VHL Family Forum

Volume 2, Number 4 ISSN 1066-4130 December 1994

Breakthrough Research

We have shared with your some interesting developments in surgical treatment. Even radiosurgery is still surgery. While there is no incision to heal, there are other risks in using radiation, and in the side-effects which can arise from the treatment.

What would be better for all of us is to reduce the need for any kind of surgery. Some interesting proposals are discussed in this issue, others are waiting in the wings.

We keep a list of trials and experimental procedures. Please contact us: If you are a researcher in search of subjects, please supply information on what you are doing. If you are a patient or physician in search of a better treatment, call and ask what's happening.

Whenever your situation can be treated with conventional surgery, a tried-and-true method is always preferable to an experimental one. Where the risks of conventional treatment are high, however, you might at least like to know what additional options are out there.

Please share with us any additional exciting information you discover. We have a powerful community here which is creating powerful new options for managing our health.

Call for Volunteers -- VHL Protocol Angiogenesis Inhibitor Trials

Dr. Judah Folkman and Dr. Emile Voest, Children's Hospital, Boston

Researchers at Children's Hospital have found that many human tumors secrete proteins which stimulate blood vessel growth. These are called *angiogenic factors*. The tumors are dependent on the new blood vessels for their own growth.

It is now possible to measure at least one of these potent angiogenic factors in a small sample of urine. It is called bFGF, basic fibroblast growth factor.

Normal levels of bFGF are known for patients of all ages, but no one has measured the level of this

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ALT for Renal Cell Carcinoma

Cellcor, Inc., is conducting Phase III trials of its proprietary autolymphocyte therapy (ALT) in patients with renal call carcinoma (RCC) or kidney cancer.

The therapeutic use of living cells that have been modified in the laboratory is termed living cell therapy, cellular therapy, or cell transplantation. Because these modified cells are living, they interact with other cells in the body, respond to changing conditions in the patient, and generate a series of biologically active molecules that are more likely to be secreted in the optimal concentration, in the correct order, and at the proper site in the body. This leads to a dynamic self-regulating therapy that leverages the body's own response to disease.

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Inside this issue!

Please Join us in Boston, April 28-30, 1995!

Angiogenesis, Continued from page 1

angiogenic protein in the urine of patients with VHL. If VHL hemangiomas are found to be secreting the angiogenic protein bFGF, this may be similar to hemangiomas of infancy which are also high secretors of bFGF. These hemangiomas in infants have been successfully treated with alpha interferon, which is one form of an angiogenesis inhibitor. Other more potent angiogenesis inhibitors are being developed or are already in clinical trial, and they could eventually be used to treat VHL patients. However, the first step is to see if we can determine what the levels are in the urine of VHL patients.

To send a urine sample to Children's Hospital, it is only necessary to call Ms. Susan Connors at the Children's Hospital 1-617- 632-2337, page #1540). She will mail a small Federal Express box with tubes in it, and we will pay for the mailing charges. Or, she will explain how to come to Children's Hospital to leave a urine sample. All of these samples and the results will be kept confidential.

An informed consent form is attached which is an agreement of your participation in this study. It should be returned with your urine sample.

From the Editor: What is Angiogenesis?

As reported in the newsletter last March,[1] angiogenesis is one of the most interesting new areas of exploration in cancer research. Angiogenesis, meaning "growth of new blood vessels," refers to the normal or abnormal creation of new blood vessels. Many VHL tumors are hemangiomas, or a mass of unnecessary blood vessels, which spontaneously decide to grow. Controlling the process of angiogenesis could lead to a therapy which would keep VHL tumors small, or prevent them from growing at all. While nothing has yet been proven in clinical trials, this is an area of research which may hold much promise.

Interferon alfa-2 was the first pure human protein found to be effective in the treatment of cancer. It is one of a family of human proteins with broad antiviral activity, and a broad regulatory effect on cell functions. It was produced in the early 1980's under a grant from the American Cancer Society. It is cell therapy, not chemotherapy, and has only mild side effects. Through extensive clinical trials these proteins have been found to be clinically useful in many diverse diseases -- including some rare forms of hemangioma in infants. Interferon was beneficial in more than 80 percent of the children treated. Not only did angiomas eventually regress but their life-threatening complications were controlled.[1]

Happy Holidays! from your Other Family

Interferon has also been shown to be effective in inhibiting angiogenesis in some other vascular proliferation disorders. "There are receptors on cells of all types. The diversity of the cellular effects of interferons suggests that they may be useful in a wider range of benign and malignant neoplasms [lesions] in the future."[2]

The study proposed at Children's Hospital will help scientists understand how the angiogenesis associated with VHL is related to the angiogenesis which occurs in other conditions.

The analysis of your own urine sample will not yield useful results. It will be a set of numbers, associated with the levels of certain proteins in the urine. We don't know yet what that means. Analysis of all the urine samples collected, however, will help the team understand what proteins are involved in the angiogenesis which occurs in VHL, and perhaps to choose an appropriate angiogenesis inhibitor for VHL. We will report the collective results in this newsletter.

Thank you very much for your willingness to participate in this exciting trial. --*JWG*

See "Scientists Unraveling Why Vegetables Retard Cancer," *VHLFF,* 2:1, March 1994. References: 1. Carl W. White, et al, "Treatment of Pulmonary Hemangiomatosis with Recombinant Interferon Alfa-2a," *New England Journal of Medicine (NEJ),* **320:**18, 1197-1200; Laurie A. Ohlms, et al., "Interferon Alfa-2A Therapy for Airway Hemangiomas," *Annals of Otology, Rhomology & Laryngology,* **103:**1, Jan 1994; R. Alan B. Ezekowitz et al, "Interferon Alfa-2a Therapy for Life-Threatening Hemangiomas of Infancy," *NEJ,* **326:**22, 1456-1463, May 1992. 2. Ernest C. Borden, "Interferons -- Expanding Therapeutic Roles," *NEJ,* **326:**22, 1491-1493, May 92. ❑

Informed Consent
Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115

Participant's Name _____ ***Date:*** _____

Protocol Title: Study of Angiogenic Molecules in Urine.

Protocol Number: 91-3682-02 ***Urine Sampling for Research Purposes***

Purpose: We would like permission to enroll you in a research study whose basic purpose is to determine whether a protein that is associated with certain tumors can be found in human urine. It may be necessary in the course of this research to ask you for additional samples.

Procedure: You will be given a small container to collect the urine.

Risks: There are no risks involved with obtaining a urine sample.

Benefits: Collection of this urine will not provide any direct benefit to you. If you choose not to participate in this study, there will be no effect on your clinical care. It is only being collected for use in laboratory research. Currently, this urine test has no known clinical utility. Therefore, no results will be returned to you because of our inability to know what the results mean.

Consent: I have been satisfactorily informed of the above described procedure with its possible risks and benefits. I give permission for my/my child's participation in this study. I know that Dr. Folkman and his associates will be available to answer any questions I may have. If I feel my questions have not been adequately answered, I may request to speak to the Hospital Consent Committee by calling 1-617-735-7052. I understand that I am free to withdraw from this consent and discontinue participation in this project at any time, even after signing this form, and it will not affect my/my child's care. I have been offered a copy of this form.

