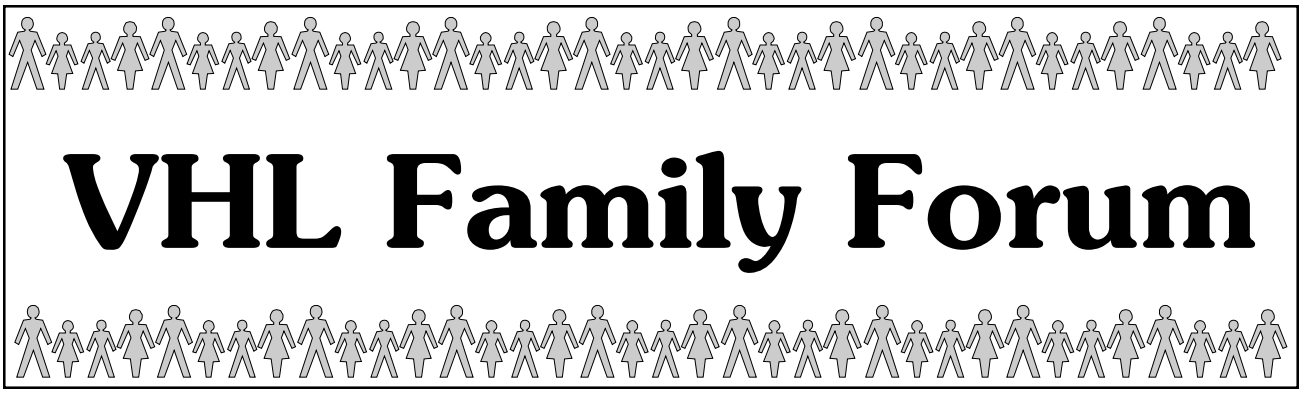

VHL Family Forum

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What is VHL?

Von Hippel-Lindau Syndrome, or VHL, is a genetic condition involving the abnormal growth of blood vessels in some parts of the body which are particularly rich in blood vessels.

While blood vessels normally grow like trees, in people with VHL little knots of capillaries sometimes occur. These little knots are called *angiomas*, or *hemangioblastomas*.

By themselves, these angiomas do not generally cause problems, but problems can develop around them. For this reason they need to be carefully monitored by your medical team.

The syndrome can be different in every patient. Even in the same family, people may show only one, or several of the symptoms of VHL. Since it is impossible to predict which one or more symptoms of VHL each person will have, it is important to check for all the possibilities.

Dr. Ernst von Hippel first described the angiomas in the *eye* in 1895. His name is usually associated with VHL in the retina.

Dr. Arvid Lindau first described the angiomas of the cerebellum and spine in 1926. His name is usually associated with occurrence of VHL in the central nervous system.

Types of Angiomas: The angioma may occur in a delicate place where the pressures it exerts may cause symptoms. Angiomas in the brain or spinal cord, for example, may press on nerve or brain tissue and cause symptoms such as headaches.

Welcome!

It is with great joy that we publish the first issue of VHL Family Forum, the newsletter of the newly forming VHL Family Alliance.

The purpose of this Alliance, and of this newsletter, is to bring us all together and benefit from the collective energy — the *synergy* — of our collective knowledge and cooperative action.

The most important thing that we can give each other here is the power of knowing that we are not alone. Together we can support each other, share our anxieties and our triumphs, and let each other know that we care.

Living with VHL, each of us has learned lessons about VHL, about our health, and about life. By sharing that information, we can help each other, and help the medical community to solve this puzzle.

This is ***your*** organization. We need ***you*** to help us shape it to meet your needs, to benefit from your experience. Please let us know what you want to hear, what you want to learn, what you are willing to share. If each of us contributes just a small amount of time and funds, we can change the world for ourselves and our children. ❑

Inside this issue!

As the angioma grows, the walls of the blood vessels may weaken and some blood leakage may occur, causing damage to surrounding tissues. Blood leakage from angiomas in the retina can interfere with vision. Early detection and careful monitoring of the eye are very important to maintain healthy vision.

Cysts may also grow around angiomas. Cysts are fluid-filled sacs which may exert pressure or create blockages which can cause symptoms.

Some male patients experience tumors in the scrotal sacs. These tumors are almost always benign, but should be examined by your urologist.

Cysts and tumors may also occur in the kidney, pancreas, liver, or adrenal glands. Symptoms here may include high blood pressure. Some of these tumors are benign, while others are cancerous. Early detection and careful monitoring are particularly important for these organ systems, usually with CT, MRI, or ultrascanning yearly.

