VHL FAMILY FORUM

Family, Friends, Physicians, & Researchers dedicated to improving diagnosis, treatment, and quality of life for people affected by von Hippel-Lindau.

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Emergency! Are You Prepared?

A patient's perspective

by Bob R., Ohio

My daughter Becky was sharing a ride back to college. When exiting the main highway and taking the off ramp, which was icy, they hit a large light pole. Police, ambulance and a tow truck arrived and took them off to the hospital to be sure everyone was okay. This all seems pretty normal for most people. However, my daughter is not "most people"—she has VHL.

Photo courtesy of National Institute of Health

Becky said she felt OK, but her neck was a little sore or stiff. To be on the safe side, they ordered a scan. Up until now, she was not overly concerned about any injuries. A random scan for someone with VHL can become an alarming thing for medical providers who are not familiar with you or VHL.

When they got the results of the scan, they admitted her to the hospital and called a neurologist and neurosurgeon. They told her that they had discovered something on her spine and brain stem that might have been a result of the accident, and advised her to call her parents.

Now at this point, Becky herself became concerned—maybe she did receive a more serious injury than first thought! I received a telephone call from a very concerned daughter about possible severe injuries resulting from a car accident. She asked if my wife and I could come. Obviously, we said that we would be there as soon as possible, but the 150 mile drive would take a little while. I asked if the doctor was available to speak to me.

The Emergency Room doctor came to the telephone and expressed his concern about the possible injuries to both my daughter's spinal cord and brain stem because of spots that showed up on the scans.

You can imagine my relief knowing that I had in my house previous copies of MRIs and radiology reports that would show these areas with the spots already there. The doctor was extremely helpful and appreciative of the information that I had. He agreed to wait until we arrived with the copies of the reports and scans before anything further was done.

When we arrived at the hospital, it was very obvious that the doctor, my daughter, and everyone involved were much more relaxed. After reading the reports and viewing the scans, they released her from the hospital and told her to follow up with her regular doctor if there was any change in her condition.

If I never need this level of medical information for myself or my family again, this one experience has shown me how important it can be.

In an accident, there is always the possibility that the injured may not be able to communicate with anyone. We really do need, at the minimum, the ability to alert medical personnel when someone has VHL.

Inside this issue!

A physician's perspective

John G. Wallace, Jr., M.D.
Fellow, American College of Emergency Physicians
Diplomate, American Board of Internal Medicine

Can one prepare for a medical emergency? or is preparing for the unexpected impossible? Is it possible to help your treating physicians better understand your illness and presenting symptoms?

As an Emergency Physician, I see many patients with a significant medical history who arrive in the Emergency Room unprepared to ensure that their caregiver, who may be seeing them for the first time, is properly informed regarding the particulars of their case. Most egregiously, sometimes they don't know their medications either, stating "it's the little blue pill" or in response to questions about medical history state: "You have my medical history" or "Can't you call my Doctor? He has all my records". Caregivers make every effort to obtain the information that some patients are unable to convey, but it is possible to eliminate the unknown and the medical errors that can stem from the unknown when patients present with a typed and orderly version of the following:

- cogent medical history and germane surgeries
- (unrelated surgeries can be listed separately)
- exact list of medicines and recent treatments
- medical allergies
- names and contact info of regular caregivers and specialists
- recent lab test results, if germane
- copies of the written radiology reports, or the discs/films themselves
- if cardiac history, a copy of an EKG, echocardiogram or catheterization report.

The premium in value goes up for presenting this information if the pre-existing illness is rare and one normally seen only at referral centers, or if the patient is being seen in a facility where they are have had no prior visits. In the event that the patient presents with an altered mental state from a medical condition or injury, having a medic alert bracelet or emergency contact info contained in a cellphone (ICE) to provide this information would be most helpful.

Yes, by being proactive, you can prepare for the unexpected healthcare encounter and help caregivers provide you the best care possible for your presenting symptoms and illness. By way of example, please read the attached medical visit history and medical resume (see page 4).

Communicating with First Responders

by Joyce Graff, Editor

According to the Centers for Disease Control, accidents are the fifth leading cause of death in the United States. While it is easy for people with VHL to focus their attention on that condition, we should not forget the other events that may occur in our lives.

I spoke with Rod Brouhard on the *Powerful Patient* about the special needs for people with rare diseases to communicate with first responders and Emergency Rooms. Rod is the Guide to First Aid at about.com, which is owned by the *New York Times*. He is a full-time paramedic, serving on an ambulance in Northern California. He writes a column for about.com, and articles for a number of magazines.*

In that interview, Rod helps us understand what information is really needed by an emergency worker in the field, where they are likely to look, and how to connect emergency workers and Emergency Room personnel with the key information from your medical history. Medical alert bracelets are still the most widely recognized device you can carry with you. There are techniques for using that bracelet to refer to more information when you reach the Emergency Room.

The easiest thing for all of us to implement is to define a telephone number in our phone named ICE (for In Case of Emergency). Emergency workers are trained to check for this. If there is room to write additional information in this entry, list the name of the person they need to call, and the most essential bits of emergency information. Some phones have security locks which would make that info unavailable. If so, carry a wallet card.

Rod advises working with your doctor to compile a one-page "history and physical assessment" to be passed to another medical professional. This is the normal quick handoff information that doctors routinely pass to one another, so it will make sense to your physician to compile such a document with two possible scenarios in mind:

- What kinds of predictable crises might occur as a result of my medical condition? Is there anything about my condition that might cause me to lose consciousness? (e.g., lack of adrenal glands, low insulin production, or other pancreatic dysfunction)

*See http://firstaid.about.com/. Joyce's interview with Rod can be found at http://powerfulpatient.org/emergency.

- If I were in an accident, what is the most important information that the ambulance personnel should know about my medical condition?

For example, some first aid practices must be modified for patients with chronic medical conditions. Medications, blood clotting disorders, decreased pain tolerance, and chronic dehydration all complicate attempts to render first aid to those with chronic illness. Drugs you are taking might interact badly with emergency meds; allergy information might be critical.

Think of it this way: if you are unconscious or unable to speak up yourself, what would you need to communicate to make sure you are treated correctly?