_____ _____

Signature of Patient Signature of Parent/Guardian if patient is under 18 years old

ALT, Continued from page 1

Living cell therapies involve the application of biotechnology to the medical care of an individual patient. The three essential steps in all living cell therapies are: (1) the collection of living cells from the patient, (2) the activation, modification, or enhancement of these cells ex vivo (outside the body, in the laboratory), and (3) the safe return to the patient of the activated, modified, or enhanced cells. Various forms of living cell therapies have been developed, and are currently being used in several clinical settings, including bone marrow transplantation, in vitro fertilization, the use of laboratory-grown skin, and adoptive immunotherapy for cancer using immunoreactive lymphocytes. Additional living cell therapies currently being studied include gene therapy and the transplantation of various living cells, including pancreatic islet cells for the treatment of diabetes and myoblasts for the treatment of muscular dystrophy.[1]

Autolymphocyte therapy (ALT) is an outpatient form of adoptive immunotherapy based upon the ex vivo general activation of killer and helper T cells which when returned to the patient are believed to search out foreign targets (cancer or virus). An earlier Phase III clinical trial in advanced kidney cancer at five U.S. sites published in *Lancet*[2], reported ALT's potential to extend survival for people with metastatic renal cell carcinoma (mRCC). Patients who received ALT on an outpatient basis remained functional and productive. There are only minimal side effects.

Because of its success so far in trials with mRCC, the trials are being broadened to include patients with RCCs at earlier stages of development. We inquired about application of ALT to VHL renal tumors. The company will consider applications from VHL patients on a case-by-case basis.

An FDA designated Phase III pivotal trial of ALT in metastatic kidney cancer is now underway at more than 20 sites. Directed by Georgetown University's Michael J. Hawkins, M.D., the primary objective of the study is to evaluate the survival of patients with metastatic kidney cancer who receive either ALT or alpha interferon. Results of the trial will be combined with data from previous research efforts and submitted in Product and Establishment Licensing Applications, one of the final steps in the pre-marketing approval process for any biological product. Cellcor hopes that ALT for metastatic kidney cancer will be the first cellular therapy to receive market approval from the FDA.

Gary W. Cashon, Ph.D., Chairman of Cellcor's Board of Directors and General Partner of Hillman Medical Ventures, Inc., stated, "We are excited that the Company can press this novel technology forward in this pivotal trial. We believe ALT is the first cellular therapy to reach this stage of approval in the process of the U.S. Food and Drug Administration (FDA) since the creation of its new Division of Cellular and Gene Therapies."

"Kidney cancer affects 27,000 new patients each year in the United States. Treatments currently available for mRCC are limited, highly toxic, and cause side effects requiring patient hospitalization," explains Richard R. D'Antoni, President and Chief Executive Officer.

Participating academic research centers for the trial are: Cleveland Clinic; Emory Clinic, Atlanta; Georgetown University Medical Center, D.C.; University of Southern California Medical Center - LA; Columbia Presbyterian Medical Center, New York; Vanderbilt University Medical Center, Nashville; Northwestern University Medical Center, Chicago; Duke University Medical Center, North Carolina; University of California-Davis Medical Center; University of California-SF; Lankenau Hospital Cancer Center-Philadelphia; Pittsburgh Cancer Institute; St. Joseph's Hospital Cancer Center-Tacoma; University of Miami, Florida; MD Anderson Cancer Center, Houston; Sparrow Hospital, Lansing, Michigan; Presbyterian/St. Luke's Medical Center, Denver, Colorado; Boston University Medical Center; H. Lee Moffitt Cancer Center, Tampa; University of Iowa Hospital, Iowa City; and Cedars-Sinai Medical Center-LA. The Jewish General Hospital in Montreal, Canada, is also participating.

> "This leads to a dynamic self-regulating therapy that leverages the body's own response to disease."

Clinical development of ALT, an outpatient procedure, has focused primarily on the treatment of mRCC to extend survival. The Company is also conducting a Phase III clinical trial in the use of ALT in non-metastatic RCC. Cellcor scientists believe ALT may have application for the treatment of other forms of cancer and serious infectious diseases either alone or in combination with other therapeutic agents.

Interested patients and physicians should contact one of the sites, or call Cellcor more information on eligibility requirements. Call Colleen Hill, R.N., 1-800-441-7901 or 617-332-2500. Headquartered in Newton, Massachusetts, Cellcor, Inc., is a biotechnology company working on the development and commercialization of cellular therapies.

1. G. C. du Moulin et al., "Implementation of an Effective Program for Quality Assurance and Quality Control in Living Cell Therapy: a 2-year experience with Autolymphocyte Therapy," *Transplantation Proceedings*, **24:**6, Dec 1992, 2803-2808. 2. See also Michael E. Osband et al, "Effect of autolymphocyte therapy on survival and quality of life in patients with metastatic renal-cell carcinoma," *The Lancet*, **335:**8696, 28 April 1990, 994-998. Sam Graham, "The Use of Ex Vivo-Activated Memory T Cells (Autolymphocyte Therapy) in the Treatment of Metastatic Renal Cell Carcinoma: Final Results From a Randomized, Controlled Multisite Study," *Seminars in Urology*, **11:**1 (Feb 1993), 27-34. ❑

The Multi-Step Nature of Cancer

Condensed from an article by Bert Vogelstein and Kenneth W. Kinzer, Johns Hopkins Oncology Center, Baltimore

One of the most important developments in genetics over the past decade has been the proof that cancer is, in essence, a genetic disease. However, there are two key differences between cancer and most other genetic diseases. First, cancer is, for the most part, caused by *somatic* changes—changes that happen to cells during one's lifetime--whereas all other genetic diseases of mammals are caused solely by *germline*, or inherited mutations. Second, each individual cancer arises not from a single mutation, but from the accumulation of several mutations. This "multi-hit" concept is central to understanding *neoplasia*.

While most types of VHL tumors do not become malignant, the process of *neoplasia*, or new growth of angiomas and tumors, follows the same general principles and patterns of abnormally accelerated cell growth which leads to cancers. VHL is therefore classed as one of the familial, or inherited, cancers.

If we look at the incidence of sporadic cancer, which occurs in the general population, we find that there are significantly more cases among older people. While there are many possible explanations, one of the most attractive is that three to seven "hits" are required for a cancer to form. These "hits" could represent insults to separate cells, but because each cancer appears to arise from a single cell, it is more likely that they represent sequential mutations of growth-regulating genes in a single cell and the cells it creates.

According to this idea, tumors grow by a process of evolution and mutation. The first mutation would result in a limited number of the *progeny*, or offspring, of a single cell. One of these cells would later acquire a second mutation, perhaps allowing growth of a small benign tumor. One cell within this benign tumor would then undergo a third mutation, overgrow its sister cells, and form a more advanced tumor composed of progeny cells with three mutations. Eventually the cell would accumulate a sufficient number of hits to make it malignant, enabling it to invade surrounding tissues and metastasize to other organs. In this sequential multi-hit model, the fact that most cancers occur in older people is explained by the decades required for an individual to accumulate the number of mutations necessary to cause malignancy.

This theory is also backed by other observations. For example, patients exposed to radiation often develop cancer, but the cancers do not form immediately. In the case of patients who underwent X-ray therapy for tuberculosis, breast cancers develop an average of 15 years after the initial exposure. Why the long time lag? One explanation is that the radiation induced a mutation in a cell, but additional mutations in the progeny of this cell were required for a cancer to form. Again, because of the low incidence of additional mutations after the radiation therapy had ended, long periods were required for the cancer to appear.

These examples suggest that multiple mutations occurring over decades drive the process of cell change that may result in a tumor. Exceptions to this general scenario provide important lessons. Tumors that occur in children obviously do not take decades to develop. The timing of the tumor growth in such cases stimulated Knudson to propose his now well-accepted model for neoplastic development. The model relies on two principles. First, in childhood tumors of the eye and kidney, only two mutations are needed for cancer formation. Second, either the two mutations can both develop after birth, or one can be inherited and the other not. In the case where one is inherited, every cell of that individual has a "head start" on the neoplastic process, and such individuals have a high risk of developing these specific cancers. One important finding from these pediatric studies is that the number of hits required is likely to vary in different cell types. Similarly, it may vary in different species. For example, rodent cells are generally easier to transform than human cells, and this may be because fewer hits are required.