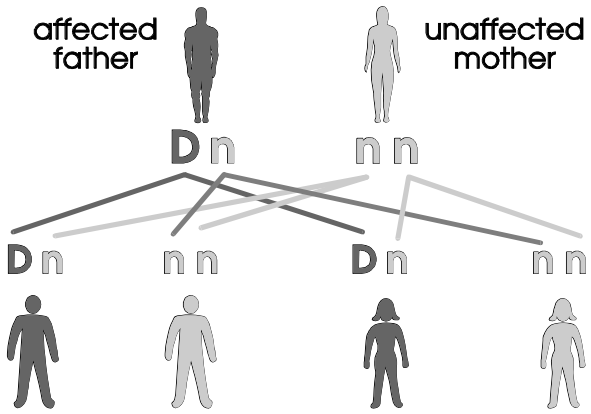
How Do People get VHL? Von Hippel-Lindau Syndrome is a genetically transmitted disease. It is caused by a dominant gene. Even in people who have this gene, however, there is a wide variation in the date of onset of the disease, the organ system in which the problem occurs, or the severity of the involvement. Every person is different.

The VHL Family Alliance is preparing a booklet, *What you Need to Know about VHL*, which discusses VHL in greater detail, and helps to explain some of the medical terminology your medical team may use in discussing your diagnosis and treatment.

Early Detection: Because VHL varies so widely, there is not a consistent set of symptoms in each person. Each possible evidence of the disease has its own diagnostic evaluation.

If you have a family history of VHL, it is important to begin screening early, before any symptoms occur. Confer with your doctor about the best time to begin screening, and the right schedule for return visits. It is generally recommended to begin regular screening at age six, or even earlier.

One clear screening does not necessarily mean there is no VHL present. The first evidence of VHL may occur later in life. Most physicians feel that if no VHL is found by age 50, it is fairly certain that there is none.



A child receives one gene in each pair from each parent. If one parent has a Dominant gene (D), each child has a fifty-fifty chance of inheriting the condition. Dominant genes dominate their normal counterparts (n). A dominant gene can be inherited by either a male or female child.

Depending on the outcome of your screening, your doctor will tell you what particular symptoms need to be followed closely. Certainly any vomiting, headaches, balance problems, or persistent pain lasting more than 1-2 days and which stays in one place, should be checked with your doctor.

Once VHL has been diagnosed in any one part of the body, it is important to undergo a full screening for other possible evidences of the syndrome in other parts of the body, and to return for additional screening on the schedule recommended by your medical team.

With early detection and treatment, there is more hope today for families with von Hippel-Lindau syndrome than ever before. Research on VHL and related diseases has led to better methods of diagnosing and treating it. Our knowledge about VHL is increasing rapidly. The VHL Family Forum will bring you the latest news about VHL. ❑

Prepared with the kind assistance of Dr. Lloyd M. Aiello, Debra L. Collins, and Dr. Gladys Glenn. **References:** Glenn et al., "Von Hippel-Lindau Disease: Clinical Review and Molecular Genetics," *Problems in Urology*, **42** (1990) 312-330; Glenn et al., "Screening for von Hippel-Lindau Disease by DNA Polymorphism Analysis," *JAMA* **267** (1992) 1226-1231; Jennings et al., "Von Hippel-Lindau Disease in a Large British Family: Clinicopathological Features and Recommendations for Screening and Follow-up," *Q. J. Medicine*, **66** (1988) 233-249; Jennings and Gaines, "The Abdominal manifestation of von Hippel-Lindau disease and a radiological screening protocol for an affected family," *Clin-Radiol.* **39:4** (1988); 362-367; Lamiell et al., "Von Hippel Lindau Disease Affecting 43 Members of a Single Kindred," *Medicine* **68** (1989) 1-29; Malek et al., "Renal Cell Carcinoma in von Hippel-Lindau Syndrome," *Amer. J. of Medicine* **82** (1987) 236-238; Neumann et al., "Hemangioblastomas of the Central Nervous System," *J. Neurosurg* **70** (1989) 24-30. ❑

Families under Stress

VHL is not caused by stress. Having a disease like VHL induces stress. Having a parent, child, sibling, spouse, or friend with VHL creates stress. Add this to the stress you normally live with in your life, and you have a potentially harmful level of stress.

Eating well, keeping our bodies healthy and strong, is good for everyone, and is especially important for every member of a family affected with VHL. For the affected individual, it is important to see yourself first as a healthy person, with an annoying condition you have to keep an eye on and deal with as necessary. For all members of the family, it is important to deal constructively with the range of emotions that will surface, as well as the many stresses — physical, emotional, and financial — that come with dealing with a serious illness.

