Family History Use in Pediatric Primary Care *A Parent's Perspective*

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Use of Family History Information Pediatric Primary Care:

Chronic Diseases: Predictor

Life Threatening Genetic Disease: *Screening and Intervention*

Can Save Lives

Use of Family History Information Pediatric Primary Care:

Chronic Disease Family History

- Parent Intervention: Diet, Exercise to Prevent Disease (e.g. heart disease)
- Genetics: Discrimination Considerations
  - Health and Life Insurance Discrimination
  - Employment Discrimination
- Safeguards to prevent discrimination

Use of Family History Information Pediatric Primary Care:

Autosomal Dominant Disorder

- Family History Crucial
- Concerns
  - Results from Genetic Testing in health history.
  - Accurate family history data in history?
  - Sharing of family history data in medical records.

Use of Family History Information Pediatric Primary Care:

In HHT Benefits Outweigh Risks

Previously Thought to be…Rare hereditary disease of epistaxis and telangiectasia

⇩

Now Known To Be…Common Rare Multisystem Vascular Disorder causing sudden DEATH AND DISABILITY in 20 %.

HHT: A Common "Rare" Disorder

Disorder	*Incidence*	*Total (U.S.)*
HHT	1 in 5,000	60,000
Hemophila	1 in 10,000	30,000
Cystic Fibrosis	1 in 2,500	120,000
Lou Gehrig	1 in 14,000	21,000
Tuberous Sclerosis	1 in 6,000	50,000

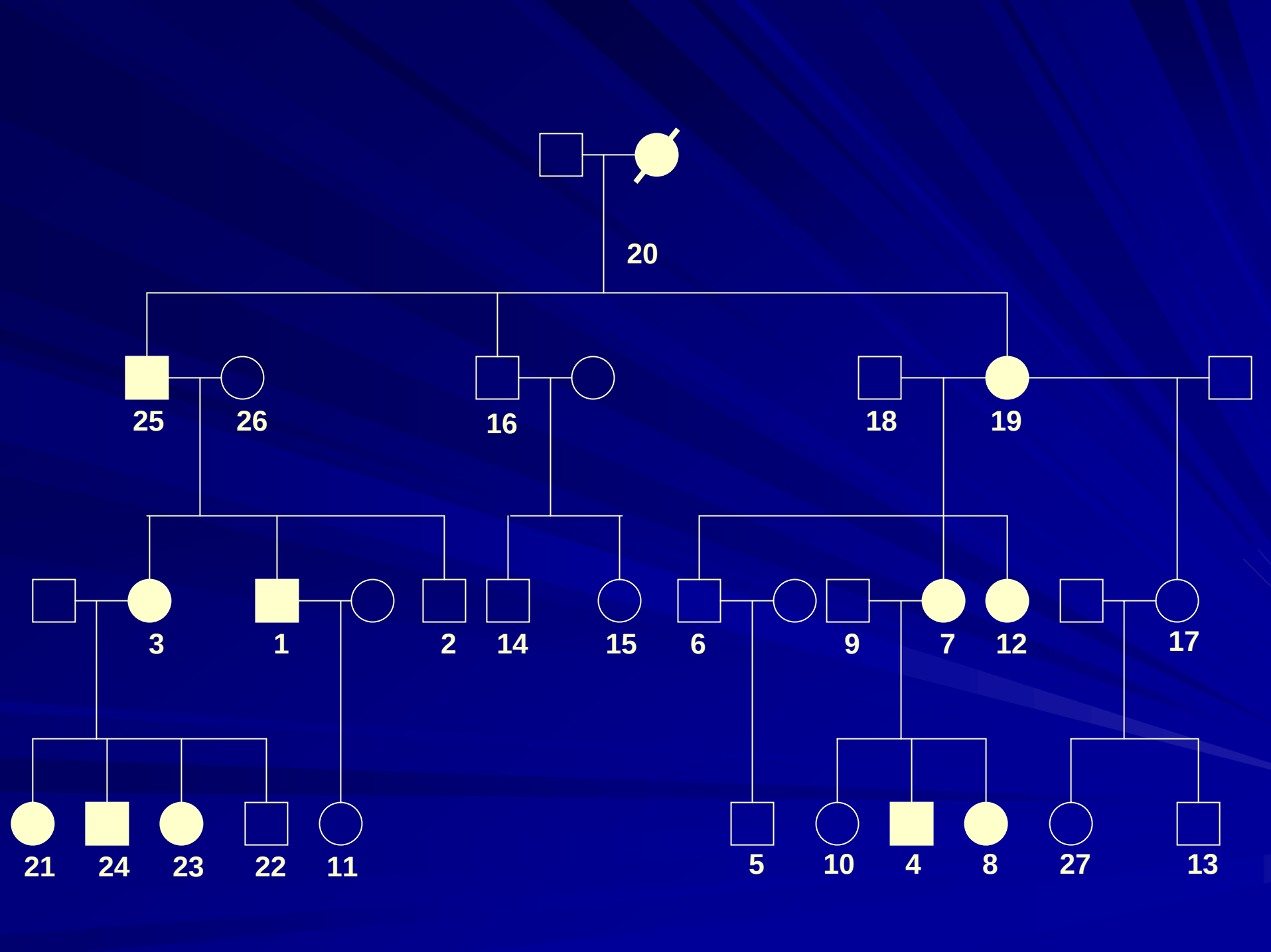
Optimal Management Requires Multidisciplinary Team