But all this is only indirect evidence. More direct evidence is provided in gene transfer experiments. An oncogene can be defined as a gene whose activity leads to more rapid cell growth. If an oncogene is transferred to cultured mouse fibroblast tumors, no changes in growth are observed. However, if two oncogenes are transferred simultaneously, the growth rate speeds up markedly, forming sites of piled-up cells which grow tumors in mice.

The VHL gene, on the other hand, is not an oncogene (a growth promoter), rather it is a tumor-suppressor gene. The weakness of the tumor-suppression system in a cell, combined with one or more of these 'hits' or insults to cells may be what permits tumors to grow, more often and at a younger age than in most people.

Because the oncogenes and tumor suppressor

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see pages 11-12

genes so far identified appear to control different cell growth circuits, one might expect that the order in which the circuits are interrupted would be unimportant, and that so long as a sufficient number of critical pathways were disabled, tumor growth would begin. In fact, different kinds of changes have clear preferences for tumors in particular organs.

Understanding the complexity and multiplicity of genetic events is the first step towards understanding the various diseases provoked by them. Multiple mutations provide multiple chances to intervene and change the course of the disease. Indeed, it has been shown that when a single normal gene or chromosomal region is introduced into a cancer cell with multiple mutations, cell growth and/or invasion can be dramatically constrained, at least in the test tube. While it is likely to be some time before we can successfully apply this type of therapy to human cancers in the body, it may eventually be possible to develop drugs that will mimic the effect of normal suppressor genes or interfere with the effect of mutant genes.

A highlight of the last decade was the discovery of many of the genes that are responsible for human cancer. The next decade should see the characterization of the biochemical and physiological mechanisms that underlie the action of these genes, facilitating novel approaches to both therapy and prevention.

Vogelstein et al, "The Multi-Step Nature of Cancer," *Trends in Genetics,* **9**:4, April 1993.

Silencing the VHL Gene

Reporting an article by James G. Herman, Farida Latif, Stephen Baylin, et al., National Cancer Institute and Johns Hopkins Medical Center

The majority of cases of renal cell carcinoma in the general population appear to be caused by some sort of inactivation or "silencing" of the VHL gene. This gene normally encodes a protein. The normal effect of the gene, and of the protein, are silenced by any number of changes in the genetic structure of the gene. This article reports a new kind of change, called *cytosine methylation*. Even where the gene has not actually been mutated or changed, the effect of methylation serves to stop it from doing its normal job.

One form of renal cell carcinoma may occur in people at risk in families who inherit changes in the VHL gene. In addition, some 26,000 cases of "sporadic" renal cell carcinoma occur each year at random among the general population, in which there is some change which causes the VHL gene to stop doing its job.

This *hypermethylation* was found in 5 of 26 (19%) of the sporadic RCC tumors examined. Four of these had some change in the VHL gene; four of the tumors with hypermethylation had no detectable mutations. Abnormal methylation appears to be an event which happens before a tumor metastasizes.

Some cells did not have changes to the VHL gene, but the gene was not functioning because of methylation. When these cells were treated with a "demethylating" agent, the VHL gene began expressing itself normally again. This is not a clinical treatment, but is an experiment which chemically proves that when the effects of methylation are reversed, an otherwise normal VHL gene began to function normally. This indicates that the effects of methylation alone can serve to silence the gene.

> ❝ Multiple mutations provide multiple chances to intervene and change the course of the disease. ❞

These findings suggest that abnormal methylation may play a role in the tumor-suppressor gene inactivations which initiate or cause progression of common human cancers. This represents the best characterized example of the direct relationship between methylation and lack of expression of a tumor-suppressor gene in a common form of human cancer. This is exciting news in the field. Methylation may prove to be a relatively common mechanism for silencing tumor-suppressor genes in other forms of human tumor growth.

James G. Herman, Farida Latif, Yongkai Weng, Michael J. Lerman, Berton Zbar, Sue Liu, Dvorit Samid, Dah-Shuhn R. Duan, James R. Gnarra, W. Marston Linehan, and Stephen B. Baylin, "Silencing of the VHL tumor-suppressor gene by DNA methylation in renal carcinoma, *Proceedings of the National Academy of Sciences, USA,* **91:**9700-9704, October 1994.

What Does All This Mean to Us?

Scientists are making significant headway toward understanding how genes function in general, and how oncogenes (cancer promoters) and tumor-suppressor genes regulate cell growth. They now understand that as a normal cell changes into a cancer, it goes through a sort of "morphing" process, changing its nature from an innocent normal cell to a pre-cancerous cell to a cancerous cell to a metastatic cancer cell which then goes out and invades other tissues. The fact that it has to go through multiple changes provides a number of opportunities to keep the cell from making further changes, or in fact reversing the process.

Already we are seeing some new therapies, like the ALT article in this issue, which take cells from the patient's own body, change certain characteristics to turn on the body's natural defenses, and reinject these modified cells back into the same patient, to promote the body's natural ability to heal itself. Within the next decade we will see some pretty amazing advances in gene therapy, leading us toward a cure. ❑

Karen Koenig, 1937-1994

Artist and poet, wife and mother,
Karen tells her story in poetry.

"My wife Karen has enjoyed doing art all her life, realizing from the age of twelve that she had a mysterious gift for creating a likeness. Her career as an artist began with portraits of her three children in 1972. As time passed, she grew increasingly active as a professional portrait artist. As her children became older and more independent, art filled her life with ever-greater challenges, enjoyment, and satisfaction.

"In 1966, three months after the birth of her third child, Karen discovered that she had von Hippel-Lindau disease (VHL). VHL began to affect her eyes more than twenty-five years ago, and she eventually lost all sight in one eye. But it was not until January, 1992, that impairment of vision in her only seeing eye ended her career as an artist. It was out of these circumstances, and with the encouragement and guidance of my poet brother, David Koenig, that this book came into being." — *Steven P. Koenig, M.D.,* from the introduction to *Sacred Process*[1]

I Thank God (for Steven)

(December 8, 1991)

I thank God
For skies and trees
And gentle breeze,
For rabbits, bears,
For joys and cares,
For ice
And mice,
For vegetables and rice,
For you
For me
For I and thee.
Life here's the best —
We are so blessed!
For merriment and sorrow
To share today, tomorrow
With YOU —
For this
I never really stop
Thanking God.

I Feel Like a Wild-Eyed Doe

(December 8, 1991, after her second son's diagnosis and surgery)

I feel like a wild-eyed doe.
All deer know
That there are wolves out there,
But life goes on.
We do our best
To be alert,
To be careful,
To use all of our wit and instinct
And when danger swoops in close,
To fight, fight!
Use all of our strength and resources,
And to hopefully fend off the peril.

When we're young, agile and strong,
And when we're only needing to protect ourselves,
Evading the threat is a relatively simple thing.
But now I have a fawn—no, two—in danger!
And the wolves are close, menacing.
I hear their stealthy moves toward us now.
The tiniest crackle and rustle tell me they approach.
My heart pounds.
I strain to be ready
To protect not just myself, but now my babies.
I see glowing wolf eyes,
Their gleaming fangs!
I rear up on hind legs
And find a roar in my throat
Which I never before knew to exist.
My precious young, huddled in the thicket,
Get up on shaky legs to run/resist.
The predators bound toward us, leaping.
I rear up, eyes bulging,
Hoofs flashing, thundering.

Can we survive?
Will all we have to fight with be enough?
How much will we have
Of ourselves or each other
When this onslaught
Is over?

Self-portrait by Karen Koenig, oil, 20 x 23½, 1988.

Thank You

(January 2, 1992, St. Mary's Hospital, before the angiogram. Abridged.)

