-term labor, and had a cesarean under epidural anesthesia. The reason they chose cesarean in this case is that there was another spinal cord hemangioblastoma they were worried about rupturing during labor.

Here again, pre-conception evaluation and baseline CNS imaging studies are critical to make the diagnosis early, to have the information early. Neurological status should be monitored carefully throughout the pregnancy. You can use CT scans, you can use MRI. It is possible to do elective repair if you make the diagnosis during pregnancy, but of course it is preferable to do repairs in the post-partum period.

However, if there are symptoms of acute or subacute spinal cord compression it's a surgical emergency and regardless of fetal maturity you need to intervene. Frequently people can get very confused during pregnancy about the priorities. The priority is the mother. If you have a sick Mom, you're going to have a sick kid. It's really useless to focus on the baby and forget that your main patient, your main priority, is the mother.

Avoiding intraoperative hypotension is an important factor during neurosurgery. Hypotension is frequently used in neurosurgery, but in a pregnant woman that can cause poor blood supply to the uterus, a drop in the fetal heart rate, and fetal distress. The data on hypothermia, another technique used in neurosurgery, is limited. It has been associated again with fetal distress and bradycardia (an abnormally low fetal heart rate). Osmotic diuretics and loop diuretics are frequently used to decrease the intracranial pressure. Limited use of these agents is reasonable in pregnancy. The concern, though, is that if you are too aggressive with them you are going to lower the blood volume, damage the perfusion of the placenta, and result in fetal distress.

Dexamethasone decreases intracranial pressure and is used in patients with increased intracranial pressure. It does cross the placenta, but actually can have a beneficial effect. We use it in patients in preterm labor to enhance fetal lung maturity. So in the proper setting, dexamethasone is quite appropriate.

Prednisone is also used. It is metabolized by the placenta, and the baby doesn't really see it.

Anesthesia. There is also a lot of controversy about choices of anesthesia, especially in regards to the use of spinal and epidural anesthesia. Cerebellar herniation is a concern in the case of a spinal block where you have increased intracranial pressure. Rupturing of a hemangioblastoma by the spinal needle is a concern, and in the case of a pheochromocytoma,

the sudden profound drop in spinal pressure that you can get with a spinal block can be problematic, both to the mother and to the fetus. But there are important benefits to spinal and epidural anesthesia.

With epidurals you get a reduction in the cardiac output during labor, which can be helpful in cases of pheochromocytomas and CNS hemangioblastomas. It decreases arterial pressure, and decreases the bearing-down reflex in the second stage of labor, where the mother has the urge to push.

While general anesthesia has no known long-term ill effects on the fetus or placenta, it has its standard risks, one of them being maternal hypertension during rapid-sequence induction intubation. So it's not a panacea.

Again, it's important to individualize the care: to evaluate the extent of the patient's disease, to review the imaging studies of the CNS. If you are going to use regional anesthesia you need to know where these tumors are located, and an epidural is generally felt to be preferable to spinal for two reasons. One, it is thought to introduce less risk in terms of rupturing a hemangioblastoma, and second, the degree to which it reduces spinal pressure can be minimized. Both epidurals and spinals in the setting of pheos are very controversial.

Ergot medications, routinely used after delivery to treat post-partum hemorrhage, can cause hypertension and should be avoided in patients with pheochromocytomas and patients with CNS hemangioblastomas.

If surgery is performed during pregnancy, especially during the third trimester, appropriate positioning of the mother is going to be critical. It is important that she is not lying flat. She has to be tilted, to take the weight of the uterus off the major vessels in the pelvis and abdomen.

During any such surgery where there is a viable fetus, the fetus should also be monitored closely. In such situations we have used continuous fetal heart rate monitoring during surgery. If it's the third trimester and there is fetal distress, you can intervene and perhaps deliver the baby early.

There are more questions than answers. The data is very limited. The patient needs to be a real participant in all of this. The patient, family, and medical team need to work closely together. It's a tricky situation that calls for counseling, consent, and understanding of the ambiguities that are likely to arise.

Mode of Delivery. During labor the pressure rises both in the blood vessels and in the cerebral spinal fluid. Each contraction affects the pressure. In that setting there is risk of rupture of the CNS hemangioblastoma, and the risk of a hypertensive crisis in labor with pheochromocytomas.

