



VHL Family Forum



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Taking a Closer Look at Phytochemicals

By Thomas Dao, M.D., et al., the American Institute for Cancer Research¹

If you saw them listed as ingredients on a cereal box you might be alarmed: isoflavones, terpenes, indoles, phenolic acids. But these tongue-twisters aren't artificial additives, they're naturally occurring chemicals found in foods like fruits, vegetables, and grains — chemicals our bodies may use as part of their disease-fighting arsenals.

These substances are called phytochemicals (phyto is Greek for plants). Some, such as digitalis and quinine, have been used for medicinal purposes for centuries. The anticancer effects of many of them, however, are only beginning to be explored.

Phytochemicals differ from vitamins and minerals in that they have no known nutritional value. Some are antioxidants, protecting against harmful cell damage from oxidation. Others perform different functions that help prevent cancer. Today's laboratory pioneers are still deciphering the many ways phytochemicals in foods may offer front-line defenses against cancer.

Isothiocyanates, for example, found in cruciferous vegetables like broccoli and cabbage, protect against cancer through their effect on enzymes. Saponins, found in beans and legumes, may prevent cancer cells from multiplying by influencing a genetic material in the cells.

A single tomato or orange contains hundreds, and possibly thousands of phytochemicals. Indeed, much of the work thus far has been simply cataloging and classifying them.

Phytochemicals as cancer preventives

One reason scientists are so excited about phytochemicals is their apparent ability to stop a cell's conversion from healthy to cancerous at so many different stages. Indoles, a family of phytochemicals found in cruciferous vegetables, stimulate enzymes that perform many functions. One impact is to make the hormone estrogen less effective, possibly reducing breast cancer risk. Research shows that allyl sulfides, in the garlic and onion family, increase enzymes that

affect cancer-causing substances and help the body get rid of more of them. And Ellagic acid, a type of phenolic acid found in strawberries and raspberries, reduces the genetic damage caused by carcinogens like tobacco smoke or air pollution. It does this by affecting the carcinogen, and also, possibly, by directly protecting the cell's genetic material.

One scientist who gives a hill of beans — soybeans, that is — about phytochemicals is Stephen Barnes, Ph.D., a pharmacology professor at the University of Alabama at Birmingham. Barnes has spent the past decade investigating the anticancer properties of soy foods.

"We're trying to determine if certain compounds in the soybean are responsible for the lower rates of cancer, particularly breast and prostate, that are seen in people who consume soy as a significant part of their diet," said Barnes.

Tofu, soy milk, and other foods made from soybeans are rich in isoflavones, which may inhibit cancer cell growth and division under some conditions. Since cancer is the result of the cell growth process gone awry, isoflavones may provide a means for switching off the unusual growth.

Barnes is currently overseeing two pilot studies he

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hopes will provide promising evidence for large clinical trials in the future. In one, 37 healthy pre- and post-menopausal women in San Francisco are consuming diets with and without soy. Researchers are examining their breast fluid for properties that may mean greater risk of breast cancer. In the second trial, at the University of Alabama at Birmingham, 40 elderly men with elevated prostate-specific antigen (PSA) levels, which means they may be at risk for prostate cancer, are drinking soy beverages to see if the isoflavones lower the PSA levels.

Phytochemicals in cancer treatment

Phytochemicals are also being studied in cancer treatment, where they are used in amounts so concentrated they qualify as drugs. Pamela Crowell, Ph.D., an assistant biology professor at Indiana University-Purdue University at Indianapolis, has found the perillyl alcohol, found in cherries and lavender, causes pancreatic tumors to regress in laboratory animals. She says these compounds appear to cause tumor cells to shift to a less malignant type. Perillyl alcohol belongs to a class of phytochemicals called terpenes. Limonene, contained in the peel of citrus fruits, is one of the best known phytochemicals in this class. In laboratory animals it blocks the development of breast tumors and causes existing tumors to regress.

Taxol, another member of the terpene family, is not found in food, but is a phytochemical already being used in clinical trials. The Food and Drug Administration approved the compound, derived from the Pacific yew tree, for treating ovarian cancer in 1992 and breast cancer in 1993. Taxol is now made in a semisynthetic process, so there is no shortage of the drug.

Molecular pharmacologist Susan Band Horowitz, Ph.D., has been studying taxol since the 1970s. It was her laboratory at the Albert Einstein College of Medicine in the Bronx, New York, that first determined how taxol works to prevent cell division. Although it is used in very low concentrations, it does have side effects such as hair loss, says Horowitz. She stresses that people and animals have died from ingesting taxol in its natural state.

Phytochemicals, like many other chemicals, can be toxic and must be properly formulated and tested before using.

Designer Foods Fanfare

Although there's still much that is unknown about phytochemicals, what scientists do know, at least from many human studies worldwide, is that people who eat large quantities of fruits and vegetables have reduced cancer risks. Some researchers are looking at the effects of other aspects of a lifestyle associated with eating lots of fruits and vegetables, like eating less fat or exercising more. Many scientists, however, think a lifelong diet of phytochemicals plays an important role.

Is an anti-cancer cocktail brimming with extra-strength phytochemicals soon to be on supermarket shelves? Many experts predict it won't be long before some of the better-known phytochemicals start appearing in pills or packaged foods the way vitamins, calcium, beta-carotene, and other nutrients are now. Indeed, the National Cancer Institute's (NCI) major foray into phytochemicals was dubbed the Designer Foods Research Project when it was first announced in 1989 by Ritva Butrum, Ph.D., then Chief of NCI's Diet and Cancer Branch, and now Vice President for Research at the American Institute for Cancer Research. Carolyn Clifford, Ph.D., who directs the program today, says the technology is far ahead of the science at this point.

"You can modify the chemical constituents in food

“ Supplements do not make up for a bad diet. -- Mark Messina, Ph.D.

”

through plant breeding, bioengineering, and food processing, but before we get to that stage we need to know: What compounds? What levels are effective?" says Clifford.

In other words, would megadoses of certain phytochemicals really head off cancer? Could they have harmful side effects? Does the preventive punch of phytochemicals depend upon dozens or hundreds of them working together in a complex ballet, as they do in foods?

Seattle-based nutritionist Mark Messina, Ph.D., does not endorse the trend toward souped-up cereals or what might be called "phytamin" pills. "I think we should focus our time on getting people to consume the type of diet we already know will reduce cancer risk. The notion of "designer foods" is in essence trying to supplement your way to good health. It doesn't make up for a bad diet, says Messina, formerly with the NCI and now a nutrition consultant.

Messina, like Barnes, is a big booster of soy foods and recommends Americans eat one serving (1/2 cup of tofu or 1 cup of soy milk) daily for the isoflavones, which aren't readily found in other foods. He says

From Our Cookbook . . .

Some delicious ways to cook with soybeans . . .

Soybean Soup, page 13, from Darlene S., California, contains lots of bright, cheery and crispy vegetables and great vitamins.

Tofu-Vanilla Pudding, page 92, from Gale S., Florida, is a delicious way to eat soybeans for dessert!



Perfect Recipes . . .

. . . Perfect Gifts !!

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studies have shown that one serving daily is enough to lower cancer risk.

The Take-Home Message

Although cruciferous vegetables and citrus fruits are developing reputations as phytochemical power-houses, keep in mind that these are simply the most studied foods and scientists are learning more every-day. Eating a variety of vegetables and fruits is more important than concentrating on particular kinds to get the full gamut of phytochemicals found in nature.

Here are some easy ways of increasing your intake of phytochemicals.

Eat more grains. Don't limit your choices to bread, rice, and pasta. Try couscous, quinoa, bulgur, barley, kasha, and wild rice for variety. Once available only in health foods stores, most of these grains have become supermarket staples.

Eat a variety of vegetables. Broccoli is very nutritious, but you don't have to eat it every day. Don't forget carrots, cauliflower, greens, winter and summer squashes, green and red peppers, snow peas, red cabbage,... the list is endless. Bags of mixed vegetables in the frozen foods section make getting an assortment at a single meal easy. Don't feel you have to eat a wide variety every day; your weekly consumption is what's important.

