VHL Family Forum

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VHL Tumor Suppressor Gene Found!

In the May 28 issue of *Science* magazine, an international genetic research team reports that it has located the von Hippel-Lindau Disease Tumor Suppressor Gene.

Congratulations go to Farida Latif, Masahiro Yao, Mary Lou Orcutt, Igor Kuzmin, Fangwei Zhou, Berton Zbar, Michael I. Lerman. and Michael Dean of the National Cancer Institute, Frederick, Maryland; Kalman Tory, Fuh-Mei Duh, Thomas Stackhouse, William Modi, Laura Geil, Laura Schmidt, Hua Li, Ming Hui Wei, Fan Chen, and Damjan Glavac[v] of Program Resources Inc./DynCorp., Frederick, Maryland; James Gnarra, McClellan M. Walther, Yongkai Weng, Dah-Shuhn R. Duan, W. Marston Linehan, Gladys Glenn, and Peter Choyke of the National Cancer Institute, Bethesda, Maryland; Frances M. Richards, Paul A. Crossey, Malcolm A. Ferguson-Smith, and Eamonn R. Maher of Cambridge University, Cambridge, England; Denis Le Paslier, Ilya Chumakov, and Daniel Cohen of the Centre d'Étude du Polymorphisme Humain, Paris, France; and A. Craig Chinault of the Institute for Molecular Genetics, Baylor College of Medicine, Houston, Texas.

"They definitely have it and it's very exciting. It means real help for the von Hippel-Lindau families," says Wayne State University molecular geneticist David Smith, who was also racing to find the gene.[1] This achievement builds on a great deal of work done not only by this team but by many others whose published works along the way provided pieces of the puzzle. Credit is also due to the many families affected with VHL who have contributed the blood and tissue samples used in this research.

The VHL gene is "an important one to know about. It's really nice to have it join the club," says Alfred Knudson of Fox Chase Cancer Research Center in Philadelphia, whose work more than two decades ago laid the foundation for current tumor suppressor gene research.[1]

Using a number of different techniques this team was able to map almost completely the relevant area of chromosome 3. They found "nested constitutional deletions" in three unrelated VHL patients. This finding and the availability of cloned DNA accelerated the speed of their search for the VHL gene. "We reasoned," says Dr. Latif, "that the smallest of these three deletions should either encompass or interrupt the gene." Like a Russian doll that gets smaller and smaller, explains Dr. Zbar,[1] the study of these nested deletions narrowed the location of the gene.

They used probes[3] to determine what genes were in this area, and began to work primarily with two genes, referred to as g6 and g7. They then tested blood samples from VHL patients to see which of these were present. They found 120 VHL patients in which g6 was not involved.

"By contrast," says Dr. Latif, "g7 proved to be a strong candidate for the VHL gene." They found that g7 was expressed in a variety of VHL tumor tissues, including brain and kidney tissues.

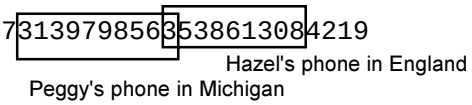
"Furthermore Southern (DNA) analysis showed that the g7 sequence is highly conserved across species as diverse as mammals, drosophila [fruit fly], and sea urchin." Evidence that this genetic material has changed very little in the course of evolution suggests that it performs a very basic cellular function.

Finally they tested for deletions in the g7 gene in the blood of 221 unrelated VHL patients, including eight patients classified as "new mutations." They found deletions in at least 18%. The entire gene is 6

Inside this issue!

Framing, additions, and deletions

Let's say that we have a string of 25 numbers, containing a telephone number, but we don't know exactly where the telephone number begins or ends. If we move a "frame" the size of a phone number up and down this string of numbers we could reach a wide variety of people and places.



If we add a number into the middle of this string, or delete a number or two from the middle, and we try to use the remaining numbers within the same frame, we will reach someone entirely different. The effect of these additions and deletions is called a "frameshift error".

to 6.5 kilobases in length; the identified sequence is 1.8 kilobases in length.

They were able to confirm that the VHL gene behaves as a typical tumor suppressor gene, as defined in Knudson's theory of human carcinogenesis[2]. According to that theory, a tumor suppressor gene normally keep tumors from forming. It is the loss or inactivation of one or more of these tumor suppressors that leads to cancer. If this is the case, they reasoned, then this altered form of the gene would be present in VHL tumor tissue.

They decided to look and see if there were deletions or mutations in the g7 genes in random or sporadic renal cell carcinoma (RCC) in the general population.

"We chose to study RCC because Knudson's model predicts that sporadic cancers should be associated with mutations in the same loci [locations] affected in the corresponding hereditary cancer."

A team under Dr. Linehan looked at a number of samples of tissue from random RCC tumors. They identified small mutations that created frameshift errors, and presumably result in the building of the wrong protein in the body. In another set of patterns there was a "nonsense mutation" where two components were reversed (instead of CA, it was AC).

In VHL patients they also saw deletions or mutations among the samples, which supported the conclusion that g7 is the VHL tumor suppressor gene and that it has a role in some sporadic RCC.

They compared this string to genes and proteins already registered in the databases of genetic information, and found no immediate matches. "It already looks like it will be a new type of tumor suppressor gene," says Dr. Lerman.[1]

The sequence obtained so far in the g7 gene shows that the gene encodes 284 amino acids, the building blocks of proteins. There may yet be more. There is one known protein which contains the pattern seen so far, one which is involved in the passing of signals among cells, telling them, for example, when to multiply or not. Evidence indicates, though, that they may be looking at a new protein, not previously identified. "The presence of this acidic [pattern] suggests that the VHL protein may be localized in the cell membrane and may be involved in signal transduction or cell adhesion. Further clues to the function of the VHL protein may emerge as more sequence information is obtained."

What does this mean to us now? The DNA testing which we reported in March uses *indirect* testing, analyzing multiple samples in a family to determine a repeated pattern associated with VHL which is unique to each family. This new information allows us to use a method of *direct* testing, which is easier to do and less prone to errors. In the families for which this testing works, it is much more reliable, and it can be used for individuals without other affected family members; but as explained above, it will only apply immediately to about 18% of families. When the rest of the VHL gene has been sequenced, the percentage of people for whom this test works will increase.

Researchers are hoping to have the gene's full sequence within the year, and a 100% accurate diagnostic test for VHL should soon follow. Dr. Zbar also hopes to be able to correlate specific mutations on the gene with the distinct forms of cancer that strike different VHL families. This could greatly improve patient monitoring by suggesting which tumors to look for most carefully.[1]

The DNA testing laboraties at Johns Hopkins in Baltimore and at Addenbrooke's Hospital in England are gearing up to do this new testing. Requests for testing may be submitted *by a genetic counseling center* to: Ms. Corinne Boehm, DNA Diagnostics Laboratory, Center for Medical Genetics, Johns Hopkins Hospital, Baltimore, MD 21205, Tel: 1-410-955-0483, Fax: 1-410-955-0484; or Dr. Eamonn R. Maher, Clinical Genetics, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, U.K., Tel: 44-223-216446, Fax: 44-223-217054.