Radiology (Interventional and Diagnostic)
Otolaryngology
Genetics
Pulmonology
Gastroenterology
Neurosurgery
Neurology
Hematology
Cardiology

Use of Family History Information: Pediatric Primary Care

HHT Genetics

- Autosomal Dominant Inheritance
- High Penetrance
- Significant Variability
- Genetic Heterogeneity
- Medical Records: Family History Information vs. Genetic Test Results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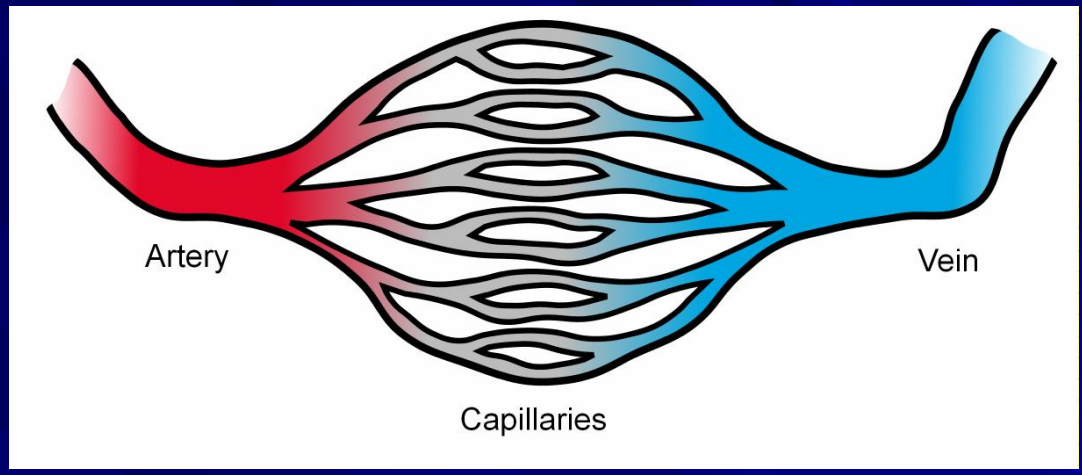
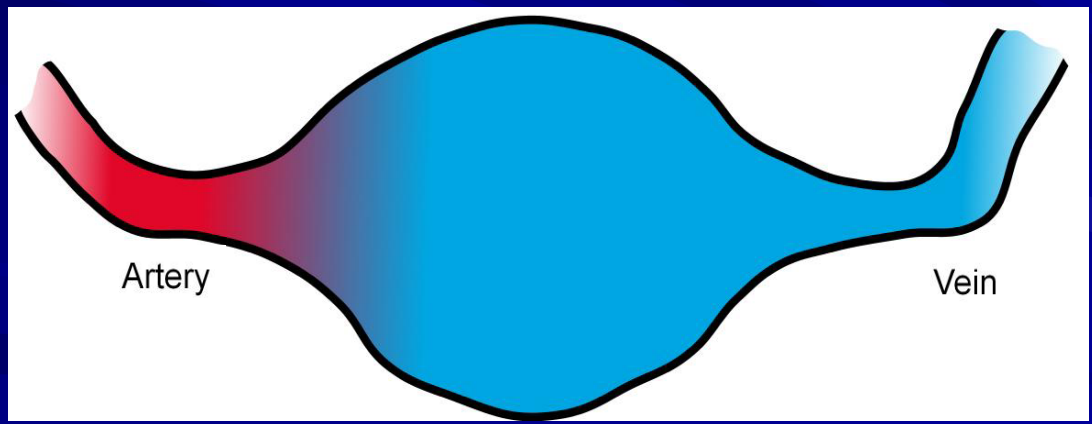
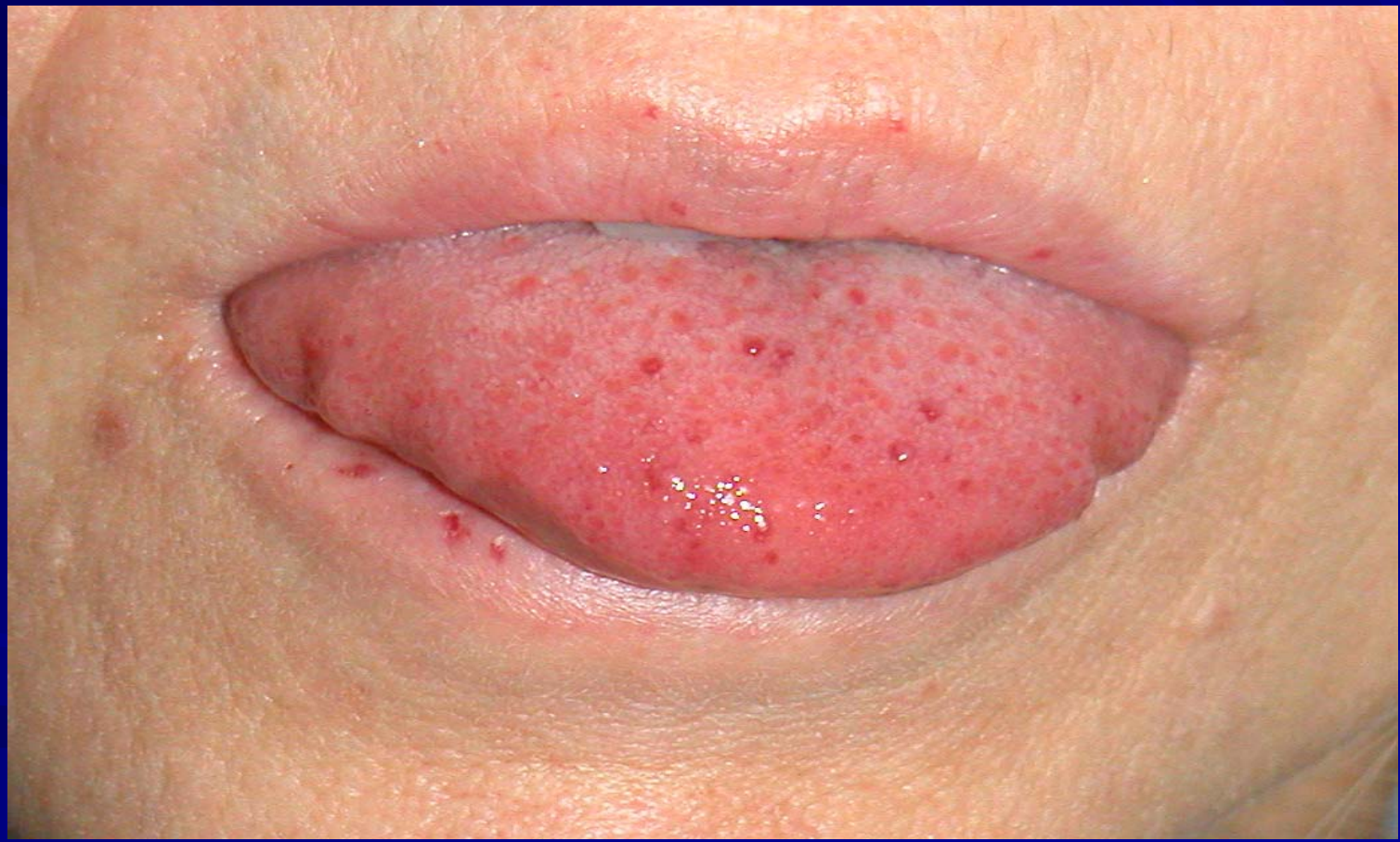