Eat more fruits. Research shows the average American eats about one serving a day. A glass of juice at breakfast is nice, but how about some bananas, blueberries, or peaches atop your cold or hot cereal? A crisp apple or fragrant orange as a midday snack or perfectly ripe strawberries for dessert?

Don't forget herbs and spices. Even though you don't eat much of them, they contain phytochemicals too. Garlic, hot peppers, basil, parsley, and other fresh and dried herbs add zip to low-fat foods.

Decrease portion size of meat, fish and poultry. You'll naturally eat more grains and vegetables if you do. Remove half the filling from an overstuffed deli sandwich. Update a favorite dish by changing the meat-to-vegetable ratio: chicken and pasta casserole with peas can become pasta and pea casserole with chicken.

Explore new foods and new recipes. Tofu may be a phytochemical-filled option, but how to prepare it may be a challenge. The same may be true for other unfamiliar offerings in the produce department, like jicama, fennel, tomatilloes, daikon, papaya, or passion fruit. Some supermarkets offer recipe cards or fliers to encourage customers to try the more exotic fare. Or check out one of the many new low-fat healthy cookbooks for tips.

"Five years ago we didn't know about half the phytochemicals we know of today; five years from now we'll know about that many more," says nutritionist Mark Messina, Ph.D. "I think the bottom line with phytochemicals is that they just give us more

reasons to consume a plant-based diet."

Phytochemicals: The Next Frontier

<i>Phytochemical Family</i>	<i>Food Sources</i>
Ally Sulfides	Onions, garlic, leeks, chives
Indoles	Cruciferous vegetables (broccoli, cabbage, kale, cauliflower)
Isoflavones	Soybeans (tofu, soy milk)
Isothiocyanates	Cruciferous vegetables
Phenolic acids (ellagic acid, ferulic acid)	Tomatoes, citrus fruits, carrots, whole grains, nuts
Polyphenols	Green tea, grapes, wine
Saponins	Beans and legumes
Terpenes (Perillyl alcohol, limonene)	Cherries, citrus fruit peel

1. Edited by Thomas Dao, M.D.; Jan Kasofsky-Flynn, Ph.D., R.D.; Adrienne Rogers, M.D.; David Rose, M.D., D. Sc., Ph.D.; Karen Collins, M.S., R.D.; Melanie Polk, M.M.Sc., R.D., L.D.; Reprinted with permission from the American Institute for Cancer Research, 1759 R Street, NW, Washington DC 20069.

References: 1. *American Institute for Cancer Research Newsletter*, "Foods 'Designed' to Prevent Cancer," Spring 1992, Issue 35; "Green Tea: Drink to Your Health?" Spring 1993, Issue 39; "Linking Plants to People," Winter 1995, Issue 46. 2. Berkowitz, Kathy Field, "Will 'Designer Foods' Fortified with Phytochemicals Fight Cancer?" *Environmental Nutrition*, March 1993, pp. 1-2. 3. Interviews with: Stephen Barnes, Ph.D., University of Alabama at Birmingham; Carolyn Clifford, Ph.D., National Cancer Institute; Pamela Crowell, Ph.D., Indiana University-Purdue University at Indianapolis; Susan Band Horwitz, Ph.D., Albert Einstein College of Medicine, Bronx, NY; and Mark Messina, Ph.D., Port Townsend, WA. 4. Schardt, David, "Phytochemicals: Plants Against Cancer," *Nutrition Action Healthletter*, April 1994, pp. 1-4. □

Resources

Rare Should Not Mean Alone, a 35-minute video about individuals who have Treacher Collins Syndrome and their families, the physicians who provide treatment, the researchers conducting studies across the country, and the Treacher Collins Foundation. This closed caption video addresses issues faced by families at various times during the life cycle of an affected individual and is a comprehensive educational tool for families and professionals.

While this is not directly about VHL, Treacher Collins is a related disorder (another of the *phakomatoses*), and the information about living with a rare disease is quite pertinent. Local chapters may find it useful. To purchase a copy, contact the Treacher Collins Foundation, P.O. Box 683, Norwich, VT 05055. Tel: +1 (802) 649-3050

The VHLFA office in Massachusetts has one copy which may be borrowed for chapter meetings. □

Cryotherapy

by Robert B. Welch, M.D., Associate Professor of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland

Cryotherapy is the therapeutic use of cold. The name is derived from the Greek word for cold, *kryos*. Its use is based upon the principle that extreme cold damages tissue by freezing, thus creating an inflammation that destroys an area and replaces it with a scar. As early as 1918 experiments with cold using carbon dioxide snow had shown that inflammation could be produced in the eye. In 1933 this led Professors Deutschmann and Bietti in Europe to apply this clinically in the treatment of detached retinas, using the scar as a fastener, to "tack" the retina in place. However, since instrumentation for applying cold was crude at that time, cryotherapy was soon abandoned in favor of diathermy (heat) introduced by Professor Weve in the late 1930's.

Interest in cryogenics, however, continued in various fields, and in this country Fay in 1936 attempted to induce low temperatures in the brain to destroy malignant tumors. With continued research in this field Cooper in 1961 was able to report successful cryogenic neurosurgical procedures. With new technology now available to produce instrumentation using liquid nitrogen, carbon dioxide, or freon as the source of the cold (freeze), its use in the treatment of retinal detachments was reborn and soon became the most prevalent form of treatment of the retina.

One of the advantages of cryotherapy was that the cold probe could be applied to the outer wall of the eye and the freeze delivered through the coats of the eye to the retina without significantly damaging those layers (conjunctiva and sclera). Thus retinal tears could now be treated without cutting surgery which made it similar in that respect to photocoagulation (laser surgery). With the realization that freezing destroys tissue, various investigators soon tried this technique on various tumors of the eye with some success in retinoblastoma. However, treatment of von Hippel angiomas was reported to be unsuccessful in cases reported in 1967 and 1968, which led Dr. Shea to state in 1967 that cryotherapy "cannot be used to sclerose vascular lesions such as angiomas of retinae."¹ However, in 1966 I had begun to treat angiomas with cryosurgery using a repetitive freeze-thaw cycle (two or three cycles), based on the observations of Cahan that repetition of the cycles of freezing and thawing is one of the criteria for producing cryonecrosis of tissues.² The cases treated were those where the angiomas were anterior (in the far periphery of the retina) and they were treated transconjunctivally.³ The angiomas responded favorably, shrinking and being replaced by scar tissue.

Thus I added cryotherapy to the use of laser and



Fig. 1, Illustration of the Human Eye, by Vincent Giovanucci, O.D.

diathermy in the treatment of angiomas. The procedure is performed with local anesthesia and the post-operative course is similar to that of laser. I use it predominantly on large anteriorly placed lesions that I feel will not respond well to laser or as a subsequent treatment to an angioma that has not responded well to laser. It is planned to treat all cases on several occasions since overtreatment should be avoided to reduce complications. Whether it be cryo or laser therapy, I always anticipate several treatment sessions. Over the years I have found that this conservative approach has considerably lessened complications from treatment.

1. *sclerose* as a verb means to cause them to harden; *angiomatosis retinae* is the Latin name for von Hippel-Lindau in the eye, literally a disease of vascular tumors of the retina. 2. *cryonecrosis*, causing the cells to die by freezing them. Just as a closed bottle of liquid will burst when frozen, the cell bursts and dies when frozen. 3. *transconjunctivally*, the probe directs the cold through the conjunctiva to the retinal lesion, without damaging the conjunctiva. See illustration. Excerpted from "Von Hippel-Lindau Disease: The Recognition and Treatment of Early Angiomas of Retinae and the Use of Cryosurgery as an Adjunct to Therapy," Transactions of the American Ophthalmological Society, 1970 68:367-424.

After the Procedure

Follow carefully the instructions of your physician. Even though you don't feel sick, you have had a surgical procedure, and you have a wound in the back of your eye. It is important not to cause this wound to bleed or enlarge, but to allow it to heal naturally. Pamper yourself for 3-7 days to avoid bleeding. Bleeding in the eye can take months to clear, so an investment of these few days is very important.