This article is based on Latif et al, "Identification of the von Hippel-Lindau Disease Tumor Suppressor Gene," *Science* **260**, 1317-1320, 28 May 1993. Prepared with the kind assistance of Dr. Frances Richards, Ms. Corinne Boehm, Dr. Berton Zbar, and Dr. Gladys Glenn. 1. As quoted in John Travis, "New Tumor Suppressor Gene Captured," *Science* **260**, 1235, 28 May 1993. 2. Knudson's theory is presented in A. Knudson, *Proc. Natl. Acad. Sci. U.S.A.* **68**, 820 (1971); *Annu. Rev. Genet.* **20**, 231 (1986). 3. ***To understand the terms in this article*** you will want to read our articles "Tracking Down the VHL Gene" and "Why so Many Errors in our DNA?" in the March 1993 issue of *VHL Family Forum*. ❑

The Secret

by Lois E., Minnesota

Von Hippel-Lindau (VHL) was a secret word in our family for years. We believed if we didn't talk about it, it would go away. Unfortunately, that left us very uninformed.

My father, Rudy, was the first of our family to be diagnosed with VHL. His first brain tumor was removed at age 22. The surgery was performed in 1942 at the Mayo Clinic in Rochester, Minnesota. My father experienced total blindness and severe headaches days before surgery. During the 1950's another inoperable brain tumor was found at the stem of his brain. Our understanding at the time was that the second tumor may have been caused by not fully removing the first. Now that we know more about VHL, it is more probable that this was a second tumor. VHL tumors of the brain do not spread from one location to another. Doctors now believe that each one grows from a single defective gene. Complications from the second tumor caused my father's death at the age of 52 in 1967.

> "I think of myself as a healthy person and try to keep busy all the time."

Rudy was the father of five children, four daughters and a son. Two of the five children have been diagnosed with VHL -- myself and my sister Mary. My oldest sister and younger brother have yet to be tested.[1] Tests on my younger sister have proved negative.

Mary, the second child, died of a brain tumor at age 22 in 1962. At the time of her death Mary was pregnant with her fourth child in four years. Due to the pregnancy her symptoms, such as fainting, were not identified as VHL. Mary's three daughters have all been tested, and only one has VHL.

Mary's oldest daughter MaryBeth had a tumor removed in 1975 at the age of 16. Her first symptom of VHL was headaches. As her tumor grew, she experienced spells of vomiting, fainting, and blackouts. MaryBeth has two young daughters who have not been tested for VHL.[1]

My first symptom of VHL was extremely sensitive teeth. This was followed by an disturbance of my equilibrium. At that time, doctors attributed the symptoms to a different disease which had taken 70% of my hearing in my left ear at age 21, so they referred me to an ear, nose, and throat specialist. They decided to do a CT scan and it was then that a brain tumor was discovered. I had the tumor removed

1. The VHL Family Alliance strongly urges family members at risk to have regular check-ups. Experience has shown that it is best to deal early with VHL issues if you want to avoid permanent damage.

Chad, Carmen, Lois, and Don.

in 1982 at age 39. Since the operation doctors have found tumors on my cerebellum, spinal cord, and eye. The tumor on the eye was treated in August 1992. In addition to the tumors, doctors continue to monitor cysts on each kidney.

I think of myself as a healthy person and try to keep busy all the time. I enjoy my job, my co-workers, and my family.

I have two children. My daughter Carmen has been tested and shows no signs of VHL. My son Chad was diagnosed with VHL in the spring of 1985. He began experiencing headaches in the fall of 1984. We attributed them to growing pains, as he had grown an inch a month for fourteen months. The headaches persisted. Due to our family history, I scheduled a physical to have Chad examined for VHL. The seriousness of his case grew quickly. On Monday March 29 he experienced flu-like symptoms along with the headaches.

By Wednesday he had increased pain in his head. We scheduled a CT scan for Thursday. I called the doctor immediately Friday morning because the pain in his head was more severe and he began vomiting uncontrollably. The doctor identified a brain tumor from the scan. Chad was rushed to Children's Hospital and given medication to reduce the swelling around the brain caused by the tumor.

On Monday doctors removed two large tumors from Chad's cerebellum, one from the right hemisphere and one from the left. He recovered quickly from surgery and returned to school in two weeks.

Chad did not experience any additional symptoms of VHL until the fall of 1991. He had difficulty seeing the blackboard in school. His optometrist found tumors and referred us to a specialist. Chad had eight lesions in his left eye and three in the right eye. He has been treated with laser treatments.

Although the laser treatments have been effective in controlling the lesions, Chad will have permanent retina damage that is not correctable with glasses. The doctors have since found additional tumors on Chad's spinal cord and brain. We now make sure we have regular checkups, to reduce the number of surprises and minimize permanent damage.

For years I have been searching for information on VHL to give to our doctors. Our goal is to make all those as uninformed as ourselves recognize the signs and symptoms of VHL. We have learned that we must become advocates in our own personal and family health care. I am excited to listen and learn from all families in order to learn from their experiences. I would greatly appreciate any information from other families and from doctors. I would also like to thank everyone for their involvement in the VHL Family Alliance and for taking the time to help us all. ❑

David, Sally, Shannon, and David Jr.

Preventive Maintenance

by David T., Hawaii

For the past 13 years, I have been walking proof of what it means to get a new lease on life. In 1980 I walked away from Tripler Army Medical Center on Oahu with somebody else's kidney transplanted into my body.

I and forty-three other members of my family are known to be affected with von Hippel-Lindau disease. Doctors first found VHL lesions in my eyes 14 years ago.

At that time I had two weeks remaining on active duty with the U.S. Navy before I was scheduled to get out. At age 22, married, and with a six-month-old son, I had my life mapped out, with a civilian job as an electrician waiting for me.

I was a lean 160 pounds, a runner, and felt great. I was shocked to receive a letter asking me to come to Tripler to be screened for VHL.

For years my family had puzzled over the early deaths of relatives including my father, Elias, who died at 33 of a brain tumor. Other relatives had died or were ill with cancer of the pancreas and kidneys, or had spinal cord tumors. There was some sickness in our family, and it affected the same areas all the time. We kind of knew there must be something, but we couldn't put our finger on it.

It was Tripler physicians James Lamiell and Fernando Salazar and University of Hawaii geneticist Y. Edward Hsia who began to see a link in our family, dating back to at least my father's parents. They received a grant from the government to study the disease in my family.

I felt the picture of health, but doctors were advising me not to get discharged until they had completed my testing. They found tumors in my eyes. I just could not believe it. I was young, I wasn't sick, I didn't have any problems, I was healthy.

Once doctors found the eye tumors, they went forward with a more extensive screening. It was hard on my wife, I think more so on her than on me. But either way, it was real difficult. I was going through a denial and kept telling myself this cannot be, it's a mistake. Not me! I'm not sick, I don't feel bad, I feel good. I'm in perfect shape.

I learned that the disease cannot be stopped, it can only be managed. Affected areas can be treated. I began to see it as an opportunity to apply the Navy's preventive maintenance system (PMS) to my own life.