Work with your doctor to compile a one-page "history and physical assessment" to be passed to another medical professional

There are a number of high-tech solutions being marketed these days, some of which are listed at the end of this article. Not all ambulances have a way to read a USB drive. The first line of defense is a wallet card with the most essential bits of information—allergies, diabetes, medications, lack of adrenals or one or both kidneys. Similarly, this information might be posted on your refrigerator or in the medicine cabinet, two places that ambulance personnel are trained to look if they are called to your home. If you have an issue that might cause you to lose consciousness, a bracelet or other wearable item might be a good idea. These might refer people to a service, device, or file of information that would provide additional information needed by the hospital.

This would give you an opportunity to provide additional important information such as:

- Whom to notify
- Living Will or Advance Directive
- Health Care Proxy
- Authorization to treat a minor
- Organ donation wishes
- Copies of recent scans and/or radiology reports showing your latest health status, so that the hospital can compare them with your status following the incident.

In some accidents or disasters, there is a risk that anything you are carrying with you might be lost or damaged. For example, in hurricane, flood or fire, a USB drive might be made unusable. For this reason, a backup system that houses data on the internet might be the safest place to keep your records. A bracelet or wallet card might lead emergency personnel to that repository.

Where you live and where you are likely to travel may also influence the way you house this information and the service you choose. There are programs specially designed for runners, for children with autism, or for adults with Alzheimer's or other dementia. There are fewer services that operate in multiple countries.

And as Bob learned following Becky's experience (see page 1), having the latest set of scans and radiology reports available can assist emergency personnel in evaluating your scans following an accident. In addition to seeing what you look like AFTER the incident, emergency personnel can then have a picture of what you looked like BEFORE, and understand what "normal" looks like for you.

Here are some resources you may like to consider for keeping your medical information on file in the event of an emergency:

MedicAlert Foundation—founded 1956, has branches in many countries including Canada, the UK, Australia, and South Africa. They sell medical ID jewelry including bracelets, necklaces, dogtags, children's wristbands, watches, shoe tags, etc. MedicAlert Membership, for adults 18 and above, allows you to manage your own emergency medical information record (EMIR℠). The live 24/7 MedicAlert emergency response center transmits medical information to emergency responders and will speak for you when you cannot—anywhere, in over 140 languages. Their "gold" service allows for storage of documents via fax, and even the scans themselves. http://www.medicalert.org or 888-633-4298.

EmergenTAG—a USB drive you can wear on a chain or keep in your pocket or purse. It has an installed program that allows you to enter your medical information. Nothing is stored on any computer, so you can fill in the form even on a public computer and it will not be stored there. The information is not stored on the internet. http://emergentag.com, 888-660-6367.

Road ID—a wristband designed for runners, with seven lines for custom engraving. http://www.roadid.com or 800-345-6336 or +1-859-341-1102. Road ID interactive is an optional associated service. You build a fully updateable, secure Emergency Response Profile (ERP) that is available to first responders via telephone and internet. You can also personalize the first 2 lines of text on the bracelet; the remaining lines and a secure code on the back of the bracelet guide responders to the ERP. http://www.roadid.com or 800-345-6336 or +1-859-341-1102.

Sample Medical Resume

Ryan Bloggs

14 Spring View Way
Anytown, MD 20755 USA
Home: (555) 685-8650 Day: (555) 379-8995
Cell: (555) 549-6568

Medical History

September 1985, Age 10 (Dr. Allan Pierce, University Hospital)
Right Adrenalectomy; pheochromocytoma

August 1996, Age 21 (Dr. Steven Johnson, Central Eye Assoc.)
Cryotherapy, right eye; retinal angioma

September 1996, Age 22 (Dr. Charles Evans, University Hospital)
Genetic Evaluation; testing done at University of Pennsylvania

Results:

G to A mutation on nucleotide 685 of the von Hippel-Lindau gene; VHL Type 2, (VHL with pheocromocytoma)

January 23, 1997, Age 22 (Dr. Mark S. Blum)
Repair of retinal detachment, right eye

Used liquid perfluorochemical and scleral buckle with laser

May 1997, Age 22 (Dr. Mark S. Blum)
Removal of epiretinal membrane, removal of posterior subcapsular cataract, implantation of artificial lens, right eye

Lens Information: Alcon Laboratories, Inc.
Model: LX90BD
Power: 20.5
Length (dT): 12.0mm

April 1998, Age 23 (Drs. Allan Pierce and Raymond Feldman, University Hospital)
Left adrenalectomy; pheochromocytoma

June 1998, Age 23 (Drs. Allan Pierce and Arnold Baron, University Hospital)
Right partial nephrectomy; renal cell carcinoma, removed with clear margins

April 1999, Age 24 (Dr. Mark S. Blum)
Focal treatment, right eye; retinal angioma at about the 11:00 position

July 2001, Age 26 (Drs. Robert Ostroff, Allan Pierce, and Ari Baron, University Hospital)
Partial hepatectomy; benign tumor on liver

Current Physician Contact List:

Sallie Adams, M.D.
Sylvan Medical Group – Endocrinology
455 Main Street
Anytown, MD 20755 USA
T: 555-665-3700; F: 555-665-8232

Sunil Patha, M.D.
Sylvan Medical Group – Medical Oncology
455 Main Street
Anytown, MD 20755 USA
T: 555-665-3300; F: 555-665-3733

Joel Pearlman, M.D.
Vitreoretinal Associates
634 Main Street
Anytown, MD 20755 USA
T: 555-454-4861; F: 555-454-3603

Past Physician Contact List:

Robert Ostroff, M.D.
University Hospital – Liver Disease Management
19 Main Street
Anytown, MD 20755 USA

Raymond Feldman, M.D.
University Hospital – Pediatric and Adult Urology
719 Main Street
Anytown, MD 20755 USA
T: 555-775-9690; F: 555-775-9695

Mark S. Blum, M.D.
Vitreoretinal Associates
634 Main Street
Anytown, MD 20755 USA
T: 555-454-0231; F: 555-454-6385

Diagnoses:

Von Hippel-Lindau disease, Type 2 (with pheocromocytoma); Addison's disease

Medication:

Hydrocortisone: 15 mg morning; 5 mg evening
Florinef: 1 mg every other day

Regular checkups (films available):

- Annual physical exam and neurological assessment
- Annual eye/retinal examination with indirect opthalmoscope by opthalmologist specializing in diseases of the retina
- Annual CT of chest and abdomen (with and without contrast)
- Annual MRI of head, chest, spine and abdomen (with and without contrast)
- Every six months: Screening for epinephrine levels, norepinephrine and catecholamines via 24-hour urine collection

Having Healthy Babies

by Joyce Graff, Editors

The drive to reproduce and have children is built into everyone. Nearly everyone wants to have children and given a choice, we would like to have healthy children. Those of us affected by VHL would prefer to have children with two healthy copies of the VHL gene.

