VHL Family Forum

Volume 3, Number 3 ISSN 1066-4130 September 1995

A Coup for Cancer Research

Progress in Understanding the VHL Gene

When the gene was found in June 1993, many people said that that event would greatly promote research on VHL. This year we are seeing the fruits of new labor based on that work. "The identification of tumor suppressor genes whose loss of function results in predisposition to cancer has taken center stage in our attempts to understand human cancer."[1] Mutations in these genes are responsible not only for inherited cancer syndromes like VHL, but for similar sporadic cancers too.

In the last several months four teams have published significant strides forward in understanding how the VHL gene works: a team at the U.S. National Cancer Institute (NCI) under Drs. Richard D. Klausner and W. Marston Linehan; one at the Oncology Drug Discovery Department of Bristol-Myers Squibb Research Institute in Princeton, New Jersey, under Dr. Bernd Seizinger; one at the Dana-Farber Cancer Institute in Boston under Dr. William G. Kaelin, Jr., and a team at the Oklahoma Medical Research Foundation under Drs. Ronald and Joan Conaway.

The VHL gene is a code for a protein. These teams are pursuing the same goal: to identify the specific protein encoded by the VHL gene, understand what it does and how it effects the life of a cell. Once we know how it works and what it does, then various medications and therapies can be proposed to restore the missing function.

The Klausner/Linehan, Seizinger, and Kaelin teams began by creating an antibody to the VHL protein in the bloodstream of a rabbit. When confronted with a foreign substance, the normal function of the immune system is to create an antibody, a neutralizing agent specially formulated to bind with the foreign substance and neutralize its effect. "It's like making a key to fit a lock," says Dr. Jean Whaley of the Seizinger team. The antibody can then be used to determine whether the VHL protein is present, and in what quantities.

The Kaelin team developed antibodies which are capable of recognizing the human VHL protein in cells. Using these antibodies, they confirmed that the human protein contains 213 amino acids. Ironically, the partial gene sequence published in 1993 by Drs. Michael Lerman and Berton Zbar and co-workers contained all the genetic information necessary to encode the complete VHL protein. As predicted from DNA analysis of human kidney cancers, the Kaelin team found that some renal carcinomas fail to produce any normal VHL protein.

At the same time, the NCI and Seizinger teams went on to identify genes in other animals which are similar in molecular structure to the VHL gene, referred to as "homologous" genes. They looked for a similar pattern of amino acid sequences in the genetic encoding.

> "The identification of tumor suppressor genes whose loss of function results in predisposition to cancer has taken center stage in our attempts to understand human carcinogenesis."

"The isolation and characterization of gene homologues from diverse species often provide important insights into the functional characterization of the respective human protein."[2] Discovering what portion

Continued on page 2

Inside this issue!

of the VHL gene is conserved in evolution, in other animals, can help to indicate which region of the gene might be the most important. The Seizinger team found that the second half of the VHL gene is almost identical to a similar gene in a mouse (mVHL1). As with the human VHL gene, the mouse homologue is found in lots of different tissue types. The NCI team identified a rat gene which is "88% sequence identical to the 213 amino-acid human VHL gene product."[3]

The NCI and Kaelin teams are studying the other kinds of proteins the VHL protein tends to bind to. "The finding that the VHL protein forms relatively tight complexes with specific sets of cellular proteins suggests that the identification of these associated proteins will yield clues about the function of VHL and may also lead to identification of other genes critical in growth and/or cell cycle control." Further, these findings promise "that the identification of these VHL-associated proteins will likely lead to understanding the role of this tumor suppressor gene product in the life of the cell."[4]

The Kaelin team has also conducted experiments using nude mice. Nude mice have no hair; they also have no immune system. When such mice are injected with cells from a human renal cell carcinoma, these cells begin to form tumors. When the healthy VHL protein was reintroduced into the renal cell carcinoma cells, and these cells were subsequently injected into the mice, these cells were inhibited in their ability to form tumors *in vivo*. (The term *in vivo* means that it occurs within the body of a living animal.) What tumors did form were consistently smaller. This confirms that the VHL gene is a bona fide tumor suppressor.

> "*Our previous studies of the VHL gene led us to an understanding of the genetic basis of VHL and sporadic kidney cancer. This work takes us from clinical medicine to genetics to molecular characterization of specific events that may lead to the development of the cancer. -- W. Marston Linehan, M.D., National Cancer Institute*"

This same effect was not seen outside living organisms in the lab. This might indicate that the VHL protein action depends on a cell-to-cell interaction that only occurs in a living organism. This, and the fact that that there are so many new blood vessels in VHL, "suggests a possible role of the VHL protein in the ability of cells to sense changes in the levels of oxygen, and perhaps other nutrients, in their microenvironment."[5]

In the September 8 issue of *Science* Magazine, these teams published the next step in their research.

The Conaway team reported their findings about a substance important in cell growth, called Elongin.

We Need Your Help!!

You can help encourage research -- with contributions of tissue to the *Tissue Bank*, and by helping us fund one or more *VHLFA Research Grants* -- through your own donations, asking friends and family to contribute, and local fund-raising activities.

Research is Expensive!

This complex of three small proteins A, B, and C is suspected to play a key role in the cycle of cell progression, development, and cell death. All cells must make new proteins every day. Each gene (which is made of DNA) carries the information necessary to construct a particular protein. The gene must, however, first be converted, or transcribed, into RNA which then serves as the actual blueprint for protein synethesis.

The *transcription* process begins with *initiation*, then *elongation*, then a series of other steps. Elongin is the key factor in this elongation process. The VHL protein "binds to Elongin B and C and inhibits Elongin (SIII) activity . . . and raises the possibility that Elongin (SIII) may be an integral component of a transcriptional regulatory network controlled at least in part by the VHL protein."[6] The Kaelin lab showed that the portion of the VHL gene that is most important in this process is the very region which is most often mutated in VHL families.[7]

In the Duan study, the VHL protein was shown to bind tightly and specifically to Elongin B and C, and to inhibit Elongin (SIII) transcriptional activity in the laboratory. These findings show a potentially important network of factors that regulate transcription, in which the VHL protein may play a key role.[8]

What is clear is the ability of the VHL protein, produced by a healthy VHL gene, to suppress tumor growth. As we learn more about the basic biochemistry of the protein and how it stops tumor cells from growing, it will point the way to possible therapies. We are at the beginning of a very exciting time.

The new results reported in *Science* "are not just a coup for cancer research. The identification and cloning of the VHL gene and its target Elongin will help to elucidate transcriptional elongation, a key regulatory mechanism. . . .We will now be able to move forward without pause in understanding how transcriptional elongation regulates gene expression, cell growth, and neoplasia."[9]

Notes: 1. Duan(e) 1402. 2. Gao (a) 743. 3. Duan (b) 6459. 4. Duan (b) 6463. 5. Iliopoulos (c) 824. 6. Kibel (f) 7. Aso (g) 1443. 8. Duan (e) 1402. 9. Krumm (d) 1401. Neoplasia is the spontaneous growth of a tumor from a single aberrant cell, as in VHL.