Thank you,
Drs. von Hippel and Lindau.
You have given me
The concrete guideposts
To a marvelously full life.
Some people have called me "Hyper."
But I have only been hurrying
So that I could enjoy
And participate in
As much of life as possible.
Since age nineteen,
An insistent inner voice

Has kept telling me
My life might be abbreviated.
So I have worked hard,
Played and prayed hard,
I have run fast, yes,
Have had a wild schedule
Sometimes.
But sometimes
I have lain very still
For very long periods.

Some people have called me
"Intense" and "intentional."
But I have only been trying
To make meaning,
Take in the meaning of life.
When there is a small space
Or a limited time factor
Things get a bit crowded,
Condensed.
People who have more time,
Who feel less pressured,
Naturally cannot relate.
They resist, even get hostile
Sometimes.
But heavenly things have been accomplished!
Mending and washings
Of dishes, clothes, and cars,
Mundane "little things"
That weave the fabric
Of a sunny, peaceful life.

Love-making and pregnancies,
Blessed mystery of gestation and births.
Infinite preciousness
Of infants, toddlers,
Children growing.
Lunches with the kids
In the Morton Arboretum,
Then lying on the blanket,
Watching the clouds
Through the branches of
The amazing variety of trees.
Church school teaching,
A weekly meeting of twelve Cub Scouts
In the basement.
Batavia Little League and Girls' Softball games,
Sometimes in three parks
Simultaneously!
Talking on the phone
While baking a cake
And making dinner
And helping with homework.
A dining room table holding
Oil paints and portrait-in-progress,
Sewing materials
For eight Christmas aprons,
And a stack of presents and wrappings
Two feet high. . . .
I have loved every minute of it,
Hectic as it has been.
I thrive on activity.
I relish challenge
It is all so precious,
So holy.

Some people have called me
"Weird."
I went out and marveled
At the fuzziness of new soybeans
In the spring fields.
I took my children,
And later my best friend,
To share my awe
At how the corn stalks grow upwards
In ever-opening spirals:

One of the countless examples
All around us
All the time
Of ultimate order —God's handiwork,
God's incredible, irresistible,
Artistic design,
Always ours for the taking in.
My joy was unbounded
In those fields.
I hugged trees too,
And I'm so very glad
I did.
Again,
Precious, holy.
My viewpoint hasn't changed one iota.
This level of appreciation,
To me,
Is weird
Like ecstasy is weird.
I wish everyone this weirdness.

Some people have found it
Amusing, confusing,
Some very tiring, even exasperating,
How so much,
So many people especially
Could be so beautiful,
So dear to me.
I have never seen a person
In whom there is no beauty.
And I am always looking!
The unending variety of people
In New York City
Delights and fascinates me.
Whether on the streets
Or the subways,
The potpourri of faces makes me feel
Like a kid in a candy shop.
Loveliness everywhere!

And so I have had
This wonder-filled
Love affair with Life
All of these years.
Where will it lead next?
Wherever it is,
I will surely find
Beautiful things there.

Thank you,
Drs. von Hippel and Lindau.
Thank you, Lord.

Sacred Process — As I See It Now III

(March 14, 1993)

Physical sight dimmed and threatened
Hearing diminished
Partial facial paralysis
Poor sense of balance
Post-radiation-impaired memory,
Knowledge of my disease's progression,
Down several considerable
Body parts.
(I've laughingly said
It turns out they were
Spare parts.)
Pieces of my physical self
Already gone ahead of me
Into the other reality.
With all of this,
I will go on,
Loving life as I live it
With as much gusto and dignity
As I can muster.
Life continues to awe me,
Tickle me,
Thrill me,
And, yes, nurture me.
What more could I ask?
The love affair continues.

1. Sacred Process, a book of the poetry and art of Karen Koenig, is privately published and not available at bookstores. One free copy is reserved by Karen's family for each person with VHL, or as a premium for your contribution to VHL information services and research. See pages 11-12 for ordering information. ❑

Partnership

by Michael A. Greenberg, M.D.

We humans have an incredible gift: The knowledge that we are going to die. This knowledge is rarely used as a gift. It is, instead, suppressed and ignored. When we are sick, have a broken arm, or a suspicious lump, we are forced to face our own mortality. Bringing this fear to the doctor's office often limits the effectiveness of our communication.

Other problems arise from the fear of death: The creation of our doctors as demi-gods, and the pursuit of "magic bullets" and remedies.

Currently, too many of us subscribe to the "fix me" mentality. We constantly see it on television--the cold or flu sufferer who takes two of the advertised pills and within minutes is off to work. It's easy to buy into this because we see these dramatic cures as triumph over disease and ultimately death. They are not.

We do not want to take responsibility for our own well-being. We abuse our bodies--smoking, drinking too much, eating too much, not exercising--and then expect it to be "fixed" by **The Doctor**. Shocking as it may seem to some, doctors do not have all the answers. One day we won't be able to fix you.

Having exposed and confronted these ideas, how should you interact with your doctor or healer? We can use healthcare professionals as advisors. But first we must create a partnership with them. By that I mean, we must understand the ground rules of good communication.

These rules are simple; however, we often do not follow them. Let us explore a few of them and make them part of our commitment to good health.

Rule number one is to be willing to accept your doctor as a coach and not as a person *who is going to cure you.*

The second rule is to be prepared before your visit to your doctor or healer. Don't be distracted by your fear and fail to obtain the help and information you are seeking. List your questions and be organized. Know any medications you are currently taking and anything you may be allergic to.

Be prepared to listen. Remember that your fears will distract you from listening carefully. Notice when you get distracted. Notice when you stop listening to the doctor because you are busier listening to your internal voice wondering whether you have something seriously wrong or whether you are going to get a shot. Politely say, "I'm sorry; I haven't been listening. I'm scared." Doctors can fully understand your fears, so get them out.

Don't let your shyness stop you from questioning your doctor. If you don't understand, ask questions. Be certain that you understand your coach. Don't get home and wonder about what you think the doctor may have meant. "Wondering about" is an unhealthy environment, breeding anxiety and fears. If you have trouble listening in the doctor's office, bring a portable tape recorder with you and ask if you can record your doctor's instructions and information about the problem in order to review it later. Your doctor should not refuse, as this will only save phone calls and confusion later.

The next rule is to always tell the truth. If your doctor is judgmental about your lifestyle or habits, find another doctor. There are many wonderful healers out there who want to help and serve you. But do not withhold information even though it might be embarrassing. Withheld information can be dangerous to your health. Tell you doctor if you smoke or drink.

Not telling your doctor about drug usage and unsafe sex practices can put your life at risk.

All of these suggestions are the basic parts of effective communication. Communication is a very difficult process; yet so often, we consider speaking and listening a very casual process. This results in much misunderstanding. When there is a partnership in communication, both parties are intentional about getting their point across, and are equally intentional about trying to understand what the other is expressing. You know how you feel when you are fully understood by another; it's a delightful feeling! I believe it is a feeling of connectedness with another, when you both are receptive and giving to each other. This is a powerful environment for healing to take place. As a billboard for a local hospital reads: Sometimes the best medicine is just listening. That goes for both patient and healer.

> "Rule number one is to be willing to accept your doctor as a coach and not as a person *who is going to cure you.*"

My suggestion is that you tell each of your doctors you want to change the way the two of you speak and listen to each other. Talk to your doctors about being your partner and your coach. They might not understand you at first, but stick with it. This might be a good time to talk about any past incidents where you were angry with your doctor. Or you might want to thank your doctors for all of the compassion and concern they have shown you over the years. These acknowledgments will be a good foundation for your new partnership.

Dr. Greenberg calls for a shift from the "me generation" to the "we generation" in his book, *Off the Pedestal.* He has been about the business of "transforming medicine" for several years. One of his projects, the Making Medicine Work Foundation, is dedicated to removing the "big business" concept from healthcare and "returning American medicine to the loving, nurturing profession it once was."