PMS is what we did to take care of our equipment in the Navy. I began to apply that to my own life, to my own health. Preventive maintenance is necessary if you know that you have the disease. I know I have it, so there are certain steps that I have to take to watch it.

At 22, I learned that there were cancerous tumors on my left kidney. Even though I felt well, I understood that if I left the tumors in, the cancer could spread. I decided to have it removed. They did an exploratory surgery at the same time to check everything, and then found small growths in the right kidney. These they felt were not cancerous, but they told me that there was a chance they could become cancerous at some point, and they couldn't tell me just when.

In one of the hardest decisions I've ever made I decided to have the right kidney removed, go on dialysis, and wait for a transplant. There was a required one-year wait, to make sure that the cancer

had not spread to other parts of my body.

The whole time I was on dialysis, I was sick as a dog. I hated it. I always felt bad. I used to get a blood transfusion every two weeks and boy, that would pick me up! Today there are much better methods of dialysis than there were back then.

My mother volunteered one of her kidneys, even though doctors couldn't guarantee that her one remaining kidney would work well enough to support her. She too might face dialysis in the future. To me, that was the ultimate expression of her love, that she was ready to sacrifice everything and go on dialysis. It just overwhelmed me.

I think I know what real love is -- not sentimentality or emotionalism or feelings. Looking back on that, I've grown to see what real love is -- the ability to deny everything you've got and give it all up for someone else.

I couldn't face the thought of my mother possibly having to go on dialysis herself if her remaining kidney failed. I waited until a kidney became available from an unrelated donor, from someone who had died of other causes.

> "Friendship is born at that moment when one person says to another, "What! You too? I thought I was the only one." -- *C.S. Lewis*"

I was the first person on my island to have a transplant. Thirteen years later my new kidney is going strong. A year ago I had surgery to remove a tumor in my spinal cord at the base of my brain. I'm relieved that I don't have to worry about that one any more! Going into surgery I knew that there would be some postoperative spinal cord damage. I'm adjusting to some physical limitations, learning to take them in stride.

Sometimes I feel disappointed about the hand of cards I've been dealt in life. There are things I miss, like a good game of basketball. I used to go hiking, running every day. Now I'm never going to hike that mountain or lift heavy things.

Sometimes I think my physical limitations are hardest on my son. I worry that he feels cheated. You look forward to when you have a son to go out and shoot baskets. I play as much as I can. He understands I'm limited. He won't run into me. Sometimes he lets me win.

The next thing I have to worry about are the tumors that have developed in my pancreas. They are growing, and we are watching them. I am educating myself about pancreas implants. Even without one, though, it is possible to manage with insulin, like a diabetic.

Living like this, waiting for that thing to develop more, is stressful. I feel like OK, that's going to be the next thing I will have to face. What is it going to happen? It is going to be six months? Is it going to be in a year?

The price of my health is constant vigilance, and I've gotten pretty skilled at it. Once I was angry about getting VHL, but no more. I'm just thankful I'm here. I think I've got it good. There are babies born without a chance and terminal cancer patients without a handle to hold onto. I'm just happy to be here.

God put me here; he can do with me what he wants. One thing I feel God wants me to do is to be the pastor of my church. My congregation looks out for me, making sure I don't overdo it. I give all credit to God, and ultimately I'm grateful. He promised to take care of me, and He does.

I don't see myself as a poor thing -- far from it. I have a loving family. I am surrounded by wonderful friends. God is gracious. I have a good life. ❑

Keeping Healthy Kidneys

Much has been learned about kidney treatment since David's experience in 1979. Dialysis and transplant are not the only options for VHL patients with kidney involvement.

According to the literature, 25-40% of people with VHL will have kidney involvement. There are generally no symptoms to watch for. It is critically important that you begin monitoring the kidney and pancreas long before any symptoms occur.

The kidney is a wonderfully redundant system. With only 25% of one kidney, it is possible to live a healthy normal life and not even make significant restrictive changes in your diet. Working closely with their medical team, most people should be able to stay on their own kidney power.

It is not unusual for adults to have a cyst in the kidney, so the presence of cysts is not a problem in itself. However, it is also possible to have tumors, called *hypernephromas*, which are potentially malignant.

Think of it as having a mole on your skin. Usually there is no cause for alarm. It is only when the mole begins to grow or change in suspicious ways that your doctor would recommend that it be removed and examined to make sure it is not a skin cancer.

Similarly, when the rate of growth of a kidney or pancreatic tumor becomes suspicious, your medical team may recommend surgery.

In watching your kidneys and pancreas, your medical team is working to evaluate whether you have

cysts or tumors, and whether the tumors are benign or troublesome. They will need tests such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) to keep an eye on them. They will watch the tissue density, the position of the tumors, and the rate of growth. Each of these diagnostic methods gives them a different kind of information. Depending on where the tumors are, and your own medical history, your team will select the method which provides the best information with the least risk to you.

There are a number of options which you and your medical team can discuss. Options will vary depending on the number of tumors, where they are, their characteristics and growth rates.

Techniques for partial removal of a kidney *(partial nephrectomy)* are improving constantly. This allows removal of many suspicious tumors while leaving enough kidney to provide you with normal kidney function.

Usually, when a urologist sees "hard tumors" (what looks on the diagnostic image like a cancerous tumor) in both kidneys, it means that the cancer has already spread from one kidney to the other, and is in danger of spreading to other parts of the body. New analyses, however, are showing that VHL tumors are different from standard renal cell carcinoma (RCC). Each VHL tumor is a *neoplasia*, or new growth, arising from a single cell. Having VHL tumors on both kidneys is not unusual; in fact bilateral tumors are present in the majority of cases of VHL kidney involvement.

A number of physicians now believe that, depending on the size and position of the tumors, it is reasonable to consider removing only the tumor and an appropriate margin of healthy tissue, and leaving the kidney. It is, of course, not possible in every case. You need to discuss your options thoroughly with your medical team.

Prepared with the kind assistance of Dr. George T. Klauber, Chief, Pediatric Urology, New England Medical Center, Boston, Massachusetts, and Dr. Hartmut P. H. Neumann, Department of Nephrology, Medizinische Klinik der Albert-Ludwigs-Universität, Freiburg im Breisgau, Germany. **References:** Keeler & Klauber, "Von Hippel-Lindau Disease and Renal Cell Carcinoma in a 16-year-old Boy," *J. Urology* **147:6** (1992) 1588-1591; W. R. Morgan and H. Zincke, "Progression and Survival after Renal-Conserving Surgery for Renal Cell Carcinoma: Experience in 104 Patients and Extended Followup," *J. Urology* 1990 **144:4** (1990) 852-857. ❑

I really enjoyed the first copy of the *VHL Family Forum.* It is written so it is very easy to understand. All of the articles were great, especially "What is VHL?" Most of the time the subject is written in a language only the medical people understand."

-- Catherine G., Massachusetts

Organ Donation Saves Lives

More than 30,000 Americans are now waiting for an organ transplant. According to Elizabeth Strock, public education director for the New England Organ Bank (NEOB) and former director of public affairs at Beth Israel Hospital in Boston, the number of people waiting for organ transplants has increased sharply over the past few years. "In fact, a new name is added to the national waiting list for transplants every 20 minutes," she says.