References: (a) Gao, Whaley, Seizinger et al., "Cloning and Characterization of a Mouse Gene with homology to the human von Hippel-Lindau disease tumor suppressor gene," *Cancer Research* (Feb. 1995), **55:**743-747. (b) Duan, Linehan, Klausner et al., "Characterization of the VHL tumor suppressor gene product," *Proc. Natl. Acad. Sci., USA,* (July 1995) **92:**6459-6463. (c) Iliopoulos, Kibel, Gray and Kaelin, "Tumour suppression by the

human von Hippel-Lindau gene product," *Nature Medicine* (Aug. 1995), **1**:822-826. Four articles from *Science*, September 8, 1995: (d) Krumm and Groudine, "Tumor Suppression and Transcription Elongation," 1400-1401; (e) Duan, Linehan, Klausner et al., "Inhibition of Transcription Elongation by the VHL Tumor Suppressor Protein," 1402-1406; (f) Kibel, Kaelin et al., "Binding of the von Hippel-Lindau Tumor Suppressor Protein to Elongin B and C," 3pp.; (g) Aso, Lane, Conaway & Conaway, "Elongin (SIII): A Multisubunit Regulator of Elongation by RNA Polymerase II, 1439-1446. ❑

Steps Toward an Effective Medication

- ☒Map some large VHL families (began 1977)
- ☒Find the chromosome where the gene is located (1988)
- ☒Find the gene itself (1993)
- ☒Determine how the gene functions normally in the cell (1995)
- ❑ Determine how the damage to the gene leads to the manifestations of VHL disease
- ❑ Find pharmaceuticals that mimic the role of the VHL protein
- ❑ Evaluate some of those medications in clinical trials with people

VHL Tissue Bank

-- William C. Dickson, Chair, Research Mgt Comm.

There was a mistake (incorrect zip code) on the Tissue Bank registration form that appeared in the last issue of the VHLFF. We apologize for the mistake and hope it did not cause you any inconvenience. A corrected form appears below.

The research community remains in need of VHL tissue. If you have not yet registered, please consider giving *a gift that only you can give.* Filling out and mailing the registration form now will greatly simplify the process at those stressful times when surgery may be required, or for the family in the case of death. Once you have registered, it only takes a phone call to the Tissue Bank at 1-800-847-1539 to notify them of any scheduled surgery and they will make all necessary arrangements to recover the tissue.

Please note that tissue must be collected as soon as possible to insure that it is usable for research. Researchers interested in access to tissue on file should submit research proposals to William C. Dickson, VHL Family Alliance Research Management Committee, 10613 Creamcup Lane, Great Falls, VA 22066, (703) 759-3665, Fax: (703) 759-7992, or e-mail: vhlres@usa.pipeline.com ❑

Donor Registration Form -- Tissue Bank for VHL Research

I, _____, wish to register myself (or a dependent minor) as a VHL tissue donor with the **Brain and Tissue Banks for Developmental Disorders** at the University of Maryland at Baltimore. This donation grants permission for the Brain and Tissue Bank to make every attempt within its means to coordinate recovery of surgically removed tissue of the above named donor. Further, if death should occur, I (**do___** or **do not___**) hereby grant permission for recovery of brain and other tissues. All tissue is donated for the expressed purpose of furthering the research of **von Hippel-Lindau disease**.

Donor name_____ Next of Kin _____

Address _____ Address _____

City _____ City _____

State _____ Zip _____ State _____ Zip _____

Phone Day _____ Phone Day _____

Phone Evening _____ Phone Evening _____

Donor's Date of Birth _____ Sex _____ Ethnic Group _____

If the Donor was diagnosed with VHL: When? _____ By whom? _____

Please enclose a brief Medical/Family history on other paper.

If you (the Donor) are not diagnosed with VHL, are you the parent/relative of someone who is?

Yes__ No__ (Describe relationship)

Signature of Donor or Legal Guardian: _____ Date _____

Feel free to include any further relevant information.

Please mail to: Brain and Tissue Banks for Developmental Disorders
University of Maryland at Baltimore, Department of Pediatrics
655 West Baltimore Street
Baltimore, Maryland 21201-1559

IMPORTANT: IN CASE OF SURGICAL EMERGENCY OR IN CASE OF DEATH, PLEASE NOTIFY THE TISSUE BANK ***IMMEDIATELY*** (ANY TIME, DAY OR NIGHT) ON 1-800-847-1539. TISSUE NOT RECOVERED WITHIN 24 HOURS CAN NOT BE USED FOR RESEARCH.

Caring for your Reproductive Health

by Peggy Graham, R.N., Michigan

People with VHL should follow the cancer-preventive precautions and self-examinations recommended for everyone. Just because you have VHL does not exempt you from other conditions which occur in the general population. Follow the normal guidelines for breast and testicular self-examinations and take good care of your reproductive health.

There is one notable occurrence in men which is associated with VHL: epididymal cystadenomas, and women have been reported to have cystadenomas of the broad ligament, the embryologic counterpart to the epididymis.

Epididymal cystadenomas are found in 10-26% of men with VHL.[1] What are they, and what do they do?

First, what is the *epididymis*? This little-known gland lies behind the testicle, in the scrotum, on the path to the *vas deferens,* the vessel which carries the sperm from the testicle to the prostate gland. "The epididymis is as long as the testicle, lying in a flattened C shape against one side of the testicle. It's a complex tubular system which gathers the sperm and stores them until they are needed," says Dr. Harry Wilcox, Professor Emeritus of Anatomy at the University of Tennessee Center for the Health Sciences. "It's a little like the coil on the back of an air conditioner, where the condensation takes place." After having been stored in the epididymis, sperm then move through the vas deferens to the prostate, where they are mixed with seminal fluid from the seminal vesicles and move on through the prostate into the urethra.

The epididymis was previously considered only a conduit through which sperm passes. It is now understood to be a highly specialized portion of the male reproductive system responsible for sperm maturation, mobility and storage.

Second, what is a *cystadenoma*? Let's divide it into its two basic parts: a cyst and an adenoma.

A *cyst* is a fluid-filled sac, an enclosed space within a tissue or organ filled with fluid. A small number of cysts are found in the epididymis of some 23% of men in the general population.[1] By themselves, cysts are not an occasion for concern, and are not even particularly noteworthy.

An *adenoma* is a benign tumor. A *cystadenoma* is a benign tumor with one or more cysts inside it. In other words, it has more mass to it, more density than a cyst.

Papillary [nipple-shaped] cystadenomas of the epididymis are a rare occurrence in the general population. These cysts can occur on one or both sides. When they occur on both sides, they are almost a definitive diagnosis of VHL. They range in size from 1 to 5 centimeters (1/3 to 1 2/3 inches). The man may feel a "pebble" in the scrotum, but they usually are not painful and do not continue to progress.

They may occur during the teen-age years or later in life. One man reported finding them for the first time in his forties. They can be removed if they are annoying, but removing them is much the same operation as a vasectomy, and may result in the disabling of the delivery of sperm on the operated side.

Only one case has ever been reported which seemed to indicate that the cystadenoma had become cancerous. This is much more likely a coincidence, since people with VHL, like others in the general population, occasionally do get cancer in this area. It is important to monitor a cystadenoma, just as you would continue to check a wart on your skin, to make sure that it is in fact a cystadenoma and not another kind of more worrisome tumor. Monitoring is usually done by the urologist with a manual examination or with ultrasound.

In most cases the only "problem" associated with cystadenomas is the minor annoyance of knowing it is there. Occasionally, depending on their position, cystadenomas may block the delivery of sperm and cause infertility. However this is a very rare occurrence. If a cystadenoma is painful you should definitely check with a doctor, since on rare occasions they can become inflamed and rupture.

A corresponding tumor in women is a cystadenoma of the broad ligament.[2] The broad ligament is a folded sheet of tissue that drapes over the uterus, uterine tubes and the ovaries. This tumor is felt to arise from the same embryonic tissue as epididymal cystadenomas. In the experience of the National Institutes of Health[1] cystadenomas of the broad ligament are very rare. Much more common are the ovarian cysts or endometriomas which occur in the

Illustration from Kahle et al., *Color Atlas and Textbook of Human Anatomy,* Volume 2: *Internal Organs* (Stuttgart, 1978), p. 261.

general population. However if an "unusual" tumor is seen in the area of the broad ligament, a cystadenoma associated with VHL should be considered. Please report confirmed cystadenomas of the broad ligament to the VHL Family Alliance research database to help increase our knowledge.