Even in this modern age, with all the technology available to us, the first thing to remember is that baby-making is never entirely under our control. We can try our best, but there is still some room for chance to happen. In fact, there are so many things that have to happen right that it's a miracle there are any healthy babies!

VHL is of course not the only concern, but for us it is a big one. Each parent contributes half of his or her genetic material to the baby—one copy from each pair of genes. Each egg or sperm contains one copy of each of 22 chromosomes in the parent's body and one copy of the sex chromosome. Mothers provide an X chromosome while fathers provide either an X (for a girl) or a Y (for a boy). Thus, even though Henry VIII blamed his many wives for not producing a healthy boy, it is actually the father who determines the sex of the child. That alone is a good example of how little control we have over the genetic makeup of our children.

We should say at the outset that more than half of all pregnancies are unplanned, and many of us had children before any of the genetic testing was available. Every person has an important role in the world and in the lives of those around them, and we welcome every child into the world. Each of us is made up of a random combination of genes and a wealth of experiences, hopes, dreams and choices that make us who we are. Genetics is only one element in the total human being. While it is important, it is not the sole defining factor in who we are.

We have little control over what genes we pass to our children. The most important things we can give them—which are certainly under our control—are love, a firm sense of self-confidence, and the skills to live a happy and successful life.

That said, people often ask: is there any way to make sure that our baby will not have VHL?

At this time, there is no way to inspect the egg or sperm before conception to determine whether this egg or sperm has the perfectly formed VHL gene or the altered gene from the affected parent. The work needed to do that inspection destroys the egg or sperm. There are ways to inspect the embryo after conception but before birth, and to give the parents the choice whether or not to proceed. We leave it to the parents in question to decide what course of action is right for them. We should emphasize here that the parents of this child—the people who will bring this child into the world and make a commitment to raise this child in a loving and nurturing environment—those are the only two votes that count on this matter. Even the grandparents may express their opinion, but they do not get to vote. The doctors too can provide data to assist in the decision-making, but they do not get to vote.

At some point, we have to accept the chance we all take in accepting responsibility for this child. The only real choice we have is to accept this package or not. We can make every effort to have a child with two healthy copies of the VHL gene, and we may still have a child with autism, or another serious genetic condition; or a perfectly healthy child might still have a terrible accident. Babies don't come with warranties. We get to love them and care for them, no matter what.

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There are special cautions for women with VHL. Be sure to read the Handbook section on pregnancy and to have a thorough check-up to make sure that you and your doctors are aware of any special health concerns. vhl.org/handbook.

People with VHL have babies in one of several ways:

1. The old-fashioned way, either by chance or by choice
2. Prenatal genetic diagnosis, using CVS or amniocentesis
3. Pre-implantation genetic diagnosis (PGD).

Once a conception has occurred and an embryo is implanted in the womb, the choices are to proceed or not. CVS or amniocentesis can provide information to assist you in making this decision. Couples sometimes choose prenatal diagnosis simply in order to prepare themselves, in the same way that they may choose to know the sex of the child before birth.

A genetic counselor can have a conversation with you about your own particular health issues, risk factors in your family and your partner's family (more than VHL), and any other questions or considerations you may have. We strongly encourage you to visit a genetic counselor, assemble health and family history information, and make the decision that is right for you in the context of your own ethics and beliefs.

The personal stories shared here will give you a glimpse into the situations others have faced and the choices they have made. These build upon another group of stories we assembled a dozen years ago, before PGD was an option. Please read that series as well to get a more complete picture of the choices people have made to have children in their lives. http://www.vhl.org/newsletter/vhl1998/98aachld.php

Happiness is a choice. Life happens, no matter what plans we make. We wish you a happy family.

Our Experience

By Maria S., Spain

As with many young couples, we were looking forward to having children one day. However, our situation was not like that of a normal couple, as one of us suffers from VHL. If we were sure about one thing, it was that we did not want our children to suffer from the same condition.

Before the "call to fatherhood/motherhood", we started to look into the options we had, as we knew it might be a long process. Since we did not know about a previous case in the Spanish VHL Association, we turned to our Community Hospital, to be more precise to the human reproduction unit. There, we presented our case and were given three alternatives:

1) Becoming pregnant in a natural way, and after three months having a specialized amniocentesis (different from the usual amniocentesis). This test would allow the doctors to see if the embryo had inherited the disease or not. In case it had, the option was abortion;
2) Achieving pregnancy through an egg/sperm donation from a healthy donor;
3) Becoming pregnant through in vitro fertilization after pre-implantation genetic diagnosis.

Our preference was for both of us to be the biological parents, so we had options 2 or 3—becoming pregnant with the possibility of an abortion if the fetus had inherited the disease and in vitro fertilization after pre-implantation genetic diagnosis. We opted for the latter because we considered it less difficult, although it might take many tries before getting pregnant and take a toll on the woman on a physical level (the hormones injected) and a psychological level (the emotional roller-coaster of not becoming pregnant after several tries). However, the possibility of an abortion after the fetus was diagnosed with the disease seemed even harder to us.

As our community hospital did not offer this option, the assisted reproduction unit put us in touch with the IVI (Infertility Institute in Valencia), and we were granted funding for up to three tries, which is the number of tries all couples with fertility problems get.

The initial process was rather long, as we both had to send blood samples (the one with the VHL mutation and the one without it), and the medical report indicating what our specific VHL mutation was. This information is helpful for the entire family as all affected family members share the same VHL mutation. After several months (approximately seven months), we were informed by phone that it was possible to detect the mutation in the fertilized egg, and from that moment on we could try to have children when we pleased.

