



Pregnancy and Family Planning



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VHL: Pregnancy and Family Planning

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Overview

- Issues in pregnancy for women with VHL
- Inheritance of VHL and risk for children
- Genetic testing for VHL – when and who?
- Options for family planning including:
 - Prenatal testing
 - Preimplantation genetic diagnosis



Pregnancy and VHL

- Normal changes during pregnancy have potential to create/worsen VHL related complications
- Issues for the health care team:
 - Pheochromocytomas
 - Hemangioblastomas of brain/spine



Pheochromocytoma

- **Undiagnosed** pheos can cause symptoms similar to other pregnancy complications (preeclampsia)
- Can lead to misdiagnosis and mismanagement
- Can result in serious complications including hypertensive crisis, insufficient blood flow to fetus, placental abruption
- **CRITICAL** for medical team to know about diagnosis or family history of VHL



Pheochromocytoma

- Pheo diagnosed during pregnancy -
- Goal is to protect health of mother while continuing pregnancy
 - May be managed with medication
 - May be managed with surgical intervention
- Good outcome is possible, but high risk management is necessary



CNS Hemangioblastomas

- Blood volume and cardiac output increase in pregnancy
- Raises concern about growth of existing tumors
- Important to monitor location of tumors and any symptoms or changes in symptoms throughout pregnancy – intervention may be needed
- Important to know location of any spinal tumors when considering anesthesia for delivery



Pregnancy management

- Pre-conception evaluation and imaging is the best approach – know what you are dealing with before pregnancy begins
- If that doesn't happen – let your doctor know ASAP about diagnosis or family history of VHL
- Monitor neurologic status throughout pregnancy for changes in symptoms
- Mode and timing of delivery may be affected



VHL Genetics

- Caused by mutations in the VHL gene
- Mutations can be found in *close* to 100% of people with VHL with current testing techniques



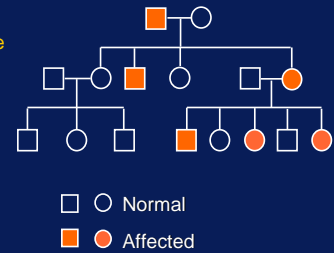
VHL Genetics

- About 80% of people with VHL will have a family history of VHL
- The other 20% will be the first person in their family to have VHL = *de novo* mutation



Autosomal Dominant Inheritance

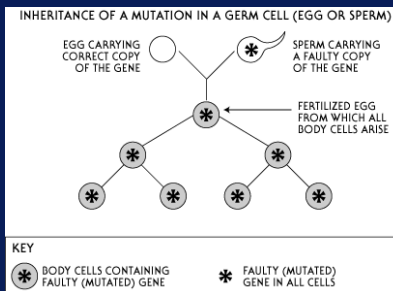
- Each child has 50% chance of inheriting the mutation
- No "skipped generations"
- Equally transmitted by men and women



ASCO



Autosomal dominant inheritance

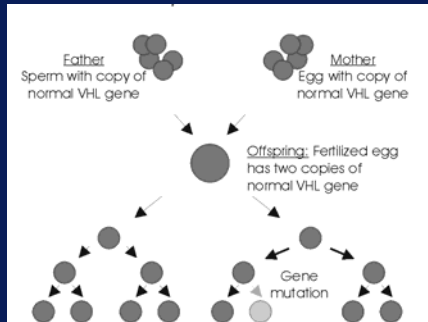


VHL Genetics

- Some patients with VHL will have mosaicism:
 - One way this shows up: patient has VHL with normal gene test
 - Another possibility: person does not have VHL, but has more than one child with VHL (mosaicism in sperm or egg cells)



VHL Genetics - Mosaicism



www.vhl.org



Genetic testing for VHL

- Best if person with known diagnosis of VHL has testing first – confirm that mutation can be identified
- Once mutation is identified, testing can be offered to any at risk family members, including children
- Testing for children is standard of care since screening for VHL starts in childhood



Family planning

- Options include:
 - Having children, testing after
 - Having children, testing prenatally
 - Pre-implantation genetic diagnosis
 - Sperm or egg donation
 - Adoption

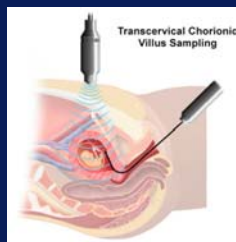


Prenatal Diagnosis/Testing

- Chorionic villus sampling
 - Usually available 10-12 weeks gestation
 - Ultrasound guided, small catheter through vagina to remove small piece of placental tissue
 - Tissue can then be used for genetic testing



CVS



<http://fmsccc.msu.edu/healthvc4/0996.jpg>



Prenatal Diagnosis/Testing

- Amniocentesis
 - Usually done after 15 weeks gestation
 - Ultrasound guided needle inserted through abdominal wall into amniotic sac
 - Fluid is collected – this contains skin cells that have been shed by the fetus
 - Cells can then be tested for VHL mutation



Amniocentesis



<http://images.main.uab.edu/healthycet/0023.jpg>



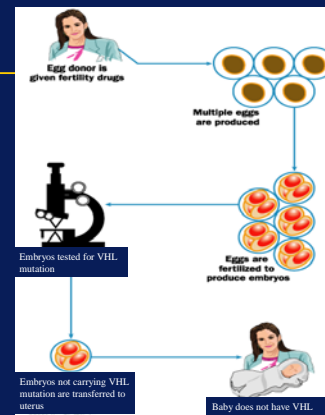
Risks of prenatal testing

- Miscarriage – 1/100 for CVS, 1/300-1/500 for amnio (can ask for statistics for specific center)
- Cramping
- Vaginal bleeding or spotting
- Rare complications:
 - Amniotic fluid leak (after amniocentesis)
 - Infection



Preimplantation Genetic Diagnosis (PGD)

- Requires in vitro fertilization (IVF):
 - Mother has course of fertility drugs, monitored for ovulation
 - Procedure for egg retrieval
 - Eggs fertilized in lab, grown to embryo stage
- One or more cells removed from early embryo for genetic testing
- Select non-carrier embryos for transfer



Preimplantation Genetic Diagnosis (PGD)

- Offers possibility to have unaffected child without pregnancy termination, but...
- Cost of IVF may be prohibitive (and not likely covered by insurance for people who are not infertile) – about \$10,000 per cycle
- Chance of achieving pregnancy with 1 IVF cycle – 25-30%
- Possibility of error in testing, up to 11% for PGD of dominant disorders – follow up CVS or amniocentesis recommended



Conclusion

- Individuals have options depending on personal preferences and circumstances
- Explore options with your partner, doctors, genetic counselor



For the handout . . .

- <http://vhl.org/support>
Click on "webinars"
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Teamwork for Health

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working together
to improve diagnosis, treatment, and
quality of life
for individuals and families
affected with von Hippel-Lindau

VHL Family Alliance