Unfortunately, the number of organ donors has remained fairly constant over the past few years, despite advances in medical technology that have increased the number of people who are eligible for organ transplants. "Part of the problem," says Dr. Michael Shapiro, surgeon, and chief of the Beth Israel Hospital Transplant Division, "is that the public is not aware of how great the need for organ donors has become. We have advanced medical technology so that we can perform more transplants and improve the likelihood of favorable outcomes, but none of this will effect a real change if people are not willing to become donors."

Beth Israel performs 22 to 30 kidney transplants annually, and plans to do three to five pancreas transplants in 1993. BI's waiting list for transplants, however, continues to escalate because of the shortage of donors. Heart, liver, and lung donations are also critically needed by potential transplant recipients around the world.

Know the Facts

Joan Abrams, RN, clinical transplant coordinator at Beth Israel, works with patients awaiting transplants and with families of potential organ donors. "It's a very difficult subject to approach with the family of someone who has just died tragically, but it is imperative for those people to realize that they have an opportunity to offer someone else the gift of life," explains Abrams. Organ donation can even help a family during the grieving process, she says, because donor families might find solace in the knowledge that the donation is a way to extract some good from the death of a loved one.

Many issues cloud the subject of organ donation, and an important component of Abrams' role is to clarify some of these misconceptions. "It's a matter of public awareness," Abrams says. "If people understand the facts about organ donation, they probably will feel less uneasy, and hopefully be more inclined to consider becoming donors."

Dr. Michael Shapiro, Robert Garnett, and Joan Abrams, R.N.

To address some commonly asked questions, Abrams highlights these facts about organ donation:

Organ donation never compromises the donor's own health care.

Transplants are performed at no cost to the donor or the donor's family.

All major religious denominations in America support organ donation.

Allocation of organs is guaranteed to be fair, with no preference given on the basis of the potential recipient's race or wealth.

The family's approval for donation must be given, even if the donor has signed an organ donor card.

The donor's body is not disfigured and the procedure does not delay funeral arrangements.

One of the main concerns that people have regarding organ donation is that the donor's life might somehow be compromised in order to provide needed organs.

"This is absolutely not true," contends Abrams. "A medical professional's first priority is to do everything within their power to keep a patient alive." The medical team treating the patient is not involved in the transplant process and an objective neurological specialist must pronounce that an individual is brain dead before the question of organ donation arises. The term "brain dead" refers to the *irreversible* loss of all brain function. The person's other organs may still be maintained artificially by a respirator, but will *never* function again without external means.

A Donor Recipient's Perspective

Robert Garnett is one patient who clearly benefited from a kidney transplant. Owner of "Strutters," a vintage clothing store in Back Bay, Boston, Garnett also supplies costumes for films. Before his transplant operation at Beth Israel in 1989, Garnett required three- to five-hour dialysis treatments three times a week. "I travel a lot in order to procure clothing for my stores and for the films that I costume," he says. "It's a relief to be free from dialysis when travelling."

Shapiro emphasizes that donor recipients must be committed to their follow-up care because transplantation is a treatment, not a cure. Garnett now receives complete follow-up care at BI once every two months. While he had some difficulty adjusting to the immunosuppressive drug treatment following his surgery, he takes it all in stride. "I've had tremendous support from the staff at BI. I regard the people here as my medical family," he says with a grin.

What would he recommend to people who are unsure about organ donation? "Go for it!" Garnett replies emphatically, "I'm living proof that transplant surgery works and that donating organs posthumously can make a real difference."

Becoming an Organ Donor

VHL patients themselves are not kidney donor candidates because of the possibility of tumors developing in their kidneys. However, we can all be advocates raising everyone's consciousness of the importance of signing up for a donor program. In many states and countries, it's as easy as filling out a card when you renew your driver's license. You should carry a Donor Card with you, and you should advise your family of your wishes.

Many people do not even think about becoming donors until they meet someone who has received a transplant, or who may need one. Whatever the impetus, says Abrams, signing up to be a donor is easy. Call a large medical center near you, or one of the following numbers:

In the U.S.: 1-800-24DONOR
In Eastern Canada: 1-800-387-6673
In Western Canada: 1-416-340-3587
In England: (0800) 555777
In Germany: (06102) 3590
In Australia: (02) 391-9184

The Examiner, newsletter of Beth Israel Hospital, Boston, April 1993. Photograph courtesy of Beth Israel Hospital Photographic Services Department. ❑

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VHL Family Forum

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Ask the Experts . . .

Screening for VHL

Q: What should I do about testing my children? I don't want to find out when they're 12 that I should have had them tested at age 8. — *Mary Ellen T., Massachusetts*

A: Children born to a parent with von Hippel-Lindau disease are at a 50% risk for inheriting the gene defect. Therefore, early monitoring is recommended. The pediatrician should be alerted to the family history. Careful ophthalmologic examinations should be started at around 4 years of age and be repeated annually thereafter. Each year the child should have a careful physical examination with special attention to the blood pressure and neurologic status.

At around ages 10 to 12 it is reasonable to begin screening of the central nervous system by CT scan or MRI of the head, and MRI of the upper spinal cord. This also should be repeated every 1-2 years thereafter. Any child who develops unexplained headaches, flushing, or high blood pressure should have a urine test to assess for pheochromocytoma. This is particularly true in families in which other members with von Hippel-Lindau disease have had pheochromocytomas. Imaging of the intra-abdominal organs should be offered at around age 18 years and annually thereafter.

These are general guidelines. It is important to know that in individual cases, physicians may choose to perform different tests or at different ages.

In some families with a sufficient number of affected family members, DNA studies for presymptomatic diagnosis may be an option. Depending on the outcome of the test, it may be possible to decrease the frequency of testing. In the future, it may be possible to eliminate testing completely for those whose DNA studies suggest they are unaffected.
-- *Virginia V. Michels, M.D., Rochester, Minnesota*

VHL and Smoking

Q: Is there any reason to believe that smoking is bad for people with VHL? -- *Rachael M., Mass.*

A: There is no comprehensive study of smoking and VHL, and there probably never will be because the VHL population is too small to do a controlled study. Smoking is not good for anyone because it increases the risk of lung disease, heart disease, and cancer. For that reason alone people with VHL and their families should refrain from smoking. Beyond that, however, there are some specific risk factors for people with VHL.

Chances are that at some point VHL patients will require at least one surgery. Smoking increases the risk of postoperative complications of the lungs (atelectasis, pneumonia, hypoxemia).

Secondly, smoking has been implicated as a risk factor for developing renal adenocarcinoma (kidney cancer). Since people with VHL are already at risk for renal adenocarcinoma, it is unreasonable to increase the risk even further.

My general advice to people with VHL is to avoid all medical problems except the unavoidable one (VHL) -- i.e., don't smoke, avoid obesity, eat properly, get plenty of exercise, avoid drug use (alcohol, cocaine, etc.), and make sure you have family and friends for support.
-- *Col. James M. Lamiell, M.D., Fort Sam Houston, Texas*

Families from Germany?