This first step was really important for us, since at first we were not assured that the disease could be detected in the fertilized egg. If they were unable to set up a rapid test for the mutation in our family, we would not have been able to use this option at all. So it was wonderful news for us when we were told that we would be able to do it.

The induction of egg production turned out to be easier than I had expected. I had been told that it would be difficult and painful. At the IVI, I was taught how to inject myself with the hormones to stimulate egg production, and I found it to be very simple and not painful at all. When the eggs reached the right size, they were extracted, for which I was sedated, so this process was not painful either. In my case, the following day was hard. I went to work, but I really should have stayed home as I was not feeling well. I should have stayed all day in bed. The day after that, though not feeling completely recovered, I was much better.

Once the eggs were extracted, they were fertilized in the laboratory. Some of the eggs recovered were not mature and were lost. But the mature eggs were fertilized and grown to the point that they could do a biopsy and test them for the VHL gene mutation. They determine which embryos (fertilized eggs) have two healthy VHL genes, which ones have the VHL alteration, and which ones are questionable (these are discarded). This leaves only a few healthy embryos to implant. Typically, couples have many healthy embryos; they implant only two or three, and the rest are frozen for future use. However, in our case, this was a problem because we were left with very few healthy embryos. If we did not get pregnant on the first try, we would have to go through the process of stimulating and extracting eggs again.

Five days after the extraction, I was implanted with two embryos. This process is done without sedation, but it is not painful at all, on the contrary it is really beautiful. We were able to be together and watch the ultrasound picture while the embryos were implanted, and we were also given an ultrasound picture showing the embryos in the uterus. The truth is that it was a very special moment. We were watching what in the future would be our two children. We were very lucky that I became pregnant on that first try. Both embryos survived, and now we have our two daughters, who are really wonderful!

For me, the worst part in this process was the ten days after the embryos were implanted, until I had a blood test to see if I was really pregnant. During the hours following the blood extraction, I was even more nervous, until I got the results. Many things come to your mind, as you are keenly aware of every little symptom you might have, or wishing to have, just any little indication to give you the hope of being pregnant. Thank goodness it was only ten days! The hours waiting for the phone call to find out if everything had worked successfully…they were endless!

As I have said before, we were lucky. I got pregnant after the first try and with twins, which is what we wanted. This way, with one pregnancy, we had two children, and we would not have to go through this process again. We were just delighted.

For us, it was worth going through all this because, at the end, you are left with the peace of mind of knowing that our children have not inherited VHL.

Note: The genetic test used in this case only determines whether the embryos have inherited the altered VHL gene, but it does not rule out other anomalies, such as Down Syndrome.

Our Best Mistake

by Diana C., USA

June 17, 2006 was one of the happiest days of my life. I was married to the most wonderful man—the man of my dreams! We had a beautiful wedding and a fabulous two-week honeymoon in Hawaii. However, our "honeymoon period" quickly ended when I found out two months later that I was a carrier of the VHL gene and would also need surgery to remove a hemangioblastoma from my thoracic spine. In November 2006, I underwent a successful spinal laminectomy to remove a 4 cm tumor. Subsequent scans were done which revealed a tumor in my pancreas and one in the base of my skull. After a couple of years, my husband and I decided we were at a point in our lives when we wanted children. After seeing my father suffer for years with VHL-related problems and experiencing my own problems, I was 100% sure that I did not want to pass the VHL gene on to my children. We discussed our options in great detail and decided that IVF with PGD was the best route for us to achieve pregnancy without passing on the gene.

In March 2008, after receiving clearance from my doctors to get pregnant, my husband and I made an appointment with the Fertility Center at Massachusetts General Hospital. We had a consultation to discuss our detailed health information as well as details of the IVF/PGD process. We were informed that it would take approximately three months for the genetic test to be completed based on both of our genetic information. The genetic test was done through a laboratory in Detroit, Michigan, called Genesis Genetics. In order for the genetic "probe" to be devised, we had to send cheek swabs from me, my husband, and several of my family members (the lab needed swabs from my family because I am the VHL carrier, and it would help with the accuracy of the test).* In addition, we had to send a copy of my genetic testing DNA report, signed consent, and payment. I should note that at the time, payment for the genetic test was completely separate from the hospital and was not covered by my insurance.

Upon completion of the genetic probe, we would be ready to start the IVF cycle. However, things did not go quite as planned! I ended up getting pregnant naturally. The news came as a total shock, and we were very scared as to what the road ahead would bring. Coincidentally, I received an email from Genesis Genetics informing us that the genetic probe was ready on the very same day that I found out I was pregnant.

I was referred to a high risk obstetrician at MGH. He was the most wonderful doctor who took the time to research VHL. At our first appointment, rather than discuss VHL and pregnancy at length, we discussed what our options were with the pregnancy. There were three options: 1) continue with the pregnancy and test for VHL after the birth of the baby, 2) abortion, or 3) test the fetus through chorionic villus sampling (CVS).

We decided to go the CVS route, which meant that the doctors could test the fetus for the VHL gene between weeks 10 and 12 of pregnancy (rather than amniocentesis, which is usually done later between 15 and 20 weeks). Chorionic villi are growths found in the placenta that carry the same genetic material as the fetus. The CVS procedure was more emotional than painful. A catheter was placed vaginally through my cervix into the placenta and a sample was taken. The procedure can also

*Cheek swabs do not always provide sufficieint information. Blood samples may be required

be done by placing a needle through the abdomen, depending on the position of the baby. I was relieved that my procedure did not involve sticking a needle through my stomach!

We weren't quite sure what we would do with the information from the CVS. As adamant as I was about not passing on the gene before I became pregnant, my thoughts and feelings were starting to change. The feeling of having another life growing inside of me was so moving and overwhelming. It was rather easy for me to say the word "abortion" prior to experiencing pregnancy. However, as the days moved on and the baby was growing, my feelings were quickly changing. We were hoping and praying that the test results would be negative for VHL.

As adamant as I was about not passing on the gene before I became pregnant, my thoughts and feelings were starting to change.

