



VHL Family Forum



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Managing Pancreatic Tumors

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The most common pancreatic lesions in VHL are cysts and serous cystadenomas that can be single or multiple and can be found in 35% to 75% of patients with VHL, varying by kindred.² Cysts are by far the most common, representing 70% of lesions. While these cysts and cystadenomas can interfere with the proper delivery of enzymes and hormones necessary to digestion, and while they may compress the intestine or bile ducts, they are not cancer and will not metastasize. Most cystic lesions are benign and do not cause symptoms.

The pancreas may be so filled with cysts that there is little normal pancreas tissue left. In some cases this can lead to pancreatic insufficiency, or diabetes. Solid lesions of the pancreas associated with VHL are less common and are usually neuroendocrine tumors or microcystic adenomas, which can appear solid on contrast-enhanced CT imaging. Neuroendocrine tumors are usually "nonfunctional", meaning they do not generate chemicals that can be seen in the urine or bloodstream. They are therefore difficult to find and may not be seen unless the physician is specifically looking for them.

Cysts and cystadenomas are benign; neuroendocrine tumors, however, are cancer and can metastasize, usually to the liver.

Pancreatic lesions often occur in the same families where pheochromocytomas occur. In the Jennings study,³ 13 of the 30 patients with pancreatic lesions also had pheochromocytomas. We are still reviewing the patterns of mutation in our patient population. I am hopeful that once we have completed genetic analysis, we may be able to tell from the genetic mutation who is likely to need early surgery and who does not.

While neuroendocrine tumors themselves rarely cause death, they do metastasize, and there is a growing appreciation for the consequences of leaving

them untreated. The purpose of this study was to establish diagnostic and management criteria that would minimize the risk of metastatic cancer from neuroendocrine tumors of the pancreas and maximize the preservation of pancreatic tissue in people with VHL.

From December 1988 through November 1997, 256 patients with VHL were screened at the U.S. National Institutes of Health. This study included follow-up of these patients through March 1998. During the study period a total of 30 (12%) out of 256 patients were identified with solid lesions of the pancreas. Four of these had evidence of metastatic disease at the time of diagnosis. Of the 18 whose tumor tissue was studied under a microscope, 17 were confirmed to have neuroendocrine tumors.

Tumor sizes were measured for all patients, and a comparison was made between the size of the largest primary tumor in patients with evidence of metastatic disease. In patients with liver metastases, the largest primary tumor was 3 to 8 cm. in diameter. In patients with no metastases, the primary tumor was 1 to 5 cm. No patient with a tumor less than 3 cm was found to have any evidence of metastatic disease. There was

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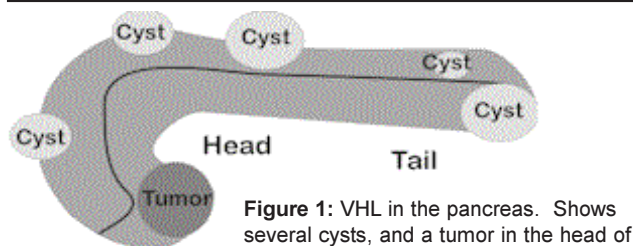


Figure 1: VHL in the pancreas. Shows several cysts, and a tumor in the head of the pancreas. Figure courtesy of Dr. Choyke.

no correlation between the number of pancreatic lesions and the presence of metastatic disease.

Given the potential for malignancy with neuroendocrine tumors and the fact that in this series of patients more than 94% of the enhancing lesions were confirmed to be neuroendocrine tumors, we have adopted a strategy of presuming that all solid enhancing lesions of the pancreas are neuroendocrine tumors until proven otherwise by careful pathologic examination. Cystic disease of the pancreas and microcystic adenomas are benign conditions. But neuroendocrine tumors of the pancreas in VHL can behave in a malignant fashion.

Solid lesions of the pancreas tend to be multiple in VHL and can occur in the head, body, or tail of the pancreas (see Figure 1). Even after resection, the remaining pancreas is at risk for development of new lesions, as is the case in other organs affected by VHL. This led us to adopt an organ-sparing strategy for the pancreas similar to the approach for managing renal tumors and adrenal tumors associated with VHL. If possible we perform an enucleation of these solid lesions, a kind of scooping out of the tumor, taking care to preserve as much normal pancreatic tissue as possible. This can be difficult in these patients, who often have many cysts at the same time. We use ultrasound imaging during the surgery, directly on the pancreas. This intraoperative ultrasound has been an important tool in these surgeries, helping to identify lesions not seen on previous imaging studies and for clearly mapping the pancreatic duct, allowing even large tumors to be safely removed.

Neuroendocrine tumors associated with VHL tend to be slow growing. In our experience, the presence of metastases appears to correlate with the size of the primary tumor. Therefore we have outlined an approach summarized in Table 1. Patients with VHL who have solid lesions of the pancreas detected on contrast-enhanced CT scans have their tumors carefully measured. Lesions less than 1 cm in size are

Back in the Swing

Well, surgery is all over and I am back in the swing of things at work and taking summer classes at school. I ended up being at NIH for about a month... my body was not very receptive to the whole idea of food. The surgery took 12 hours and they had to take out my gallbladder as well as remove the tumors. They turned out to be neuroendocrine tumors. The physicians there did a wonderful job and I felt well not long after the surgery. I was just waiting to eat real food. All is said and done and I am glad it is over. Thank you for your support during this time. It was nice to have someone who'd been there with VHL. – Sarah S., Minnesota

monitored with serial scanning performed at 12-month intervals. Tumors that are 1 to 3 cm are managed depending on location. If lesions are found to be in the head of the pancreas, they are removed when they reach approximately 2 cm in size. Because of anatomic constraints in this region and the desire to perform an enucleation rather than a resection of the head of the pancreas, we favor removal of these tumors before they reach a prohibitive size. Lesions in the body or tail of the pancreas that can be resected by removing part of the pancreas are monitored until they reach approximately 2 to 3 cm. Patients who are undergoing an abdominal exploration for the management of a different VHL-associated tumor, such as a renal lesion or a pheochromocytoma, are also evaluated for management of their pancreatic lesions.

We have attempted to establish a rational approach for the diagnosis and management of solid lesions of the pancreas. On the basis of this review of our experience with these tumors, we believe that the guidelines illustrated in Table 1 will minimize the risk of metastatic disease yet maximally preserve pancreatic function. It is our hope that by using this systematic approach we will not only gain a better understanding of the natural history of these lesions but also establish procedures that reduce the risks associated with pancreatic neuroendocrine tumors in VHL.

1. Abridged from Libutti et al, "Pancreatic neuroendocrine tumors associated with von Hippel-Lindau disease: diagnostic and management recommendations." *Surgery* (1998) 124:1153-9.
2. Neumann, HPH et al, Pancreatic lesions in the von Hippel-Lindau syndrome, *Gastroenterology* (1991) 101:465-71. Also Hough DM et al., Pancreatic lesions in von Hippel-Lindau disease: prevalence, clinical significance, and CT findings, *AJR* (1994) 162:1091-4.
3. Jennings MC et al, Abdominal manifestation of von Hippel-Lindau disease and the radiological screening protocol for an affected family. *Clin. Radiol.* (1988) 39:363-7.