1. Choyke, Glenn, et al, "Von Hippel-Lindau Disease: Genetic, Clinical, and Imaging Features," *Radiology*, March 1995, p. 639.
2. Karsdorp et al, "von Hippel-Lindau disease: new strategies in early detection and treatment," *Am J Med* 1994, 97:158-168; Korn et al., "Papillary cystadenoma of the broad ligament in von Hippel-Lindau disease," *Am J Obstet Gynecol* 1990, 163:596-598.

References: See also E.B. Price, "Papillary cystadenoma of the epididymis," *Arch Pathol* 1971 91:456-470; J.S. Meyer et al., "Papillary cystadenomas of the epididymis and spermatic cord," *Cancer* 1964,16:1241-1247. Our thanks to Dr. Gladys Glenn, National Cancer Institute, Bethesda, Maryland, and Dr. Harry H. Wilcox, Memphis, Tennessee, for their assistance in preparing this article. ❑

Sources of DNA Testing

In announcing the reopening of the VHL Clinic at NIH in our June issue, we mistakenly said that they would do DNA testing for the first member in a family. We're sorry, but that is not correct. DNA testing must be obtained from a clinical laboratory prepared to provide service to you and your physician in a timely manner. We apologize for any inconvenience caused by our error.

DNA testing services are available from the following laboratories:

Maryland: 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.

Pennsylvania: Ms. Lynn Godmilow, M.S.W., Director, Genetic Diagnostic Referral Center, University of Pennsylvania, Department of Genetics, Philadelphia, PA 19104-6145, Tel: 1-215-573-9161; Fax: 1-215-573-7760; E-mail: godmilow@mail.med.upenn.edu

England: Dr. Eamonn R. Maher, Clinical Genetics, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, U.K., Tel: 44-223-216446, Fax: 44-223-217054.

Germany, Freiburg: Dr. Hartmut Neumann, Medizinische Universitätsklinik, Hugstetter Strasse 55, D-79106 Freiburg i. Br., Germany, Tel: 49-761-270-3363; Fax: 49-761-270-3778; E-mail: Neumann@mn41.ukl.uni-freiburg.de

Germany, Munich: Dr. Hiltrud Brauch, Labor für Molekularpathologie, Klinikum rechts der Isar, Trogerstraße 32, D-81675 München, Germany, Tel: 49-89-4140-4592; Fax: 49-89-4180-5215.

Israel: Dr. David Gross, Chief, VHL Clinic, Dept of Endocrinology & Metabolism, Hadassah University Hospital, P.O. Box 12000, Jerusalem, 91120 Israel. Tel: 972-2-777648; Fax: 972-2-437940; E-Mail: Gross@vms.huji.ac.il ❑

National Brain Tumor Foundation
Conference for Patients and Health Professionals
"Health Caring - An Equal Partnership"
March 8-10, 1996, San Francisco
1-800-943-CURE

Aloha! Hawaii '96

by Rodney Belen, Hawaii

As we close in on the 21st century, in this ever-changing world, Hawaii is still Paradise. Diamond Head is the most recognizable landmark in the world, beautiful beaches you've never seen before and may never see again, it's all here in Hawaii. Flowers and birds of every imaginable color for your eyes to feast on. So much to do and see, such as snorkeling and reaching out to the fish or viewing the windy Pali cliffs where King Kamehameha pushed the enemy natives over to conquer the islands. If you enjoy history you may enjoy visiting the Arizona Memorial, the ship that sank during the bombing of Pearl Harbor. Clean air, green valleys and rainbows on a regular basis. People from all over the world, we have it all here in Hawaii. Bring your shorts, camera, sunscreen, and an adventurous appetite, we're gonna have some fun!

The VHL Conference will be held from June 17-21, 1996. A luau is scheduled for Wednesday evening, the cost of which is included in the registration fee. We are also planning a beach picnic on the 16th for "*the* Hawaii Family" with all the VHL Family Alliance members as guests. The VHL Conference will be held at the Pacific Beach Hotel across the street from Waikiki beach. With restaurants and shops galore, there is much to do.

Rooms may be reserved with the Pacific Beach Hotel. A room with Partial Oceanview, in the Oceanarium Tower, are $108 single or double, children 18 or younger stay free in the parents' room using the existing beds. For additional adults, add $15 per person. Reservations must be made by April 16, 1996. To reserve by credit card, phone the hotel at 800-367-6060 and tell them you are with the VHL International Conference.

Keep an eye out for promotional airline fares, save up those Frequent Flyer miles, or ask a nearby corporation if they would donate two frequent flyer coupons. We are very excited to have you all coming to our beautiful home, Hawaii! *Aloha*!

Monday: "Cancer in Families" general sessions, nutrition.

Tuesday: "Consumer Issues in Familial Cancers," chaired by Debra Collins: insurance, screening, genetic counseling, fetal diagnosis, registries.

Wednesday: "Family Issues," chaired by Patti Kohlen and David Torres: coping, alternative medicine, stress management. Luau in the evening.

Thursday: "Medical Issues in VHL," chaired by Drs. Hartmut Neumann and James M. Lamiell: diagnosis and treatment.

Friday: "Scientific Issues in VHL," chaired by Dr. Berton Zbar: the state of research.

For more information contact Dr. Ted Hsia or Ms. Janet Brumblay, 1-808-956-8331. ❑

Helping Children Through a Parent's Serious Illness

by Randy and Lisa W., Michigan. Reviewing How to Help Children Through a Parent's Serious Illness *by Kathleen McCue, M.A., C.C.L.S., with Ron Bonn. St. Martin's Press, 1994.*

When it became evident that we were about to face yet another brain surgery, the third in five years, and this one with a very active and inquisitive two year old observing everything, we knew that we needed to find a book that explained illness in a way that a toddler could understand. Unfortunately, bookstores and libraries were of no help, so we took our search to the Information Superhighway through the Internet.

It was here that we were alerted to a book that is a must for anyone who has to explain an illness to their children: *How to Help Children Through a Parent's Serious Illness* by Kathleen McCue.

This book is geared to all age groups of children, from toddlers to those in their teens and beyond. Topics range from initial diagnosis through treatment, surgeries, therapy, death and many others in between.

But if there is one central message that is stressed in virtually every chapter of this book, it is: *"You must tell your children the truth."* Ms. McCue hits on this point often for these three reasons:

1. Your children are affected by everything that happens in the family.

2. The more serious the situation, the more they will be impacted.

3. Lying to your children, in any way, will inevitably make things worse.

The guiding principles, from the beginning to whatever the end may be, are openness and honesty. Children can and probably will imagine much worse things than the truth, which is why Ms. McCue feels there should be three main things you tell your children:

1. Tell them you are seriously ill.

2. Tell them the *Name* of your disease or condition.

3. Tell them your best understanding of what may happen.

And not only does the book deal with telling your children of your illness, but another major area covered deals with your children's reactions to the changes that will occur. Signs that a child may be having difficulty dealing with what is happening may include: sleeping or eating disturbances, fear, developmental troubles (grades dropping, vocabulary or skill declines in young children, silence) and signs and concerns of suicide.

This book also provides excellent guidance in the following areas:

- Your children's visits to the hospital, which can be a very frightening experience at any age: how to prepare them, and whether a visit is a good idea or not.

- When the sick parent comes home: how to prepare your children, involve them and deal with their expectations and frustrations.