by Jacquelyn McCowen-Rose

Telangiectases



Use of Family History Information Pediatric Primary Care:

Ethical Legal and Social Issue:

Family History Inclusion

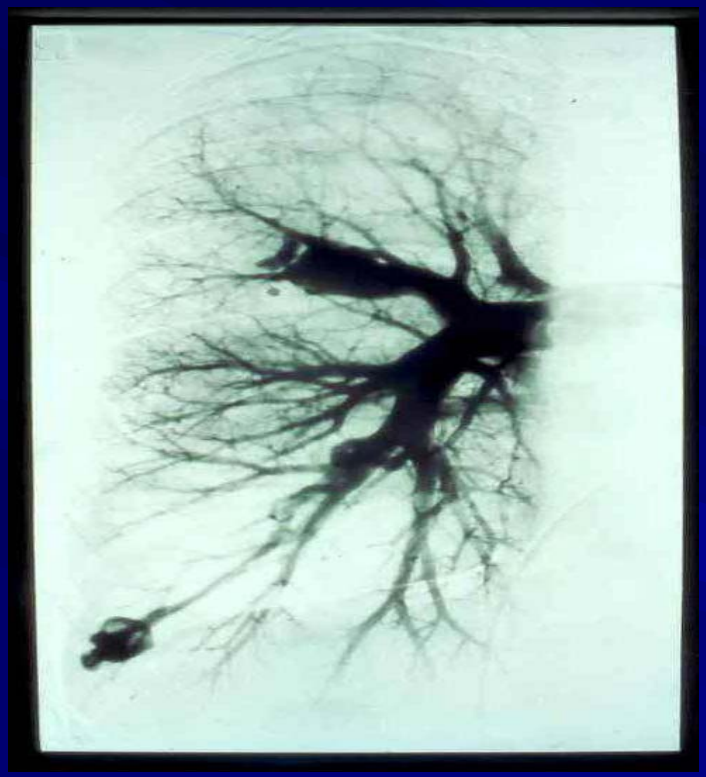
In Patient Records

(HHT as Example: Families are Information Resource)

Telangiectases

Nose	Epistaxis	95% earliest finding
Hands Face Oral Cavity	usually silent	95% decade of 30-40s
GI Tract	Bleeding anemia	20%, decade of 50-60s slow, persistent stomach, upper duodenum