Table 1: Solid pancreatic tumors in VHL: surveillance and management recommendations

Lesions ≤ 1 cm are followed every 12 months with CT, MRI

Lesions 1-3 cm: case by case assessment

Lesions >3 cm, lesions that are symptomatic or functional, lesions that are increasing in size are resected

Patients undergoing exploration for other VHL tumors are considered for resection of the pancreatic tumor

Enucleation when possible

Clinical Trials

A second anti-angiogenic drug relevant to VHL is now in Phase 2 trials and is seeking VHL volunteers.

The Novartis drug (PTK) which Dr. Kaelin is trialing in Boston (see *VHLFF* December 1998) is making good progress through Phase 1. They are doing dose escalations and expect Phase 1 to be completed by the end of 1999. A small number of people with VHL have been added to Phase 1 of the trial under compassionate exemption; more are expected to be invited into Phase 2. Novartis PTK is administered as a pill taken once a day. Volunteers who have expressed interest in this trial should hear from the team in November, or should call Sarah Alwardt to follow up.

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Another new drug from Sugen, called SU5416, has completed Phase 1 and is entering Phase 3 in colorectal and lung cancer. At the same time, Sugen is conducting phase 2 trials with VHL and other conditions. As with the Novartis drug, SU5416 is based on strategies for suppressing the signal associated with the excessive production of vascular endothelial growth factor (VEGF). It is hoped that SU5416 will inhibit the growth of new blood vessels and hemangioblastomas in patients with VHL and prevent further tumor growth.

SU5416 was featured on the television magazine *60 Minutes* in May. Reporter Ed Bradley followed several people through the Phase 1 trial. The goal of Phase 1 is to determine the toxicity level of the drug, not necessarily to achieve tumor response. All of the 100 subjects in the Phase 1 trial had very advanced cancer and were not expected to live more than one year. At the end of the year, thirty people were alive, some with stable disease and occasionally with tumor response. The worst side effects at highest doses were headaches with nausea and vomiting, which went away when the dosage was reduced. Other side effects observed were mildly painful vein irritations. One person with VHL has been taking SU5416 for only two months so far. Her eye tumor has not yet shrunk, but she is getting symptomatic relief, giving us sufficient hope to induce Sugen to write two new protocols for trying this drug with VHL in Europe and in the US.

The VHL trial in Europe will be held under one primary investigator, Professor Adrian Harris, in Oxford, UK. People who are interested should contact one of the doctors listed below.

The multicenter VHL trial in the US has just opened its first site: Dr. David Palchak, Arroyo Grande (near San Luis Obispo), California. The contact was established initially by the patient, and Sugen is willing to consider enrolling additional investigators to make the drug available more locally for qualified patients. As the process of tumor growth occurs over weeks to years, it is unlikely that long-term clinical benefit will be observed in patients after limited dosing. A patient, therefore, will be

eligible to continue to receive the drug after the completion of this Phase, as long as there is good tumor response and there are no unacceptable side effects.

The drug is administered in the doctor's office or hospital two times a week (Monday and Thursday or Tuesday and Friday). It is administered as an intravenous drip and takes about one hour.

People participating in the Sugen study of SU5416 will be required to:

- Have a VHL diagnosis verified by DNA at one time during the patient history
- Be at least 18 years old, or 16 with consent of a guardian.

- Use strong effective (barrier) contraceptives (both men and women) as this class of drugs is expected to harm a developing fetus, and because the effects on sperm exposed to the medication are unknown.

People with any of the following are not eligible for this study:

- Has absolute neutrophil count (ANC) < 1,500/mm³; platelet count < 100,000/mm³; hemoglobin < 8.0 g/dL.

- Has a significant liver function abnormality manifested by an increase in serum transaminases (AST, ALT) > 3.0 x upper limit of normal, or a total bilirubin > 2.0 mg/dL.

- Has a significant renal function abnormality (serum creatinine > 2.5 mg/dL or creatinine clearance < 40 mL/min)

- Is still recovering from a previous VHL treatment.

- Has had major surgery or another investigational drug within 2-4 weeks prior to enrollment

- Has had another anti-angiogenic therapy, or organ transplant.

- Has a known allergy to Cremophor® or Cremophor®-based drug products, corticosteroids, H1 blockers, or H2 blockers.

- Has a Karnofsky Performance Status (KPS) <60%

- Has had a heart attack or severe angina within 6 months prior to the study

- Has insulin-dependent diabetes, peripheral vascular disease, or diabetic ulcers.

- Has any other acute or chronic medical or psychiatric condition that may interfere with the interpretation of study results.

For further information on SU5416, please contact the team nearest to you:

- Dr. Adrian Harris, Med Oncology, Churchill Hospital, Headington, Oxford OX3 7LJ England, U.K. Tel: +44 (0)1865 226184; Fax: +44 (0)1865 226179; E-mail: v.berry@icrf.icnet.uk

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Spiritual Power

By Deb H, Massachusetts

In June my husband Mark and I held our first yard sale fund-raiser to benefit VHL research. Mark and I are committed to helping support the work the VHLFA does to help us live full long lives. Thanks to all the volunteers and contributors who make this work possible!

I want to just briefly recount some of what has happened to me since February 15, 1998. I was a healthy 34-year-old woman, mother of two, physical therapist, active, and leading a full life. On Feb 15 after singing at my church I went home and had a grand mal seizure. After seeing the physician and undergoing tests — a brain MRI, CT scans, ultrasounds, bone scans — my deepest fear was realized. I have the disease that my mother had. The disease is called von Hippel-Lindau, abbreviated VHL. My mother died at 37, her Mom died in her 40's, my grandfather died young. Naturally, I was scared.

The disease causes tumors to grow mostly in the brain and spinal cord, but also the kidneys, pancreas, the retinas — every place that you don't want a tumor. The scans revealed that the first thing that needed to be done was brain surgery. I had brain surgery on March 12, 1998, and kidney surgery in May.

As you can imagine, getting all these diagnoses at once was pretty hard. By the time I was finished I had eight tumors. In only a few weeks I went from thinking I was healthy to having eight tumors — it was catastrophic and I barely survived. But I recovered from those surgeries, and had another kidney surgery in October 1998. I had some catching up to do, having avoided the necessary preventive maintenance for VHL for all those years.

People ask me, and I had to ask myself, How does one go on? How do you survive something like this? It shook my image of myself, and challenged my faith as well. So I had to ask, what does God promise us? Does God promise us health and wealth? (I have to admit that I probably had thought so.) Does God promise us smooth sailing along life's oceans? That wasn't my situation! I was in trouble! So what was I going to hold on to?

I grabbed my Bible. At every CT scan, every MRI, I read my Bible. I went to the Psalms, because the Psalms gave me a voice for what I was feeling. David in the Psalms always cried out "God! Help me! Answer my prayer! Rescue me!" He gave me a voice for what I was feeling and I was able to pray through the words of the Psalms.

The Bible is full of stories of troubled times and troubled lives. But I have to tell you something: I don't like trouble! I don't want pain! Yet in spite of those fears, I found hope in God who is our steadfast help in time of trouble. "Thou hast been my high

tower, and a refuge in the day of my distress. O my strength, unto Thee will I sing praises; for God is my high tower, the God of my mercy." (*Psalms 59:17-18*)

So did God take the tumors away? No, they are still there. So what does this refuge and strength mean? Well, I started looking at it in a different way. God gives me joy in my sorrow, helps me to see the best in my situation. He helps me to be thankful for what I have. That in itself is a miracle.