Reprinted from *Healing,* the Journal of the Healing Health Care Project. ❑

1994 Index to the VHL Family Forum

(numbers indicate Issue Number:Pages)

> Never doubt that a small group of thoughtful committed citizens can change the world: it's the only thing that ever has.
> -- *Margaret Mead*

> People with VHL need to do their best to be experts at this problem and make as many informed choices as possible. No matter how fine and caring a physician may be, there will be times that he won't have the latest information about VHL, and there will be other times that his agenda will be different from mine. Leaving all the decisions to others is risky at best. Thanks for helping to keep me an informed consumer. -- *Stephen S., Washington*

Love Bears All!

From Sherry D., Tennessee

Thank you,
Drs. von Hippel and Lindau.
You have given me
The concrete guideposts
To a marvelously full life.
-- *Karen Koenig, Sacred Process*

Index of contributors

I just finished my major work project for the year -- our organizational annual report. It goes out to 6,000 international and national readers, and takes about six months of work. I'm enclosing a copy of last year's annual report. I am very proud of it. It has won international and national top awards in the communications field.

I am particularly proud that it worked out so well because during the six months I worked on it I was relearning how to walk and write following my second brain surgery. I am glad to report that I'm doing well now.

-- *Amy J., Arkansas*

Coupon

Karen's Gift to You

The family of Karen Koenig would like to give a free copy of Karen's beautiful book of poetry* to each individual or family affected with VHL, anywhere in the world. To claim your free copy, please return this coupon with your name and address to the VHL Family Alliance address in the U.S.

A voluntary donation in Karen's memory to the VHL Family Alliance would be appreciated but is not required.

Name _____

**See pages 6-7 for an excerpt from Karen's book.*

Cook Book Going to Press in January!

We need your recipes by mid-January!

Great Chefs from throughout the world-wide VHL community -- including you, your friends, and your family -- are sending us their best secret recipes for **Appetizers, Main Dishes, Casseroles, Cakes and Cookies, Jellies and Jams, Soups and Salads, Vegetables, Desserts, Bread and Rolls,** etc.

The Cook Book will be available for purchase for $10 in April.

Send us a recipe now, and get $1 per recipe off the purchase price!*

Be sure to include your name and state

Send recipes to the VHLFA office in Brookline, or directly to:

Gale Lugo, Florida Chapter, VHLFA
1990 Harmon Avenue
Winter Park, FL 32789-5306

* discounts up to $5 per person

Join us in Boston, April 28-30, 1995!

Burlington Marriott, Burlington, Mass.
Group rate, $80, single or double

Make reservations through our conference coordinator, or through your own travel agent

Jacki Hunsberger, conference coordinator
1-800-829-0022 or 1-215-489-0896

Burlington Marriott, 1-617-229-6565

Meetings will go from Friday at 6 to Sunday at 3.

What would you like to learn?
What could you present?

Please send your questions in advance so that we can be sure you will get what you want.

See you there!!

More info on page 13

Questions/Ideas for April Meeting: What do you want to learn?

Let us Hear from You!

_____

_____

_____

Recipes Needed by mid-January!

Category: _____ Recipes will be credited to the author, as "Gale L., Florida"

Your Name:_____ State or Country _____

_____

_____

_____

_____

_____

Tear Out Page

Membership, Feedback and Order Form

Name: _____

Address: _____

_____

City: _____State: _____ Zip: _____

Country (if not USA)_____Fax: _____

Phone (home): _____Phone (work): _____

❑ 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

Quantity	Description	Each	Total Price
	Membership - VHL family (per address)	$25	
	Membership - Professional	$35	
	Tax-deductible Contribution ❑ In Honor Of (see below) ❑ $250 Sustaining Members ❑ $1000 Lindau Society *Premiums available:* With your gift of $50 or more, choose a free T-shirt With your gift of $100 or more, choose book or sweatshirt		
	T-shirt #__Small #__Medium #__Large #__XL (may be requested as your premium for a $50 gift)	$12	
	Sweatshirt #__Medium #__Large #__XL (may be requested as your premium for a $100 gift)	$25	
	***Sacred Process*, poems by Karen Koenig, free with coupon on page 11** (or may be requested as your premium for a $100 gift)	premium only	
	Back issues of newsletter (which issues?_____)	$ 1	
	Extra copies of the VHL Handbook	$ 2	
	Audio tape set of Kansas City Conference	$40	
	Please make checks payable to VHL Family Alliance. TOTAL ENCLOSED *Our tax-exempt number is 04-3180414. -- Thank you!*		

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 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

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, Camberra, ACT, Australia

Tear Out Page

Boston, April 28-30, 1995!

The meeting, co-sponsored with the Lahey Clinic, will be held at the Burlington Marriott, Burlington, Massachusetts, a suburb of Boston.

The meeting will begin Friday evening and go through 2:30 pm on Sunday. Details will be mailed out in February. Meanwhile, save up a vacation day, and begin making your travel plans now!

We already have people coming from England, Canada, and Hawaii.

What would you like to learn? What would you like to contribute to the meeting?

Topics on the agenda so far:

Advances in diagnosis and treatment of eye, brain, and adrenal lesions

Cost-effectiveness of pre-symptomatic testing

Update on genetic research

Families sharing our stories and coping skills

The how and why of DNA Testing ❑

"Hahvehd is one of several
lodge schools near Bawhston."

from Sam McCool, How to Speak Bostonian,
Hayford Press, Inc., 1985. Illustration by Jim Montgomery.

Update: Clinical Care Centers

-- Susan Warnick, R.N., Maryland

The list of pilot clinics is growing and changing. Please use this list, which includes some additions and corrections to the June list.

Each of the participating institutions has agreed that they will designate a point-of-entry into the institution here the term VHL will be recognized, and staff will know how to assist. They will take responsibility for helping a patient find all the needed specialists, and check all the appropriate areas of the body which need screening. They will ensure communication among the specialists involved in a patient's care, and wherever possible will do their best to coordinate appointments to minimize the time the patient and family need to spend at the center.

These centers may also serve as a source of second-opinions, or referrals from HMO's and physicians less familiar with VHL.

We need your help in identifying additional centers where expertise in VHL already exists, and tying those centers into the system. We need your suggestions for standards of care. And we need your help with the nuts and bolts of coordinating the program. We would like to have regional coordinators assisting with communications — please contact me to volunteer your help.

The 1994-95 pilot clinics are: (* = new since June)

Canada: Memorial University of Newfoundland, St. John's, Newfoundland. Jane Green, M.S., Medical Genetics, Tel: 709-737-6807; Fax: 709-737-3374.

England: Addenbrookes Hospital, Cambridge. Eamonn Maher, M.D., Tel: +44-223-216446; Fax: +44-223-217054.

*France: Sainte-Anne Hospital, Paris. Stéphane Richard, M.D., Neuro-oncology, Tel: +33-1-4586 2406; Fax: +33-1-4565 8728.

Germany: Albert-Ludwigs University Hospital, Freiburg. Hartmut Neumann, M.D., Nephrology, Tel: +49-761-270-3363; Fax: +49-761-270-3245.

United States:

California: University of California, San Francisco. Siobhan Geary, R.N., Neurocutaneous Clinic, Tel: 415-476-3338; Fax: 415-476-7965.

Hawaii: Kapiolani Medical Center, Honolulu. Juliet Yuen, M.S., Tel: 808-973-8698; Fax: 808-973-2554.

**Illinois: Northwestern Memorial Hospital, Northwestern University, Chicago.* Maureen O'Connor, R.N., Daniel Dalton, M.D., 312-943-5353; Fax: 312-908-0376.

Iowa: University of Iowa Medical Center, Iowa City. Ann Muilenberg, Coordinator. Tel: 319-356-2674; Fax: 319-356-3347.

Kansas: University of Kansas Medical Center, Kansas City. Debra L. Collins, M.S., Tel: 913-588-6043; Fax: 913-588-3995.