With CNS hemangioblastomas, cesarean delivery has been recommended, especially where there are large lesions, elevated intracranial pressure, or neurological deterioration. In some situations, vaginal delivery and epidural analgesia is reasonable and appropriate if there is no acute neurologic deterioration. With careful management, the doctor can minimize the arterial pressure, and can do what is called a second stage assist to avoid the mother bearing down. Second stage assist is waiting for the mother to become completely dilated, and the fetal head to descend in the pelvis low enough to apply a vacuum or a forceps. There are some risks to both mother and baby with an operative vaginal delivery, but in the proper hands it is generally quite safe.

There is only limited literature on how best to deliver patients with pheochromocytomas. This data include patients who were treated and untreated, and patients who came in at term with terrible hypertension, no treatment, and no diagnosis. It shows that with vaginal delivery there is a 31% risk of maternal death; with cesarean section, the risk dropped to 0-19%.[3] As such cesarean section has been advocated, primarily now because of concerns over hypertensive crises in labor, concerns regarding conduction anesthesia, and because of the tendency until recently to do a combined delivery and resection of the tumor.

> "…pregnancy should not be discouraged in women with VHL if the screening results are negative, or if the lesions are asymptomatic and have been adequately treated."

Today there are a number of physicians, including myself, who have tried to delay resecting the tumor until after the mother has recovered from delivery. If the patient is in her third trimester, and is well controlled with established alpha blockade, we watch the blood pressure intensively during pregnancy and delivery, and decide whether we feel we can wait and do a laparoscopic procedure after recovery rather than exposing the mother to a more risky major operation at the time of delivery. Again, there is no consensus on these matters.

The largest series that I could find in the literature[9] is an analysis of 56 pregnancies in 30 women with VHL. It's a low-risk group. All but one had asymptomatic lesions. Symptoms related to VHL developed in 5.4% of the pregnancies. The live birth rate was 96.4% and all infants survived. Mean gestational age 38.2 weeks, which is well into term. Weight 3.1 kilograms. These are excellent outcomes. There are risks for women with VHL, but you can have good outcomes. Again, this is data on a low-risk group.

The authors of this paper feel that pregnancy should not be discouraged in women with VHL if the screening results are negative, or if the lesions are asymptomatic and have been adequately treated.

Counseling. There is no good data on pregnancy and VHL kidney issues specifically. In counseling women with renal insufficiency from multiple causes, it is important to explain that pregnancy places a major additional burden on the kidney. So normal renal function is important. If there is moderate or severe renal insufficiency the risks in terms of prematurity, or permanent loss of renal function, can be significant.

No matter how good our intentions are to achieve more widespread pre-conception counseling, the reality is that at least half the pregnancies are unplanned. It is important for the patient to inform the medical team that VHL is in the family, even if she herself does not have a diagnosis of VHL. In the absence of symptoms it is important to have a high level of suspicion. In a patient with VHL It is important to check for all possibilities — pheochromocytomas, CNS involvement, retinal involvement, 24-hour urinary collection, eye exam, abdominal ultrasound, MRI, CT – so you know what you're doing, and so the patient and the medical team can be prepared for possible complications.

Critical to all this is a multi-disciplinary approach. The patient who has VHL and has lesions of any kind, needs to be delivered in a place that has all the specialists necessary to take care of this patient – obstetricians, surgical specialists, anesthesiologists, endocrinologists, neurologists, radiologists, geneticists – it's a big effort on everybody's part.

See related stories beginning on page 2.

Note: Whenever you have the opportunity to check things out before entering into a pregnancy, be sure to have a complete set of "before" tests. This will also help us collect data on the question of whether and to what extent tumors grow, or temporarily inflate, during pregnancy. What is very hard to sort out is how many people in fact experience tumor growth during pregnancy, and of those, how many tumors grew because of the pregnancy, and how many of them grew simply because it was their time to grow.