I have had five surgeries since March 1998. The first surgery was brain surgery March 12, and I have to say that brain surgery was a "no brainer" — I really mean it! It was nothing! You think that brain surgery is the worst thing anybody could have. But honestly, it went well — the pain was minimal, I was in and out of the hospital in five days, no deficits whatsoever. The only problem I had was with my hair.

Right before the surgery, I was on the stretcher and getting prepared, and the brain surgeon came in and said, "Deb, we're going to shave half of your head. You might not like how that looks, so I'm going to give you 20 minutes to think about it. You can have your whole head shaved if you want. I'll come back for your answer."

I'm having brain surgery in 20 minutes, and he wants me to make a decision about my hair! So Mark and I talked, and I thought half of my head shaved might look a little punkish, and I wasn't into that, so we both talked and we agreed that I would have the whole head shaved. I thought, "I can do the Demi Moore thing — you know, *GI Jane* — I can do that!" So the surgeon came back and we told him to go ahead and shave my head.

After the surgery I woke up and there was a turban on my head. I felt around, and I felt some hair, like a tail! And I thought, "What kind of haircut did they give me in the operating room! I've got a tail!" I was out of my mind. Of course anesthesia and narcotics weren't helping! I kept thinking, "Can someone get me a pair of scissors? I have to cut off this tail. This is awful — a bald head with a tail!" The nurses assured me they could see some hair under the bandage. The surgeon had decided not to shave my head after all. He only shaved a little horseshoe on one side.

So brain surgery went well, but kidney surgery was totally different. My surgeon at Lahey clinic had also had kidney surgery himself. When I was complaining about my pain, he said to me, "Does it feel like a bull has his horn in your side and has you pressed up against the wall?" Yes," I said, "that's exactly what it feels like!" Five days after having that first kidney surgery I started to bleed internally and had to be taken back into surgery. That put me in for another seven days for a total of twelve days. Eleven of those twelve days I didn't eat anything or drink anything. It was a hard time for me. After that second surgery I felt like there were *two* horns in my side. I felt like I was never going to get out of the hospital!

When I left the hospital I weighed only 95 pounds. I couldn't eat and I was still in a lot of pain. It was difficult. But there was still joy in the midst of all that. For one thing, I got to play gin rummy with my Dad almost every afternoon. I love my Dad, and I love to play gin rummy. And I got to watch some re-runs of *Gilligan's Island* and *Happy Days* at 3 o'clock in the morning when I couldn't sleep. How much more fun can a person have!

I met some spectacular nurses that I never would have met. I had some great talks – those are precious memories for me – I was able to share my faith with some of them. I think the best thing of all was getting to know my surgeon, Dr. Libertino. He's the Chief Executive Officer (CEO) at Lahey Clinic and I'm the luckiest girl in the world, because I have the CEO of heaven and the CEO of Lahey on my case. Dr. Libertino is a very gifted man and I enjoyed his company. Spending time with people like him, being loved and cared for, showed me the silver lining in the midst of my suffering.

One bit of scripture kept coming to me during this time, a verse from *Hebrews 13:5*, that says "Never will I leave you, never will I forsake you." When this kind of thing happens to you, you really do feel lost and forsaken by God. My daughter Jessica just happened to be memorizing that verse for Pioneer Girls while I had my brain surgery. She wrote it on a piece of paper and put it on my board at the hospital so I would read it every day. In May during my hospitalization for kidney surgery Jessica was again learning this verse, this time for the Pioneer Girl mother-daughter tea. I was in the hospital and could not be there, which was very hard for me. Just before Jessica went on stage I received a phone call and I heard my daughter live, reciting her verse before the group: "Never will I leave you, never will I forsake you." I think God was trying to tell me something.

Another way that God sustains us is through the people around us. I have felt this deeply through my church. I have never before felt such support. This is why you need your friends around you. I received 3-5 cards every day for at least four months. I had meals for three weeks after each surgery. People I had never met across the country would write to me and tell me they were praying for me.

I have struggled with loneliness all my life. I was raised as an only child. My parents were divorced when I was seven, and my mother died when I was 17. I've had an emptiness in my heart for a long time. And I have to say that I haven't felt lonely for a minute since I had my diagnosis. It's unbelievable. My community of friends has just enveloped me. And I would say to you, please don't ever go through any burden without the support of your own spiritual community. I have spent twelve years of my life in churches, singing and ministering and making relationships that God turned around and gave back to me



during these trials. And there was no other way that I could have made it through all of this. So "thank you" to all of you who were part of that.

We all need this kind of support at times in our lives. Are you making yourself available? There is someone in your life who is really hurting. Maybe it's not as dramatic as my situation, but there is someone that really needs you and God is expecting you to be there for them. Sometimes people tell me that they don't know what to do when someone's ill, don't know what to say, don't know how to handle it. Well, I'll tell you a couple of things.

1) Be available. Call and check in. You can leave a message on the machine saying "I'm thinking about you today."

2) Send a card. Some people sent me a card every week.

3) Make a meal for that person

4) Offer free babysitting if they have children

5) Maybe just sit and listen.

I have had to face my own mortality in the last few months, and that's been very hard. But my faith has given me peace and given me joy. After my mother's death, when I was 17, I had a real hunger in my heart for God. I was not raised in a religious home and I didn't know how to find God. I found an old Bible. I looked up *Psalms 23*. "The Lord is my shepherd, I shall not want." I memorized it because I thought if I could have God's word close to me, then I could know God. Well, I have found Him to be everything He says He is. Hopefully I will live lots of years and raise my daughters, but I have to come to terms with the fragility of life. I am confident that He is going to be there on the other side. He is there for all of us in the storms of life with his sustaining power and his never-ending presence.

"God is our refuge and strength, a very present help in trouble. Therefore will we not fear, though the earth do change, and though the mountains be moved into the heart of the seas. . . . The Lord of Hosts is with us, the God of Jacob is our high tower." (*Psalms 46: 2,3,12*)

Complementary Therapies

By Gale Lugo, Florida

Like many of you, I also have VHL. I was diagnosed more than 23 years ago. Since then, I have had three brain surgeries (2 of which were on the brain stem), a cervical spinal cord surgery, many eye procedures, and an adrenal gland removed. Presently, I have 13 brain tumors, half a dozen throughout my spinal cord, and my pancreas and kidneys are covered with cysts. My yearly scans always showed some new activity — new tumors, more cysts, and other times these things just grew.

After my last brain surgery, I experienced swelling in the back of my head. I was told after many tests that the swelling was spinal fluid that accumulated in the muscle and not in the brain, so I was not in danger — there was no need to worry, and it would be best that we let nature run its course. Four months later I still had this swelling, which was very uncomfortable. At this time, I decided to see a doctor that dealt with nutrition and homeopathy. There was a health care practitioner in this office that I started to see routinely. I was immediately put on a detoxification program. It was a powder that I stirred into juice and drank 2 times a day. I started taking this powder during my 1994 trip to the VHL conference in Kansas City. I also did some visiting during this time. Ten days later I returned home without the fluid in the back of my head.

I continued to see Perry, the health care practitioner, to see how else I might benefit from this therapy. I was in that office every six weeks for one year until one day Perry told me he was venturing out on his own. I then asked, "could I ask you a personal question?" He said, "Sure". I then inquired, "What kind of official training have you had to do this kind of work?" His response was "Officially none although I have attended various classes." My immediate thought was, "Well, I could do this."