**Maryland: Johns Hopkins Medical Center, Baltimore.* Opening in January. Call Susan Warnick for contact information, 410-526-6858.

Massachusetts: Lahey Clinic, Boston. John Libertino, M.D., Urology, Tel: 617-273-8420; Fax: 617-273-5246.

Minnesota: Mayo Clinic, Rochester. Mary Kelly, Clinic Coordinator, Tel: 507-284-8198; Fax: 507-284-0161.

**New York: Albert Einstein Medical College of Medicine/Montefiore Medical Center, Bronx.* Robert D. Burke, M.D., Tel: 718-430-3720; Fax: 718-918-0857.

New York: Mount Sinai Hospital, New York City. Jane Halperin, M.S., Neurology, Tel: 212-722-1784; Fax: 212-860-6629.

To volunteer your assistance with the Clinical Care program, please contact Susan Warnick, R.N., 16 Ridge Lawn Road, Reisterstown, MD 21136. Tel (410) 526-6858. ❑

Computer Bulletin Boards

— Fred M. Johnson, New York

The VHL Family Alliance can now be reached at vhl@pipeline.com

Just as we manage the voice line, the computer account will be monitored by a volunteer from a VHL family who will make sure you get your questions answered. During December, Joyce Graff and Fred Johnson will be monitoring this account. Send messages to this account from your own email account, anywhere attached to the Internet. Ask your service provider how to send a message to an Internet address.

On January 15, 1995, the VHL Family Alliance will open an electronic bulletin board system sponsored by the Health and Welfare Ministries Program Department of the General Board of Global Ministries of the United Methodist Church. With a computer, you would dial into the bulletin board service, read the information stored there, and post any questions or comments you would like to share. You will be asked to record your real name privately for us, but may assign yourself an alias to maintain your privacy in the open discussion.

The VHL Family Alliance is establishing this service in order to provide an interactive electronic environment to educate, inform, and support VHL patients, families, and medical professionals around the world. The bulletin board will allow individuals a means to obtain and disseminate information on VHL that currently exists in several different locations.

We need You to make the Boston meeting complete! *See pages 11, 13*

VHLFA publications will be accessible via this bulletin board. The Computer Committee and other members will gather and post information from other medical databases and newsgroups. People will also be able to post personal notes and questions, and support one another through the bulletin board. Each member of the VHL Family Alliance has a unique experience with the disease that they can share with others via this medium.

The Computer Committee currently consists of: Fred Johnson, chair, Bob W., New York; Vernon H., Pennsylvania; Gale L., Florida; and Damon G., Massachusetts. We would be glad to have additional volunteers in the group, and of course we welcome your questions, comments, and input at any time.

When someone signs onto the bulletin board service, they will be greeted with a menu of topics. What topics would you like to see on that menu? The following is only a suggestion. We would like your assistance in building and shaping this service.

Welcome to the VHL Forum
1. VHL medical issues
2. Genetic Testing
3. Spouses Circle
4. Children's concerns
5. Supporting one another

Make a selection from the menu.

Each topic will store a series of articles or notes from participants. These articles can be read online or downloaded to a local computer for later reference. This forum will also give users the ability to communicate with other VHL members, medical professionals and individuals in other parts of the world via Internet electronic mail.

The telephone number has not yet been assigned. After January 15, 1995, the telephone number for the Bulletin Board can be obtained by calling us at 1-800-767-4VHL or 1-617-232-5946, or by writing to vhl@pipeline.com.

Forum for Brain Tumor Patients

BRAINTMR, an Internet forum for discussing all types of brain tumors, is used by patients, their families, and supporters, as well as medical professionals, educations and researchers to share information and experiences.

The BRAINTMR forum was initiated by Samantha J. Scolaniero, a brain tumor survivor herself, who moderates the unedited Internet service which now has more than 175 subscribers. "BRAINTMR will be as interesting and helpful as its participants," says Scolamiero.

To subscribe to BRAINTMR send a message on the Internet to : LISTSERV@MITVMA.MIT.EDU. The text should read: SUBSCRIBE BRAINTMR YOUR FIRST NAME YOUR LAST NAME. Confirmation of the new subscription should be received almost immediately. For questions, contact Samantha Scolamiero at 617-593-5095 or on the Internet using the address: samajane@mit.edu

Reprinted from the newsletter of the National Brain Tumor Foundation.

Kidney Cancer Bulletin Board

People can get free information on kidney cancer and health care issues from the NKCA BBS. Hundreds of information files are now online and free to the public. Need a copy of the Clinton Health Care Reform Plan? Want to know the latest clinical trials in renal cell carcinoma? View kidney cancer cells under a microscope? Do you need a list of doctors who specialize in urological oncology? It's all online at the NKCA BBS.

If you have used a bulletin board service before, connect with your computer to 708-332-1052 in Illinois, or call toll-free 800-280-2032. Write for complete instructions on computer equipment required and how to use the service to the National Kidney Cancer Association, 1234 Sherman Avenue, Suite 200, Evanston, IL 60202. ❑

Nominations, Please, for Spring Elections

Nominations are being accepted for additions to the Board of Directors and the Medical Advisory Board, for a two-year term 1995-1997. As we grow and take on new activities, we look to expand our leadership corps. Nominations must be received by January 31, 1995.

You are welcome to nominate yourself, or another person. Please send a statement describing what time, enthusiasm, talent, and VHL experience the nominee would add to the management of the VHL Family Alliance.

Even if you do not feel you are ready to assist at the national level, please nominate yourself to help at the local level. Our most important activities happen at the state and local level, working to raise consciousness about VHL and gain support for our work of putting together the tools and knowledge it takes to manage VHL.

Please send nominations by January 31, 1995, to Peggy Marshall, Nominating Committee, RR6, Box 88, Corinth, Mississippi 38834-9215, or via email to vhl@pipeline.com. ❑

People with VHL are . . .

administrative assistants
administrators
advertising salespersons
artists
attorneys
billing clerks
bricklayers
broadcasters
budget analysts
buyers
cameramen
carpenters
cartographers
chefs
chemists
child care workers
clerical workers
clinical psychologists
college professors
college students
computer products salespersons
construction workers
cosmetologists
cosmetology instructors
court clerks
customer service representatives
dieticians
disc jockeys
district managers
draftsmen
electrical engineers
electricians
elementary school teachers
factory workers
firemen
flight attendants
food service workers
government workers
grandparents
graphic designers
high school teachers
historians
homemakers
househusbands
housewives
human resources manager
insurance agents
investor reporting specialists
jewelers
journalists
laboratory technicians
licensed practical nurses
managers
marketing specialists
masonry contractors
massage therapists
mechanics
mechanical engineers
medical records specialists
medical sonography instructors
ministers
money managers
mortgage brokers
nurses
nursing students
package delivery business owners
paramedics
pastoral counselors
personal banking officers
physicians
planners
plumbers
poets
policemen
postal workers
professors
real estate salespersons
registered nurses
remodeling contractors
rescue team members
retail store managers
retired
quality control specialists
sales representatives
secretaries
ski instructors
small business owners
social workers
software product managers
stock brokers
students
supervisors
teachers
telephone operators
trainers
transplant nurses
travel agents
union laborers
waiters, waitresses

. . . just like everyone else!

Genes in Primary Care

Dr. Hilary G. Worthen, a primary care physician in Cambridge, Massachusetts, and instructor at Harvard University Medical School; Dr. David Housman, a biology professor at M.I.T.; and Alison Harris of The Cambridge Hospital put together a three-day continuing education course for internists and family physicians, which was presented in October in Cambridge. Known fondly as "The Gene Team," they decided to offer the course after a survey of more than 200 physicians revealed they had limited knowledge of genetics. "Genes in Primary Care — What You Really Need to Know" was designed to give support to doctors who may face patients with genetic disorders every day, but who often lack the training or knowledge to consider genetics in diagnosis and treatment.