I finished reading the draft of the second issue of the *VHL Family Forum*. I was especially intrigued with the letter from Siobhan G., Michigan, on page 9. I wonder if this family might have ancestors in the German Black Forest? I have seen a number of families with a lot of pheos and only a few CNS (spinal) hemangioblastomas.
-- *Hartmut Neumann, M.D., Freiburg, Germany* ❑

Carrier Detection Testing

In the March issue we carried a comment in an article by the National Society of Genetic Counselors which recommended asking your insurance company if they would cover carrier detection testing.

Since then, a series of articles has come to our attention, citing abuses of genetic testing information by insurance carriers and even employers. The National Organization for Rare Disorders is collecting information on such incidents. Please contact us, or contact NORD directly, if you wish to share your experiences.

Public policy issues on screening, privacy, and confidentiality are still being formed. If you are not already clinically diagnosed with VHL and want to participate in carrier detection testing, it might be wise to do so only as part of a research program or separately funded by yourself, not funded by your insurance company. ❑

Small World

I was pleased to notice that Dr. E. Maher from Cambridge, England, is on your Medical Advisory Board. It makes the world seem smaller. He has done initial screening on my mother and brother, who live in England. Luckily they appear to be symptom-free. -- *Patti K., California*

Ask the Family . . .

Dear Family,

In November 1991, at the age of 18, I was diagnosed with von Hippel-Lindau. I was the fourth of six children in my family to be diagnosed. I have two hemangioblastomas 2-3 cm in size on my right cerebellum. Unlike my other brothers and sister I do not have pheochromocytoma, but since they do, it may appear at any time. I was assured that my case was not severe and that no precautions need be taken aside from annual magnetic resonance imagery (MRI).

In the summer of 1992 my oldest sister went in for surgery to remove one of two hemangioblastomas of her cerebellum. It was at that time that I began to realize the seriousness of my disease. Aside from my sister's pheo, our cases are similar in the position of our hemangioblastomas. I began to realize that what was happening to my sister could happen to me.

While my case is the least serious in my family, it is still hard to cope with. I face many hard tasks ahead. One day I hope to have a family. How does one explain all this to a prospective mate? There are so many ways this can affect a person. Having VHL means having a 50/50 chance of passing it on to your children. How would someone feel about this inherited disorder and the gene their child may get? How does one cope with not knowing how long their partner might live? It is a risk one has to take, and not everyone will.

Hopefully in the near future gene replacement will play a significant role in the curing of VHL. Until then, determination, knowledge, and support will have to do.

— Siobhan G., Michigan

[Editor's note: Siobhan, pronounced "Shavanne," is Gaelic for Joan.]

Dear Siobhan,

The truth is, none of us knows how long our partners may live. People get in automobile accidents every day. 11% of women will get breast cancer. Most families in the general population will have at least one major health hurdle to deal with. Nobody has a guarantee on a trouble-free tomorrow, no matter how perfect they may think their genes are.

Yes, you may have some difficult periods to go through with your VHL. You may also have some difficult periods caused by a whole long list of other things that can happen in life, but you have some warning about VHL.

If you know there's a hurricane coming tomorrow, you have a chance to buy batteries, tape windows, and stay out of the water. If you don't know, and you go fishing, you could be in for some hard times. We wish the hurricane were not coming, but the warning gives us a better chance of weathering the storm.

When you find that special person to share your love and make a life together, you will work it out with him. The fact that you have determination, knowledge, and support is already a very great deal.

Love, Joyce G., Massachusetts

Dear Family,

My daughter just recently found out she has VHL, and she's very depressed. She is applying to college this year, and I'm terrified that she will be turned down. I don't know if she can deal with the disappointment. Should I check first with the college to see if they will admit a person with VHL?

Signed, Worried

Dear Worried:

I'm 21 years old and in college. I have VHL in the retina and spine, and had two cerebellar lesions removed at age 13.

I think you should not approach the college with this question. Why bring it up? It's not an academic problem, it's just a disease. Don't make a big deal out of it and act normal. Sure, she might need some time off. Lots of kids take time off during college, for reasons of health, mental health, or just to explore the world and grow up. Lots of perfectly healthy kids have skiing accidents and wind up in traction for a semester.

I also think you shouldn't be saying anything to colleges on your daughter's behalf. It's up to her to do it -- to get into college or not. Getting turned down by some of the schools you apply to is part of the game, part of learning about life.

If your daughter is depressed, it would be good for her to have a counselor to talk with for a while. Even just a few visits with a counselor who deals with the stresses of chronic illness can help to get her back on track. It's scary finding out, especially if you know an older relative with serious problems.

I have to take charge of my own life. There shouldn't be anything I can't do, I just have to use common sense.

Best wishes, Chad E., Minnesota

❑

Please Ask Us . . .

anything you'd like to ask

Please Tell Us . . .

what you want to say, on these or any other topics. We need to hear your opinion too!

Medical questions are passed to members of our Medical Advisory Board.

Family questions are posed anonymously to other members of the VHL Family Alliance.

Resources

While VHL always involves abnormal or out-of-control cell growth, not all VHL tumors are potentially malignant; some are. Technically, VHL is a familial cancer syndrome. Most of us don't normally like to describe VHL as a cancer. In the service realm, though, using the cancer description gives you access to a wide range of services that could benefit you and your family.

Cosmetics and Wig Care

suggested by Joanne B., New Jersey

"The 'Lipstick Theory' is the observation made by medical professionals that when a woman battling cancer starts to put on her lipstick, she is on the road to recovery," says William Cahan, M.D., Senior Attending Surgeon, Memorial Sloan-Kettering Cancer Center, New York.

The premise is: if a patient can be helped to look good, he or she will feel better and the quality of life can be improved.

Look Good...Feel Better, which was launched in March 1989, is a free national public service program dedicated to teaching cancer patients -- through hands-on experience -- techniques to help restore their appearance and self-image during treatment. Trained and certified volunteer cosmetologists conduct Look Good...Feel Better group sessions at comprehensive treatment centers, local hospitals, and salons. They help women regain control of their appearance by demonstrating how to camouflage the appearance-related side effects of treatment, including loss of hair, eyebrows and lashes, and changes in skin tone. In addition, patients are shown how to use wigs, turbans, and scarves to hide hair loss. It is important to note that Look Good...Feel Better is non medical and product neutral.

"Look Good...Feel Better reminds us in the medical community that healing the psyche can be equally as important as healing the body," says Marc E. Lippman, M.D., Director of Psychooncology Research at Georgetown University Medical Center and the Lombardi Cancer Research Center in Washington, D.C. "At Look Good...Feel Better sessions there is an almost tangible emotional shift. The participants, many of whom come into the room alone and frightened, begin to sense the care and concern of the volunteer cosmetologists and the community of survivorship they share with their fellow patients. Their spirits are visibly lifted."

Look Good...Feel Better is sponsored by the Cosmetic, Toiletry and Fragrance Association, the public service arm of the U.S. cosmetic industry's trade association in partnership with the American Cancer Society (ACS), the world's largest voluntary health agency, and over 45,000 hairstylists, estheticians, wig experts, makeup artists, and nail technicians who are members of the National Cosmetology Association (NCA).