- Basically, don't do anything that will cause additional pressure in your eye.
- Don't take aspirin. Tell your ophthalmologist about all your prescription medications.
- Keep your head above your heart, or
- Keep your fanny below your head (squat, don't bend over)
- Take your blood pressure medicine (if any) as prescribed
- No heavy lifting
- No jumping or jarring movements
- Take a mini-vacation from your exercise routine (no jogging, push-ups, tennis, etc.) ☐

Learning from VHL

by Mary P., Utah

I suppose my story is no different from the rest. I, too, am a member of the "doctor of the month club" and am affectionately referred to as "Slash" by my husband and family in honor of my many VHL scars. I, too, have cared for loved ones who have undergone excruciating and horrendous procedures, and then stood by and watched as they passed on alone to the world beyond. I, too, look into the faces of my children and wonder.

When I was first diagnosed with VHL, I saw it as a thief robbing me of my future. You, too, would understand. In desperation and fear I fought hard. Every scan and checkup that came back without change was my victory, and we celebrated. For a time, the battle consumed much of my energy and thought.

I'm not sure when it happened or how, but one day when my strength was nearly spent, I stopped fighting long enough to view my adversary. My foe presented itself and I recognized it as a part of me and a part of who I am. Together now we visit the doctor and have our scans, and I ask VHL, "What is it you are going to teach me about myself this time?" It has taught me much. You, too, would understand.

I cannot help but believe there will be much VHL will teach us about all in our human family. I join with you in this great pursuit. □

We Thank our VHL Family

-- Don and Peggy Marshall, Mississippi

Peggy and I send our most heartfelt thanks to our VHL Family. Your prayers, concerns, and encouragement and special support have made the weeks since Peggy's brain surgery very special for both of us. We have received messages, cards, and calls from all over the world. We want to give a special "Thank You" to Joyce Graff's family. They called and visited every day and brought love and encouragement to both of us. We receive love and support from our family all the time, and especially during our VHL episodes, but the additional support of our "VHL Family" is very special to us both.

Peggy is on the road to full recovery and expects to be back in action by the end of March. She personally wants to thank members of the Mid-South Chapter for their efforts in raising funds for the Research Fund. They were able to raise more than \$5000 of the Challenge Grant through raffles, letter writing, mailings and one on one contacts.

We look forward to seeing you at future meetings and would like to meet everyone in Hawaii in June.

We're Going to . . .

The VHL Symposium Hawaii, June 17-21, 1996

For hotel reservations, call the

Pacific Beach Hotel, (800) 367-6060 or (808) 922-1233

For flight arrangements, call your local travel agent or call

in Pennsylvania: Jacki Hunsberger at 610-489-0896 or 800-829-0022, Fax: 215-361-8008.

in Hawaii: Rod & Vanessa Belen, +1 (808) 623-3633

Families: Learn the latest advances in managing your health

Doctors: Share ideas with other doctors and researchers to advance diagnosis and treatment for people with VHL.

To Register:

See pages 19-20 of this issue.



advertisement

Commissions for VHL

-- from Pat Stepper, Virginia

Real Estate Brokers earn commissions not just from sales, but also from listings, rentals, and referrals. Pat Stepper, who is a member of the Alliance, is also a Real Estate Broker. Since she is affiliated with a national company, Coldwell Banker, she can earn money from referrals all over the country. She has pledged to donate one-half of the commission from any referral, sale or listing where the customer mentions the Alliance. If you, or anyone you know, is planning on buying or selling a house, anywhere in the United States, call Pat at (703) 212-800 or (800) 825-7794. You can fax information to (703) 212-0730. She will be glad to refer you to someone from a Coldwell Banker affiliate in your area. Make sure to tell her that you are contacting her because of your association with the Alliance so the VHLFA will get half the referral fees! □

VHL and Pregnancy

Before and After Pictures Needed

The National Institutes of Health is investigating the effects of pregnancy on tumor growth in VHL women. They are looking for a number of volunteers who have imaging studies from before and after their pregnancies who would be willing to participate in their study, or women with good pre-pregnancy studies who are currently pregnant and would be willing to come to NIH for post-pregnancy studies.

If you are interested, please contact Dr. McClellan Walther, Senior Investigator, +1 (301) 402-2251. □

Handbook in French!

VHL France is pleased to announce the publication of the first edition of the VHL Handbook in French! To obtain copies, write to VHL France, 87 rue de la République, 95240 Cormeilles, France. Congratulations to Mireille and Michel Proux and the team of physicians and doctors who translated and revised this text. □

Help Wanted!

There are many interesting and rewarding jobs to be done to make the VHL Family Alliance succeed and grow. We are looking for committee members for the committees listed on page 18, chapter chairs and willing workers in states and regions, internet surfers, and new Board members. Please call or write and offer your time and talent. We are growing and meeting new people every day . . .

We Need Your Help!

Ask the Experts

Question: I have a blood clotting problem for which my doctor has prescribed Coumadin. Should I be concerned about the effects of Coumadin on tumor growth in VHL? -- *Clark C., Washington*

Answer: Coumadin (warfarin) is a "blood thinner" that predisposes those taking it to bleed. It is used in people who have artificial heart valves, thrombophlebitis, pulmonary embolus, myocardial infarction, atrial fibrillation, etc. Coumadin interacts with many other drugs and has several side effects. The primary side effect of Coumadin is the predisposition to bleed. Coumadin should be used when its benefit outweighs its risk of side effects.

VHL tumors are generally highly vascular (hemangioblastoma, angiomas, renal carcinoma) but they usually do not spontaneously bleed. The predisposition to bleed caused by Coumadin could be a problem with VHL tumors, but it is hard to know exactly how much. As usual, one would have to carefully weigh risks versus benefits, and act accordingly. I personally do not want to use Coumadin in a VHL patient unless there was a very good reason to do so, that is, there were unequivocal benefits. -- *Col. J. M. Lamiell, M.D., Chief, Clinical Investigation Regulatory Office, U.S. Army Medical Education Department, Fort Sam Houston, Texas.*

Working for a Cure for VHL

The VHL Family Alliance and the Massachusetts General Hospital are co-sponsoring an event Sunday, April 14, 1996, 2-5 pm, in the Wang Building at MGH. Dr. Robert Ojemann, Neurosurgeon, and Dr. Francis McGovern will talk about advances in clinical care. Dr. Diana Griffith will explain her approach to identifying the structure of the VHL protein, and Dr. Manuel Navia of Vertex Pharmaceuticals will explain the process of moving from the protein structure model to a useful drug. RSVP by April 5 to Melissa Franks, 617-724-6438. □

Dial-a-Group!

by Altheada Johnson, New York

SupportWorks is a service which allows eight people to "meet" via a conference call. The VHL Family Alliance has arranged five meetings to take place over the weeks and months ahead. VHLFA members in three states -- Idaho, Michigan and Iowa -- will be able to meet via teleconference for one hour on the following dates. We will also have a support group meeting for the visually impaired, and one on the highlights on the Hawaii meeting.

If you are interested in joining any of these meetings, please call the hotline number at 800-767-4845 to reserve a space and get the number to call on the date of the meeting. It's first come, first served, since the system can only connect 8 people.

Saturday -	<u>Idaho Chapter</u> with Peggy L. Rudd
April 20	at 3:00 pm Mountain Time
Saturday -	<u>Vision Support Group</u> with Betty
May 18	Beebe at 3:00 PM Central Time
Sunday -	<u>Michigan Chapter</u> with Fran Mott
May 19	at 3:00 PM Central Time
Saturday -	<u>Iowa Chapter</u> with Diane Mansheim,
June 8	R.N., at 3:00 PM Central Time
Sunday -	<u>Highlights of the Hawaii Meeting</u>
June 30	with Altheada Johnson at 3:00 PM Eastern Time.

Assistance is available for telephone charges. □

Online Services

Connect with us! All questions welcome!