- When things get very bad, or won't be getting better, are very definitely difficult times. The book touches on different situations and how to explain them to your children, and also how you and your children can help each other through difficult times.

In the introduction to the book, we found Ms. McCue's rationale for creating this book, and our reason for buying it, reading and re-reading it:

"If you are reading this manual, something terrible and frightening is happening to your family. It is happening to you, it is happening to your partner, and it is happening to your children, and you are worried about them. You want them to come out strong and sound, ready for future happiness and success, whatever the medical outcome."

This is how we felt. My wife was about to face another surgery, the sixth in five years, but this time with a child to be concerned about. She knew Mom was sick and had a boo-boo in her head, and that the doctors were going to try to make her better. But we didn't know how much we should explain to her and expose her to.

How to Help Children Through a Parent's Serious Illness answered the questions we had in a very insightful and informative way. We would recommend this book to anyone who is unfortunately in a position to have the same questions and concerns that we were faced with. This book helped ease the anxiety of not knowing what to say and do and also provided information that we could use immediately and as she grows.

One last point that is true not only for your children but could also apply to family and friends:

"All life is terminal. Even if one's own time is tragically shortened by a medical diagnosis, the end is not yet. There is still time, time for children and parents who love each other to make the most of. Don't try to shield your children from making the most of that time." ❑

Introducing our Medical Advisory Board

The medical professionals listed on page 14 may not always be very visible to you as readers, but they are very visible to the members of the Board of Directors. They very generously lend us their expertise as consultants on difficult questions from members, in the writing or reviewing of material for this newsletter, in presenting or helping design presentations for our annual meeting, and in advising us on various aspects of our programming. We continue here the introductions begun in previous issues. We have purposely sought out people with depth and breadth of experience with VHL — people whose formal training has been enriched by working with a number of patients with VHL over a number of years.

Yujen Edward Hsia, M.D.

Born in Shanghai, China, Dr. Ted Hsia (pronounced Shaw) studied at Oxford University and began his medical career in England, at the London Hospital. He taught for five years in medical school in Malaysia, and ten years at Yale University, before settling in Honolulu where he heads the departments of Genetics and Pediatrics at the Kapiolani Medical Center, and teaches at the John A. Burns School of Medicine.

In his early days in Hawaii he joined with Drs. Lamiell and Salazar to study a large family with a hereditary pattern of kidney cancer, which proved to be VHL. Their mapping of 220 members of a single VHL family [*Am J Med Genet*, **36:**1310142, 1984] was the groundwork for the genetic research reported in this issue. He has published widely on issues of genetic counseling, neonatology and birth defects.

New VHLFA CookBook

Where else can you find the best recipe for Country Squirrel from New Mexico? or Kangaroo Steak from Australia? VHLFA members and friends from around the world contributed their favorites for good food, good fun and gastronomical exploration!

Cookbooks are only $12 postpaid in the U.S. and Canada. Proceeds help to promote education and research on VHL. ❑

With Drs. Neumann, Lips and Zbar he published a recent survey of VHL [*Brain Pathology* **5:**181-193, 1995.]

Dr. Hsia continues to care for the Hawaii family. He is chairing the 1996 VHL Symposium and Conference in Honolulu [see page 5].

Allan E. Rubenstein, M.D.

A graduate of Cornell University in 1966, Dr. Rubenstein completed his medical training at the University of Rochester School of Medicine, Tufts University School of Medicine, and Columbia-Presbyterian Medical Center in New York City. He is certified in Psychiatry, Neurology, and Neuroimaging.

He has been with the Mount Sinai Hospital since 1974, and holds concurrent appointments at Beth Israel Hospital and Catholic Medical Center of Brooklyn and Queens. He teaches neurology at the Mount Sinai School of Medicine.

Dr. Rubenstein co-founded the National Neurofibromatosis Foundation in 1978 and still serves as its Medical Director. He established the first interdisciplinary clinic devoted to neurofibromatosis (NF) in the world. The clinic has been a model for over 25 other NF clinics in the U.S. and Europe. The clinic at Mount Sinai now has the largest NF population in the world. The clinical care centers of the National Neurofibromatosis Foundation have served as models for our own VHL clinical care centers.

Neurofibromatosis and VHL are classed together in a group of diseases called phakomatoses, all of which have a wide variety of symptoms including cysts and tumors involving the central nervous system. Dr. Rubenstein has written and presented world-wide on neurofibromatosis and the phakomatoses. His experience and expertise in multi-disciplinary clinical care centers have been particularly helpful to our Clinical Care Program. ❑

Casual Day

Wauwatosa Realty Company, Wisconsin's largest home seller, and its affiliate companies sponsored a "Casual Day" in July when employees and Sales Associates were allowed to wear casual clothes if they donated $2 to the VHL Family Alliance. The company matched the donations, for a total of $721.40! *Many thanks* to all our friends at Wauwatosa Realty Company and its affiliates, Heritage Title Service, Wisconsin Mortgage Corporation, and Wauwatosa Real Estate Institute. ❑

Ask the Experts

Got a question? Please send it in! We will be happy to help you find an authoritative answer. We'll send you a VHL teddy bear if we publish your question in the newsletter.

MRIs and dental work

Question: "Since VHL patients have lots of MRIs, are people finding that they are having trouble with their teeth? Fillings loosening and falling out frequently?" -- *Thea F., Massachusetts.*

The effect of strong magnetic fields on dental fillings is a natural concern for anyone undergoing an MRI. Fortunately, MRI poses no risk to the vast majority of dental fillings, implants and appliances.

A magnetic field only exerts a force on substances that are *ferromagnetic*, most commonly iron, nickel and cobalt. The substances used in fillings are *non-ferromagnetic*: that is, no force is exerted on them by a magnetic field.

Materials commonly used for fillings (officially known as dental restorations) include composite resins, dental amalgams, gold alloys, porcelain and porcelain fused to a non-ferrous metal.

Composite resins are made of a plastic base (typically Bisphenol A-Glycidyl Methacrylate) in which silica particles are embedded. This substance produces a hard tooth-colored surface with which chipped front teeth can be repaired. It is non ferromagnetic and thus unaffected by magnetic fields. Composite resins typically last 1-5 years although some may last longer.

Dental Amalgam is made of mercury and a mixture of silver and tin with tiny amounts of zinc and/or copper. Mercury is used to harden the amalgam. This material is also non-ferromagnetic. Dental amalgams typically last 5-10 years but some amalgams can last a lifetime.

Gold Alloys, porcelain and porcelain fused to a non ferrous metal. These materials are alternative means of restoring teeth. None of them is ferromagnetic. They can be expected to last 5-10 years.

Thus the commonly used materials used for fillings are non-magnetic and should not be influenced by MRI scans. Unfortunately, dental fillings do not last forever and what the reader may be experiencing is simply deterioration due to "wear and tear." It is known that when subjected to the severe pressures of chewing some restorations deteriorate faster than others.

There are some very specialized dental appliances used for orthodontics of complete dentures which actually have small magnets within them that may be disturbed by a magnetic field, but these are rarely employed.[1] However, if you have any doubts about the composition of a dental appliance you should check with your dentist before having an MRI.

-- Myles Koby, D.D.S., M.D. and Peter L. Choyke, M.D., Department of Radiology, National Institutes of Health, Bethesda, Maryland. Dr. Koby is a dentist turned neuro-radiologist, so this question was right up his line.

1. Shellock, F.G., and Kanal, E. *Magnetic Resonance, Bioeffects Safety and Patient Management,* New York, Raven Press, 1994, p. 105.

Can Essiac Tea control Tumor Growth?

Question: "A friend who has VHL told me that at his last checkup, his spinal and brain tumors were unchanged, but his kidney tumors had disappeared!