As a parent or spouse, it is easy to get caught up in self-sacrifice, spending long hours at hospitals, robbing yourself of sleep. Remember that on an airplane, when they give you the instructions about putting on those oxygen masks, they always say to put on your own mask first, then assist your child. If you pass out, what good are you to the person you want to help? It is critically important to the health of your loved one that *you* stay healthy. It's not selfish, it's common sense.

Dr. Herbert Benson and his associates at the Mind/Body Medical Institute at the New England Deaconess Hospital and Harvard Medical School, have done extensive research into the relationship between mind and body. The things you do every day — even the things you think about — contribute to your health profile. Their experience indicates that the way we think can aggravate symptoms, interfere with healing, and hinder our self-improvement.

"The secret," says Dr. Benson, "is understanding how your body and mind work together, and then using them to improve your health and sense of well-being." In their clinic in Boston and in cooperation with physicians around the world they have devised techniques which can be used to treat and deal more effectively with insomnia, high blood pressure, infertility, cancer, AIDS, and many other conditions.

They have proved that patients with healthy attitudes and strong spirits respond more rapidly and more completely to the treatments prescribed by their doctors. Using relaxation techniques in the hospital, surgical patients require less pain medication and recover more rapidly from surgery.

They have recently compiled a workbook which people can use at home. "The reader can easily follow the provided information as well as the numerous examples and exercises," says Dr. Alice Domar, a Senior Scientist at the Mind/Body Medical Institute. "It is designed to be very interactive. There are chapters on numerous relaxation techniques, multiple stress-management strategies, information on nutrition, easy, safe exercise suggestions, and special chapters on certain medical conditions."

Some people find it useful during relaxation to envision the outcome they want for their treatment. Since VHL involves the loss of one tumor-suppressor gene, you might choose an image where your other tumor-suppressor genes take over the job of the missing one. Family members should begin with strong visions of themselves, and add strong images of healthy eyes, spinal cords, and organs in their loved ones if they wish.

VHL is a stressful challenge to any family. Stress management techniques, such as those compiled by the Mind/Body Medical Institute, help you maintain control of your real life, put VHL and other issues into the minor position they deserve, and stay well.

The Wellness Book: The Comprehensive Guide to Maintaining Health and treating Stress-related Illness by Herbert Benson, M.D., et al., Hardcover, 480 pages, $24.95. Birch Lane Press/Carol Publishing Group. 1-800-447-BOOK. ❑

Dr. Arvid Lindau 1892-1958

One hundred years have passed since birth of Dr. Arvid Lindau who first described what he called "angiomatosis of the central nervous system."

Arvid Lindau was born 23 July 1892 in Malmö, Sweden. He was the son of a regiment doctor. After completing school (B.A. 1910) he was trained as a military officer and physician. He got his medical training in Lund (M.D. 1923, Ph.D. 1926). He was a pathologist at the hospital in Lund 1918-1933, and held a concurrent appointment as a military doctor beginning in 1924. He was secretary of the Lund Medical Society from 1926.

It was during this time that he observed and studied a condition involving hemangiomas of the central nervous system and linked this condition to the similar condition of the retina which had been described by Dr. Eugen von Hippel. This became his doctoral dissertation work. He published his findings in a Swedish journal of microbiology in 1926. He was awarded the Lennmalm's prize (1929) from the Swedish Medical Society. The syndrome he described is now called von Hippel-Lindau Syndrome.

Dr. Lindau traveled to Germany, Czechoslovakia, Holland, England, and the United States to learn from colleagues in different parts of the world. He was a fellow at the University of Freiburg under Professor Ludwig Aschoff; at the Massachusetts General Hospital under professor Hans Zinsser; at the Peter Bent Brigham Hospital, Boston, under Dr. Harvey Cushing; and in the Danish Serum Institute under Dr. Thorvald Madsen. In the U.S. he worked on bacteriology and immunology as well as blood transfusions and practical blood grouping. He published more than 40 papers on pathology, neurology, and bacteriology.

An article in *Reader's Digest*,
"This 'Tree' Can Save Your Life"
by Sue Browder, March 1993, p. 66,
mentions von Hippel-Lindau Syndrome!

photo of Dr. Lindau here dated 1933

Professor Harvey Cushing visited Lindau's laboratory in the 1930's and was fascinated with the samples Lindau had collected. It was Dr. Cushing who made Lindau's work known in the United States.

In 1933 Lindau was appointed professor of pathology, bacteriology, and general health care at the University of Lund. For the remainder of his career his primary interest was in bacteriology and immunological problems. He had special opportunities to exercise his professional skills when the German concentration camps were emptied at the end of the Second World War and refugees in large numbers relocated to Lund.