Pulmonary AVM



30-40% of HHT patients

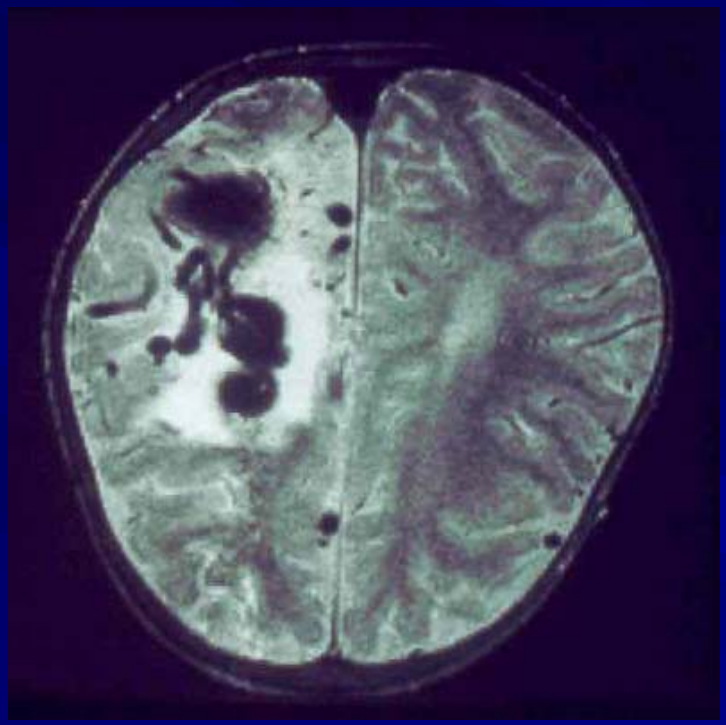
Symptoms

- **exercise intolerance**
- **shortness of breath**
- **migraine**
- **TIA**
- **none**

Risks

- **embolic stroke**
- **brain abscess**
- **hemorrhage**

Cerebral AVM



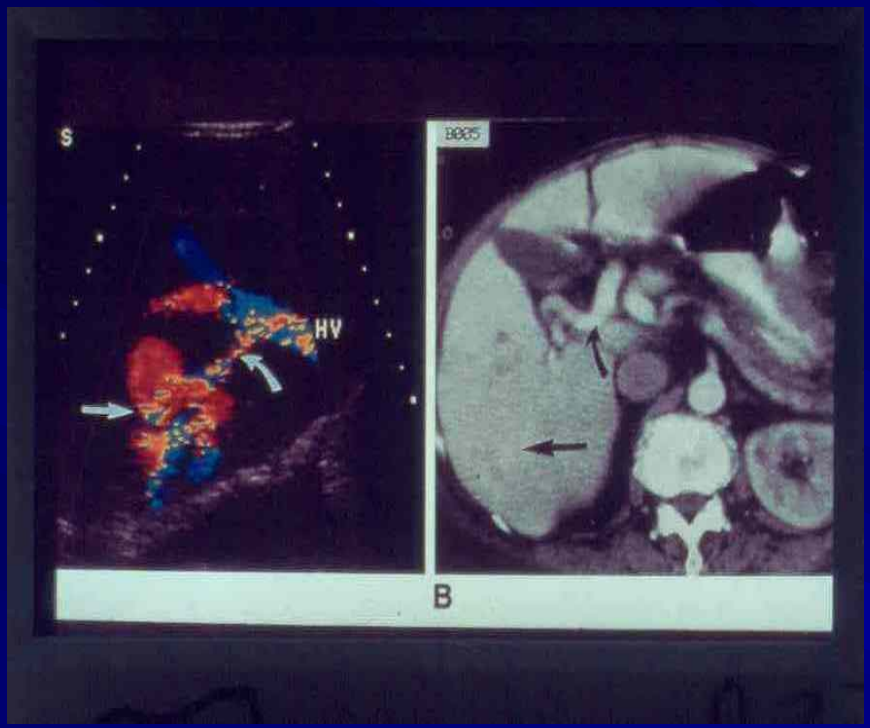
10% of HHT patients
Congenital lesions

Symptoms
- headache
- seizure
- hemiparesis
- none

Risk
-intracranial hemorrhage

can be fatal in asymptomatic children

Hepatic Involvement



70% of HHT pts by CT
5-10% symptomatic

Clinically silent
Lower quadrant pain

Risks
- heart failure
- portal hypertension
- biliary disease

Presymptomatic Treatment

Manifestation	Considerations
Pulmonary AVM	Size of feeder vessel(s)
Cerebral AVM Spinal AVM*	Size Location Structure