The CVS was performed at 11 weeks, and we found out three weeks later that we were having a boy (the CVS test can also test the gender of the baby)! It took a bit longer for the genetic results to be complete. The 6 weeks following the CVS were the most stressful of our lives. The feeling of "not knowing" and not being able to do anything about it was awful. Around 17 weeks of pregnancy, I received the call that we were waiting for...the baby boy growing in my belly was not a carrier of the VHL gene!! Tears of happiness were flowing from my eyes as I was able to pass along such amazing news to my husband, our families, and friends! Several months later, our beautiful baby boy was born via planned C-Section.

As for my VHL tumors during pregnancy, both of my tumors did grow while I was pregnant.* However, a few months after pregnancy, the tumor in my head got smaller while the pancreas tumor continued to grow. Also, my doctors were able to monitor the tumors throughout pregnancy with MRI scans—without contrast. For me, the pregnancy was normal with no complications despite my VHL condition.

After experiencing the extreme stress and anxiousness of "not knowing," my husband and I decided that we never want to experience those feelings again. In addition to be being extremely careful to prevent pregnancy, we decided if we want to try for another child that we will most definitely go the IVF/PGD route.

*It is now recommended to do an MRI without contrast in the 4th month of pregnancy to check CNS lesions.

Ultimately, the decision is extremely personal and should be discussed in great detail. What was "right" for my husband and I might not be the right decision for another couple dealing with VHL and pregnancy. We were lucky and fortunate that what was considered a "mistake" turned out to be one of the greatest gifts of our lives.

Expecting a Boy

By Mireille N., France

As you all know, there are happy periods when one wants to forget about VHL, sometimes easily, sometimes with difficulty.

I would like to share with you some hope and some moments of joy after certain battles have resulted in some great victories. Today I am happy to announce that I am expecting a little boy on the 23rd of January.

Now that I am nearly 40 years old, I am just now touching with the tips of my fingers the happiness that I have desired. VHL nearly made me give up. I was living in fear and anxiety from this disease.

I was not able to benefit from pre-implantation genetic diagnosis. Even though my request was initially accepted, they said that the waiting list was long and, since I was already 38 years old, the chances of success with IVF are greatest when you are under 25. I was disappointed at first that I was not in the percentage of the population more likely to succeed. It is hard to be just a number or a percentage.

Nonetheless, I did not give up in spite of the fear of having a child with VHL like myself. My grandmother who has VHL is still here, my mother also, and of course I myself am still here—why could he not also be okay with VHL? I still don't know whether he has VHL. I had them do an amniocentesis test only for trisomy (Downs).

He will be tested in time, but for the moment I am enjoying this pregnancy.

As for me, like others, I know that I have spinal cord tumors. Three years ago I had surgery on a hemangioblastoma and a cyst in the cervical spine. I am doing quite well now.

Because of the spinal cord involvement, they will take extra care during the delivery. They tell me it is okay to do epidural anesthesia, but they don't want me to push hard during delivery. It is better to do a Caesarean section.

Love and kisses to all.

P.S. Mireille had a beautiful little boy. Whether or not he has the altered VHL gene, she and her husband will work with him to keep him healthy.

Report on the Hungarian VHL Symposium, 2010 November

By Helga Süli-Vargha, PhD, President of the Hungarian VHL Society. Budapest

The first national von Hippel-Lindau Symposium in Hungary took place at Semmelweis University in Budapest on the 11th of November 2010, organized by the 2nd Department of Medicine with the support of the Hungarian VHL Society. After welcoming the participants, Helga Süli-Vargha, Chairman of the Society, reminded the guests that this symposium fits well into the current health policy of the European Union (EU) considering rare diseases as a priority in the public health area and recommending that the member states establish and implement a National Plan for the rare diseases by the end of 2013.

The scientific program was compiled by Dr. Miklós Tóth, Associate Professor, Dr. Peter Igaz, Assistant Professor, and Dr. Attila Patócs, Senior Scientist. It consisted of three major sections with presentations of 15–20 minutes duration. The presentation of Professor Hartmut Neumann, the invited speaker from the Albert Ludwig University Clinics, Freiburg, Germany, highlighted the recent molecular and clinical advances in the management of VHL syndrome.

The Symposium was attended by approximately 50–60 visitors, most of them were physicians and scientists, but affected patients and family members also attended. Session breaks gave a good opportunity for discussions between patients and experts.

Attendees at the Hungarian Sympsoium

During this meeting, a brand new book, *Pheochromocytomas and Paragangliomas, A Guide for Patients and Medical Practitioners*, edited by Professor Neumann and translated into Hungarian by Dr.

Peter Igaz and Dr. Peter Reismann—published by Semmelweis Publishing Group—was presented to the audience. All participants received a free copy of the book as a gift from the Hungarian VHL Society.

We have received positive comments from par_ticipants and so we feel that this meeting has been a real success. Therefore, in accordance with the EU recommendations, we are considering the possibility of organizing in the near future a regional workshop on VHL in cooperation with neighboring countries.

The complete agenda for this meeting may be found on the website at http://vhl.org/meetings/meet2010/hungarian_symp.php.

CCC in St. Louis, Missouri

by Joyce Graff

We welcome a new Clinical Care Center in Missouri. For the complete list of clinical care centers, please see http://vhl.org/ccc.

The Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine provides integrated, comprehensive care for Von Hippel-Lindau (VHL) patients. Siteman, the only NCI-designated* Comprehensive Cancer Center within a 240-mile radius of St. Louis, offers committed physicians with expertise in all disciplines involved for caring for VHL patients.

The core VHL team at Siteman includes 17 physicians representing Endocrinology, Hepatobiliary Surgery, Medical Genetics, Nephrology, Neurology, Neuro-otolology, Neurosurgery, Ophthalmology, Pediatrics, and Urologic Surgery. The Siteman VHL Center is led by Drs. Robert L. Grubb III (Urologic Surgery) and Paul Santiago (Neurosurgery). Our medical team is supported by a full-service patient care coordination center made up of nurses, social workers, and a supporting team. The St. Louis service area includes more than 2.7 million people, and Siteman serves more than 40,000 cancer patients annually.

To contact the VHL team at this center, please call Pam Dowling, RN, BSN, 877-251-6485 or 314-747-3046; Fax: 314-454-8103; e-mail: pad1069@bjc.org

*The US National Cancer Institute (NCI) has designated a number of Comprehensive Cancer Centers regionally around the United States.