Main address: vhl@pipeline.com

Bill Dickson re Research: vhlres@usa.pipeline.com

Publications office: vhlpub@aol.com

BBS dial-up to +1 (212) 222-4724 □

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

The Danish Association for von Hippel-Lindau

by Richard Harbud, Denmark

Like the VHL Family Alliance in the USA, the Danish Association was started in 1993, and for pretty much the same reasons. Originally the association comprised solely of the family members of our chair, Vibeke Harbud, herself a VHL patient, and one doctor. We too felt there was a lack of coordinated information on VHL, and that if we wanted more information on the subject then we had better find it ourselves. Today we have a membership of eight families and contact with some thirty doctors.

It has been our experience that the need for clear information, for patients and doctors, is of paramount importance. General practitioners and hospital doctors have not always been aware of the necessity of regular and systematic check-ups, and it follows that patients have also been unaware of the benefits. Fortunately, today we have the cooperation of hospitals, who are kind enough to inform VHL patients of our Association, and who in turn can inform their doctors.

However, establishing a contact with VHL patients is not easy. It is estimated that there are perhaps 30 to 50 families in Denmark with VHL. Few of these will have been correctly diagnosed, and fewer still are known to our Association. Despite the fact that Denmark is a rather small country, with some five million people, our Association could still be regarded as regional. Currently most members live in and around the city of Aarhus, as it was there the association was started, and there many VHL patients have their check-ups. Fortunately, Dr. Eigil Kjeldsen of Odense University Hospital (eikjeld@biobase.dk) who specializes in human genetics, hopes to instigate a nation-wide study of VHL patients. Thus a more complete picture of the extent of VHL in Denmark could be available within the next few years. Hopefully Dr. Kjeldsen will be attending the VHL conference in Hawaii in 1996.

As I stated before, our Association is very small. My wife and I take care of the few administrative tasks there are; Vibeke (pronounced *vee-b-ka*, in case you are curious) keeps in touch with doctors and I take care of letter writing, forwarding of brochures and so on. Generally speaking very little happens. Occasionally, however, the phone rings and a complete stranger introduces themselves as a VHL patient. More often than not we discover that the person on the other end of the line has just been told that they have VHL. Just as frequently we learn that they could have been helped at an earlier stage, had their families not tried to keep the disease a secret from their relatives and general practitioners. It is no easy thing, talking to a complete stranger on the phone about a

potentially dangerous disease, and despite the fact that we immediately refer them back to their own doctor and offer to supply them with copies of all the material we have on VHL, we find that we end up administering first-aid. The chain of events is almost always the same: the patient, following treatment for previously undiagnosed symptoms, is informed by the hospital that they have VHL, at which point in time the patient is ill-equipped to deal with the problem and therefore understands little of what is being said to them. The patient's family concedes that there is "something in the family;" the doctor does his or her best to explain things. The patient, by this time thoroughly confused, finds the brochure given to them by the hospital, phones us, and the battle against ignorance commences.

It has not been easy, starting and running an active association for VHL patients in Denmark, and it has been inspiring to establish contact with the VHL Family Alliance. Both my wife and I were astounded by the speed and quality of response following our first contact, and to describe the VHL Family Alliance as "dynamic" might be bordering on understatement. We know for sure that since making contact we have helped to increase the range of inter-professional resources available to doctors in Denmark, which in turn will give long term benefits to patients. We would like to take the opportunity to thank the VHL Family Alliance and wish all those involved all the best for the future.

Foreningen af Von Hippel-Lindau Patienter,
Vibeke Harbud, Fiskervejen 10, 4000 Roskilde,
Denmark. Tlf: +45 46 76 70 33 □

Meet us in Hawai'i in June!

**Learning, Play, and Hugs from
other VHL families from all over
the world.**

Sign-up info, pages 19-20

Hold that Plant!

adapted from an article by Jean McCann, National Institutes of Health

As cancer patients receive more high-dose chemotherapy treatments and undergo bone marrow transplantation in growing numbers, the opportunities for infections are rising. While a number of antibiotics exist for the prevention and treatment of bacterial infections, using them as preventives often creates a hospitable environment for equally deadly fungal infections -- for which few good treatments now exist.

While people with VHL are not treated with chemotherapy, treatment with radiation therapy, can also result in a temporary weakening of the body's immune system which can put them at risk for such infections.

At the recent International Congress of Chemotherapy, held in Montreal, a number of speakers discussed developments that could improve the diagnosis and treatment of these serious fungal infections in people with weakened immune systems.

Françoise Meunier, M.D., Ph.D., director of the Central Office of the European Organization for Research and Treatment of Cancer in Brussels, said that, while deaths from fungal infections that have spread to the bloodstream are more common in hematologic malignancies (such as leukemia), even in solid tumors, "5% [of cancer patients who die] have evidence of invasive fungal infection at autopsy." She estimated that 300,000 of the 6 million worldwide cancer deaths each year result from fungal infections that have spread to the bloodstream, also known as fungemia. The more aggressive the treatment, the greater the risk. Some 30% of bone marrow transplant patients show evidence of fungal infection. "It is clearly a catastrophe for a patient to enter a hospital for a bone marrow transplant and then have to explain that this patient is going to die because of invasive *Aspergillus*."

Meunier said that *Aspergillus* infection is particularly important to prevent by any means necessary, because there are no good treatments. Prevention of *Aspergillus* infection may mean something as simple as removing plants from a patient's room (the soil can harbor the fungus) or something as drastic as shutting down an entire bone marrow transplant unit as a result of widespread contamination, which Meunier said was done recently as a unit in France where 21 deaths from invasive *Aspergillus* occurred. *Candida* fungus is also a threat.

Elias Anaissie, M.D., associate professor of medicine at the University of Texas M. D. Anderson Cancer Center in Houston, has studied strategies for detecting and preventing fungal growth. While there are drugs which can be administered as preventives,

they can permit the growth of other dangerous fungi which do not respond to the preventives. For this reason, preventive drugs are generally given only to patients at high risk, such as those undergoing bone marrow transplant, or patients with acute leukemia and other patients who have prolonged neutropenia. Dr. Anaissie and others are working toward earlier diagnosis of fungal infection. In his own practice, he supervises patients with weekly cultures, and gives preventive treatments if any signs of fungi are found.

Taking drugs such as Decadron can mask the symptoms of fungi. Be alert to signs of infection and report to your doctor without delay. But the best defense remains prevention. People who are being treated with immune-weakening treatments such as radiation and transplantation should decline to accept live plants and flowers in their rooms or homes. They can be put on display at the nurses station, or sent home with a friend. You can suggest that people send cards or balloons or silk flowers instead.

condensed from "Deadly Fungal Infections Spreading in Cancer Patients," *Journal of the National Cancer Institute*, 87:19 (October 4, 1995), pp. 1434-1436.

Resources

The **National Association of Hospital Hospitality Houses, Inc.**, is an association of residences for outpatients and family accompanying patients being treated for serious illnesses away from home. Contact Shirley LaBerteaux, NAHHH, 4013 W. Jackson Street, Muncie, IN 47302, (317) 288-3226 or (800) 542-9730; fax: (317) 287-0321.

The **National Parent-to-Parent Network** of Mothers United for Moral Support, Inc., (MUMS), connects families with similar conditions, esp. children with special needs. Free newsletter. Julie Gordon, MUMS, 150 Custer Court, Green Bay, WI 54301-1243, Tel: 414-336-5333; Fax: 414-339-0995.

When your mate can no longer be your social partner, parenting partner, financial partner, emotional partner, or sexual partner, you are a **Well Spouse**. Support meetings for husbands, wives, and partners of the chronically ill and/or disabled, U.S. and Canada. Contact Well Spouse Foundation, P.O. Box 801, New York, NY 10023; Tel: (800) 838-0879; Fax: (212) 724-5209.

Long Distance Love is a national non-profit support network that links individuals with similar health problems for telephone support and correspondence. Contact Roxanne Black, P.O. Box 114, New Brunswick, NJ 08903, +1 (908) 418-1811 or <http://www.njin.net/~ldl/>

Cancer Care Counseling Line is a toll-free telephone counseling service of Cancer Care, a non-sectarian social service agency founded in 1944 to help cancer patients, their families and friends cope with the impact of cancer. (800) 813-HOPE. □

A Family Affair

by Gay V., Sydney, Australia

My husband Paul was 24 when he was diagnosed with von Hippel-Lindau disease following the discovery of an angioma that virtually blinded his right eye. He was not told that the disease was genetic, or any of the other possible affects. For the next 17 years all was apparently well.