Diagnostic Criteria

Shovlin *et al*., Am J Med Genet, 2000

1) Epistaxis

2) Telangiectases-multiple, characteristic sites

3) Visceral lesion

4) Family history

Diagnostic Criteria

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4) Family history

definite	**if three or four**
suspected	**if two**
unlikely	**if one**

HHT Genes

Endoglin (*ENG*)

9q34.1

HHT1 locus - identified 1995

45-50% of HHT

Activin receptor like kinase 1 (*ALK1, ACVRL1*)

12q13

HHT2 locus – identified 1996

45-50% of HHT

At least one other gene

5-10% of HHT

Intracranial Hemorrhage
151 pedigrees

- ICH/CVM confirmed (Utah records) 10
- ICH/CVM confirmed per MD report 23
- ICH/without CVM confirmation 9

TOTAL **52**

Use of Family History Information: Pediatric Primary Care

HHT: Who To Screen?

- Determined by Accurate Family History
- Playing Detective: Following Family Clues
- Familial Nosebleeds are a Common Thread
- Clinically Silent

Use of Family History Information: Pediatric Primary Care

IDENTIFICATION OF AT RISK CHILDREN

Vascular Time Bombs: Adolescence

- Screen All Children for Brain and Lung AVMs
- PAVM: 40 %
- CAVM: 10 %

Patient History

- Patient 1: JS, is currently 19 years old.
- At age 12 he began to experience frequent upper respiratory infections and could not stay up with other children in sports.
- Aunt had mild spots on lips and in liver and was told she had Osler-Weber-Rendu;

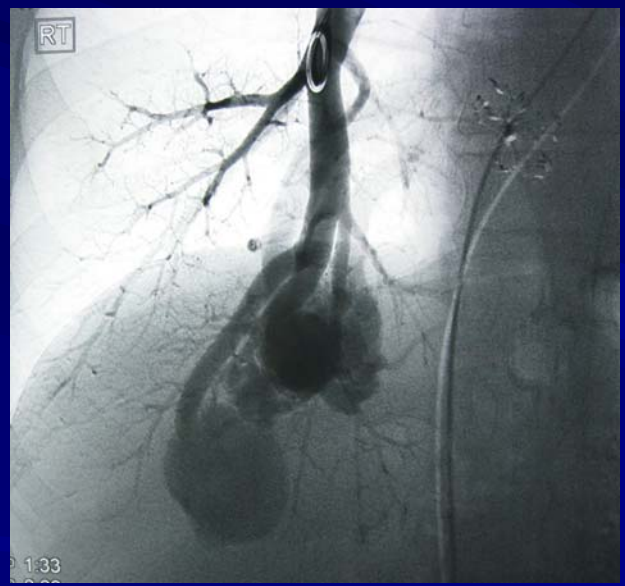
. Pediatrician at first did not make any association.

- At 12 years of age, Pediatrician drew a blood sample and found red blood cells were greatly increased; Concerned about blood cell leukemia.
- JS was referred to major medical center and underwent bone marrow exam and other exams without diagnosis being established.
- By February of the following year, he was growing more symptomatic and the Pediatrician was concerned.
- JS had mild nosebleeds as did his father but no one had considered that his increased red blood cell count was due to low level of oxygen. Finally, out of frustration, the Pediatrician ordered a chest x-ray.
- The radiologist made diagnosis of large PAVM; referred for lung embolization and repair for large PAVM.