In some areas you can apply for a free wig if you can't afford one and your insurance does not cover it. When you call, say that you have VHL, which is a familial cancer, and they will be happy to include you in the program.

The program is operable now in U.S., Canada, Australia, and New Zealand. It is expected to be operating in the U.K. in 1994.

In the U.S., call your local office of the American Cancer Society or 1-800-227-2345.

Before and After photographs courtesy of Look Good . . . Feel Better, The Cosmetic, Toiletry, and Fragrance Association, Washington, DC

VHL News

Another good source of information and services for VHL patients is the Von Hippel-Lindau Syndrome Foundation, Inc., P.O. Box 733, Toms River, NJ 08754-0733. Telephone (908) 244-7635.

Corporate Angels

suggested by Lee-Anne B., Connecticut

If you need air transportation to treatment, you can apply to the **Corporate Angel Network**, Westchester County Airport, Building One, White Plains, NY 10604. Judith Haims, Administrator, telephone 1-914-328-1313. This is a charitable organization of the U.S. corporations that own aircraft. They volunteer empty seats on business to cancer patients in need of transportation to or from recognized treatment. This service is not dependent upon financial need.

Patients must be able to board the aircraft unassisted, not require special equipment or services en route, and have proper medical authorization for the flight. CAN will transport one friend or family mem-

ber with the patient. You are responsible for your own ground transportation. You do not have to be in financial need.

Being flexible on airports and dates increases your chance of getting a flight. Lee-Anne says it's worth it -- "they really are angels!"

In Canada, **Mission Air Transportation Network** arranges free flights for patients if they must travel outside of their communities to obtain recognized medical care and they cannot afford the airfare. If required, an escort may accompany the patient. Mission Air utilizes aircraft seats donated by corporate, commercial and government sponsors.

Patients must be Canadian residents, may be any age and require treatment or diagnosis for any type of illness. Medical clearance is required and although wheelchairs can often be accommodated, patients must be able to sit in a regular aircraft seat and must not require medical care during the flight. A minimum of three full business days are required to arrange a flight. For more information contact Mission Air Transportation Network, 10 Alcorn Avenue, Suite 200, Toronto, Ontario M4V 3B1. Tel: (416) 924-9333, Fax: (416) 924-5685.

When we inquired about similar services in Europe, we were told that the distances are less vast and air service is not as essential. Where needed, courtesy train or taxi transportation can usually be arranged through physicians. ❑

Coping

"I keep VHL in its little compartment, and take it out when I have to, for check-ups and treatment."

— *Mary Ellen T., Massachusetts*

"You need to cry; you also need to laugh."

-- *Lee-Anne B., Connecticut*

Teamwork

by Joanne B., New Jersey

My doctor brought me in to explain the course of treatment he was recommending for my lesion. I asked him to explain what was going on, and why he was recommending the treatment. He looked startled and frankly a bit offended.

"I went to school four years beyond medical school to learn how to do this, and you want me to teach it to you in one hour?" he asked, somewhat sarcastically.

I looked at him and said, "I don't want to know everything you know, but I want to know how this treatment is going to work on me. How did you come up with this plan? Why? Show me on my films just where the treatment will be working and how."

There was a lot of tension and a long pause. "I think I know what you're asking me to do. Most patients don't ask to know, so I'm not used to answering questions like these."

I explained to him that I needed to know. I wanted to be able to visualize clearly what he was doing, and participate in helping the treatment work. I wanted to look in the mirror, straight at that lesion, and order it to shrink!

Eventually the tension subsided and we had a very pleasant, constructive conversation. At the end of the meeting I said, "Thank you for explaining. Now I understand."

He shook my hand warmly and said, "We'll get through this together."

We're a good team now.

Don't hesitate to ask your doctor to show you X-rays and explain test results. If you don't understand, ask for clarification. It is your right to have as much information as you wish about your own body. ❑

Uncertainty

I explain what's going on, how it works, what we're trying to fix, what could happen if it isn't fixed. I'm educating my patient in a way, but I'm also dispelling uncertainty. Uncertainty is the worst illness. The fear of the unknown can really be disabling.

--Dr. Thomas Delbanco, Beth Israel Hospital, Boston, Massachusetts

as quoted in Bill Moyers, *Healing and the Mind*, ©Public Affairs Television, Inc. and David Grubin Productions, Inc. Doubleday Books, New York, 1993, p. 18.

Pen-Pal Wanted

Catherine G. from Massachusetts is 62, a grandmother, with VHL, recently widowed. Her hobbies include crocheting, reading books, watching the soaps, football and baseball. She is looking for a female pen-pal with similar interests. Please send your letter to Catherine G. in care of the VHL Family Alliance.

Dr. Eugen von Hippel, 1867-1938

Eugen von Hippel wrote in 1904 "about a very rare disease of the retina" and in 1911 added "the anatomical basis" of that disease, which he named *angiomatosis retinae*. He studied one extended family, with several generations exhibiting numerous lesions typical of those of von Hippel-Lindau Disease (VHL).

Dr. von Hippel was honored in his lifetime as a physician, clinician, teacher and researcher. He spent his entire life in service to others.

Eugen von Hippel was the son of another exceptional ophthalmologist, Arthur von Hippel (1841-1917), professor of ophthalmology, founder and head of the University Eye Clinic in Göttingen, later succeeded in that post by his son Eugen. Eugen studied at the best schools -- Giessen, Freiburg, Berlin, Heidelberg, and Göttingen -- and received his doctorate in medicine in 1890.

As a young physician he first worked in pathology under Dr. Arnold at Heidelberg. During this time he studied cadavers with severe infections, which influenced the course of his later research. In 1892 he began to specialize in ophthalmology and became assistant to Dr. Leber. He studied and lectured in ophthalmology and won a prize for his research.

He became fascinated with disorders in formation of the eye, including hydrophthalmus (a form of glaucoma), corectopia (abnormal situation of the pupil), corneal defects, congenital cataracts of various types, and angiomatosis of the retina, which has become known as von Hippel's disease. He not only took great pains to describe these malformations in exquisite detail, but also sought to determine just how they came about, and how they might be tied to damage during embryonic development. His paper on *angiomatosis retinae* was published in 1895.

From 1909 to 1914 he taught at Halle and published his research in a series of publications dealing with the diagnostic signs and clinical results of these disorders. Later he taught at Göttingen, and produced a series of studies on sympathetic ophthalmia, tuberculosis of the eye, and chorioid membrane sarcoma, and on diseases of the optic nerve. He contributed to a number of textbooks, notably on diseases of the optic nerve, pathological anatomy of the cornea, and malformations of the eye.

In his tribute to Dr. von Hippel, Dr. Baurmann of Karlsruhe admires him for his astounding breadth and richness of creativity. He took an active role in the work of his students, helping them think and talk through the problems they were tackling. "His participation and positive input in each task, and his obvious interest in everything, added a very special element to his clinics. Von Hippel always created an atmosphere in which everyone felt extremely fortunate to be actively participating in the scholarly scientific work of the clinic."