Then in 1990, when Paul was 41, he became very ill. Two cerebellar tumors were picked up by CT scan. They were successfully removed in 1991, but an MRI scan then showed two smaller tumors, one of which eventually developed a cyst. They were removed successfully in 1994.

Meanwhile, 16 members of his family were tested for von Hippel-Lindau disease, including our children Lana and Brent. None showed any signs of the disease.

Paul's monitoring continued, and in early 1994 the two additional tumors were successfully removed. Then in April 1995 a tumor was removed from his spinal cord. Even though only 50% of the tumor could safely be removed, surgeons were successful in cutting off its blood supply, and a subsequent MRI showed that it had dried up. Some small cysts in his kidneys are now being watched.

We were told to have the children's eyes checked every three years. If we had known then what we know now, Lana would not have lost the sight she has. In 1993, when Lana was 12, she was treated for a large angioma which nearly destroyed the vision in her right eye. A smaller one in her left eye was successfully treated. Later the same year Brent, then 14, also had a small angioma successfully treated.

Our family had been feeling very isolated and alone through all of these traumas. Lack of information was the main thing. The doctors who were treating us had never treated this disease before, and did a very good job with little information. Now that there is so much more information available, we feel confident that our medical team is much stronger. It is wonderful to have more information coming on a regular basis. Paul, Lana, and Brent are now regularly monitored by neurologists, ophthalmologists, and urologists as well as their general practitioner. Everyone has had their check-ups and all is fine, so we can put VHL back in the bottom drawer for a while. Paul is feeling well at the moment, which is a pleasure to see.

There are an estimated 600 people with VHL in Australia. Because of Australia's small population, getting information about the disease, let alone finding anyone else who has it, has been impossible until now. Late in 1993 I was listening to the radio during "Gene Awareness Week" and heard a genetic counselor being interviewed. They suggested that interested families with genetic diseases might like to contact Dr. Kathy

Brent, Lara, Paul, and Gay, Sydney, Australia.

Tucker at the Prince of Wales Hospital in Randwick, Sydney. I was feeling pretty stressed and alone at that time. The first thing that Kathy told me was that the gene had been found. She sent me a patient information leaflet prepared by Dr. Eamonn Maher in England. I wrote to him, and he replied, enclosing a copy of the *VHL Family Forum*! So by going around the world we will at long last have the information we have been looking for so long."

I wrote to the U.S., and Joyce put me in touch with Jennifer K. The two of us have worked together to set up an affiliate of the VHL Family Alliance in Australia. Jennifer and I have become good friends and are in regular contact with each other. It is very exciting when another VHL family makes contact with either of us. Four families called me after an article was published in *The Medical Observer*, a medical magazine, in August.

Spreading information about von Hippel-Lindau disease is my way of fighting back. The VHL Family Alliance, Australia, will hold three meetings in March in Brisbane, Sydney, and Melbourne, in conjunction with the visits of Dr. Y. Edward Hsia and Joyce Wilcox Graff to Australia and New Zealand. A chapter is being set up in New Zealand as well, which will collaborate closely with us in Australia.

A VHLFA Clinical Care Center is being set up in Melbourne under Dr. Mac Gardner, Genetics Dept., Murdoch Inst, 10th Floor, Royal Childrens Hospital, Flemington Road, Parkville, Melbourne, 3052 Australia. Phone: +61 (03) 9345-5157; Fax: +61 (03) 9348-1391.

DNA testing for VHL is offered by Dr. Jack Goldblatt, Director of Genetics, Princess Margaret Hosp for Children, Roberts Road, Subiaco, 6008 West Australia, Phone: +61 9 340-8222; Fax: +61 9 340-8111; E-mail: tedkins@uniwa.uwa.edu.au.

We hope to meet you in Hawaii!

Our thanks to Raelene Allen and the *Medical Observer*, Sydney, Australia, for their assistance in the preparation of this article. □

Genetic Discrimination and Health Insurance

— Reporting an article by Kathy L. Hudson and Francis S. Collins, Natl Ctr for Human Genome Research; Karen H. Rothenberg, U. Maryland School of Law; Lori B. Andrews, NIH-DOE Working Group; Mary Jo Ellis Kahn, NAPBC¹

The ability to obtain sensitive genetic information about individuals, families, and even populations raises profound and troubling questions about who will have access to this information and how it will be used. With the accelerating pace of gene discovery, we will soon be able to identify quickly a wide range of risk factors, and to find effective preventive and treatment strategies that will lower the personal, social, and perhaps the financial costs of disease in the future. Every human being carries genes that predispose to common illnesses. In many circumstances, as with VHL, knowing this information can be beneficial, as it allows individualized strategies to be designed to reduce the risk of illness.

As knowledge about the genetic basis of common disorders grows, so does the potential for discrimination in health insurance coverage for an ever increasing number of Americans. While health care itself is not in jeopardy for people who live in countries with health care for all citizens, similar concerns frequently arise in obtaining life insurance.

The use of genetic information to exclude high-risk people from health care by denying coverage or charging prohibitive rates will limit or nullify the anticipated benefits of genetic research. In addition to the real and potentially devastating consequences of being denied health insurance, the fear of discrimination has other undesirable effects. People may be unwilling to participate in research and to share information about their genetic status with their health care providers or family members because of concern about misuse of this information. As genetic research progresses, and preventive and treatment strategies are developed, it will be increasingly important that discrimination and the fear of discrimination not be a roadblock to reaping the benefits.

Genetic information has already been used by insurers to discriminate. In the early 1970's, some insurance companies denied coverage and charged higher rates to African Americans who were carriers for the gene for sickle cell anemia. Recent studies have documented cases of genetic discrimination against people who are healthy themselves but who have a gene that predisposes them or their children to a later illness such as Huntington's disease. In a recent survey of people with a known genetic condition in the family, 22% indicated that they had been refused health insurance coverage because of their genetic status, whether they were sick or not.²

Because of the high costs, insurance is essentially required to have access to health care in the United States. Over 40 million people in the United States are uninsured.³ Group insurance, individual insurance,

self-insurance, and publicly financed insurance (for example, Medicare and Medicaid) are the principal forms of health insurance in the United States for the ~240 million Americans with coverage. Most people get their health insurance through their employer. For individuals and small groups, insurance providers use medical history as well as individual risk factors, such as smoking, to determine whether to provide coverage and under what terms. This is known as underwriting. Insurers argue that underwriting is essential in a voluntary market to prevent "adverse selection," in which individuals elect not to purchase insurance until they are already ill or anticipate a future need for health care. Insurers fear that individuals will remain uninsured until, for example, they receive a genetic test result indicating a predisposition to some disease such as breast or colon cancer.

While some states have enacted laws to protect individuals from being denied health insurance on the basis of genetic information,⁴ (See Fig. 1) Insurers can use other phenotypic indicators, patterns of inheritance of genetic characteristic, or even requests for genetic testing as the basis for discrimination. Meaningful protection against genetic discrimination requires that insurers be prohibited from using all information about genes, gene products, or inherited traits to deny or limit health insurance coverage.

No federal laws are currently in place to prohibit genetic discrimination in health insurance.⁵ It is not clear if the current health insurance reform proposals would prohibit insurers from denying coverage on the basis of genetic information. If enacted, current health reform proposals would prohibit denying insurance to those currently suffering from disease or with a past history of disease. But these proposals may not protect people who are healthy but have a genetic predisposition to disease.