In 1995, I started my quest, searching the field to see what was available. The opportunities were endless. After much research, I decided on a nutrition and fitness program. I found this information to be interesting and I wanted to learn more. After additional research, I chose a degree program in Natural

Healing from the Clayton College of Natural Health. I was afraid to begin something not knowing if I would be able to finish. I did not know if I was going to survive much longer, never mind two years of studying. I weighed the pros and cons and the pros won. I then embarked on this journey in Natural Healing. There were many times that I wanted to drop out because of all the work involved, the endless projects and reports. I felt I had told too many people what I was doing to drop out gracefully — including Joyce Graff — so I continued. I graduated in 1997 with a Bachelor of Science degree in Natural Healing, focusing on herbs. I practiced what I was learning with diligence. I lost 45 pounds, spasms decreased or diminished altogether, numbness went away, and a lot of the pain I experienced subsided. My tumors even seemed to cooperate. I felt so much better. At this point I started reading whatever I could get my hands on pertaining to natural healing. I was busy making tinctures, ointments, and salves. The more I delved into natural healing, the more I wanted to learn. I did some more investigating and found a program in anatomy and physiology. I am always interested in learning more about the human body.

This is where I am today. I still continue to practice what I preach and I look at life and what it has to offer in a new way. My life is so different now; death no longer feels like one surgery away. I cannot even begin to tell you how I feel today compared to how life was 6½ years ago. Today I feel empowered. Back then I was averaging a surgery every 1.89 years. My last surgery was 6 years ago. What I am about to share with you is strictly my own observation and opinion. It does not necessarily reflect the opinion of the Family Alliance.

Our care should be two-fold; *prevention* — prevent any additional surgeries — and *improvement* — improve our present condition. The magic pill that we are all waiting for has not yet been developed. Therefore, it is up to us to take control of our health. You may say to yourself, I can't do this I don't know where to begin. My response is Yes, you can do this, and it all begins with what you have been hearing for years—eat plenty of fruits and vegetables and exercise on a regular basis. But let me explain why these things are important to your well-being. The body is remarkable. If given the right nutrients the body tries to restore homeostasis, a state of natural balance among all the organs. The body has a difficult time with items that cannot be digested. My philosophy is my body has a difficult time to begin with, so why feed it things that it cannot use? This energy is better utilized by my body's normal functions in trying to restore health. Would you put oil in your gas tank? Of course not! So why would you put a substance into your body that it



Gale answers questions in Atlanta. Photo by Fred Johnson.

cannot use? Many of you probably only put high-octane gas in your car. Why do we sometimes treat material things better than we do our own body? I feel that I am not a fanatic, but there are certain rules that I do live by and I would like to share them with you.

- Eat simple, healthy meals
- Eat plenty of fruits and vegetables
- Exercise regularly
- Eat butter rather than margarine
- Eat plenty of onions and garlic
- Drink at least 6-8 8oz glasses of water a day. Know your water. It may be necessary to purchase bottled water
- If you eat pork, do so in small quantities
- Do not smoke
- Limit alcoholic beverages
- Avoid unnecessary drugs
- Avoid processed foods as much as possible
- Avoid nitrates and sulfites. These are usually found in processed meats like ham, hot dogs, corned beef, and bologna
- Avoid products with monosodium glutamate (MSG). This can be found in many processed foods like salad dressing, soup, even barbecue potato chips, and Chinese food. Although, in many Chinese restaurants you can request no MSG, this will only eliminate it from the main dish. If they cook with MSG, it will still be in the egg rolls and soup.
- Limit caffeine intake
- Avoid fast food
- Stay away from artificial colors and flavors, as well as dye colors
- Avoid foods that have been burned
- Limit fried foods
- Read labels. Stay away from chemicals. If you can't pronounce it, don't eat it!

As many of you know, our tumors are formed by the abnormal growth of blood vessels. I have worked with various people with VHL. All of them, 100%, including myself, have problems with one or more of breathing, circulation, or blood pressure (high or low). Oxygen plays a major role in each one of these. Page 29 of the VHL Handbook states: "New research also shows that the VHL gene plays a role in a signaling system which tells the cell how much oxygen is available to it. When the VHL protein is missing, the cell believes—even if it isn't true—that it is starving for oxygen. So it puts out distress signals to the body, Help! I need more oxygen! The body responds by building more blood vessels to bring more blood to bring more oxygen."

Whether the body is starving for oxygen or not I feel it is necessary to do some form of cardiovascular training. In my opinion one of my biggest accomplishments was to become aerobically conditioned. I have had trouble breathing since I was about 12 years old from childhood asthma. I no longer have asthma, but I still find it difficult to catch my breath. I do much better now that I do some form of cardiovascular conditioning consistently. As long as I do it regularly, I am able to take that deep breath that my body desperately wants. Some cardiovascular exercises include a

stationary bicycle, treadmill, and walking at a brisk pace. Start out very slowly and increase your activity appropriately.

Another problem I have noticed in a number of people with VHL, is an improper elimination cycle. Elimination is extremely important in maintaining health. This process eliminates dead cells, bacteria, and toxins. If these toxins are not disposed of, they will accumulate in the body. If they stay there, where do you think they might go? To the weakest link. This usually means to an area where we are already having problems. Therefore it is important that this process work efficiently. Maybe you just need to add more water to your diet or look at the food-combining method.¹ Exercise will also stimulate this action.

What can I do to feel better? No one knows you better than yourself. Identify your problems: is it stress, are you in a lot of pain, or do you have trouble walking, or are you possibly depressed. For any problem first ask yourself, Why do I think this is happening? Do I have control over the situation? If yes, begin here, If no, ask why not. Then ask, Can I work around this problem? Whatever the problem is, there are many things one can do to feel better — from massage to macrobiotics, from meditation to herbology from ayurveda¹ to guided imagery. We have this illness to deal with, we will never be like we once were, but there is always room for improvement no matter what our condition is. I have compiled a list of natural therapies.¹ There are 48 complementary therapies on this list and many are useful. The information includes a synopsis of the therapy, as well as a reference if you want to learn more about any one of them. For example, if you have trouble digesting food, look at nutrition with the food-combining method. If you suffer from stress and tension, perhaps you may want to look into exercise and music therapy, or even the Alexandria Technique. If pain is a problem, look into guided imagery. It also depends how and why you are having this pain, perhaps it is because of the stress you are under. In that case there are many things you can do to relax. You might even include some chamomile herbal tea to help reduce tension.

I believe there is no single therapy, medical, complementary or otherwise, that will solve all of our problems. But a combination of many is extremely helpful.

1. Explained in Gale's list, which may be obtained from <http://www.vhl.org/nutrition>. Print copies will be sent free to paid-up members on request; non-members pay \$5 photocopy, printing, and postage.



Teamwork for Health in Atlanta

The Sixth International Patient/Provider Conference on von Hippel-Lindau was held June 4-6, 1999, in Atlanta, Georgia. One hundred fifty people attended, the largest attendance so far at a U.S. VHL conference. Speakers and attendees came from as far away as Canada, England and Germany. U.S. attendees came from the five corners of the U.S. -- Hawaii, California, Washington, Massachusetts, and Florida -- and a total of 30 states.