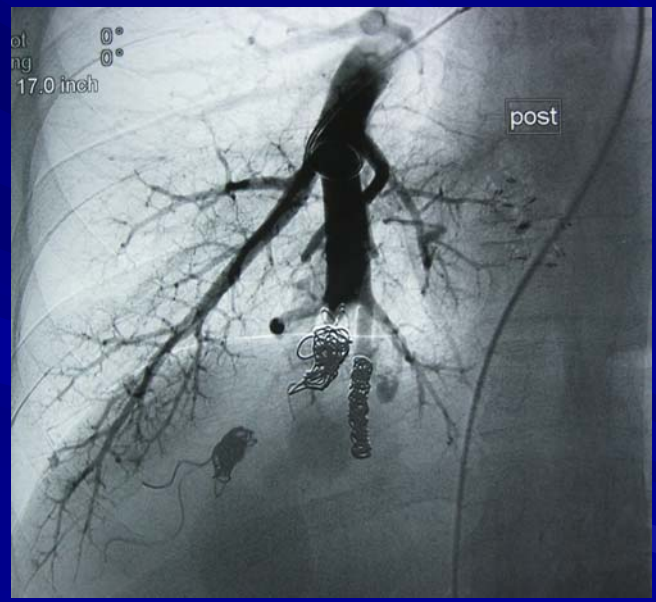
FAMILY HISTORY HAD BEEN IDENTIFIED BUT LACK OF AWARENESS OF GENETICS RESULTED IN MISDIAGNOSIS AND DELAY OF PROPER TREATMENT

Treatment Consideration

- Pre-Embolization



- Post-Embolization



Patient History 2

- A mother lost a son due to a brain hemorrhage.
- He had had nosebleeds, but had not been diagnosed.
- HHT listed on autopsy, but the mother was told son's condition was not relevant to the rest of the family's health.
- The mother became ill with and they took out her appendix! Low oxygen was noted, but she was told to take no action and not worry.
- She had her second son, now 4 years old, who has nosebleeds.
- She took him to seen by a Pediatric Pulmonologist who gave her the referral to an HHT Center.
- Both had previously undetected lung AVMs. They were treated successfully and will be monitored every 3-5 years for the rest of their lives.

FAMILY HISTORY HAD BEEN IDENTIFIED BUT LACK OF AWARENESS OF GENETICS RESULTED IN MISDIAGNOSIS AND DELAY OF PROPER TREATMENT

Family Risks with Genetic Disorder Identification!

- RA- died at 1 mo of age from ruptured brain AVM. Family had known HHT.
- SA- brain hemorrhage at 11yo due to AVM. Survived with severe disability after lengthy hospitalization and brain surgery. Lived until age 26 in a facility for severely disabled adults.
- LH- Spinal AVM detected at 7 yo after 3 years of suggestive symptoms in a known HHT family. Surviving with minimal deficits after surgery.
- MM - multiple hospitalizations for bleeding, daughter with 2 brain hemorrhages, disabled, died 52 years old.
- S Family – 22 year old died from brain abscess, mother had stroke and long rehabilitation, both due to PAVM.
- G Family – mother had life threatening lung hemorrhage, niece had seizures from brain AVM which required emergent surgery.
- K Family – 2 girls with brain AVM, one with paralysis and long term care needs, Grandfather died from clot through pulmonary AVM to brain and intestine, long hospitalization.
- M Family – father died of pulmonary AVM, several children with lung and brain AVM.
- K Family – Grandfather died of undiagnosed lung AVM, grandchildren with multiple lung AVM.
- M Family – son misdiagnosed with multiple sclerosis, had lung AVM, multiple treatments before diagnosis, mother with transfusion dependent nosebleeds.
- R Family – daughter with life threatening hemorrhage during pregnancy from pulmonary AVM.

Conclusions

- Safeguards must be put in place to prevent health insurance and employment discrimination
- Software to assist with family history data gathering in busy pediatric and family practices
- Recognition of familial patterns

Conclusions

- Family History: Genetic Medicine

  Prevents Childhood Death, Morbidity and Disability

  - “ If a proper family history had been taken at any number of points, there might have been a realization that nosebleeds, pulmonary hemorrhages, deaths in adolescence, gastrointestinal bleeding, strokes, TIA’s and brain abscesses, *in multiple generations* were *more than just coincidental*, and death and disability in my family might have been prevented. HHT is a treatable disorder if it is diagnosed, and family history is the first place to start. “