Personal Report from the Rio Symposium

By Christiane Golz, Germany

When I sat down on the plane headed home to Germany, I had four days full of exciting events behind me. We started on Thursday afternoon with a meeting about changes to the screening protocol for the new Handbook. With representatives from Denmark, the Netherlands, Germany, Spain, USA, Brazil, and Argentina, we were able to get a good picture of the international experience.

Chris Golz, Pr. Jochen Decker, Joyce, and Elena from Brazil

In the evening, we were invited by Dr. Rocha (Brazilian head of the Tumor Bank) to a traditional Brazilian barbecue. Many of the researchers knew each other from prior Symposia. For me, it was still uncharted territory. With a fruity drink with caipirinhas and delicious food, the atmosphere was perfect to meet and exchange ideas.

During the next two days, we turned to basic research and the medical aspects of VHL disease.

During the scientific contributions from Brazil, some families were present. They were very warm and friendly. Language barriers were overcome by hands and feet, smiles and hugs.

Sunday was dedicated to the patients and their families. Dr. Rocha described the genetics and biochemical basis of VHL disease. For many of the families, this was their first such meeting and probably the first time they had heard information at this depth. Later, several of the families had the opportunity to tell their stories and exchange ideas. It quickly became clear that the Brazilian families have had experiences very different from my own. In my family, my mother and I have been followed carefully and have received good preventive medical care for VHL, so we are both healthy and doing well. For most families in Brazil, while VHL has been in their families for generations, they have only recently received the right diagnosis.

Most families had lost loved ones or seen serious disability from VHL. And even once the diagnosis was made, many patients did not know what they should do it because there was no doctor in their area who knew anything about the disease. I think it is even more important for the Brazilians to have an Alliance like ours so that they can share information and support one another. There is now a website for the VHL organization in Brazil so that everyone has the opportunity to learn. (http://www.abvhl.com/)

On Monday, I went with Joyce Graff, Jochen Decker, and Arnim Pause to visit the offices of Dr. Claudio Casali da Rocha at the Tumor Bank of the National Cancer Institute of Brazil. We were told how the tumor bank works and some of the many issues you have to consider. Brazil is a very large country, larger than all of Europe. In addition, he is part of a consortium among all the countries of Latin America (from Mexico south). The geographic distances and the wide variety in the capabilities of the medical centers in each region provide hurdles and complications that we do not have in Germany. Dr. Rocha uses RNA-later, an alternative preservation method for surgically removed tissue, to preserve the RNA for research while permitting tissue to be sent by regular courier. The preferred method, preservation in liquid nitrogen, is not available in most hospitals in Latin America and requires investment in equipment and training of operating room personnel, which is not realistic in most areas and requires specially licensed couriers to transport it, especially across country boundaries.

All in all, it was a very informative experience for me. I am very grateful that I had the opportunity to attend this conference and learn so many new things.

Reporting from Rio

by Joyce Graff, Editor

In October, it is springtime in Rio de Janeiro. This beautiful port city on the east coast of Brazil in South America is situated on Guanabara Bay, so wide and deep that the Portuguese sailors who first visited thought it was a river. In fact, it is a bay which they named the River of January. In the bay are scattered granite monolith mountains reaching high up out of the sea and into the sky.

In the unique logo created for this conference, you will see Copacabana Beach stretching as a crescent to the right, Sugar Loaf Mountain, and "Christo", a statue of Jesus Christ the Redeemer, as high as a football field is long, standing atop another of the monoliths, dominating the view of the harbor.

We met in one of the hotels that line Copacabana Beach. Right across the street from wonderful white sand beaches the city is bustling with all the myriad activities of a city of 6 million people in a metropolitan area of 12 million people, with twice as many people per square kilometer as in New York or London. Rio is the second largest city in Brazil (after Sao Paolo), and the third in South America.

The first day of the conference was dedicated to understanding the molecular genetics of VHL, an essential element in the life of the cell in organisms from yeast to humans. Inside the cell, there is a complex system of sensors and controls that keep all the body's activities in balance and respond to changes in circumstance and environment. Each time we meet, there is a deeper understanding of the normal role of the VHL protein in the cell and of the chain reaction that occurs when the VHL protein is not present or not doing its job properly. It's not just a simple single-file process; it's a complex waterfall of events.

The abstracts, or short summaries, of the presentations are contained in the Program from the conference. See http://vhl.org/conf2010.

I will give a brief overview of the presentations on the second and third days of the conference, which were devoted to the more clinical aspects of VHL and to the family experience of VHL. These issues are of course more familiar and more immediate for most of us. On Saturday we heard from experts from all over the world; on Sunday we heard from Brazil itself.

Four neurosurgeons from Spain, Brazil, and Japan presented reports of cases of VHL they had treated in different ways. The standard of care for nearly all brain, brain stem, and spinal cord tumors is still open microsurgery in the hands of a surgeon with experience in VHL. Dr. Jose M. de Campos, the leading neurosurgeon operating on people with VHL in Spain, shared a series of 12 patients who underwent 14 surgeries. In all, 20 hemangioblastomas were successfully removed and all but one patient returned

to full function. Dr. Maria Elena Kusak (Spain) and Dr. Douglas Guedes (Brazil) reported cases where stereotactic radiosurgery (SRS) was used to good effect. Dr. Kusak has used gamma knife to stabilize VHL tumors for as much as four years. Dr. Guedes was able to stop the growth of an ELST, but there was no benefit to hearing or vestibular function. There was general agreement that open surgery is still the preferred method, and that SRS should ONLY be used in VHL where surgery is not a safe option in a VHL-experienced neurosurgical unit.

Dr. Hiroshi Kanno (Japan) shared his series of 62 central nervous system (CNS) hemangioblastomas in 34 patients from 1992 to 2010. Laboratory data often revealed polycythemia due to secretion of erythropoietin from the tumor. Most results were quite good. Larger tumors tended to have less good outcomes (>4 cm in the brain or >2 cm in the spinal cord). He found that SRS did not always control the tumor. His recommendation was to operate earlier rather than later in order to avoid deterioration of neurological function.