The meeting was co-sponsored by Emory University School of Medicine Division of Medical Genetics and the VHL Family Alliance. Dr. Louis Elsas II, Chief of Genetics, and Eva Logan, VHLFA Georgia Chapter Chairperson, co-chaired the event. The governor of Georgia declared May to be VHL Awareness Month, and the Peachtree State welcomed us with gracious Southern hospitality.

This meeting boasted a number of "firsts". It was our first meeting south of Kansas City. For the first time Emory University awarded Continuing Medical Education credits (CMEs) to attending physicians who registered with Emory's CME department. And our first magician, the Amazin' Grayson, Grayson Smith of Memphis, circulated throughout the crowd performing illusions for small groups.

The meeting began on Friday afternoon with a rousing "Howdy!" from Eva Logan, conference chairperson. Peggy Marshall and Joyce Graff, VHLFA Co-chairs, welcomed everyone, introduced the Board Members, Chapter Chairs, and 800 Line Committee, putting faces to those names and voices from the telephone and the internet. They also set the tone for the meeting. Nearly half the attendees were there for the first time. Even though they were armed with Handbooks and the glossary in the back of the handbook, there would be unfamiliar terms. They were invited to ask questions of the board members during the session, or between sessions. Everyone would have a tender moment when they would need a tissue or a hug. Everyone was encouraged to reach

out for support -- just extend a hand -- and to be ready to give it to the person next to them.

Peggy then introduced the VHL Video, "VHL - Quest for a Cure", thanking the many volunteers who participated in bringing it to reality, and dedicating it to Craig Warnick, Linda Turner, and Thea Franzini. Susan McGuire, Public Relations Director from North Carolina, reported on PR activities for the year, and introduced Jay Platt, whose inspiring Thru-hike along the Appalachian Trail led our fund-raising effort in 1998-99.

Joseph A. "Jay" Platt, retired from the US Marine Corps, gave an inspiring half-hour talk about his experiences on the Trail, and the lessons he has learned through that experience -- lessons about self-discipline, motivation, and the courage and perseverance to see a difficult task through to completion. People loved him, found him a marvelous speaker and very upbeat, dynamic and inspiring. He spoke from the heart and reinforced the challenge to be the best you can.

Joyce Graff gave a brief report on the clinical care centers, explaining our intention in setting up the program, and soliciting input from everyone: their experiences with the various centers, and their suggestions for strengthening the program.

Dr. Gladys M. Glenn introduced the work of the National Cancer Institute's Clinical Program, and discussed the learning of her team about Clinical Evaluation and Molecular Genetic Diagnosis of VHL. As usual, her talk was very instructive, both for families and for physicians. Barbara Redding of the VHLFA Information hotline led a discussion with Dr. Glenn about this work.

Patricia Foote of California shared some thoughts from her book, *How Are You?* outlining recommendations for managing your own health. Putting yourself in charge of your health and your health care team is an empowering step.

We adjourned for dinner in the Crown Room at the top of the Sheraton Colony Square Hotel, followed by two very interesting presentations. First was a panel discussion about "Coping with VHL" among Tania Durand of Canada, Kathy Braden of Indiana, David Torres of Hawaii, and Fred Johnson of New York. Kathy and Fred represented the viewpoint of the spouse, and the other two their own unique perspectives as people with VHL. Don Marshall chaired the discussion. People found it personal and pertinent.

Following the panel, Gale Lugo, the VHLFA Chapter Chair for Florida, shared her story and experiences with Complementary Therapy, supplementing her good standard medical care with healthy eating and exercise (see page 6).



Dr. Walter Rayford, Louisiana; Altheada Johnson, New York; Don Marshall, Mississippi. Photos by Fred Johnson.

Saturday morning we convened early for a panel of experts on Genetic Testing for VHL. Dr. Paul Fernhoff of Emory University did an excellent job of explaining the terminology of genetics, the different kinds of alterations in the VHL gene that can be found, and the process of sequencing the gene to locate the particular alteration in a family. People found it "awesome, fun, and understandable," especially when he used children's pop-beads to depict the series of segments of a gene, their rearrangements and truncations.

Debra Collins, genetic counselor from the University of Kansas Medical Center, discussed the issues surrounding DNA testing. More than a simple blood test, DNA testing comes with a set of social and emotional issues that take careful consideration and discussion with genetics professionals and family members. How will you feel if the answer is yes? or no? Will the answer affect family dynamics, insurability? Should you secure health and life insurance before the testing so as to avoid future issues? Do you really want to know if your small child is affected? With a condition like VHL, where testing can help to prevent serious damage, there are sound medical reasons for testing children from about age five. If the family chooses not to test children until they are older teenagers and can participate in the decision, then children must be screened as if they were known to have VHL. Dangerous complications can arise in young children, especially pheochromocytomas (pheos) and eye lesions. Damage can be avoided with early diagnosis and treatment.

Angela Trepanier expanded on the psychosocial, ethical, and legal issues involved in genetic testing. She answered a series of questions posed by callers on the VHL hotline. There followed a panel discussion among the three presenters and the audience. The panel discussion got very high marks. This was the best DNA testing presentation we have ever had at a VHL meeting, and the audience was consistently grateful for the careful planning done in conjunction with the VHL hotline team.

The Neurology panel followed. Dr. Edward H. Oldfield, Chief of Surgery at the National Institute for Neurological Disorders and Stroke, gave a talk on Brain and Spinal Hemangioblastomas, outlining the points he weighs in making a decision whether or not to operate. It is rarely a clear-cut decision. Most of the time it is a careful balancing of pros and cons, determining what course of action will produce the best outcome for the patient.

Dr. Daniel Choo of the Department of Otolaryngology (ear and throat) at Children's Hospital Medical Center in Cincinnati presented highlights of the work he has done at NIH and Cincinnati on the endolymphatic sac tumors of VHL which can cause hearing loss. He explained the screening process they devised to determine the progress of such a tumor, and the

approaches he has used to remove the tumor and save the hearing. Left untreated, these tumors lead to progressive hearing loss over time, sometimes sudden hearing loss.

Dr. Dheerendra Prasad of the University of Virginia presented his work with the Gamma Knife machine doing stereotactic radiosurgery on a variety of tumors, including hemangioblastomas. While he was very enthusiastic about the capabilities of this technology, he was also very straightforward in presenting the limitations of the technology as well. Not all tumors are good candidates for stereotactic radiosurgery. It has to be used with caution, in order to avoid secondary complications which can be at least as damaging as open surgery.

Thomas D. Rodenberg, Esq., an attorney from Kansas City, Missouri, shared his experiences in dealing with insurance companies as the family negotiator for a large VHL kindred in Missouri. He presented excellent tactics for dealing with refusals to pay. In short: never give up. If they turn it down, appeal the decision. Insurance companies often turn everything down on the first round, hoping you will give up. Keep going. Tom answered many questions during the discussion period, and we could have kept him going all afternoon, but we had a schedule to keep. Hopefully we will see more from Tom in future meetings and in the *VHL Family Forum*.

At the Annual Meeting over lunch, Maria Shipton of Pennsylvania was elected to the Board of Directors, and awarded the VHL Chapter Chairperson of the Year for her excellent work in public relations around Jay Platt's hike. Jay Platt was honored as the Volunteer of the Year for his extraordinary effort in hiking the Appalachian Trail. He was given a plaque, and an American Flag that had been flown over the Pennsylvania Statehouse in his honor, and a beautiful scrap book prepared by Susan McGuire.