Dr. Lindau was a highly respected member of the faculty. He took a great interest in athletics and worked with physical education programs for youth. He was very interested in music, and was also engaged in local politics.

We remember Dr. Lindau for his powers of observation, intuition, and synthesis of information. As he did, we have the opportunity to combine our collective experience and make progress on the road to resolving the puzzle of von Hippel-Lindau syndrome.

Prepared with the kind assistance of Dr. Arne Brun, Institute of Pathology, Lund, Sweden; Dr. Raymond Adams, Massachusetts General Hospital, Boston; Mr. Richard Wolfe, Countway Library of Medicine, Boston; and Dr. Harry H. Wilcox, University of Tennessee, Memphis. **Photo** from *Nordisk Medicinsk Tidskrift*, 7:1 (1934), 249, courtesy of the Rare Book Collection, Countway Library of Medicine, Harvard University, Boston. **Reference:** "Studien über Kleinhirn- cysten, Bau, Pathenogenese und Beziehungen zur Angiomatosis retinae." *Acta Path. Microbiol. Scand.* 1926, Suppl. 1. ❑

Tracking Down the VHL Gene

"I'm thinking of a number between one and one hundred." One child chooses a number, and the other must guess the number by asking yes and no questions. Looking for a gene is a similar undertaking, but on a much broader scale. It is somewhat like looking for a particular house, not knowing at the beginning which continent the house is on.

There has been considerable progress in the molecular genetics of VHL disease. Dr. Bernd Seizinger and his team, then at the Massachusetts General Hospital, began by doing genetic linkage studies on nine families with VHL. They collected genetic markers which had already been identified, and tried them on samples from affected individuals.

The researchers watched the pattern of inheritance of particular genetic markers in VHL families to see whether they were present in the affected parent and not present in the unaffected parent, present in affected children and not in unaffected children. This method was used to determine whether a particular marker was associated or "linked" with the VHL gene.

Researchers then compared these inheritance patterns with the inheritance patterns of that same marker in a control study, a Venezuelan family whose genes were mapped in great detail by Dr. Nancy Wexler for the purpose of studying Huntington's Disease. While this family is affected with Huntington's Disease, it is normal for VHL, and therefore provides a good reference.

They found that one marker which mapped to chromosome 3 was pretty tightly linked to VHL, and announced this finding in 1988. This finding has since been confirmed by Dr. Berton Zbar at the National Cancer Institute, by Dr. Eamonn Maher at Cambridge University, by Dr. David Smith at Wayne State University, and by Dr. Jeff Vance at Duke University Medical Center.

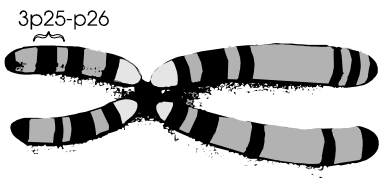
Now at least they knew which continent the house was on. With an ever-growing group of families participating in the study, they continued to do comparative analysis of the genetic information in the family samples. The researchers examined the markers found on chromosome 3 in each in sample, and recorded the pattern for family members with and without clinically diagnosed VHL. Using additional markers on chromosome 3, and LINKAGE, a computer program from the Howard Hughes Medical Institute, to calculate the probability of linkage of a particular area to VHL, they have narrowed the search to an area known as 3p25-p26, near the tip of chromosome 3.

They are in the right general area. While these markers may seem close, there are between 5 and 8 million base pairs of genes between them. The house we're looking for is somewhere in the Middle West. There is still a long way to go.

Dr. Berton Zbar and his team at the National Cancer Institute, working in parallel with the Seizinger team, have discovered another set of five markers which take him to the same area, and which can also be used to predict whether the VHL gene is present.

The markers find genes which are found throughout the normal population. "The marker is unrelated in any functional sense to the VHL gene. It is only related in its proximity to the VHL gene," says Corinne Boehm, director of the DNA Diagnostics Laboratory at Johns Hopkins Center for Medical Genetics. "Because these markers are so closely located on chromosome 3, they usually get inherited together as a complex with the gene, and that pattern can be used to predict the probability of VHL inheritance in other family members."

Even though the gene itself has not yet been identified, Dr. Zbar finds that some arrangement of these markers tends to be inherited along with the VHL gene in a consistent pattern in a given family. While the pattern in each family will be different, once a family's unique pattern has been worked out it can be used to do some initial



The VHL gene is in the region 3p25-p26, near the tip of the short arm of chromosome 3.
Illustration by Karen Barnes, Stansbury Ronsaville Wood Inc., for Howard Hughes Medical Institute, as published in *Blazing a Genetic Trail,* 1991.

testing to determine whether someone in this family is at risk of developing VHL cysts and tumors.