"What he didn't tell his doctor is that he had been drinking Essiac Tea for three months. He believes that the disappearance of his kidney tumors is due to the tea. Essiac Tea is marketed under the name Flor*Essence.

"I asked Dr. Todd Magnum, a medical doctor who uses a variety of holistic treatments, including herbs, in his practice. He said that `trying Flor*Essence as a cancer treatment is a good idea. There are no side effects.'

"Maybe this is something which could slow down or even reverse the growth of tumors? Do you know of others who have had good results from Essiac Tea?" -- *Altheada Johnson, New York*

The Essiac Formula is a very old American Indian Remedy given by a Native American to a Canadian nurse after he watched his horse cure himself of a cancer with these herbs in the pasture. It has helped thousands and done nothing for others. It is hard to know when it will help and when it won't. No doubt, age and length of symptoms play a great role. I would recommend it but not as a sole agent against VHL -- but along with diet, exercise, meditation, etc. it would be helpful in addition to regular medical treatment.

-- Dr. Rosita Arvigo, D.N., Director, Ix Chel Tropical Research Foundation, San Ignacio, Belize, Central America. Author, with Dr. Michael Balick, of Rainforest Remedies.

Scientists do not know everything, and perhaps there is some significant unknown factor in Essiac tea which can help VHL patients. We just don't know. A beneficial effect of Essiac tea cannot be ruled out. We can never prove the null hypothesis (no difference between Essiac tea and a placebo,) we only conduct experiments or studies that may provide evidence that allows us to reject the null hypothesis. Any serious side effect or excessive cost would make administration of Essiac tea unreasonable. This or any other homeopathic remedy should now only be an adjunct to standard therapy, and its use should be revealed to health care providers.

--- James M. Lamiell, M.D., Colonel, U.S. Army, Chief, Clinical Investigation Regulatory Office, U.S. Army Medical Department Center and School, Fort Sam Houston, Texas.

Taking Charge of your Health Care

-- by Cathy C., New York

About a year ago now I started feeling sickly but did not go to a doctor. In November and early December I started seeing a doctor who told me I was stressed. In late December, my father passed away. Since the stress brought on by this did not make me any sicker, I decided it was time for a new doctor.

I went to a new doctor in January who declared I had colitis. But the medications were not helping. Both my father and sister have had pancreatitis caused by a cyst, so I pushed for a CT scan. My CT scan not only revealed cysts on my pancreas, but also on both kidneys, with some possible tumors on the right kidney. A possible diagnosis of VHL was made in February, and I began researching what VHL was, since none of my doctors had ever heard of it.

All my research took me to a major hospital on the east coast in April. The visit went well, but I heard nothing from them afterward. After three months and many follow-up telephone calls they told me I needed a biopsy of the right kidney. No local doctors here wanted to do that biopsy since they were not skilled in partial nephrectomy. I would need to find a urologist who could remove only the tumors and leave as much of the kidney as possible.

I was looking for someplace to turn and connected with the National Organization for Rare Disorders (NORD) who in turn directed me to the VHL Family Alliance. I called later that day, and Altheada Johnson called me back. Finally I felt I was not alone any more! She gave me some helpful advice and directed me to the National Institutes of Health, where they are reviewing my scans this week and will be helping me make a decision on what to do next.

Through Mrs. Johnson I also learned that the hearing loss in my left ear might be connected with VHL. This was confirmed by NIH, and we will have to decide soon what to do about that.

I am so glad to know that there's someone out there who understands! It makes dealing with all this so much easier. My father's doctors still deny that he had VHL, even though he had so many symptoms which are typical of VHL -- pancreatic cysts, high spiking blood pressure, and cancer starting in his kidneys. He died from an infection from a pancreatic cyst.

I appreciate all the information you have given me, and especially Altheada Johnson. Now that I understand what I am dealing with, I am better prepared to negotiate with our doctors and find the help I need to manage my own health.

Editor's Note: While pancreatic cysts in many patients with VHL have caused no problems, occasionally abdominal symptoms may develop such as discomfort due to pressure from a large cyst. Incidental infection of a cyst can occur, as described here. Medical attention should not be delayed if you have abdominal pain or fever or nausea and vomiting. We are preparing an article on pancreatic involvement and will appreciate your sharing your own experiences. ❑

Federal Funds for NIH

-- William C. Dickson, Chair, Research Mgt Comm.

Much of our time in the last several months was spent organizing a "write your congressman" campaign, urging Congress to continue their funding support for NIH. It was felt that doing whatever we could to prevent a cut in NIH funding would be the most significant thing any of us could do to enhance VHL research. A very large percentage of genetic research on VHL in the U.S. is being conducted at NIH, or with assistance from NIH grants.

Earlier this year the House and Senate Budget Committees proposed significant cuts in NIH funding. The original Senate Budget Committee proposal called for a 10% cut now, with a freeze at that level through the year 2002. The House Committee proposal called for a 5% cut with the same freeze. The Senate Committee later modified its proposal to request no current cut but to freeze NIH funding at its current level for the next seven years. Considering the current rate of increase in the cost of health care and medical research, any such freeze would amount to a devastating cut.

Thanks, in part, to the letters so many of you sent to Congress, this trend is beginning to turn. The Congress is realizing how much money is saved in health care throughout the country through the advances in diagnosis and treatment made possible through the NIH. The House Appropriations Committee passed and sent a great Appropriations Bill to the floor of the House. The House Appropriations Bill not only eliminated the proposed cuts in NIH funding, it included a 5.7% increase for NIH.

The struggle is not yet over. The Senate Appropriations Committee must complete their version of the Bill and then a joint version must be passed by the House and Senate before it can be sent to the President for his signature. All U.S. voters are encouraged to write a letter to your Congressman and to your two Senators urging them to support an Appropriations Bill that includes an increase in funding for NIH that is not less than that proposed by the House Appropriations Committee. For additional information, such as names and addresses of Senators and Congressmen, sample letters, etc., contact Bill Dickson, Phone: 703-759-3665; Fax: 703-759-7992; E-mail: vhlres@usa.pipeline.com. ❑

Pete Wamble, 1958-1995

-- Arleen Wamble, Illinois

Pete and Arleen were high school sweethearts when they got married in the fall of 1976. In less than three years Pete was diagnosed with von Hippel-Lindau. His father and two half-brothers had been affected for several years.

In 1979, within three weeks of each other, Pete had two surgeries for cerebellar hemangioblastomas. The outcome was great and he had no further problems for the next six years. At that time he had two craniectomies five months apart. During the fourth surgery a VP shunt was also placed to manage a cyst. In 1992 Pete had his fifth surgery once again for multiple cerebellar hemangioblastomas. In 1993 he was treated with stereotactic radiosurgery using the Gamma Knife. 1994 brought surgery for placement of another VP shunt. On May 13, 1995, Pete was laid to rest after a long and courageous battle with VHL.

Pete was admired by his family and friends for the strength and courage to keep a cheerful and joking attitude while dealing with the many challenges of von Hippel-Lindau.

Those who share their laughter
and their smiles with everyone,
And help others feel
a sense of their own worth
Are God's own special angels
who may pass this way but once,
but who truly make a difference
here on earth.
-- Emily Matthews

Matthew P. Rider, 1963-1995

--Ann Marie Rider, New Jersey

Matt and Ann Marie started dating their senior year of high school and married three years later in June, 1985. Matt was diagnosed in 1983 with von Hippel-Lindau. Matt was an adopted child and had no family history of VHL until he searched in 1994 when he was diagnosed with renal cell carcinoma. He learned that his biological mother and grandmother also died of VHL which was misdiagnosed at the time of their deaths in 1956 and 1981.