Board Officers were elected by the Board at their meeting on Friday morning and announced at the Annual Meeting. Altheada Johnson continues as Chairman of the Board. Peggy Marshall continues as Chairperson of the Alliance, essentially the chief operating officer of the VHLFA. She will be assisted by Vice Chairpersons Don Marshall and Kathy Braden, secretary Melissa Minster, and treasurer Kelly Heselton.



The Amazing Grayson performed illusions at tables.

When the VHLFA was founded, the Bylaws were written to include a provision that no one person could serve more than two consecutive terms on the Board of Directors. After two consecutive terms you have to take at least one year off and then you can run again. This provision is to keep the organization from becoming too dependent upon any one individual, and to encourage the development of a number of strong leaders. Joyce Graff retired from the Board after two consecutive three-year terms on the Board, as Chairman or Co-chairman. Joyce was honored for her steadfast leadership, and given a plaque naming her Founder Emeritus of the VHL Family Alliance.

In the afternoon, Dr. Emily Chew of the National Eye Institute headed the Ophthalmology panel with a presentation on Ocular Manifestations of VHL Disease - Prevention and Treatment. Dr. Chew has now seen more eyes with VHL than any other single ophthalmologist, and has a unique perspective on treatment. Dr. Hans E. Grossniklaus of Emory University talked about his research in retinal disease, some of which was done in conjunction with Dr. Chew. The goal is always to save vision, and to save the eye.

In some circumstances, however, it is not possible to save the eye. Once the retina is gone, the eye tends to atrophy over some years, eventually becoming painful and requiring removal, or enucleation. Robert A. Thomas, an ocularist from Memphis, Tennessee, presented a series of photographs showing artificial eyes and facial and eye restorations, showing that people can look completely natural with a well-made ocular prosthesis. He explained the process, the decisions that need to be made before the eye is removed, and the work done by the ocularist after the eye socket has healed, similar in many ways to making dentures.

The Urology panel was headed by Dr. Hartmut Neumann from Albert-Ludwigs University Hospital in Freiburg, Germany. Dr. Neumann's study is the largest and longest study in Europe. He has published widely in more than six languages, and was the first to propose delaying operation on the kidney. He was followed by Dr. Walter Rayford of Louisiana State University in New Orleans. These two physicians described their work -- Dr. Neumann's in Germany and Dr. Rayford's at the NIH -- and the issues they weigh in deciding when to operate on a kidney and how long one can watch the tumor without actually taking action. The goal in all cases is to maintain normal organ function while avoiding metastatic cancer.

Dr. Berton Zbar shared his current work on inherited cancers of the kidney. While he began this work by studying VHL, he is now working on other familial forms of kidney cancer, learning additional

ways that kidney cancer can develop. It is through learning about all the inherited predisposition factors that we will truly come to understand this complex disease. The audience had many questions for these three excellent presenters.

Sunday morning we heard from two very fine speakers, Karen Lair of the Methodist mission in Atlanta, and Pastor David Torres of Hanapepe Baptist Church in Kauai, Hawaii. David is a member of the Board and chairs the Dialysis and Transplant committee. Their presentations were warm and inspirational, showing that spirituality is an important aspect of coping with disease.

Dr. Steven K. Libutti of the National Institutes of Health headed the Endocrinology panel with a talk on Pancreatic Lesions in VHL. The pancreatic lesions have been poorly understood, leading some physicians to overtreat and others to undertreat. Dr. Libutti showed that there are no pancreatic tumors in VHL that produce chemical tracers that can be seen in the urine. That would be too easy. Instead, we have to rely on imaging and on knowledge derived from studying many pancreatic tumors over the years to determine which tumors can be watched, and which ones require immediate removal. Over the years at the NIH they have come to apply the 3-centimeter rule from kidney tumors also to most tumors in the pancreas. If the tumor is in the head of the pancreas, they watch tumors only to a size of 2 cm. and then remove them. If they are symptomatic or if they are growing at a particularly fast rate then they move more quickly to remove the tumors. Cysts do not require removal, but many large cysts can cause discomfort which sometimes requires drainage. (See article, page 1.)

Dr. McClellan Walther, a "son of the South" from Atlanta, Chief of the Neurodynamics Laboratory at the National Institutes of Health, spoke about pheos in VHL. Pheos can grow anywhere along a line from the base of the skull to the bladder, along the sympathetic nervous system. Very few (1.6%) metastasize in VHL, but all pheos can be dangerous because of their effect on the cardiovascular system. They have developed a new test of "free metanephrines" which is reported in a new article, now in press. It is a biochemical test which is much more sensitive and reliable, and easier to administer than a 24-hour urine collection. 75% of the pheo patients in his series had missense mutations, and all those with extra-adrenal pheos (pheos occurring outside the adrenal glands) had missense mutations.

Dr. Nutzet O. Atuk, Emeritus Professor from the University of Virginia, described his work studying a large kindred over the course of 30 years. Altogether he studied 97 cases of VHL in 4 generations in this one family, and followed closely 64 patients. Pheos occur frequently in this family, and renal cell carcinoma is rare. Our three speakers answered many important questions from the audience.



Lois Erickson and Vicki Couch, genetic counselor from Mayo, key planners of next year's meeting. See page 16 for details.

The last segment of the day was on Research: Hope for the Future. We brought five research scientists to report to the group, three of whom have received funding from the VHL Family Alliance to support their work. The biochemical study of the VHL gene and the VHL protein have become so highly technical that it is sometimes hard for anyone who is not a research geneticist to understand what they are saying. Next year at the International Symposium in July at the Mayo Clinic we will be focusing on having one research session designed for the lay person.

- Biology of the VHL Gene Product, Professor Robert D. Burk, M.D., Albert Einstein College of Medicine, New York
- Functional Analysis of the VHL Tumor Suppressor, James Gnarra, Ph.D., Louisiana State University, New Orleans, Louisiana
- Evidence for a Stepwise Progression Model for VHL Tumorigenesis, Steven T. Lott, Ph.D., M. D. Anderson Cancer Research Center, Houston, Texas
- Clinical Anti-angiogenesis Research, Jeffrey Humphrey, M.D., Bristol Meyers Squibb, Connecticut
- Functions of the VHL Tumor Suppressor Protein, Othon Iliopoulos, M.D., Dana Farber Cancer Research Center, Boston, Massachusetts

It was explained that the VHL gene functions as a tumor suppressor gene. The VHL gene is a recipe for the VHL protein (pVHL). When the normal VHL protein is present in the cell, cell division starts and stops as designed and all goes well. When the VHL protein is missing, cell growth can go out of control. We do not yet understand all the mechanisms that go on, but these researchers and others have identified a number of associations or bindings that pVHL makes. When pVHL is missing, those associations are not made and a number of normal processes don't work. One result is the over-production of Vascular Endothelial Growth Factor (VEGF), which is implicated in the growth of new blood vessels, resulting in a hemangioma in VHL, or in blood supply to a number of other kinds of tumors in other conditions.