"Physicians admitted that they could not understand enough terms to get through fairly basic medical journal articles," said course organizer Alison Harris. "Few were comfortable teaching genetic concepts to their students and even fewer knew how to counsel patients properly."

A New Field

"When I was a first-year medical student at New York University in 1950," writes Dr. Robert Schwartz[1], "neither the biochemistry curriculum nor the 650-page textbook we used mentioned DNA or genes. For the entire year, I studied carbohydrates, fats, and proteins; the composition of milk and urine; and energy metabolism. Molecular biology as we know it today was only a dream."

Today, however, we are beginning to understand the causes of disease at a previously unimaginable level of detail. More than 5,000 genetic disorders have already been identified, and the number is constantly growing. More than 900 genes for hereditary disease have been identified, and more are cloned each week.

Dr. Francis Collins, Director of the National Center for Human Genome Research, who spoke on Wednesday morning, said that genetics will be part of most medical examinations within the next decade. "This is going to fundamentally change the way care is done."

> "We're all going to have pre-existing conditions pretty soon.
> -- *Dr. Francis Collins, Human Genome Project*"

One in Five

One in five people have genetic disorders in their family and one in 100 babies is born with a single gene defect. With genetic research providing advance knowledge about potential medical problems, insurance coverage will be one area of concern for the public, Collins said. "We're all going to have pre-existing conditions pretty soon," he said. Someday everyone will know the potential for a genetic illness that would be discovered through DNA testing.

Pre-existing health conditions are one factor insurance companies use to determine whether they will issue a policy for someone. If the person is a bad health risk, the policy might be denied. The impact of pre-existing conditions on health insurance was raised during the debate over the now dead national health care legislation. Collins said the Clinton administration is considering whether to raise that issue again in the next session of Congress by separating it from a broader health care reform. "I think the public has a great desire to see this issue resolved," said Collins.

Patients are the best resource

Voluntary support groups of and for patients are a prime source of information for doctors who are trying to keep up with the rapid developments in the field. "Those who have genetic disorders and their families are really the experts," said Joan Weiss, director of the Alliance of Genetic Support Groups, a coalition of organizations helping patients and their families.

Patient support groups often inform doctors about advances in treatment and research. "If you can convince them you know what you're talking about, physicians will listen to you," said Jeffrey Hollis, who has neurofibromatosis, which causes tumors and cysts. Jeffrey and Barbara Hollis participated on a consumer panel along with Weiss; Richard Saltus representing the Marfan Society; and Joyce Graff, representing the VHL Family Alliance.

The Hollises and Graff, said they are also starting to get calls from couples who are planning to start families and want information about genetic testing and counseling. Graff says that the Alliance provides information, and that members share their own stories and opinions, "but whatever anyone else says, there are only two people who get to vote" on how to use that information—the couple who are planning their family.

"This conference should be cloned and sent out through the country," said Dr. Maimon Cohen, the president of the American Society of Human Genetics. Cohen said the speed with which scientific research is being applied by doctors in their practices necessitates more forums to discuss genetics and its implications.

The course was video-taped and may be made available in other areas. For information, please contact Alison Harris, The Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139. Phone: 617-498-1584; Fax: 617-498-1814.

1. Editorial, *New England Journal of Medicine,* 331:1, July 7, 1994.

Compiled from Bill Premo, *The Cambridge Tab*; Amy Miller, *The Cambridge Edge*, Richard Saltus and Pamela Ferdinand, *The Boston Globe*; and M.A.J. McKenna, *The Boston Herald.* ❑

Introducing our Medical Advisory Board

There are twelve medical professionals listed on page 19 who may not always be very visible to you as readers, but who 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 the September issue. 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.

James M. Lamiell, M.D., Texas

Dr. Lamiell is a Colonel in the Medical Corps of the U.S. Army, serving as Chief of the Department of Clinical Investigations at Brooke Army Medical Center in Fort Sam Houston, Texas. He graduated from the Massachusetts Institute of Technology (MIT), and earned his M.D. from the University of Colorado School of Medicine. He also holds a Master of Computer Science from the University of Texas and is working on a degree in mathematics.

He has earned a number of awards and decorations from the armed services, including the Distinguished Flying Cross and the Vietnam Cross of Gallantry with Palm Leaf.

It was during his service at Tripler Army Medical Center in Hawaii 1977-1980 that he was asked to see a woman with polycystic kidney disease (PCK) who claimed her family had von Hippel-Lindau disease. At first they thought she had both VHL and PCK, but eventually they realized that her kidney condition was also VHL. He joined with Dr. Y. Edward Hsia at the University of Hawaii to study all members of this family, both military and civilian. Their study became one of the first and one of the largest systematic studies of a VHL kindred, and initiated the genetic screening work which laid the foundations for the genetics work now going forward at the National Institutes of Health.

"Without question, Hawaiian VHL family members are among the bravest people and patients I have known. As a group, they face the adversity of VHL with admirable courage. After knowing this VHL family and observing them over 15 years, I have learned that although VHL cannot be cured, it can be effectively managed provided all involved have sufficient VHL knowledge, honesty to face VHL problems, and courage to prevail against VHL."

Dr. Lamiell has published widely on VHL 1978 to present, including "Segregation and linkage analysis of von Hippel-Lindau disease among 220 descendants from one kindred" (*Amer. J. of Human Genetics*, **36:**131, 1984); "Von Hippel-Lindau disease maps to the region of chromosome 3 associated with renal cell carcinoma" (*Nature*, **332:**268, 1988); and "Von Hippel-Lindau disease affecting 43 members of a single kindred" (*Medicine* **68:**1, 1989).

He continues to be involved with VHL education. "Few health care providers have experience with VHL, so their VHL knowledge is often inadequate. VHL patients and their families cannot sensibly deal with VHL unless they know what to expect." Dr. Lamiell spoke and participated in the VHL Patient/Provider Conference in Kansas City earlier this year. "The organization has grown and matured considerably, and is very important for those affected by VHL. It is safe to say the VHLFA will endure. Good work!"

Hartmut P. H. Neumann, Germany

Dr. Neumann completed his medical degree and thesis at the University of Bonn and the University of Heidelberg, completing his Germany medical degree of Privatdozent Dr. med. He holds multiple specializations, with degree in General Medicine, Pathology, and Internal Medicine, and subspecialties with degrees in Nephrology and Endocrinology.

Until 1983 he worked at the Institute of Pathology, City Hospital, Ludwigshafen (Rheinland). Since 1983 he has been at the Albert-Ludwigs University in Freiburg (Breisgau), Department of Medicine, Division of Nephrology and Hypertension.

His primary research project there is on inherited diseases affecting the kidney, and inheritance of hypertension.

Since 1989 he has built up one of the largest studies on von Hippel-Lindau syndrome in the world in the last decade, consisting of 120 patients with VHL. His publications have appeared in the *New England Journal of Medicine*, the *Lancet, Gastroenterology,* the journals of Neurology, Neurosurgery, and Psychiatry, the *Journal for Neurosurgery,* and others. He has presented papers at the congress of the American Society of Nephrology, the International Congress of Nephrology, the International Congress of Human Genetics, and the Congresses of the German Societies of Endocrinology and of Nephrology.

He has lectured on von Hippel-Lindau disease at Massachusetts General Hospital, Boston; Columbia University, New York; Memorial University, St. John's, Newfoundland; Dalhousie University, Halifax, Nova Scotia; University of California, San Diego; Fox Chase Cancer Center, Philadelphia; Johns Hopkins University Medical School, Baltimore; the National Institutes of Health, Bethesda, Maryland; and at the VHL Family Alliance meeting in Kansas City in April.

He organized and co-chaired the First International Symposium on VHL in Freiburg in May 1994. His tireless efforts have helped to bring a new level of attention to VHL throughout the world.