Through the 1980's and 1990's Matt underwent several laser surgeries and cryotherapy for angiomas of the retina. The 1990's were to bring brain and spinal hemangioblastomas, which were small in size until 1995. In December 1994, doctors found renal cell carcinoma on his left kidney and cysts on his right kidney. In February Matt underwent a partial nephrectomy on his left kidney.

In March doctors felt the brain tumors were growing, as well as the spinal tumors, which were giving him pain. He was started on the steroid Decadron to control brain swelling from radiation therapy. Radiation therapy was also started on his spine. The radiation had knocked out his immune system, and the steroid masked his fever; pneumonia developed and an Aspergillus fungus spread throughout his body.

On May 8, 1995, Matt died peacefully in his sleep. The last shirt Matt wore in the hospital under his hospital gown was the "VHL Family Alliance" T-shirt he bought at the VHL Conference in Boston. He truly fought VHL until his death. His courageous battle was greatly admired by his family, numerous friends and co-workers. It was Matt's wish and prayer that a cure for VHL be found for all his Family members -- his immediate family and all his 4000 VHL Family members. ❑

In Memoriam

We are sad to share with you the passing of some of the people in our community. Whenever you have a community of 4000 people there will be some sadnesses. We feel these especially keenly because they are part of our family.

Pete Wamble passed away from complications from his repeated surgeries. Arleen was with us in Kansas City.

Matt Rider passed away quite suddenly in May from an infection which was evidently masked by the steroids he was taking to manage swelling during radiation therapy. Matt and Ann Marie were with us in Boston.

Carolyn Flanagan passed away in June from metastatic cancer. By the time she was diagnosed with VHL a year ago, the kidney cancer had already spread to her hip bone. She fought hard, and was on crutches in Boston, recovering from a total hip replacement. Carolyn's family asked us particularly to work for early diagnosis.

Clay Castleberry died suddenly on an airplane in July. We met his mother, Charlotte, in Boston. There is still no conclusive answer to why, except that he had a tumor in the part of the brain that controls breathing, and had had some difficulty with his breathing before.

We send our heart-felt wishes to their families and wish them the comfort of their "other family." If you would like to write to any of these families, we will be happy to pass your notes along to them. ❑

Resources

Family Resource Center on Disabilities, 20 E. Jackson Blvd, Room 900, Chicago, IL 60604. Two newly revised resource guides -- *How to Get Services by Being Assertive* and *How to Organize an Effective Parent/Advocacy Group* are now available for a nominal fee. Call 312-939-3513 for prices.

Living with Low Vision, *A Resource Guide for People with Sight Loss.* A comprehensive Large Print guide to services and products that help individuals with vision loss throughout North America. This guide provides people with sight loss the information they need to keep reading, working and enjoying life. Chapters on self-help groups, relevant laws, high tech equipment that promotes independence and enjoyment, and special resources on the internet. A bit expensive, but you could recommend that your local library purchase a copy so that you and others can use it. ISBN 09-929718-14-3, $43.95.

Printer Receives Award

-- reprinted from The Daily Corinthian, Corinth, Mississippi, June 16, 1995

The VHL Family Alliance recently presented Wayne and Gayla Hodges, Hodges and Sons Printing of Corinth, an award and certificate of appreciation.

The Hodges provide printing services for all national and international publications to medical professionals, family, friends and patients with von Hippel-Lindau (VHL) disease. During the past two years, their services have been instrumental in providing educational information to more than 20,000 individuals.

VHL is a familial cancer affecting one in 35,000 individuals. VHL is genetically transmitted, caused by a mutated tumor suppressor gene which has a 50 percent chance of being inherited by the next generation. It is under-reported and misdiagnosed in many cases. The VHL Family Alliance has its Mid-South Chapter and national publication office in Corinth.

Peggy Marshall, vice chair of the Board of Directors, and husband Don, National Publications Coordinator, co-chair the Mid-South chapter.

"With the dedicated support and assistance of Wayne and Gayla, the VHL Family Alliance has been able to reach out to many new families that are in need of information to be able to manage their VHL involvement and live very happy lives," Mrs. Marshall said. "Thirty five years ago I was diagnosed with VHL. At that time I was told I was one of only a handful of cases in the world. Don and I just returned from our second international conference in Burlington, Mass. We were able to meet over 100 other VHL families and 24 dedicated physicians from all over the world working to improve diagnosis, treatment and quality of life for people with VHL. We have contact with over 4,000 VHL members in over 20 countries. VHL has affected four generations of my family. It is because of the dedicated support of friends like Wayne and Gayla we are able to reach more families." ❑

Resources

National Patient Air Transport Hotline 1-800-296-1217. the NPATH hotline offers free information about all long distance patient air transport options -- free, charitably assisted and commercial. Patients, families and medical professionals can all use NPATH to find the best transportation options to reach necessary medical care.

A Woman's Guide to Coping with Disability addresses the special needs of women with disabilities and chronic conditions, such as social relationships, sexual functioning, pregnancy, childrearing, caregiving, and employment. Special attention is paid to ways in which women can advocate for their rights with the health care and rehabilitation systems. Written for women in all age categories, the book has chapters on diabilities including spinal cord injury. Includes information about service providers, psychological aspects, and special assistive devices. ISBN 0-929718-15-1, $39.95.

Intro to VHL for Doctors

There are three new reviews of VHL this year in the medical literature, two in English, one in French, all very useful as a handy reference for physicians. These articles should aid physicians in making earlier diagnoses of VHL, and will help specialists understand the importance of full body screening for all the manifestations of this complex syndrome.

The Choyke article assembles the learning of the U.S. National Institutes of Health into a succinct desk reference which explains the kinds of manifestations, how to test for them, and some guidelines on when and how to treat them. Choyke, Glenn, et al, "Von Hippel-Lindau Disease: Genetic, Clinical, and Imaging Features," *Radiology*, March 1995, 639ff.

The Neumann article reviews the manifestations of VHL and has a very good explanation of the genetics of the disease and the state of DNA testing. Neumann, Lips et al, *Brain Pathology,* 1995, **5:**181-193.

For a good review in French, see "La maladie de von Hippel-Lindau," by Stéphane Richard, Sylviane Olschwang, Dominique Chaveau, and François Resche, Synthèse Médicine/Sciences (1995) 11:43-51. ❑

Online Services

by Fred Johnson, Computer Committee

VHLBBS/UMC available via Telnet

The VHLBBS free bulletin board sponsored by the Global Ministries of the United Methodist Church may be reached at 1-212-222-4724 or

telnet hwbbs.gbgm-umc.org

ftp hwbbs.gbgm-umc.org

VHLFA contacts on the net

Our primary contact point, the electronic equivalent of our 800 number, is vhl@pipeline.com Here are a few other handy addresses:

Publications: vhlpub@aol.com

Research Committee: vhlres@usa.pipeline.com

Georgia chapter: gavhl@aol.com

Mid-South Chapter: vhlms@aol.com

Newsletter articles and other info

including the Handbook are available on the Internet through the University of Kansas Medical Center Genetics home page, or through the Harvard University Medical Center Neuro-genetics home pages, listed at the bottom of this page. The most popular items are "What is VHL?" and the Handbook.

Have fun! ❑

Dialysis and Transplant

Do you know people beginning renal replacement therapy -- dialysis or transplant -- within the next year? or are on these therapies now? Are they currently working or not?

The International Center for the Disabled is opening a special program to help people stay employed, prevent problems at work, or help resolve problems that have already arisen.

For all people with VHL there are opportunities to increase our knowledge about VHL, dialysis, and transplant.