"But," Dr. Zbar cautions, "because the test does not measure the disease gene itself, errors in risk prediction can occur." Where informative markers are present on both sides of the gene, the accuracy of the test is above 99%. This is the case in only about 44% of the families studied. It is possible to improve the ease of risk prediction by isolating more markers, or by locating the gene itself.

Determining risk: "When it is not possible to predict whether an individual in a VHL family is a VHL gene carrier, that individual must be screened as though they were carriers of the VHL gene. Otherwise, persons who do not yet have symptoms but who may have potentially dangerous kidney and other tumors may go untreated." Dr. Zbar is hopeful that the gene will be isolated within a year.

Dr. Vance at Duke is working with yet another group of markers, building on the work of the Seizinger team. "Some markers are not very useful in every family," says Dr. Vance. "We are trying to make more informative markers." Dr. Maher at Cambridge is following a similar pattern to that of Drs. Zbar, Vance, and Seizinger.

Dr. Smith and his team at Wayne State are using yet another technique called Yeast Artificial Chromosomes (YAC) which latch on to twenty points along chromosome three and essentially form overlapping markers which map the entire area where the VHL gene is located. They are now in the process of isolating genes in this region and testing them individually as candidates for the VHL gene. "It is amazing how fast the research is moving now," says Dr. Smith. "The tools are getting better, the reagents are getting better — it's a very exciting time."

What does this gene do? "The hypothesis," says Dr. Jean Whaley of the Seizinger team, "is that the VHL gene is one which normally produces a protein relating to cell growth or DNA replication. When someone has VHL, the ability to produce this protein is in some way deactivated or altered." To determine just what its function is, researchers must first isolate the specific gene, and study its normal activity in the laboratory. They also have to show clearly that this gene is in fact normal in unaffected people and deactivated in people affected with VHL, and that this inactive form of the gene is present in VHL tumor tissue.

Potential benefits for everyone: By studying inherited forms of tumor conditions, like VHL, scientists hope to unlock the mysteries of tumor conditions in the normal population. One interesting hypothesis is that there are two copies of this gene, one inherited from each parent. Both copies need to be deactivated in order for the cell to lose its control over cell growth. In a person with VHL, there is one normal copy and one inactive copy, so it is only necessary for one to drop out of function. Normal cell division and gene replication is complex. It is usually accurate, but occasionally a mistake is made during this replication process.

Why? "We often think of cancer as a disease of older people," says Dr. Whaley, "because statistically more older people have cancer. For example, the average age of onset of kidney

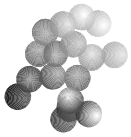
A Brief Key to Basic Genetics

A human cell. *Each of the 100 trillion cells in the human body (except red blood cells) contains the entire human genome — all the genetic information necessary to build a human being. This information is encoded in 6 billion base pairs, subunits of DNA. (Egg and sperm cells each have half this amount of DNA.)*

The cell nucleus. *Inside the cell nucleus, 6 feet of DNA are packaged into 23 pairs of chromosomes (one chromosome in each pair coming from each parent.)*

A chromosome. *Each of the 46 human chromosomes contains the DNA for thousands of individual genes, the units of heredity.*

A gene. *Each gene is a segment of double-stranded DNA that holds the recipe for making a specific molecule, usually a protein. These recipes are spelled out in varying sequences of the four chemical bases in DNA: adenine (A), thymine (T), guanine (G), and cytosine (C). The bases form interlocking pairs that can fit together in only one way: A pairs with T; G pairs with C.*



A protein. Proteins, which are made up of amino acids, are the body's workhorses — essential components of all organs and chemical activities. Their function depends on their shapes, which are determined by the 50,000 to 100,000 genes in the cell nucleus.

cancer in the general population is about 62. In persons with VHL, the age of onset is significantly younger — about 45, and often much younger. Perhaps there is some influence from the environment — from exposure to sunlight, food additives, air and water pollution, smoking, or any of a number of other possibilities — which causes this tumor suppressor to become deactivated. In persons with VHL, this happens earlier because only half of the system is active to begin with. But by understanding this mechanism we would learn useful lessons for the entire population."

Specifically for VHL families, the immediate short-term goal is to be able to do reliable predictive testing, and with the methods which Dr. Zbar and other researchers are proposing, we are partway there. "The clinical examinations are costly, inconvenient, and may not yield definitive diagnostic information," says Dr. Gladys Glenn of the Cancer Diagnostic Branch, National Institutes of Health. "If it were possible to identify disease gene carriers, medical attention could be directed to those individuals at high risk of tumor development."

Dr. Maher is following patients clinically to determine the value of screening and presymptomatic diagnosis in reducing the severity of VHL.