The key take-away message was that there is progress in understanding the function of the normal VHL protein in the cell. Once we understand what it is doing, it is easier to talk about ways to restore normal function. For example, let's say that your car doesn't work, and the only tool you have available to fix it is a paper clip. Can you fix the car? The answer is "maybe," but we will have to know a lot about what is wrong with the car, and about how a car works, in order to know how to bend the paper clip and where to put it so that it will fix the problem.

Dr. Humphrey talked about a drug going into clinical trials soon. Dr. William Kaelin in Boston and Dr. Adrian Harris in Oxford are beginning VHL trials of two anti-angiogenic drugs, one from Novartis and one from Sugen, testing them specifically for their effectiveness in treating VHL (see page 3). How soon will a drug come to market? Probably another four years. But trials are now under way, which is much closer than we have ever been before. Scientists are working on strategies to emulate the function of VHL; to go around the VHL function and control the levels of VEGF directly; and to perform gene therapy on the VHL gene itself.

It should be noted that both Dr. Walther and Dr. Gnarra mentioned that there is now clear evidence that kidney tumors grow faster in people who smoke. People with VHL should avoid smoking, both primary and secondary.

Peggy Marshall and Joyce Graff led the final audience discussion and meeting summary and thanked everyone. Comments from the audience were quite positive, even with their difficulties with the research segment. "This is the first conference I have attended. It was extremely informative, well run and doctors were extremely generous in answering questions after their speeches." "The conference has given me the opportunity to meet and make new friends who are going through the same problems with VHL." "We were very impressed and grateful for all the information we can take back with us." Best of all, one attendee said, "The VHL Family Alliance made me feel welcomed and loved." "Thank you for all the work you have done to help me feel better about my future."

"Great work, wonderful information, great fellowship."

Special thanks to Peggy and Don Marshall who organized the agenda, to Eva Logan who worked with the hotel and made all the local arrangements for us, to Kim Torando at Emory University for organizing the badges, handouts, and CME details, to the volunteers who staffed the registration and service tables in the hallway so that the rest of us could attend the meetings, to Chris Logan and Andy Braden for their support of audio, lighting, and logistics, and to the Amazin' Grayson for his light-hearted interludes of illusion. **Next year in Rochester!** (See page 16.)

No Better Time

-- Anonymous

We convince ourselves that life will be better after we get married, have a baby, then another. Then we are frustrated that the kids aren't old enough and we'll be more content when they are. After that we're frustrated that we have teenagers to deal with. We will certainly be happy when they are out of that stage. We tell ourselves that our life will be complete when our spouse gets his or her act together, when we get a nicer car, are able to go on a nice vacation, when we retire. The truth is, there's no better time to be happy than right now. *If not now, when?*

Your life will always be filled with challenges. It's best to admit this to yourself and decide to be happy anyway. One of my favorite quotes comes from Alfred D Souza. He said, "For a long time it had seemed to me that life was about to begin -- real life. But there was always some obstacle in the way, something to be gotten through first, some unfinished business, time still to be served, a debt to be paid. Then life would begin. At last it dawned on me that these obstacles *were* my life."

This perspective has helped me to see that there is no way to happiness. Happiness is the way. So, treasure every moment that you have. And treasure it more because you shared it with someone special, special enough to spend your time...and remember that time waits for no one. So stop waiting until you finish school, until you go back to school, until you lose ten pounds, until you gain ten pounds, until you have kids, until your kids leave the house, until you start work, until you retire, until you get married, until you get divorced, or until your spouse becomes the person you think he or she ought to be, until Friday night, until Sunday morning, until you get a new car or home, until your car or home is paid off, until spring, until summer, until fall, until winter, until you are off welfare, until the first or fifteenth, until your song comes on the radio, until you've had a drink, until you've sobered up, until you die, until you are born again to decide that there is no better time than right now to be happy.

I want to *thank you for all* you have done to help us understand VHL and the *opportunity* to be in Atlanta!! My daughter and I had such an *informative time!!* I have had VHL since 1962 *but* -- as everyone else -- *thought* we were the *only family* that had it!! It's so good to know we have this whole *other family!!*

-- Bonnie S., Minnesota

Mary and I had a great time at the Atlanta meetings! Outside of our family this was the first time in 43 years that we have ever met anyone else with VHL. This was a real great experience for us!

-- Todd and Mary G., New York

Resources

Job Accommodation Network (US, Canada). Advice in situations where people are in difficulty in doing their jobs or are coming under undue pressure from an employer. They will assist the worker and employer in making accommodations in the work environment that will allow the worker to continue the job, and will help achieve a balance between compassion and business need. If needed, they can assist in filing a complaint with the Equal Employment Opportunity Commission. Their website has a list of important links to other resources on the internet. Job Accommodation Network, West Virginia University, P.O. Box 6080, Morgantown, West Virginia. 1-800-232-9675 or 1-800-526-7243; <http://janweb.icdi.wvu.edu>, select "points of interest." Assistance in English or French.

Disability Rights Commission (UK). The DRC has been set up in England to enforce the Disability Discrimination Act of 1995, intended to protect workers from discrimination in recruitment, terms of employment, and opportunities for promotion, training, and other benefits, as well as protection from dismissal. DDA Information Line 0345 622 633 (local rate in the U.K.), TDD 0345 622 644. DDA Information, FREEPOST MIDO2164, Stratford-upon-Avon CV37 9BR. <http://www.disability.gov.uk/>

Protection and Advocacy (US). A U.S. federally mandated system in each state and territory which provides protection of the rights of persons with disabilities through legally based advocacy. NAPAS agencies will investigate problems, provide information and guidance, provide legal counsel and litigation services to eligible persons, and provide education and training for advisory councils and volunteers. The National Association of Protection and Advocacy Systems, 900 Second Street, NE., Suite 211, Washington, DC 20002. Tel: +1 202 408-9514; Fax: +1 (202) 408-9520; E-mail: NAPAS@earthlink.net. <http://www.protectionandadvocacy.com>

Through the Looking Glass (US), TLG provides direct service, information and referral, concerning adaptive equipment for parents with physical disabilities and their babies; training; support groups in the Bay Area; advocacy in custody cases. TLG's staff includes psychologists, social workers, marriage, child, and family therapists, special educators, childbirth educators, occupational therapists, physical therapists, speech and language therapists, and researchers. Nearly 80% of the staff are disabled, parents of disabled children, or members of families with disabilities. National Resource Center for Parents with Disabilities, 2198 Sixth Street, #100, Berkeley, California, 94710-2204. +1 (510) 848-1112 or 1-800-644-2666; Fax: +1 (510) 848-4445; E-mail: TLG@lookingglass.org; <http://www.lookingglass.org>

New Ultrasound Software

The leading manufacturers of ultrasound equipment have announced advances in ultrasound imaging called Harmonic Imaging and Contrast Ultrasound. This advanced ultrasound technique gives clinicians a new tool for evaluating cancer and determining the health of vital organs. This new contrast software enhances blood flow details in the body's tiniest capillaries.

"Used with ultrasound contrast agents, Siemens patented Ensemble™ Contrast Imaging technology may open up new doors for diagnostic and therapeutic use of ultrasound in medicine," said Markus Kirchgeorg, M.D., vice president of worldwide marketing for Siemens Medical Systems, Inc., Ultrasound Group.

Ultrasound contrast agents are tiny, highly reflective, gas-filled microbubbles which, once injected into the blood stream, can travel into even the smallest capillaries. When exposed to an ultrasound beam, these agents return signals that are thousands of times more reflective than blood.