For people in Northern New Jersey, New York and Long Island there is free assistance from expert vocational specialists to help retain their jobs.

Please call the hotline 1-800-767-4VHL, or send E-mail to vhl@pipeline.com. Outside the U.S. and Canada please write, or call 1-718-622-1996. ❑

Find information about VHL on the World Wide Web! Connect to the VHLFA Home Page, at URL
http://kumchttp.mc.ukans.edu:80/instruction/medicine/genetics/vhl/vhlhomep.html
or http://neurosurgery.mgh.harvard.edu:80/vhl-fa.html

We're Growing!

We are thrilled to welcome four new chapters since our Annual Meeting: Vermont, North Carolina, Texas and Virginia. In the December issue we will introduce some of the new chapter chairs.

Big Texas Meeting

-- Mark and Cindy B., Co-Chairs

The Texas Chapter of the VHLFA has its first meeting at M.D. Anderson Cancer Center in Houston, Texas, on August 5, 1995. We had families come from as far as Baton Rouge, Louisiana. Don and Peggy Marshall came from Mississippi. The meeting lasted from 1 to 6. Everyone wanted to know when the next meeting would be held. I'm going to shoot for January or February.

I can never than Dr. Stephen Lott or Don and Peggy Marshall enough for their taking time out of their busy schedules to make our meeting a success. Stephen Lott's knowledge and work in genetic research was wonderfully presented. Don and Peggy were able to help many of us with questions.

Mark and I want to thank each of the 19 people who attended and ask them to come and bring someone with them to the next meeting!

New York Meeting

-- Altheada J., Chair

The New York Chapter held its second meeting on September 10. Members from Brooklyn, the Bronx, Long Island, Queens, and Westchester attended.

Dr. Robert Burk, Coordinator of Clinical Care Center at the Albert Einstein College of Medicine, hosted the meeting. He discussed the importance of the recent genetic advances and the possibility of developing a drug therapy for the treatment of VHL tumors. We all know a little more about what mutations on genes look like and how they occur.

Donna Russo, Genetic Counselor, discussed linkage vs. direct testing, pros and cons of genetic testing, and explained the components of a cell. Both Dr. Burk and Donna Russo have agreed to make themselves available to answer questions on-line by giving us their e-mail addresses.

Fred Johnson, Computer Committee Chair, discussed and explained VHLFA online services. Now we know what a Home Page is, and how to use the United Methodist Bulletin Board.

It was a pleasure to meet. Even participants with a great deal of knowledge and experience with VHL, who have attended the Kansas City and Burlington conferences, said they learned something new! The Alliance needs the participation of everyone to continue its goal of offering support to others. In the process we can learn from each other and have a nice time as well. It is very important to know that you are not the only one.

Up-coming meetings

Please call 1-800-767-4VHL for further information and a referral to the state chairperson. If you don't find one near you, how about helping to create one? Please contact us to volunteer your assistance.

Louisiana/Southern Mississippi - September 16, North Oaks Hospital, Hammond, LA

Florida - October 14, Orlando

West Tennessee, Arkansas, Northern Mississippi - October 21, Memphis, TN

Wisconsin - October 29, Madison

Iowa - November 1, Des Moines

Nebraska - November 2, Omaha

North Carolina, South Carolina - November 11, Fayetteville, NC

California - April 13, 1996, San Francisco

Hawaii - Annual Meeting, June 17-21, Pacific Beach Hotel, Honolulu (see also page 5)

Here's a suggestion for your holiday gift-giving!

Also see p. 15 for CookBooks T-Shirts VHLFA Pins

Your support helps keep the information building!

As my gift to you
this Holiday season,
I have made a donation to the

Von Hippel-Lindau Alliance Fund for Cancer Research

giving everyone a chance
for a very healthy, happy life.

VHL Family Alliance
Families Allied Against Cancer
171 Clinton Road
Brookline, MA 02146

Donor Services: 1-800-767-4VHL

This issue is sponsored
in memory of Pete Wamble, Centralia, Illinois, by his family and friends:
Jeff & Gale Beatty, Ken & Fay Buchanan, Dwain & Martha Chapman, Paula Chatterton, Melvin & Doris Croan, Toni Densmore, Karen Dinkelman, Michael & Debra Dunbar, Mr. & Mrs. Danny Holmes, Ryan and Cindy Holmes, Synda & Jerry Holmes, Mr. & Mrs. Edward F. Jarvis II, Duane & Becky Kleibocher, Steven & Beth Koester, Mr. & Mrs. A. R. Love, Mila J. Malone, Mr. & Mrs. Bill McDaniel, Mr. & Mrs. Thomas McMillan, Lindall & Donna McMillian, Pamela S. Meredith, Mabel Peterson, David & Pam Bauer Schaeffer, Robert & Pamela Soltis, Travelectric Company, Jody & Hal Waller, Aldora J. Wamble, Arleen Wamble, Michael & Melissa Whalen, Nettie Whalen, June Wilkin, Donald & Norma Wittenbrink, Mr. & Mrs. Benny Yorick, Mr. & Mrs. Larry Yorick, Mr. & Mrs. Leon York

Our thanks for Contributions...
In Honor of . . .
...Judge & Mrs. Willard Dixon on their 50th wedding anniv, by Margaret & Grayson Smith
...Damon Graff & Jessica Sorkin on their engagement by Florence Kaunfer, Mass.
...Altheada Johnson, by the International Center for the Disabled, New York
...Jean Lima, by her friends
Roselyn S. Butterworth, Michigan
Amber Grimm, Michigan
Becky Lima, Michigan
Carolyn & Howard Rubin, Michigan
...Don Marshall, for the wonderful job he did on the Resource Manual, by Patti Kohlen
...Sheldon & Pearl Marshall's 53rd Wedding Anniversary, by Peggy & Don Marshall
...the members of our Medical Advisory Board, for their continuing support, by Peggy & Don Marshall
...Stacey M. Regal O'Hare by her mother, Sharon Luttazi
...our brave son Gregory Dale Roper, California, by his parents, Robert & Louella Roper
...Craig Warnick, by Michael C. & Heidi E. Brown, Maryland
..."B" and the Rev. Addison Woestemeyer on their 50th wedding anniversary, by June & Harry Wilcox

In Loving Memory of . . .
...Margaret Appleton, Tennessee, by June & Harry Wilcox
...Lillian Arriaran, New York
...Mr. Bayard Boyle, by J & H Wilcox
...Clay Castleberry, California, by
Dr. and Mrs. James M. Lamiell
Peggy & Don Marshall
...Alex Dickson III, Tennessee, by Margaret & Grayson Smith
...Robert Dobberpuhl by Wauwatosa Realty Company, Wisconsin
...Magdalena Fedinec, Tennessee, by June & Harry Wilcox and Sally Overman
...Carolyn S. Flanagan, Rhode Island, by
Beavertail Lighthouse Museum Assn, Rhode Island
Adrianne Cady, Rhode Island
Mary L. Coulombe, RI
Wilma Elkins, Kentucky
Cheryl A. Foster, RI
Mr. & Mrs. Carl W. Hedberg, R.I.
Timothy Kennedy, RI
Laurence R. Kessler, Massachusetts
Kathy Maloney & Tom DeMello, RI
Anahid D. Nalbandian, Rhode Island
Mary Pigman, Kentucky
her co-workers and friends at the Rhode Island Dept. of Mental Health
Claire Sarli, Rhode Island
The Sun Chronicle, Attleboro, MA
...Miss Alberta C. Gaines, by J & H Wilcox
...Frank Warren Graff, by Joyce, Damon & Jessica
...Rose Kleinon, by Holly Cashman, Mass.
...Mr. Mancil Abernathy Milligan, by J & H Wilcox
...Willoughby W. Moyer, Pennsylvania, by
Marilyn Baldwin, Indiana
Fred & Elizabeth Crawford, Ohio
Reba Mohan, Pennsylvania
Leonard & Joyce Schmiege, Indiana
Sondra Sykes, Pennsylvania
...Dr. John D. Peeples, Jr., Tennessee, by June & Harry Wilcox
...Barry F. Regal, by Sharon Luttazi
...Phyllis Richner, Pennsylvania, by June & Harry Wilcox
...Matt Rider, by Holly Cashman
...Rabbi Norman E. Singer, Williamsport, Pennsylvania, by Rachael Morgenstern
...Robert Snyder, Tennessee, by Margaret & Grayson Smith
...Arlene Bieler Sullivan, Pennsylvania, by June & Harry Wilcox
...Mrs. Rowena Valladares, by Margaret & Grayson Smith
...Jerry Walsh, Florida, by Regina O'Brien, Illinois