Carrier Detection Testing: Using genetic analysis, the Johns Hopkins Center for Medical Genetics in Baltimore, Maryland, and Addenbrookes Hospital in Cambridge, England, are beginning to perform some testing in families. In order for a member of a VHL family to be tested, there usually need to be DNA samples from two affected family members. The Center asks that you work with a local geneticist to do the background collection of family history information, and to provide you with a local team to assist you in analyzing the results. Your geneticist can contact the lab to determine whether the testing would be useful in your family.[1]

"It is also important for families to realize," says Ms. Boehm, "that this testing is still experimental and is not 100% reliable. At this point it should be used primarily to determine levels of risk in an affected family, to tell who should be followed more closely than others. In some families with the right kinds of markers present, it may even be reliable enough to do prenatal testing. In families where we have sufficient samples it can be used to determine who is a carrier of VHL, and can therefore provide some useful genetic counseling information."

The longer term possibilities and dreams are endless. Once the gene has been cloned and we understand its operation, we might discover a missing protein or enzyme, or the operation of

Why so many errors in our DNA?

As scientists learn to read the instructions in our genes, they are discovering that much of our DNA is riddled with errors.

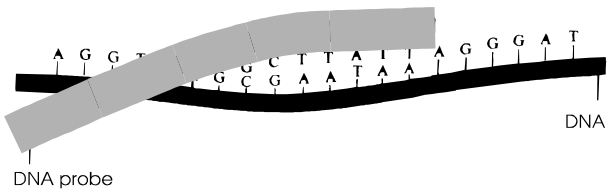
Fortunately, most of the errors are harmless. Considering the difficulties involved — the 6 feet of DNA in a human cell consists of 6 billion subunits, or base pairs, coiled and tightly packed into 46 chromosomes, all of which must be duplicated every time a cell divides — our general state of health is something of a miracle.

We each inherit hundreds of genetic mutations from our parents, as they did from their forebears. In addition, the DNA in our own cells undergoes an estimated 30 new mutations during our lifetime, either through mistakes during DNA copying or cell division or, more often, because of damage from the environment. Bits of our DNA may be deleted, inserted, broken, or substituted. But most of these changes affect only the parts of DNA that do not contain a gene's instructions, so we need not worry about them.

Problems arise only when an error in DNA alters a message that tells certain cells to manufacture a particular protein.

To stay alive and functioning, the human body requires a daily crop of billions of fresh protein molecules — about 50,000 different kinds of proteins that must be supplied in the right quantites, at the right times, and in the right places. Our cells are kept extremely busy linking together amino acids — the building blocks of proteins — in the right order to produce these diverse proteins.

An error in just one base can bring the wrong amino acid, altering the protein. Much of the recent progress in reading DNA has come from analyses of genetic errors.



A DNA probe, a strip of radioactively labeled DNA, seeks out a complementary fragment of DNA and sticks to it. This method is used to locate the markers *which have been determined to be associated with the VHL gene.*
Illustration by Karen Barnes, Stansbury Ronsaville Wood Inc., Annapolis, Maryland, for Howard Hughes Medical Institute, as published in *Blazing a Genetic Trail,* 1991.

the tumor suppressor, and learn how to stimulate the tumor suppression mechanism artificially. Dr. Seizinger's lab has recently moved to Bristol-Myers Squibb Laboratories in New Jersey. Clearly Squibb is gambling that this research will lead to a commercially viable treatment — or cure! — for cancer. It will probably take another decade or two, but the prospects are more real now than ever before.

Be Part of a Modern Miracle: At this point, there is a race to identify the VHL gene, with teams in a friendly mix of collaboration and competition with one another. This is good news for VHL families, since it means that researchers are highly motivated, and are making good progress toward identifying the gene. It is in our interest to keep them all going, and to supply them with as much information as we can. They are using different techniques. No matter which team identifies the gene first, we gain the diagnostic information we need for our families.

Families from various part of the United States including Hawaii, from Canada, the Netherlands, France, Germany, and Iceland have participated in the U.S. studies, and families in Europe are participating in a parallel study in England under Dr. Eamonn Maher. This work would not have been possible without the willingness of patients and physicians to provide family history information, blood, and tumor tissue samples. Every team we spoke with was effusively grateful for the cooperation of their participants.

Researchers still need more families, especially ones where there are a number of affected individuals. In addition to blood samples, they need samples of tumor tissue. To keep the research moving quickly, contributions of blood and tumor tissue to the teams would be appreciated.2 Dr. Vance is willing to coordinate collection of samples and ensure that samples are made available to all four U.S. teams.