Conference logo

Dr. Eric Jonasch (USA) presented a progress report concerning three clinical trials in progress at MD Anderson Cancer Center in Houston. Sunitinib has gotten a significant response in kidney tumors, but not in CNS. He will be treating 14 VHL patients with VHL and hemangioblastomas with TKI258, a small molecule inhibitor of FGFR and VEGFR. He will also be opening a multicenter 40-patient study treating VHL patients with pazopanib, a well tolerated small molecule VEGFR inhibitor.

Several presentations from Germany, France, and Brazil described a number of studies of kidney cancer, searching for biomarkers that would give us a good "measure" of the level of tumor activity in the kidney without going to the cost and trouble of getting an image. While there are no confirmed biomarkers yet, there is a great deal of activity in this race.

Dr. Karel Pacak (USA) presented his extensive work on pheochromocytomas, not only caused by VHL but also by any of five other genetic flaws. While VHL is the largest of these genetic promoters of pheochromocytoma and paraganglioma, all genetic causes so far account for only 30% of the pheos there are—70% are sporadic in the general population or have other genetic causes we have not yet identified. The tools to diagnose a pheo exist—the biggest hurdle is finding a doctor who will believe that the patient is not crazy, run the tests, and take the time to learn what the resulting numbers mean. There is a protocol open now at the US-NIH to assist in arriving at a diagnosis, and to help us learn as a community how we can move more quickly to a diagnosis. See http://vhl.org/pheo.

Dr. Surena Matin (USA) presented his experience in treating VHL renal tumors. He has found the 3 cm strategy to be quite effective. Open partial nephrectomy is the primary modality he uses, but each successive surgery becomes more difficult. Dr. Ian McCutcheon (USA) presented a series of cases where he worked with five people with VHL who suffered intractable nausea from a hemangioblastoma located in or near the distal medulla. Relief in all cases occurred within one week following removal of the tumor. While nausea can be caused by other conditions associated with VHL (e.g., pancreatic cysts or tumors), this symptom should trigger a search for a hemangioblastoma of the distal medulla, which should be clearly seen on an MRI.

Dr. De Campos (Spain) presented a series of 62 patients with a total of 291 diagnosed tumors from 30 families in Spain, and followed in the Spanish national health system their whole lives, in which they tracked the age of onset of the first symptom and the course of the disease. They demonstrated that in 10% of the cases the first issue arose before age 19. Having an early symptom did not predict an aggressive clinical course for subsequent tumors. He is happy to see the recommendations for early DNA testing and regular screening in order to find and address any early tumors in a timely manner.

Dr. Sven Gläsker (Germany) reported that he is using color Doppler ultrasound during neurosurgery to guide the surgical approach and resection of CNS hemangioblastomas.

Dr. Valérie Krivosic (France) presented the work of Dr. Alain Gaudric on the role of vitreoretinal surgery in the management of advanced retinal capillary hemangioblastomas (RCH) of VHL. While he was able to treat the RCH successfully and save the eye, in most cases there was a high rate of vision-threatening RCH recurrence in the long run.

Pregnancy and VHL

From the earliest days of the VHL Family Alliance, families have been asking whether pregnancy promotes tumor growth. Dr. Caroline Abadie (France) reported that the French team has recently completed the first scientific study of this important topic.

They went back through the records in the French National VHL clinical database to study 269 women from 172 families. Their aim was to analyze the onset of new hemangioblastomas and potential tumor complications in patients compared to their pregnancy status. They collected follow-up data on CNS and retina for 176 women with at least one pregnancy (Group 1) and 93 women with VHL who have had no pregnancies (Group 2). More complications of hemangioblastomas were found in Group 1. Because of this finding, the French VHL Study Group now recommends an MRI without contrast in the fourth month of pregnancy to check on the health of the mother. This is especially important for women with a previously identified CNS lesion.

Hearing Testing and ELST

We know that if there is a significant drop in hearing, we should immediately suspect an ELST. For that reason, we include in the annual screening recommendations an audiology test to quantify the hearing and allow us to compare year over year. Before 2009, none of the 42 people with VHL in Denmark had ever been diagnosed with an ELST. Since the international averages indicated that 11–16% of people with VHL can have ELST's, the Danish team asked all their patients to be examined for ELST. So far, they have identified 2 out of 39 people (5%) who have ELST's. One had hearing and balance symptoms, while the other had no symptoms but an ELST can be seen on the MRI.

We do not yet know whether there are more subtle early signs of trouble that might be learned from an audiology report. The Danish team proposes to study these annual audiology reports and would like to invite patients and physicians throughout the world to contribute to this important learning. Please contact Marie Louise Poulsen, Genetic Counselor, University of Copenhagen, Denmark.

On Sunday we focused on Brazil—reviewing for Brazilians with VHL and their families what VHL is, the genetics, DNA testing, and management. Dr. Claudio Casali da Rocha is the geneticist who has introduced DNA testing for VHL into Brazil and has made it possible for each of these families to finally learn the name of their disease—sometimes after three generations of mysterious and devastating medical problems. Brazil is a large country with some outstanding medical centers and a lot of local hospitals with limited facilities. They are still working to set up a chain of information and escalation of problem cases to support doctors throughout Brazil in managing the health of their patients with VHL. The VHL Family Alliance in Brazil (ABVHL), under the presidency of Jamila Mansour Najar, is providing coaching by e-mail and telephone to help people get the best care.

Joyce Graff spoke about VHL in the world and the progress we have made in the last 20 years. She remarked that what Brazil is going through now is where we all were in 1993—few people with diagnoses, few doctors who remembered more than one paragraph from medical school about VHL, and very little information available on the ground. Today we have a good base of information available in the world and on the internet, and we have the tools to tap that knowledge for people in Brazil. While many people in Brazil can read or speak Spanish or English, it would be best if the Handbook were in Portuguese. Claudio and Jamila are working to make that happen. Also, all the other Family Alliance groups around the world stand ready to assist people in Brazil in getting the best information possible to help in a particular situation.