The innovation may offer clinicians a new, less-invasive method for evaluating tumor characteristics. VHL hemangioblastomas grow their own recognizable networks of blood vessels. In healthy tissue, blood vessel networks are tree-like networks, where large vessels branch into smaller ones at every bifurcation. VHL lesions and various malignant tumors develop more complex and less predictable vascular networks, featuring greater numbers of small capillaries. The ability to review these networks at the capillary level may help clinicians assess tumors and, ultimately, may offer clues to the tumor's aggressiveness.

Ultrasound contrast can also be used to detect a lack of blood flow in organs, such as the kidneys and the heart, and in transplants, providing clinicians an early warning of poor organ health. It may also be used to evaluate the type of tumor in many other organs, evaluating the vascularization around the tumor.

Ultrasound contrast agents are administered through a simple intravenous line and the microbubbles dissolve harmlessly within the body, typically within a few minutes.

In response to our request for comment on its relevance to VHL, Dr. Peter Choyke, at the National Cancer Institute said, "This is a very interesting area of development for Ultrasound technology. A number of manufacturers of ultrasound equipment offer harmonic imaging which accentuates the effect of the ultrasound contrast agent. Unfortunately, the Food and Drug Administration (FDA) has not yet approved ultrasound contrast agents for general use in the United States so availability outside of research centers is limited.

When it does become widely available it might permit

some people with VHL to be screened by ultrasound alone. We are especially interested in it for intraoperative ultrasound where lesions can be difficult to see. I am following this area with great interest. However, one of the major limitations of ultrasound remains that it is highly dependent on who is doing it and the specific anatomy of an individual. For instance, it won't be possible to examine most hemangioblastomas because the surrounding bone will block the sound waves. Nonetheless, I think it could be a huge development for the worldwide market where CTs and MRIs are less common."

Harmonic Ultrasound software is available from Siemens, Philips ATL Ultrasound, Hewlett-Packard Ultrasound, and others. <http://www.aium.org/News%20Releases/3dharmonic.htm>

Ask the Experts

Question: We have a long history of VHL in our family. Although we have known of the disease since 1969, when it was first diagnosed in my sister-in-law, we still don't know how VHL can be recognized in our children without going for all these numerous scans and un-ending sonar screenings. As far as I know, no genetic tests are being done in the Republic of South Africa. How can we get someone in RSA interested in starting such tests? — Dorie V., Republic of South Africa

Answer: You can inquire of various genetic testing labs in RSA, or you can deal with an experienced VHL testing lab. Unless a center has a number of requests for VHL testing, they are unlikely to want to go to the expense of obtaining the markers that improve the accuracy of testing.

The blood samples do not require refrigeration, but would need to be shipped via a courier service (like DHL) in a special biohazard container, and would need to be delivered within 5-7 days of being drawn. Blood samples coming into the USA require an accompanying letter that the blood has been tested and is negative for infectious diseases, i.e. AIDS. Samples often get held up at the border and then when they finally arrive are not usable for testing.

For samples from outside the country I generally recommend sending only the DNA because there are no problems with customs. It is usually possible to arrange for the DNA to be extracted at a genetics lab in the originating country, and the DNA alone can then be sent via regular mail.

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In Honor Of . . .

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Family Reunion

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In Memory Of . . .

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Homework Machines Available

Canon Corporation gave us a number of word processing machines for the chapters, and we have some left over. One of these nice little word processors can be yours for a donation to VHLFA. They are great for writing and printing letters, reports, and addressing envelopes. *They will not connect to the internet.* There are two models:

The *StarWriter Jet 300* looks very much like a type-writer. Includes clip art and printer.

The *StarWriter JET 4000* has a 14" screen, clip art, dictionary, thesaurus, and printer. It will write files to a 3 1/2" disk that will load to a PC. They cannot be modified to work with the internet, so they are not the most modern equipment, but they are very serviceable in the right setting. Send your donation below, or call 617-277-5667 for more information.

Calendar Winners Announced!

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Congratulations to all the winners!

Be sure to order your calendars early! This is a limited run, so if we don't get large orders early, we could run short. We are willing to work with you on pricing for large orders as long as we know about them before the printing is done, about October 10.

See below for ordering information, or call 617-277-5667 for bulk pricing.

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Please check one: I am a ☐ Person with VHL ☐ VHL Family Member ☐ Supporting Friend
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VHL Symposium 2000 Chapter News

The Fourth Biennial VHL Symposium will be held at the Mayo Clinic in Rochester, Minnesota, co-sponsored by the Mayo Clinic. This will be the first VHL Symposium held in the Continental United States. Anyone intending to submit a paper for this meeting should contact VHLFA immediately at joyceg@pipeline.com or erickson9532@yahoo.com or via fax to +1-617-734-8233.

**July 20-23, 2000, Thursday - Sunday
Phillips Hall, Mayo Clinic, Rochester, Minn.**

Speakers already confirmed include Dr. Marston Linehan, of the U.S. National Cancer Institute; Dr. Harmut P.H. Neumann of Freiburg, Germany; Drs. Bruce Pollock and Corey Raffel of the Mayo Clinic; Dr. Stéphane Richard of Paris, France; Thomas Rodenberg, Esq., of Kansas City; Dr. Catherine Stolle of the University of Pennsylvania. This is a chance for the world leaders in VHL care and research to share ideas. It is an incomparable opportunity for local health care teams to gain knowledge about VHL. A Family Track includes sessions for families.

Blocks of rooms have been reserved at the Kahler Grand Hotel and the Rochester Marriott.

The conference will be co-chaired by Dr. Virginia Michels, Chairman of the Department of Medical Genetics, Mayo Clinic, and Kelly Heselton, Treasurer of the VHL Family Alliance. Continuing Medical Education (CME) credits will be awarded by the Mayo Clinic to specially registered attendees for the sessions they attend.

Patients are asked to help extend the invitation to members of their own health care teams, to encourage as broad participation as possible in this important event.

Three new U.S. chapters were formed this quarter:
- Terry & Rick Murphy, Co-chairs of the **Tennessee** Chapter

- Sue Buckner, Chapter Chair, **South Dakota**

- Michelle Sanchez joins Cindy Boyd as Co-Chair of the **Texas** Chapter

Myriam Gorospe, who does Spanish language communications for us, reports a great deal of activity recently. One family called from **Spain** looking for a second opinion on spinal cord surgery. Another family called from **Mexico** looking for assistance with genetic testing. It looks like a chapter is forming in Spain, with ties to Dr. Richard in Paris for expertise on VHL.

Erika Trutmann is acting as a contact person for **Switzerland** and helping the German group with German language support.

Canada is now an official Canadian Charity and can provide tax receipts acceptable to Revenue Canada. They are helping to expand our French language services on the internet, and will be distributing a bilingual newsletter at least once a year. Many thanks to Tania Durand for making this happen!

Gale Lugo and Joyce Graff have now hosted ten **internet chat** sessions, working to find the timeslots and technology that suit the majority of participants. Erika from Switzerland and a doctor from India participated in recent sessions. Write to info@vhl.org or 1-800-767-4VHL or your local affiliate for more information.

The VHL **Message Boards** at Dr. Koop's are seeing quite a bit of activity. Join in the conversation there, or send your personal questions to info@vhl.org or postal mail. We are always glad to hear from you!

VHL Family Forum

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