Planners of the Human Genome Project recognized from the beginning that maximizing the medical benefits of genome research would require a social environment in which health care consumers were protected from discrimination and stigmatization based on their genetic make-up. Genome programs at both the DOE and the National Center for Human Genome Research, a component of the National Institutes of Health (NIH), have each set aside a portion of their research budget to anticipate, analyze, and address the Ethical, Legal, and Social Implications (ELSI) of new advances in human genetics. The original planners also created the NIH-DOE ELSI Working Group, which has a broad and diverse membership including genome scientists; medical geneticists; experts in law, ethics, and philosophy; and consumers, to explore and

propose options for the development of sound professional and public policies related to human genome research and its applications. The ELSI Working Group has long been involved in discussions about the fair use of genetic information. In a 1993 report, "Genetic Information and Health Insurance,"⁸ the ELSI Working Group recommended a return to the risk-spreading goal of insurance. The Working Group suggested that individuals be given access to health care insurance irrespective of information, including genetic information about their past, current, or future health status. Because denial of insurance coverage for a costly disease such as breast cancer may prove to be a death sentence for many women, the National Action Plan on Breast Cancer (NAPBC), a public-private partnership designed to eradicate breast cancer as a threat to the lives of American women, has identified genetic discrimination in health insurance as a high priority.

Building on their shared concerns, the NAPBC and the ELSI Working Group cosponsored a workshop in July 1995 on genetic discrimination and health insurance.² Scientists, representatives from the insurance industry, and members of the ELSI Working Group and the NAPBC participated in the one-day session. On the basis of the information presented at the workshop, the ELSI Working Group and the NAPBC developed the following recommendations and definitions for state and federal policy-makers to protect against genetic discrimination:

1) Insurance providers should be prohibited from using genetic information, or an individual's request for genetic services, to deny or limit any coverage or establish eligibility, continuation, enrollment, or contribution requirements.

2) Insurance providers should be prohibited from establishing differential rates or premium payments based on genetic information or an individual's request for genetic services.

3) Insurance providers should be prohibited from requesting or requiring collection or disclosure of genetic information.

4) Insurance providers and other holders of genetic information should be prohibited from releasing genetic information without prior written authorization of the individual. Written authorization should be required for each disclosure and include to whom the disclosure would be made.

The definitions are as follows. Genetic information is information about genes, gene products, or inherited characteristics that may derive from the individual or a family member. Insurance provider means an insurance company, employer, or any other entity providing a plan of health insurance or health benefits including group and individual health plans whether fully insured or self-funded.

These recommendations have been endorsed by

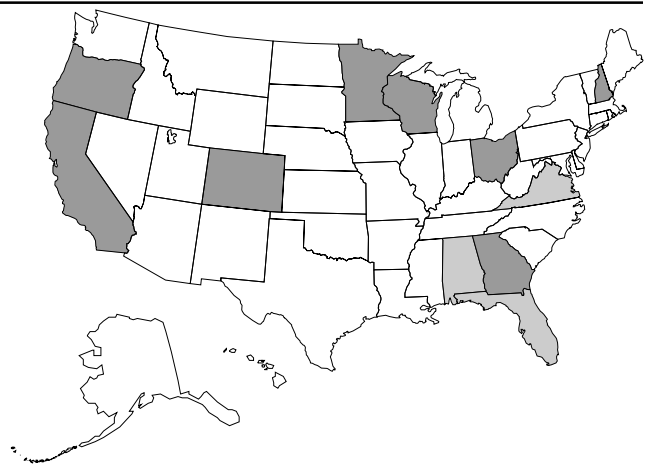


Fig. 1. State laws on the use of genetic information in health insurance. States shown in lightest gray were the first states to enact legislation addressing genetic issues in insurance. Florida and Alabama laws prohibit insurers from denying coverage on the basis of the sickle cell trait. North Carolina prohibits insurers from denying coverage because the applicant has the hemoglobin C or sickle cell trait. Maryland prohibits discrimination in rates based on any genetic trait unless there is actuarial justification. California, Oregon, Colorado, Minnesota, Wisconsin, Ohio, Georgia, and New Hampshire prohibit insurers, to varying degrees, from requiring or requesting genetic tests or their results, from denying coverage on the basis of genetic tests, and from using tests to determine rates and benefits. California, Colorado, Oregon, and Wisconsin laws include provisions to protect the privacy of genetic information. Massachusetts and Hawaii have related bills pending.

the National Advisory Council for Human Genome Research (NACHGR). The NACHGR stresses the positive value of genetic information for improving the medical care of individual patients and the need to ensure the freedom of patients and their health care providers to use genetic information for patient care. The NACHGR views the elimination of the use of genetic information to discriminate against individuals in their access to health insurance as a critical step toward these goals.

The recommendations presented here for state and federal policy-makers are intended to help ensure that our current social, economic, and health care policies keep pace with both the opportunities and challenges that the new genetics present for understanding the causes of disease and developing new treatment and preventive strategies.

1. Reporting an article in *Science*, **270**:391-393 (20 October 1995).
2. "Genetic discrimination and health insurance: A Case study on breast cancer," Bethesda, Maryland, 11 July 1995, workshop sponsored by the NAPBC, and the NIH-DOE Working Group on the ELSI of Human Genome Research. 3. *Employee Benefit Research Institute Special Report SR-28*, issue brief number 158, February 1995. 4. K. H. Rothenburg, *J. Law Med. Ethics*, in press.
5. The March 1995 EEOC guidance on the term "disability" extends protection to individuals who are discriminated against in employment decisions solely on the basis of genetic information. This is the first broad federal protection against unfair use of genetic information.
6. "Genetic information and health insurance: Report of the task force on genetic information and insurance (NIH-DOE Working Group on the ELSI of Human Genome Research, 10 May 1993).

Human Genome Education

by Patti Kohlen, California

On October 6-7, 1995, the Alliance of Genetic Support Groups and Georgetown University Child Development Center presented the second of their Human Genome Education Model Project (HuGEM) conferences in Bellevue, Washington. The purpose of this project is to educate consumers with genetic disease and health care professionals who provide preventive, diagnostic, counseling and treatment services for people with genetic conditions, about the Human Genome Project.

The Human Genome Project is being carried out at the National Institutes of Health and is mapping all 100,000 genes found on the 23 pairs of chromosomes of a human. Each gene is made of DNA, which is a packet of information that tells cells how to behave. DNA is made up of four chemicals, abbreviated to A, G, C, or T. It is the order of these chemical combinations that determines what protein the DNA will make. There are 3 billion bits of information (DNA sequences) on the 100,000 human genes. As you know, genes orchestrate the development of a single-celled egg into a fully formed adult. They influence not only what we look like, but even what diseases we may eventually get. For example, a flaw in the gene sequence found on the short arm of chromosome 3 causes von Hippel-Lindau disease. It is estimated that the mapping of the entire human genome will be complete by the year 2005.

In order to be prepared for this new information, the HuGEM project was developed, for it is believed that the Human Genome Project (HGP) will change the way medicine is practiced in the 21st century. HuGEM's goal is to educate consumers and professionals so that they will be able to work collaboratively to obtain optimal benefit from the HGP.

Participants at the conference were given an overview of the HGP. The results of a survey about the HGP and genetic testing issues that was sent to approximately 300 consumers and 300 medical professionals were reviewed. A brief summary of the results of this survey follows: 61% of consumers and 52% of professionals had heard of the HGP. 25% of consumers said they had been refused life insurance because of a genetic condition. 71% of consumers and 74% of professionals said children 10-17 years old should participate in decisions about having genetic testing. 91% of consumers said they would participate in research studies again. In response to the question: "At what age should children be involved in the decision to be genetically tested?", consumers said children should be 15 years old, and professionals said 14.

The differences between genetic testing and general medical testing were pointed out:

- The predictive nature of genetic testing
- The private nature of the information
- The ramifications for family members
- The implications for reproductive decisions
- The lack of knowledge about ways to influence or prevent certain genetic outcomes

-The relationship of test results to self perception

Consumers provided humorous summaries of real life situations. Speaking of his hip replacement surgery, one man with Gaucher's Disease said, "I left my hips in Boston!" The father of a nine-year-old with Neurofibromatosis spoke of "life in the trenches" and that "survival" is his and his daughter's middle name.