He demanded the best efforts of everyone, physicians, nurses, and all other employees of the clinic. He instilled in everyone the spirit of respect for accomplishment in everything they did. This resulted in a very unusual harmony and positive mutual cooperation which benefited the work of the clinic in very favorable ways. His students went out into practice "equipped not only with a broad knowledge of clinical medicine, but above all with the ability to think critically and scientifically, and all had learned in that clinic how to gain self-confidence."

"To those who met von Hippel briefly, he appeared reserved and withdrawn; but whoever came to him with a real human need, be it as a patient seeking advice from him, as a pupil returning to him, or as a co-worker seeking with him the same goal in a clinical and scientific task, that person would find in Dr. von Hippel a rich helpful attitude and an unlimited and unshakeable confidence."

Prepared with the kind assistance of Dr. Hartmut P. H. Neumann, University Medical Clinic, University of Freiburg, Germany; Dr. Harry H. Wilcox, University of Tennessee, Memphis; and Mr. Richard Wolfe, Countway Library of Medicine, Boston.

References: Baurmann from Karlsruhe, Obituary of Dr. von Hippel, *Klinische Monatsblätter für Augenheilkunde*, **103** (1939) 632-634; H.P.H. Neumann, "The Epidemiology and Prospective Study of the von Hippel-Lindau Syndrome in South Baden," *Habilitationsschrift,* 214 pages, presentation to the Medical faculty of the Albert-Ludwigs University, Freiburg, 1988. Translations from the German by Dr. Wilcox. **Articles on angiomatosis:** Eugen von Hippel, *Über eine sehr seltene Erkrankung der Netzhaut.* Klinische Beobachtungen, Universitäts-Augenklinik zu Heidelberg, 1904; E. von Hippel, *Die anatomische Grundlage der von mir beschriebene "sehr seltenen Erkrankung der Netzhaut,"* 1911.

Portrait: from the collection and with the kind permission of his daughter, Frau Lena Chemin-Petit, Berlin. ❑

Alliance News

The Board approved the By-Laws, Chapter Agreement, and Chapter By-Laws in April. Incorporation documents and application for 501(c)(3) tax exempt status have been filed.

Officers. We are pleased to present this first set of six officers to you, listed on page 14. They are a talented, energetic, and compassionate group of people. These six people have 135 years of experience living with VHL. Just in their own nuclear families, not counting other assorted relatives, they represent 18 people with VHL.

Nonetheless, we are all still learning as we go along. What we have learned from each other in the last few months has been, in the words of my nephew, "Awesome!"

The first set of officers will serve through next year's Annual Membership Meeting, when we will elect officers under the terms of the By-Laws. We hope you will plan to join us for the **Annual Meeting** next spring. Details will be announced in the September issue. Save up those Frequent Flyer miles!

Our **Medical Advisory Board**, listed on page 14, consists of physicians and other medical professionals with depth and breadth of experience with the various aspects of VHL. We are honored to have such an outstanding group of people who have graciously donated a portion of their very valuable time to assist us all in understanding and dealing with VHL.

Chapters are forming in ten states. Many are planning to hold meetings beginning in June. Please call us for the time and location of a meeting near you, or to set up a meeting in your own area.

In Britain, Hazel Murfitt and her daughter Anne have been very busy with speaking engagements and appearances in the media. At the forthcoming Bike-a-thon for cancer, sponsored by Action Research, **Susan Tulley,** a star of *East Enders,* will be riding for benefit of cancer *and VHL!* A portion of the proceeds of the event will go to support Dr. Maher's research on the VHL gene.

You can help **publicize VHL** in your own community. We will be happy to provide information and assistance. If each of us does a little in our own communities, we will make an enormous difference.

We have been contributing **brochures** to a number of professional events around the country, spreading the word about VHL to medical professionals. Copies of these brochures are available for the asking. If you hear of an event, or want some for a physician's waiting room, please ask for copies of "What is VHL?" or "VHL -- not so rare after all". We would appreciate feedback on these, and your ideas for additional brochures.

We have a new **800 number** -- 1-800-767-4VHL in the U.S. and Canada. This number will go to one of the Board members on a rotating basis. You are also welcome to dial any one of us directly. Please don't be shy to leave a message if we're not available just when you call -- we really want to speak with you!

Many thanks to all the Members and physicians who have helped to distribute copies of our brochures and of these first two newsletters. Please spread them around!

Special thanks to all the Members who contributed ideas, questions, and articles for this issue.

Now it's your turn!

What do you want to learn? What would you like to hear? What questions would you like answered?

Please share your thoughts and concerns with us, in any form. We read a variety of languages, including Braille. Send us a poem, a cartoon, a random thought. One Member sent in "Having VHL sucks." We can relate to that too.

We need to hear from you!

Thank you all. We hope you and your loved ones are well.

-- *Joyce, Peggy, Susan, Hazel, Lois, and Darlene*

ART CONTEST

What swam by on your last ultrasound?

What funny or poignant pictures have you or your children drawn about their experiences with VHL?

Prizes awarded for cartoons and drawings published in the VHL Family Forum.

Insurance Concerns

While Hilary R. Clinton's task force on revising the health care system in the United States is still working out its recommendations, it will be important for her to hear your views on reforming the system of "preexisting conditions".

If you or someone in your family has been denied health insurance coverage, please share your own experiences with the Task Force. Send to Mrs. Hilary R. Clinton, White House, Washington. If you are willing, please send a copies of your letter to the National Organization for Rare Disorders, 100 Route 37, P.O. Box 8923, New Fairfield, CT 06812-1783 and to the VHL Family Alliance.

Dignity

What I'd like to say to doctors: "It's not just a patient, or a number. There's a human being inside. Each person must be handled with dignity.