Before any surgery, please have your surgeon call the team or teams of your choice to arrange for quick delivery of fresh tissues, along with your written request that they be made available also to additional teams. Sharing of samples requires your permission in writing and the team's agreement in advance.

Your participation could be just what is needed to create the breakthrough we are all waiting for. ❑

1. ***To arrange for carrier detection testing,*** ask your Geneticist to contact Ms. Corinne Boehm, DNA Diagnostics Laboratory, Center for Medical Genetics, Johns Hopkins Hospital, Baltimore, MD 21205, Tel: 1-410-955-0483, Fax: 1-410-955-0484; or contact Dr. Eamonn R. Maher, Clinical Genetics, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, U.K., Tel: 44-223-216446, Fax: 44-223-217054.

2. ***The research teams are as follows.*** If you would like more than one team to have access to your samples, you have to make your wishes known in writing, and get the recipient's agreement in advance.

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

- Dr. Bernd Seizinger, Cancer Drug Discovery Dept, Bristol-Myers Squibb Pharmaceutical Research Institute, P.O. Box 4000, Princeton, NJ 08543-4000, Tel: 1-609-252-3257, Fax: 1-609-252-3307.

- Dr. David I. Smith, Molecular Biology/ Genetics, Wayne State University School of Medicine, 540 East Canfield, Detroit, MI 48201. Tel: 1-313-577-6968, Fax: 1-313-577-5218.

- Dr. Jeff Vance, Box 2900, Duke University Medical Center, Durham, NC 27710, Tel: 1-919-684-5963, Fax: 1-919-684-6514.

- Dr. Berton Zbar, National Institutes of Health, Frederick Cancer Research & Development Center, Building 560, Room 12-71, Frederick, MD 21702, Tel: 1-301-846-1288, Fax: 1-301-846-6145.

References: Glenn et al., *JAMA*, **267:9** (1992), 1226-1231; Seizinger et al., *Proc. Natl. Acad. Sci.* **88** (1991), 2864-2868; Pines et al., *Blazing a Genetic Trail*, Howard Hughes Medical

Institute, 1991. ❑

How Genes Work

If you would like more information on how genes work and on how researchers track down genes, the following two publications are available free:

(1) *Blazing a Genetic Trail*, one of their series of reports on science for the general public, from the Howard Hughes Medical Institute, 6701 Rockledge Drive, Bethesda, MD 20817, Tel: 1-301-571-0330, Fax: 1-301-571-0573; or

(2) *DOE Human Genome Program: Primer on Molecular Genetics*, from U.S. Department of Energy Research, Oak Ridge National Laboratory, P.O. Box 2008, Oak Ridge, TN 37831-6050, Tel: 1-615-574-7582, Fax: 1-615-574-9888. ❑

Finding a Genetic Counselor

by Joyce Graff

My son and I decided to try the testing at Johns Hopkins to see if our family is in the lucky 44%. Even if it doesn't work this round, the samples will be on file for when the next set of markers is ready for trial.

Our first quandary was how to find a geneticist. We decided to start with the hospital where his records are, for convenience. We "interviewed" the folks in the genetics department. We felt comfortable with the genetic counselor there. While she had no specific expertise in VHL, she expressed an eagerness to work with us and to learn along with us.

The next challenge was finding enough samples in our little family unit for Ms. Boehm and her team to study. My son is an only child. His father and grandfather, who both had VHL, passed away more than 15 years ago. What we submitted were blood samples from me and my son, and tumor tissue from my late husband's surgery in 1975, found in the archives of the Massachusetts General Hospital. If a deceased relative had surgery, especially at a teaching hospital, it is worthwhile to ask if there are samples in the archives which would be useful for DNA testing.

We're still waiting for our results! ❑

Genetic Services

from the National Society of Genetic Counselors

Where to look:

Consult with your physician or health care provider about a genetic consultation.

Call your local major medical center or community hospital. Ask for Obstetrics or Pediatrics. Genetic Services are frequently divisions of these departments.

Contact your state department of health. Ask for genetic services.

Contact the National Society of Genetic Counselors for a direct referral to a genetic counselor. *Please note:* The NSGC office does not maintain or disseminate information about specific genetic disorders, but they can refer you to genetic services in your local area. Write to: National Society of Genetic Counselors, 233 Canterbury Drive, Wallingford, PA 19086.

How to prepare for the visit:

Bring information about your family history and important medical records.

Plan to spend one to two hours at your first visit. Additional visits may be necessary to complete the evaluation.

Check with your insurance carrier prior to your visit. A growing number of companies now cover genetic services. ❑

Confidentially ...

This first issue of
VHL Family Forum
may have been
forwarded to you by your physician,
who has not disclosed your name to us.