In the end,

To conclude,

It all comes down

To Attitude

The conference presented a discussion about communication. Dr. Nuhad Dinno stressed the importance of paying attention to linguistic cultural differences. She urged professionals not to give bad news to patients on a Friday afternoon when practices will be closed over the weekend and no support would be available to patients. Professionals should admit unknowns and set up another appointment when they can present the missing answers. Professionals need to use diagrams, and pause when presenting information and check for understanding: What did the patient hear? Professionals should be empathetic, should check how much a patient knows about their condition, and should not use medical jargon or shorthand. They should try to understand the cultural belief system of the patient (i.e. does the patient believe that bad genes mean you are a bad person?)

The consumer perspective on communication emphasized that the consumer is always in charge: I set the pace, I set the standard, I want information, I will filter this information, I will decide what I will do with this information. It is important that consumers state clearly to their physicians that they wanted accurate, up-to-date information. Communication needs to be based on mutual respect.

Dr. Mark Kay, Ph.D., from the University of Washington, gave an evening presentation on gene therapy. The ultimate goal of the HGP is that prevention or intervention with genes that cause disease can occur by gene therapy.

During the conference consumers and professionals worked together on establishing steps that could be taken to help educate the general public about the HGP. The conference organizers will be assimilating these recommendations and distributing them to all participants.

Patti is a member of the Board of Directors of the VHLFA, and serves on the Education and Consumer Committees of the Pacific States Regional Genetics Network (PSRGN). □

VHL Family in Hungary

by Hannah S., Budapest, Hungary

My husband András and I are chemists. We married after finishing our university studies in 1966. Since then I have been working at a major university in Hungary. My main research activities are the investigation of the structure and activity of peptide hormones and the synthesis of peptide derivatives with selective anti-tumor activity. My husband was working in a semi-conductor research laboratory, and later he became the director of a small company dealing with computers, especially designing and building medical imaging systems.

In the spring of 1971 my husband noticed some black stains in his vision. His eye was covered with blood. He was told that it was a blood vessel tumor. He went through two unsuccessful photocoagulation operations in Budapest, and before a third one (which we feared would also be unsuccessful) we made inquiries to find a specialist anywhere in the world. At that time, behind the "Iron Curtain," it was not easy to inquire about other countries, much less to go there. Anyway we learned that Professor Meyer-Schwickerath in Essen, Germany, was the only specialist in Europe who treated this von Hippel-Lindau disease with laser. He immediately agreed to take my husband's case, and in a relatively short time he got permission to travel to Germany. I was pregnant at the time with our elder son Mark. András returned from Germany just before my delivery.

He was told to go regularly for check-ups, which was not possible, but occasionally, perhaps twice in the following ten years, he managed to return to Germany. Luckily everything was okay, and we thought that this problem was solved forever. I do not remember that we were told that this disease was inherited. Perhaps the doctors we dealt with didn't know that then.

So we were living happily, and our younger son Áron was born in 1973.

In March 1987 Áron was often complaining about indisposition in the morning. We went to the doctor but he found nothing, because the complaints were not very definitive. But one day he told us that he could not see well, so I took him to an ophthalmologist, who advised a thorough medical check-up. We turned to our friend, a surgeon at the pediatric clinic. The next day Áron was examined and was found to have a very high blood pressure. First it was thought that he had some problem with his kidneys, and there were some awful days until after an ultrasound examination it turned out that he had bilateral pheochromocytoma, the first time this had been found in a child in Hungary. He underwent surgery.

Then the whole family was checked by ultrasound for pheochromocytoma and both Mark and András were found to have pheos on one side. Mark had a

broken arm at the time, and was operated on with his arm in a plaster cast, since because of the high blood pressure the operation was urgently needed. After the operation a slightly higher blood pressure than normal remained, but nobody seemed very concerned.

András had never had high blood pressure, and had no symptoms of the pheochromocytoma, but still had the surgery because we feared that the tumor might become malignant. [We now know that while sporadic pheos often become malignant, the pheos of VHL very rarely progress to cancer. However they do have to be treated promptly to prevent damage to the heart and vascular system.]

Thus in two months there were three operations in our family and thank God all the tumors were benign.

Although the doctors advised us to go for yearly check-ups, we went only after the first year and later not, because the boys were very much against it.

“ It is most important to test for pheochromocytomas before undergoing surgery for any reasons, and before going through the childbirthing process. ”

They never talked about the operations and hated if someone mentioned it or inquired after their health. We also wanted to avoid the development of an illness consciousness. They seemed to be fine and we were not really forced to go for checkups.

Thus it was very shocking that in 1990, when we spent our summer holidays in Cyprus, Mark felt ill and when we came home and measured his blood pressure it was very high. The CT examination showed a pheo on the same side as before and he was operated again, and again after the operation his blood pressure was not perfect.

The next spring, 1991, he looked unwell, but had no specific complaints. His urine test showed some deviation from normal. I was getting desperate and decided to go to another hospital where they have more experience with pheochromocytomas. Through personal connections we went to Cologne, Germany, where he was thoroughly examined and it was found that he had a pheo on the other side. This tumor could be detected only in a rotating scintigraph [%needs a note] which was not available in Hungary, so the tumor had not been seen before. So he was operated on again, for the third time. If he had had proper diagnosis, they could probably have done the whole job in one operation. It was thought that he had multi-endocrine neoplasia type 2 (MEN2) [another rare hereditary condition which also causes pheos] and we were told to go for check-ups every half year, for urine tests and calcitonin measurements.

Last summer (1994) in connection with my research work I met Dr. Michael Price, the secretary

of the European Organization for Research and Treatment of Cancer (EORTC), and in an unofficial discussion I asked him whether he could help me to find a place where the genetic testing of my sons could be performed to locate the chromosomal aberrations causing these awful pheos. He was very kind and arranged a connection with Dr. Eamonn Maher in England.

When Mark began having symptoms of a brain tumor, we asked Dr. Maher for a referral to a neurosurgeon specializing in VHL. We thus found our way to the VHL Family Alliance, who gave us a list of European doctors and family contacts. Our son was treated by Dr. Neumann's wonderful team in Freiburg. He came through his surgery beautifully.

But enough about these depressing operations. Mark is now 24 and has finished his university studies. In spite of the brain surgery he never postponed his exams. He is a mechanical engineer. He is working now with his father and studying as a post-graduate student in economics. He is a very bright, sharp-minded, charming and generous boy, has a lot of friends, likes skiing and wind surfing.

Aron, 22, is still a student. He studied geophysics for three years, but this year he changed his mind and has turned to astronomy. He is interested in history and computers as well. He is an independent character, very warm-hearted and more introverted than Mark, with strong principles. Presently he is attending a language course in London. He does not care much for sports, although he likes to ski.

Both of them are very brave, with a good sense of humor, and they never complain or pity themselves. So you see I have the most wonderful sons in the world, as all mothers do!

According to the genetic projections, there are 300 people with VHL in Hungary, who, like us, struggle to get the right information and treatment. We are working with our physicians here to publish an article about VHL in a medical journal and to develop a VHL Clinical Care Center in Hungary.

Editor's Note: Please note that pheochromocytomas can occur on both sides, both inside an adrenal gland and outside of one. People can have more than two pheos, as Mark did here, so blood pressure and urine chemicals should continue to be checked, even after bilateral adrenalectomy. It is most important to test for pheochromocytomas before undergoing surgery for any reasons, and before going through the childbirthing process. MIBG, a specific test for a phéo, has recently been approved by the U.S. FDA and is now considered the standard test worldwide for locating a phéo, wherever it may occur in the body.

□

Testing for Pheochromocytoma

by Fran M., Michigan

It is most important to test for pheochromocytomas before undergoing surgery for any reason, and before going through the childbirthing process.

While the authoritative test for a pheochromocytoma is a nuclear medicine scan called an MIBG, not everyone can get to a hospital that offers this test, and not everyone is a candidate for the test. The urine and blood tests for phéo are most reliable when care is taken in two areas -- diet prior to the testing, and preservation of the urine sample from the start of the test until the lab processing is complete.