Dr. Neumann was recently awarded the Franz Volhard prize for outstanding contribution to the field of Nephrology by the Society of Nephrology *(Gesellschaft für Nephrologie)* of the German-speaking countries, for his work on von Hippel-Lindau disease and inherited hypertension. In his speech to the Society, he mentioned the work of "der gro□ßartigen VHL Family Alliance, einer sehr aktiven Familieninitiative" (the magnificent VHL Family Alliance, a very active family initiative) in locating and informing families with VHL. ❑

New York Chapter Meeting, September 1994, L to R: Top row: Kathy R., Stacy R., Christine M., Thomas W., Fred Johnson; Middle row: Helen D., Marge M., Bob W., Evelyn W.; Bottom row: Joyce J., Julie Kurnitz, speaker, Altheada Johnson, Chairperson, Edward H., Adam H.

Report from Montreal

— Peggy Graham, R.N., Michigan

The October meeting of the National Society of Genetic Counselors in Montreal was attended by over 700 genetic counselors from the U.S. and Canada. Peggy Graham and Siobhan Graham attended to represent the VHL Family Alliance.

As a member of the Alliance of Genetic Support Groups, the VHL Family Alliance was able to display our literature at their booth and put our pamphlets into the hands of hundreds of genetic counselors.

This annual conference explored a number of important issues of concern to genetic counselors. Some of the sessions focused on the human aspect of genetic disease: how to help families deal with their diagnosis and the hope for cures for certain conditions. There was much discussion centered around privacy issues and patient registries.

Our own advisor on genetics, Debra Collins of the University of Kansas, gave an excellent workshop on computer access for information regarding genetics programs.

Jane Green, a genetic counselor, attended from Newfoundland where her practice serves a signifiant population of people with VHL. She gave a presentation which included VHL to the American Society of Human Genetics, whose meeting followed the genetic counselors meeting. The ASHG meeting was attended by professionals and scientists from around the world. Jane distributed flyers inviting patients and professionals alike to our Second Annual Patient/ Provider Meeting, to be held in Boston April 29-30, 1995. These flyers also made people aware that our toll-free number is available to Canadian as well as U.S. callers — and hopefully put us in touch with many VHL patients in that country who might otherwise not have heard of us.

The highlight of the conference was the keynote address by Dr. Francis Collins, Director of the Human Genome Project. This is an effort which is involved in the very laborious process of mapping every human gene which number about 100,000. Many will be found to play an important role in health and disease.

The Human Genome Project is headquartered at the National Institutes of Health in Bethesda, Maryland, and is joined in this effort by scientists from many other countries such as France, Germany, Italy, Japan, and the U.K. When this mapping is completed, with a target date of 2005, it will revolutionize medicine and be of untold value in the diagnosis, treatment, and prevention of many diseases.

Dr. Collins stated in his talk that virtually all disease except that caused by trauma has a genetic component. The last four years have seen the identification of the location of over 25 disease-causing genes, VHL among them. While this mapping is of enormous importance, at this time our diagnostic abilities far outstrip our treatment capabilities. In the case of VHL, many new trials and investigations are now going on, some of which are highlighted in this issue of the VHL Family Forum.

The role of Genetic Counselors can only become more important in the future when increasing numbers of people can benefit from definitive diagnosis.❑

Chapter Happenings

Four chapter meetings were held this quarter in Mississippi, New York, Massachusetts, Hawaii, and Louisiana.

The **Australian Affiliate** is growing, and planning their first meeting in Sydney in the summer -- February, that is!.

The **British Affiliate** now reaches more than 100 VHL families. Ken Murfitt, Co-Chair, was honored by Action Research for his role in fund-raising to support VHL research. Ken and Hazel are frequently seen on the Tellie (TV) and in the news.

Fourteen members of the **Mississippi Chapter** met in September in Jackson, chaired by Don and Peggy Marshall. "There were smiles, hugs, laughter, bonding, and a true understanding of how each other felt. By the end of the meeting we were being asked, "When's the next meeting? This is great! I'm so glad I came! A very positive meeting! and it's so nice to put a face to the voice on the phone!"

Peggy remembers especially one comment from a spouse, who came very reluctantly with his wife who has VHL. "He came to me after the meeting ended and related how he had dreaded coming. He did not want to be there. His picture was one of tragic stories and a negative atmosphere. Instead, he said, 'It's all been positive and I'm so glad I came. There wasn't anything negative about the meeting, not at all what I had thought. You really do understand how we feel and what we have been through.' He made my day!"

In November, the Mississippi Chapter hosted a spaghetti supper and crafts sale in Rienzi, Mississippi, where they sold lots of VHL T-shirts too! Radio stations in Tupelo, Corinth, and Booneville announced the event. Proceeds of their fund-raising efforts are going to support VHLFA publications and for some scholarships for attendance at the Annual Meeting in Boston.

Altheada Johnson chaired the first meeting of the **New York Chapter** in September, at the Nynex building, with thirteen people in attendance. "The main reason for getting together was meeting others just like ourselves, sharing our personal knowledge and experiences with VHL, and supporting each other. I feel we accomplished that beautifully," reports Altheada.

"Julie Kurnitz, comedienne, spoke on *Humor, Creativity, and Chronic Illness.* While there is nothing funny about having VHL, it is very important to find the humor in one's life. Julie's advice was to smile often. It really does help you feel better."

They are all participating in outreach to physicians, beginning with the ones they all use, asking their doctors to share our information with other colleagues and patients. In addition to the very popular T-shirts and sweatshirts which were designed by the New York Chapter, they discussed other ideas for fund raising, including a "300 Club" raffle.

Brian Dougherty from the **Kentucky Chapter** contributed his graphic design services to create our beautiful Annual Report for the fiscal year ended June 30, 1994. Special thanks to Brian! Copies are being sent out with the December newsletter.

David Torres and Roxanne Martinez co-chaired a **Hawaii Chapter** meeting in Honolulu in September. There were thirty-five people present, all related to one another, even though David had never met half of them before! Roxanne has worked hard to round up long lost family members.

Dr. Y. Edward Hsia, geneticist, and Ms. Juliet Yuen, genetic counselor, were guest speakers. David reported on the Kansas City meeting. Dr. Hsia shared what's new in VHL research, especially in the identification and mapping of the *Lazarus gene*, named for David's great-grandfather, the particular form of the VHL gene which is inherited in the Hawaii family. Ms. Yuen has recently retired from the University of Hawaii and is devoting full time to VHL.

The group was very enthusiastic about being together and gaining more information on how to manage their health. Most of all, they were thrilled to be together and didn't want to leave! They would like to invite us all to **Hawaii for the Annual Meeting in 1996!**

Laurel and Sandra Newson chaired a meeting of twenty members of the **Massachusetts chapter** in November in Quincy. Ms. Kathy Schneider, a genetic counselor at the Dana Farber Cancer Institute, spoke about DNA testing, and answered questions from the group about available methods of diagnostic and prenatal testing.

Laurel and Sandra are readying a mailing to physicians in the area, and gearing up activities for the **Annual Meeting in Boston in 1995!** We talked about topics and activities that the group would like to see and information we would like to gain from the meeting.

The **Louisiana chapter** met outside in Hammond, outside New Orleans, in October, chaired by Peggy and Don Marshall. Twenty-three people came, including 18 new members. People were delighted with our Handbooks and other materials -- and our new VHLFA sweatshirts were very popular, too! Many of the people were related, but had not seen each other for up to five years. "It was a truly exhilarating experience!" The group is eager for its next meeting, which will be in the spring, co-sponsored with Louisiana State University Medical School, which will provide a panel of specialists to answer questions on VHL. ❑

This issue is sponsored by the California Chapter

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...Dr. Hartmut Neumann on winning the Volhard prize
...Betty Newson's wisdom and courage
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