Please fill out the form on page 11 to
ensure that you receive
the next issue.

Our membership and mailing lists are
entirely confidential, and are
not rented nor sold.

Be a Founding Member!

We are VHL families, just like you. We have lived with VHL for 4-32 years each. We spent as much as thirty years without meeting another VHL patient. We know the loneliness and isolation of having a rare disease that most of your doctors never heard of.

When we found each other and began to share ideas, we were immediately struck by the power of putting our knowledge together. We had an image of putting all the knowledge of all the families together in one pile, along with the growing pile of medical information. The scientists have their very valuable perspectives on the chromosomes and capillaries; we families see the whole human experience of VHL from a different angle. Each by itself is very valuable. Add the two together, and it's more than twice as powerful. It might well be what is needed to solve this puzzle at last.

We want to share with you what we have learned. More than that, we want to learn from you. Each of you has learned a great deal -- from your experiences, from your physicians, and from life. Please share that with us.

This is your Forum.

We welcome your experiences, thoughts, poems, art work, cartoons, clippings, ideas for articles, scientific articles to be digested for families to read. Be pensive, be funny, be wise.

Tell us some things you wish somebody had told you about how to have a positive experience in the hospital, about choosing and working with medical professionals, about living with VHL.

What would you like to say to other VHL patients and their families? What would you like to say to doctors and medical professionals?

What would you like to learn?

This is your Forum -- the podium is yours!

-- Joyce Graff, Peggy Graham, Susan Warnick
Co-chairpersons, VHL Family Alliance

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Dr. Raymond D. Adams, Harvard Univ, Cambridge, MA
Dr. Lloyd M. Aiello, Joslin Diabetes Center, Boston, MA
Ms. Corinne Boehm, Johns Hopkins Hosp, Baltimore, MD
Dr. Arne Brun, Univ Hospital, Lund, Sweden
Ms. Debra L. Collins, Univ of Kansas, Kansas City, KS
Dr. Jerry Cavallerano, Joslin Diabetes Center, Boston, MA
Dr. Alice D. Domar, New England Deaconess, Boston, MA
Dr. Gladys M. Glenn, National Inst of Health, Rockville, MD
Mr. Ferenc Gyorgyey, Yale Univ Library, New Haven, CT
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Newsletter of the
VHL Family Alliance

171 Clinton Road, Brookline, Massachusetts 02146 U.S.A.
Telephone: 1-617-232-5946 (eve); Fax: 1-617-734-8233

Co-Chairpersons: Peggy Graham 1-313-979-8563 (day) Susan Warnick 1-410-526-6858 (day)
Adviser: Debra L. Collins, M.S., Genetic Counselor, University of Kansas Medical Center 1-913-588-6043 (day)

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

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

Submissions: Your questions, comments, articles and ideas are always welcome. Please send them directly to the Editor, Joyce Graff, 171 Clinton Road, Brookline, MA 02146. Tel: 1-617-232-5946, Fax: 1-617-734-8233. Copyrighted works or their modifications must be accompanied by the copyright notice and the consent of the owner prior to publication or distribution. Opinion(s) expressed by the authors are not necessarily those of VHLFA.

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

Yes! I want to be a Founding Member!

Name: _____

Address: _____

_____

City: _____ State: _____ Zip: _____

Country: _____ Fax: _____

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

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

All Founding Members receive a Founders certificate, 3-4 issues of the Forum this year, and copies of all Alliance publications (two planned this year).

A limited number of free subscriptions are available where the dues are a hardship.

- ❑ Audio version required (please send one 90-minute tape)

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

I have some expertise which I am willing to share with others

- ❑ Telephone skills
- ❑ Writing or reviewing articles about _____
- ❑ By-laws committee, or Legal assistance for filing incorporation documents
- ❑ Advertising or public relations skills
- ❑ Artistic skills, to help with illustrations for publications
- ❑ Fundraising skills
- ❑ Other _____

Things I particularly liked in this issue of the newsletter:

- ❑ What is VHL?
- ❑ Tracking Down the VHL Gene
- ❑ Families Under Stress
- ❑ Finding genetic counseling services
- ❑ Dr. Arvid Lindau

Things I would change: _____

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

If my submission is printed in the newsletter, please sign me:

- ❑ Initials, City, State (example: A.B., Lund, Sweden)
- ❑ First name, last initial, city, state (example: Mary G., Hilo, Hawaii)
- ❑ Full name okay (example: Joyce Graff, Brookline, Massachusetts)
- ❑ Other_____

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

The Podium is Yours . . .

Here's your chance to learn and share about VHL

The VHL Family Forum is waiting to hear from *you!*

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

Address Correction Requested