-- Thea F., Massachusetts

VHL Family Alliance

Many thanks to those who helped with startup and with the current issue

ACCORD, New South Wales, Australia
Alliance of Genetic Suppt Groups, Chevy Chase, MD
Ms. Teri Barr, Mission Air Transportation, Toronto, Canada
Ms. Iris ben Zeev, Tel Aviv, Israel
Michael J. Bohnen, Esq., Boston, MA
Ms. Priscilla Ciccariello, National Marfan Fndn, NY
Dr. and Mrs. Sidney Cohn, Memphis, TN
Mr. Julian Dyke, Polycystic Kidney Res Fndn, Ks City, MO
Dr. Joal Fischer, SupportWorks, Charlotte, NC
Julie Fox, M.S., Mass. General Hospital, Boston, MA
Ms. Joan Gadon, Jerusalem, Israel
Dr. Gladys M. Glenn, National Inst of Health, Rockville, MD
Dr. Y. Edward Hsia, Shriner's Hospital, Honolulu, HI
Dr. George Klauber, New England Medical Ctr, Boston, MA
Milica Kokotovic, Beth Israel Hospital, Boston, MA
Ms. Pat Krug, Natl Neurofibromatosis Fndn, Dedham, MA
Mrs. Lisa Lisco, Belmont, Massachusetts
Anita Lustenberger, M.S., Irvington, New York
MORE Program, Toronto Region, Canada
Charles H. Morin, Esq., Boston, MA
Dr. Mytilineos, University of Heidelberg, Germany
Dr. Hartmut P. H. Neumann, Freiburg, Germany
Dr. Edward Oldfield, Bethesda, MD
Mrs. Sally Overman, Memphis, TN
Brenna Peabody, M.S., International Urological Sciences
Dr. Frances M. Richards, Cambridge, England
Ms. Luanne Roark, CTFA, New York, NY
Dr. R. Elizabeth Roebuck, Newton, MA
Anne Smiley Rogers, Esq., Boston, MA
Dr. and Mrs. Joseph Sabbath, Newton, MA
Ms. Betsy Strock, New England Organ Bank, Boston, MA
Ms. Julia Warren, UK Transplant Support Service Authority
Jeff and Barbara Weener, Brookline, MA
Ms. Janet Weiner, Brookline, MA
Dr. Jean Whaley, Bristol-Myers Squibb, Princeton, NJ
Dr. and Mrs. Harry H. Wilcox, Memphis, TN
Ms. Mary Ann Wirtz, UNOS, Richmond, Virginia
Mr. Richard J. Wolfe, Countway Libr of Med, Boston, MA
Dr. Berton Zbar, National Inst. of Health, Frederick, MD
Members of the VHL Family Alliance

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Volume 1, Number 2, June 1993 Editor: Joyce Wilcox Graff, 1-617-232-5946 (eve)

Newsletter of the VHL Family Alliance 171 Clinton Road, Brookline, Massachusetts 02146 U.S.A.
Toll-free in the United States and Canada: 1-800-767-4VHL Telephone: 1-617-232-5946 (eve); Fax: 1-617-734-8233

Adviser: Debra L. Collins, M.S., Genetic Counselor, University of Kansas Medical Center 1-913-588-6043 (day)

This newsletter is distributed to members of the VHL Family Alliance. It is supported by dues, fundraising, and advertising. We welcome your comments, suggestions, ideas and submissions.

Annual Dues: $7 for individual, $10 for family, $25 for professional, $100 for corporate/facility membership.

Submissions: Your questions, comments, articles and ideas are always welcome. Copyrighted works or their modifications must be accompanied by the copyright notice and the consent of the owner prior to publication or distribution. Opinion(s) expressed by the authors are not necessarily those of VHLFA.

Postmaster: Please send address changes to VHL Family Forum, 171 Clinton Road, Brookline, MA 02146.

Yes! I want to be a Founding Member!

Name: _____

Address: _____

_____

City: _____ State: _____ Zip: _____

Country: _____ Fax: _____

Phone (home): _____ Phone (work): _____

My check includes $ _____ for dues
$ _____ to help with start-up expenses (telephone, postage, printing)
($7 for individual, $10 for family, $25 for professional, $100 corporate/facility)
Make checks payable to VHL Family Alliance -- *Thank you!*

VHLFA has applied for 501(c)(3) tax exempt status. Please consult your tax advisor regarding deductibility. All Founding Members receive a Founders certificate, 3-4 issues of the Forum this year, and copies of all Alliance publications (two planned this year).
Free subscriptions are available where the dues are a hardship.

In Britain, membership dues are not required. Your donation is very much appreciated.
Please make cheques payable to *VHL Patient and Relative Contact Group.*

- ❑ Audio version requested (available for visually handicapped)

I am a
- ❑ VHL patient
- ❑ VHL family member
- ❑ Supporting Friend
- ❑ Professional (physician, nurse, dietitian, social worker, etc.)
- ❑ Other (please specify) _____
- ❑ I am interested in participating in a local support group

I have some expertise which I am willing to share with others
- ❑ Telephone skills
- ❑ Writing or reviewing articles about _____
- ❑ By-laws committee, or Legal assistance for filing incorporation documents
- ❑ Advertising or public relations skills
- ❑ Artistic skills, cartooning, to help with illustrations for publications
- ❑ Fundraising skills
- ❑ Other _____

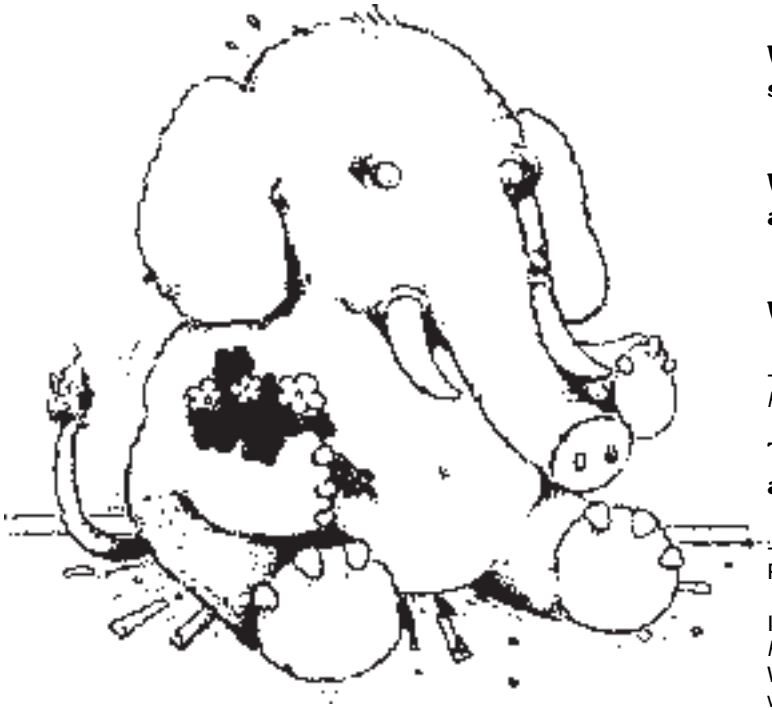
Things I particularly liked in this issue of the newsletter:
- ❑ VHL Gene Found
- ❑ Healthy Kidneys, Transplant
- ❑ Resources
- ❑ Personal stories
- ❑ Ask the Experts
- ❑ Ask the Family
- ❑ Other: _____

Things I would change: _____

Please share your own thoughts and experiences -- use as much paper as you wish.

Return to: VHL Family Alliance, 171 Clinton Road, Brookline, MA 02146

In Britain, send to: VHL Patient and Relative Contact Group, 114 Longfield Rd, Littleport, Ely, Cambs CB6 1LB



What's gray, visits you when you're sick, and breaks a chair?
A get-wellephant.

Why do elephants have tusks that aren't straight?
Their parents can't afford braces.

Why did the rabbit go to the doctor?
He was feeling jumpy.
--Joanne E. Bernstein and Paul Cohen, *Dizzy Doctor Riddles*, Whitman, IL, 1989.

Today we will discuss the kidney, liver, and pancreas.
Just another organ recital.
-- adapted from Charles Keller, *What's Up, Doc?*, Prentice-Hall, NJ, 1984.

Exciting Late-Breaking News on page 1!

VHL Family Forum
Newsletter of the VHL Family Alliance
171 Clinton Road
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Address Correction Requested

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