with our thanks for Donations & Assistance from ...
...Peggy Graham, Michigan
...Luisa Guerra and B. Bogatch, Italy
...Dr. Myrian Gorospe, Maryland, for Spanish translation
...Mr. & Mrs. Roberto Guerra, Italy
...Mr. Abouakry Guiro, Senegal, for French translation
...Robert & Ellen Lydon, Illinois

... and from all the Members of the VHL Family Alliance

Membership, Feedback and Order Form

Every contribution helps! Thank you

Name: _____

Address: _____

_____

City: _____ State: _____ Zip: _____

Country (if not USA)_____ Fax: _____

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

❑ New Member ❑ Renewal

❑ My employer will match my contribution. I have enclosed the appropriate forms.

All Members receive 3-4 issues of the Forum during the year, and one copy of each Alliance publications. Free subscriptions are available where the dues are a hardship.

❑ Audio version available if needed for a handicapped member

I am a ❑ VHL patient ❑ VHL family member ❑ Supporting Friend

❑ Professional (physician, nurse, dietitian, social worker, etc.)

❑ My occupation is _____

❑ I am interested in participating in a local support group

❑ ***Membership*** *($25 per mailing address, $35 for medical professionals)*

❑ ***Tax-deductible donation*** *to support the work of the Alliance*

❑ *1994 Conference audio tapes (7 tapes & album) #__ @ $40* $ _____

❑ ***1995 Conference audio tapes*** *(12 tapes & album) #__ @ $60/set* $ _____

or $7.50 per session: Total sessions: #____ @$7.50 $ _____

___(1) Brain & spinal; ___(2) Stereotactic Radiosurgery; ___(3) Eye;
___(4) Kidney & Adrenals; ___(5) Inspiration & Meditation; ___(6) Mapping the Gene;
___(7) DNA Testing: How & Why; ___(8) DNA Risks & Issues; ___(9) Cost-Effectiveness, Best Care

❑ ***T-shirts*** #__Small #__Medium #__Large #__XL @ $12 $ _____

❑ ***Sweatshirt*** #__Medium #__Large #__XL @ $25 $ _____

❑ ***Sacred Process,*** *poems by Karen Koenig #__ @ $15* $ _____

❑ ***VHLFA Teamwork Pin,*** *gold filled #__ @ $27* $ _____

❑ ***VHLFA Teamwork Pin,*** *silver #__ @ $18* $ _____

❑ *****NEW ** VHLFA Cookbook*** #___@$12 $ _____

Total donation for membership & materials (U.S. Dollars) **$ _____**

In Honor Of . . . donations (minimum $5 each):

I am enclosing a donation ❑ In Memory Of ❑ In Honor Of ❑ OK to list in VHLFF

Honoree's Name _____

In Honor of Occasion: _____

Please send card to (name and address) _____

_____

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

Sales of materials are used first to fund local activities. If you are in one of the countries with a local affiliate group, please send money to one of the following addresses:

In Britain, send to VHL Patient and Relative Contact Group, 114 Longfield Rd, Littleport, Ely, Cambs CB6 1LB
In France, send to VHL France, 87, rue de la République, 95240 Cormeilles-en-Parisis, France
In Italy, send to Alleanza VHL, Loc Malvicina, 19, 15066 Gavi (AL), Italy
In Australia, send to VHL Family Alliance, 2/51 Musgrave St, Yarralumla 2600, Canberra, ACT, Australia

VHL Family Forum, Newsletter of the VHL Family Alliance
Volume 3, Number 3, September 1995, ISSN 1066-4130
E-mail: vhl@pipeline.com; Phone: 1-617-232-5946; Fax: 1-617-734-8233
Toll-free in the United States and Canada: 1-800-767-4VHL
Editor: Joyce Wilcox Graff, 1-617-232-5946 (eve)
Adviser: Debra L. Collins, M.S., U. Kansas Med. Center, 1-913-588-6043
http://neurosurgery.mgh.harvard.edu:80/vhl-fa or via OncoLink
171 Clinton Road, Brookline, Massachusetts 02146 U.S.A.

New NCI Director does VHL Research

Richard D. Klausner, M.D., was sworn in August 1 as the 11th director of the National Cancer Institute (NCI) at the National Institutes of Health (NIH) in Bethesda, Maryland.

NIH director Harold Varmus, M.D., said, "Dr. Klausner brings to this important post an extraordinary record of scientific achievement, admirable personal qualities, and a firm commitment to advancing the nation's health through vigorous and innovative science. I am sure that he will provide the leadership that NIH's largest and most visible institute needs as it carries forward the fight against cancer."

Trained as an internist, Klausner combined patient care and basic research in the early days of his career. He earned his undergraduate degree from Yale University in 1973 and his M.D. degree from Duke Medical School in 1976. He was a resident in internal medicine at Duke Medical Center from 1976-1977. From 1979-1981, following additional training in internal medicine at Massachusetts General Hospital and post-graduate research at Harvard Medical School, Klausner began his research career at the NIH in the NCI's Laboratory of Mathematical Biology at NCI. He worked at NIH s National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases from 1981-1984, when he became chief of the Cell Biology and Metabolism Branch at the National Institute of Child Health and Human Development.

Klausner is one of the most highly cited scientists in the world in cellular and molecular biology. His work has greatly contributed to our understanding of the regulation of complex genetic networks in human cells. He is a renowned leader in the study of iron metabolism and hemochromatosis, a disease of impaired regulation of iron uptake by body tissues which is associated with subsequent development of cirrhosis and liver cancer. He also illuminated the structure and function of the T-cell antigen receptor, the central molecule of the immune system. He is an expert on how certain cell surface receptors enable antigens to activate the immune response, and he has contributed to an understanding of the molecular basis for how the cell recognizes abnormal or incompletely synthesized antigens, and retrieves and eliminates them. His studies illuminated novel pathways by which molecules traffic and speak to each other within the cell. Most recently, Dr. Klausner has collaborated with NCI scientists to study the VHL gene, a member of a new class of tumor suppressor genes, which play a key role in the development of human kidney cancer.

"The identification of what may be a new tumor suppressor gene pathway will simultaneously have implications for understanding the basic biology and the essential steps that transform a normal cell to a cancer cell," says Dr. Klausner. "I will be surprised if this pathway is limited to von Hippel-Lindau and kidney cancer."

Dr. Klausner has written textbooks on medical immunology and internal medicine, and has been recognized with numerous awards and honors. ❑

VHL Family Forum
Newsletter of the VHL Family Alliance
171 Clinton Road
Brookline, MA 02146

NONPROFIT ORG.
U S POSTAGE
PAID
Permit No. 37
Tarpon Springs, FL

Address Correction Requested