There were many very moving presentations from Brazilian families about the difficulties they had gone through in trying—sometimes for decades—to find out what was happening and find competent care. There is a temptation to want to fly your child anywhere in the world to find that care. Joyce said, though, that while in some cases that might be the right approach for a very specialized problem, for most people most of the time, the best place to get care is right where you are, with your own local doctor. The Handbook is designed to help you and your doctor learn together, find things early, understand what choices exist for treatment, and with whom to discuss the problems. In Brazil today, that starts with Dr. Casali, Dr. Bruno Vilhena, Dr. Marcelo Reis, Dr. Renato Faria, Dr. Leonardo Machado, Dr. Yonder San, Dr. Cristiano Guedes, and all the other physicians and researchers from Brazil who participated in this meeting. Even more than that, it starts with every patient and every family member. You spend more time with your own body than any doctor ever will. You need to understand what to watch for, what you can do to keep your body and its own immune system strong, and how to seek the help you need when you need it.

It was a very emotional day. We applauded our translators who kept us all in the conversation by providing excellent simultaneous translation throughout the day, and the head of the translation team tearfully hugged Joyce at the end of the day as she was so moved by all the family stories and the compassionate exchange she had witnessed.

All of us from US and Europe went away grateful for what we have learned together in the last 18 years and the progress we have made ourselves. We all need to remember that there are lots of other families out there struggling to get a diagnosis. Some are in foreign countries and some are right in our own towns. While in the past it took tumors in at least two organ systems before anyone would have considered a diagnosis of VHL, today there is DNA testing to confirm a diagnosis in a younger person with only one kind of tumor and get them into a surveillance program that will hopefully save them a great deal of suffering in their lifetime. Will the doctor think to check for it? Will the family find the clues on the internet? And will we be ready to hug them too?

Updating the Screening Protocol

by Joyce Graff

The screening protocol in the VHL Handbook has been working well throughout the world. It has been evaluated in studies in the US, UK and Denmark, and has been found to be very helpful in identifying issues early enough to be helpful in influencing treatment decisions.

The only issue we have had with it since the beginning is that it calls for a great deal of imaging, which is expensive and requires a lot of time on the part of the patient each year. In light of the concerns raised in the press in the last year about radiation dosages in imaging, we convened an international working group (12 people from six countries) prior to the Rio meeting to see what adjustments we might want to make in the 2011 version of the Handbook, especially in the Screening Protocol.

As ever, the Handbook is intended to be used by a patient and their local doctor, to help both get up to speed on the recommendations of the experts on VHL. It is not intended to replace your local medical team, but to supplement what they know, add information about what is different about VHL that they might not be familiar with, and provide leads to key journal articles and sources of second opinions. In the case of the screening protocol, it outlines what we have learned about how best to manage the health of someone with a diagnosis of VHL, but who has not yet experienced symptoms in a particular area of the body. Once there are symptoms, the local team will be assumed to know best and can contact one of the experts listed if they would like assistance. But in the absence of symptoms, the relevant section of the screening protocol should apply.

We decided that CT's should be avoided for all pre-symptomatic people. That allowed us to simplify the categories to only three: ages zero to four; ages 5–15; and ages 16+. Once a tumor has been identified, CT still has an important role to play.

In testing for pheochromocytoma or paraganglioma, the new handbook should state that the Plasma Free Metanephrines (PFM) blood test is the preferred test. Because it is not always available, 24-hour urine is still good, but PFM is better. It should also be noted that MIBG only finds about 85% of pheos, whereas F-DOPA PET finds 98%. Again, F-DOPA PET has only limited availability, so MIBG will still be used.

In the 16+ age category, the recommendation is to schedule an MRI of the abdomen every two years, alternating with a Quality Ultrasound. We define Quality as having a good quality ultrasound machine and an operator experienced in sonography of the kidneys, adrenals, and pancreas. Ultrasound results are highly dependent upon the quality and experience of the operator. While ultrasound is less expensive, it can also miss a large number of tumors. It was felt that it is better to avoid the radiation of a CT, and having the MRI every two years should catch anything missed on the US in time to make a difference in treatment.

Also in the 16+ category, for monitoring of the central nervous system, the group recommendation is every two years to perform "MRI with contrast of brain and cervical spine, with thin cuts through the posterior fossa, and attention to inner ear/petrous temporal bone to rule out both ELST and hemangioblastomas of neuroaxis." The thinking is that these are the areas where early diagnosis is critical, and symptoms are sometimes slow to develop, so that imaging is particularly important in finding issues before they become difficult to treat successfully. This combination image can be done in one sitting, lowering the total cost of CNS scanning.

We will be validating these recommendations with the worldwide community of VHL clinical care centers and physicians treating people with VHL. Please share this information with your own team. We will be happy to hear comments from families or physicians. Please send comments to editor@vhl.org. something here or a picture?

Please join us in Houston or at another meeting closer to home.

Seee vhl.org/meetings or page 20

VHL Family Forum, Newsletter of the VHL Family Alliance and the Cancer Research Fund / VHL

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Please join us at one or more of the following events coming up! see also vhl.org/meetings

Meet Montefiore

April 18, 2011 - Monday 10 AM–noon
Montefiore-Einstein Center for Cancer Care
1521 Jarret Place, Bronx, New York 10461
For more information, visit http://vhl.org/meetings

Patients as Partners

April 28, 2011
Cincinnati, Ohio
Topic: **A family perspective on the VHL genetic cancer syndrome**
For more information, visit http://vhl.org/meetings

New York Regional Meeting

Saturday, June 11, 2011
Memorial Sloan Kettering
For more information, visit http://vhl.org/meetings
or contact us-ny@vhl.org

10th International Medical Symposium on VHL

January 27-28, 2012
Houston, Texas
For more information, visit vhl.org/conf2012
Hold the date! Plan to come!

VHLFA National Meeting

Saturday, June 18, 2011
Houston, Texas

Educate and Empower Yourself!

- **Dr. Scott McLean re DNA testing**
- **Dr. Eric Jonasch re new clinical trials**
- **Dr. Jeffrey Kim re ELST**
- **Dr. Ian McCutcheon re neurosurgery**
- **Evaluating & Monitoring Children with VHL**
- **Coping and Managing Stress**

Latest info about clinical trials, ELST, pheos and more!

Sunday: Chapter Leaders' Meeting
Come join the team!

http://vhl.org/meetings/meet2011/

Please check http://vhl.org/meetings for updates and directions
or call the office, 800-767-4845, ext 4