Footnotes:

1. Delisle MF et al. Central Nervous System Complications of von Hippel-Lindau Disease and Pregnancy; Perinatal Considerations: Case Report and Literature *Review. J. Matern.-Fetal Med. 2000*;9:242-247.
2. Postural hypotension: a significant drop in blood pressure when standing versus when sitting.
3. Schenker JG, Granat M. Pheochromocytoma and pregnancy: An updated appraisal. *Aust NZ J Obstet Gynaecol* 1982;22:1-10.
4. Harper MA. et al. Phaeochromocytoma in pregnancy. Five cases and a review of the literature. *Br J Obstet Gynecol* 1989;96:594-606.
5. Burgess GE. Alpha blockade and surgical interventionof pheochromocytoma in pregnancy. *Obstet Gynecol* 1979;53:266-270.
6. Kothari A et al. Massive bilateral phaeochromocytomas in association with Von Hippel Lindau syndrome in pregnancy. *Aust N Z J Obstet Gynaecol* 1999 Aug;39:381-4.
7. Naidoo K, Bhigjee AI. Multiple cerebellar haemangioblastomas symptomatic during pregnancy. *Br J Neurosurg* 1998;12:281-4.
8. Ogasawara et al. Pregnancy complicated by von Hippel-Lindau Disease. 1995;85:829-831.
9. Grimbert P. et al. Pregnancy in von Hippel-Lindau disease. *Am J Obstet Gynecol*, 1999;180:110-1.

California coverage for people with VHL

The Genetically Handicapped Persons Program (GHPP) provides health coverage for Californians 21 years of age and older who have specific genetic diseases including von Hippel-Lindau. GHPP also serves children under the age of 21 with GHPP-eligible medical conditions who are not financially eligible for California Children Services (CCS). The program is administered statewide through the GHPP office in Sacramento.

Although there are no maximum income eligibility requirements, families with Adjusted Gross Incomes (AGIs) exceeding 200 percent of the federal income guidelines pay an enrollment fee and treatment costs based on a sliding fee scale for family size and income.

For further information about GHPP, please call 1-800-639-0597

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David's Marathon

by David I., California

The Portland Marathon was on Sunday, September 30. Portland weather was clear and hot, quite unseasonably so. About 8000 participants gathered at 4th and Jefferson for the 7:00 start, which was delayed while the attendees paused for a moment of silence in recognition of the September 11th tragedies. The marathoners, as well as I can determine it, were about half walkers and half runners.

Marilyn G. and I are coworkers with the City of Palo Alto, California. We strapped on our walking shoes and were primed for the 26.2 mile event.

I was diagnosed with VHL in 1994 and used memories of that time as inspiration. In 1994, a brain tumor had caused severe headaches and severe dizziness. I could only walk to the bathroom from my bed with the aid of walker. I felt so sick that I couldn't eat. That tumor was removed and I have had several others treated over the intervening years with stereotactic radiosurgery. I also have kidney complications.

To explain the marathon undertaking goes back a few months. Marilyn and I have both enjoyed walking as a healthful activity for many years. One day, Marilyn approached me with the notion that she was going to prepare for and participate in the Portland Marathon. Would I mind, she asked, if she solicited contributions to the VHL Family Alliance as a fundraiser allied with her effort? I thought that was a wonderful idea, but would she mind if I did the training and the marathon also?

We both carefully followed the suggested training regimen for walking a marathon that was posted on the Portland Marathon web site, so we were well conditioned for the distance. We had the enthusiastic interest of our colleagues and family and friends to sustain us early on, as well as the commonly shared drive to 'just finish'. What we did not expect was the hot weather on the day of the race. Fortunately, the Portland event was beautifully organized with ample water service along the route.

Marilyn and David

Participants were walking for a number of worthy causes, including breast cancer and diabetes. There is a psychological advantage to having a cause to propel your effort.

I actually improved on my expected pace for the walk. In training, I aspired to maintain a fifteen minute mile pace. My actual pace in the marathon was influenced a little by the other participants around me, and at times I clocked miles at close to fourteen minutes. Marilyn and I walk at different paces, so we did not do the distance together.

Those of us with von Hippel-Lindau have been aided a great deal in the identification and management of our illness through the guidelines and support of the Family Alliance. I have always felt that managing my illness is only half the battle. The other half is managing my health. Walking and swimming are part of a regular regimen that allows me to keep fit and ready for the next VHL ordeal or really any ordeal that I happen upon. It might even be said that my quality of life has improved since the 1994 onset.

I am grateful for the interest and support that Marilyn and my friends have shown me over the years, and for the guidance and information of the Alliance.

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