To get the best information from a 24-hour urine test, it is critically important that the patient -- *that's you!* -- follows carefully the phéo test instructions that go with the test. An informal survey of hospitals and VHL patients in my state discloses that not all hospitals provide these instructions to the patient, and not all patients follow them conscientiously.

If your own hospital lab staff has provided instructions, that's great! If not, ask them if these would be good to follow, to ensure that the sample is fresh and that the chemical levels for which they are testing are not artificially influenced by things in your diet. It is also very important that the urine be carefully refrigerated and preserved throughout the 24-hour urine collection period, and delivered fresh to the lab for immediate processing.

Preparation for Blood Testing

Do not take any medications without the testing doctor's knowledge and agreement. In particular, be sure to discuss theophylline, anti-hypertensives (blood pressure medicines), methyl dopa, reserpine, guanethidine, L-dopa, or any diuretic.

Refrain from eating or drinking anything except water from 10 P.M. the evening prior to your blood test and that you not take any medications the morning of the test unless specifically okay'ed by the doctor administering the test. If you are instructed not to take your morning medications, please take them with you to the test so that you can take them right after the completion of the test.

In addition, it is recommended that you refrain from anything containing nicotine or caffeine at least three days prior to your test (i.e. cigarettes, cigars, coffee, tea, colas, etc.) If you have questions regarding your diet, please contact your physician.

The procedure usually takes about 45 minutes. It is important that you be quiet and calm for 30 minutes prior to the blood draw to ensure accurate results. Bring a book to read, or your walkman with some favorite music, something you will find relaxing.

Preparation for 24-hour Urine Testing.

For Vanillyl Mandelic Acid testing (VMA): Avoid chocolate, fruit (especially bananas) and any vanilla containing substance (cake, ice cream, pudding, etc.) for 48 hours prior to and during collection. Check with your doctor if you are taking Aldomet.

For Catacholamines, Metanephrines, Epinephrine, Norepinephrines: Avoid medications, chocolate, fruits (especially bananas) and any vanilla containing substance (cake, ice cream, pudding, etc.) for 48 hours prior to beginning collection and during collection.

Collection instructions: Do not begin collection on Friday or Saturday. This ensures that your sample will be delivered to the lab on a working day and can be processed promptly.

1. Start the collection in the morning. Empty the bladder and do not save this urine specimen

2. Write this date and time on the jug.

3. Save all the urine passed for the next 24 hours in the jug provided, include the final specimen passed exactly 24 hours after beginning the collection.

4. Keep the urine refrigerated at all times. (I know this seems gross. We kept ours in a paper bag in the fridge.)

5. Write this date and time on the jug when the collection is finished.

6. Bring the collection, along with the paper work, to the lab as soon as possible after collection. (Drop it off on the way to school or work. Labs are usually open early in the morning, or have a place where you can arrange to drop it off early).

* If there is a preservative added to the jug, be careful not to get it on the skin. If this happens, wash the area immediately with water.

Test instructions provided by Partners in Health, General Medicine Outpatient Service of the University of Michigan, Department of Internal Medicine.

We remember . . .

Thea F., who died of lung cancer after a long bout with VHL. She was 43. "She was the bravest person I've ever known, and I and many others loved her very much."
— Jack F., Mass.

Jerry Walsh. Jerry was very gifted in music and art, and delighted us with his creations. We as a family feel that Jerry had the heart of a lion. We feel lucky to have had him with us."
— Michelle O., Fla.

Thank you!!

Thanks to each and every one of you, we brought in the \$26,000 within the forecasted time. Many thanks to everyone who made it possible for us to meet this goal, and to award our First Annual VHLFA Research Grant to Dr. Diana Griffith of Harvard Medical School for her project "Derivation of the Crystal Structure of VHL."

The majority of it came in with little pink slips attached -- responses to our mailing, and to members' outreach to their friends and family.

This is only the beginning. With mention in the March issue of *Scientific American* and a spring issue of *Science*, and our new research presence on the Internet, we are generating a lot of interest. We are receiving additional proposals, and hope to be able to award at least one more grant this year.

Please continue to remember the Fund for Cancer Research in your own regular charitable contributions, and whenever an opportunity arises to suggest it to friends and businesses near you. You will find among our list of thank-yous a number of businesses who have matched the gifts of employees, donated in honor of an employee, or simply responded to a neighborly request from their community.

The biggest reason people don't give is that they were not asked. With your help, we can increase the visibility of the need to solve VHL and tumor conditions for everyone.

Thank you!! -- *The VHLFA Board*

This issue of VHLFF is sponsored. . .

This issue is dedicated to the memory of Ken Murfitt, who died of a heart attack in January, and in gratitude for his loving and devoted service to all of us, in England and around the world.

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- ☐ **VHLFA Teamwork Pin**, silver #__ @ \$18, gold filled #__ @ \$27 \$ _____
- ☐ **VHLFA Cookbook** #__ @ \$12 \$ _____

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

Make checks payable to VHL Family Alliance, and Send membership and order information to
 VHL Family Alliance, 171 Clinton Road, Brookline, MA 02146

In Honor Of . . . donations (minimum \$10 each):

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Second International VHL Symposium Third Annual Meeting of the VHL Family Alliance

Five days of meetings are planned for June 17-21 in Honolulu, focusing on "Cancer in Families," with specific emphasis on von Hippel-Lindau disease. The five chairpeople are developing high quality programming to deal with family, insurance, legal and counseling issues for families with hereditary disorders, and on the state of treatment and research on VHL.

Monday: Opening Session: Family and Nursing issues, organized by Janet Brumblay, R.N.

Tuesday: Insurance, pre-symptomatic screening, counseling, registries, and consumer issues, organized by Debra Collins, M.S., and Dr. Jane Green.

Wednesday: Consumer Session: family-oriented topics sponsored by the VHL Family Alliance and the Rosado family, followed by a Luau. Chaired by Rev. David Torres.

Thursday: Medical session: podium presentations by various professional experts regarding VHL management, organized by Drs. J. M. Lamiell and H. P. H. Neumann.

Friday: Scientific Session: podium presentations by various experts regarding VHL molecular genetics. Organized by Dr. Berton Zbar.

We know already that we have representatives coming from Australia, Canada, France, Germany, Holland, Japan, and mainland U.S.A. Please come and join in this unique learning experience.

Families gain new medical information, and the medical perspectives of many disciplines and many medical cultures. Most of all, meeting others who are going through the same experiences is a gift without price. As one family said to me, "We can never miss another one of these! We learned more in days than we have been able to glean in years of struggle!"

Medical professionals gain from interaction with the spectrum of professionals involved in the care of

cancer in families, and most important from interaction with members of the families themselves. Every year, the doctors who attend tell us how very much they learned from the conference. "There were more people with VHL in the room than are reported in most journal articles."

Registration - if you register by May 15, you can obtain discount rates (\$50 more after May 15) which includes lunches five days, and a special luau Wednesday night. See page 19 to register.

Family: \$150 per person for family members

Professional: \$350 for nurses, genetic counselors, and other medical professionals

Physicians: \$500 for physicians and researchers

Attendees are responsible for making their own *hotel arrangements*. The conference will be held at the Pacific Beach Hotel, where we have a special conference rate of \$108 for 1-2 people, \$123 for three, or \$138 for four people in one room. *Reservations must be made by April 15 to obtain these low rates.* Call 1-800-367-6060 to reserve rooms.

Ground transportation to and from the Honolulu airport is available by shuttle for \$7 or by taxi for \$20-25. Once in Waikiki, the local bus system is easy and fabulous. For \$1 U.S. you can go just about anywhere on the island.

At the hotel you will find numerous brochures about local sights to see.

Reserve Wednesday evening to join us for a Hawaiian Luau at Germaine's Luau in West Oahu. Bus transportation will be provided from the hotel. This exotic evening will include tropical drinks, Hawaiian food, and Polynesian entertainment.

It is wise to book your travel very soon now, to ensure a good rate. Travel Monday thru Thursday is least expensive, so add a few days and enjoy!

We will be happy to answer any questions that you may have about the meeting, so don't hesitate to call us. -- Rodney & Vanessa Belen, +1 (808) 623-3633



VHL Family Forum

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

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