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There's More to Nosebleeds-Think HHT

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Objectives

- Describe the diagnostic criteria of hereditary hemorrhagic telangiectasia (HHT)
- Recognize the clinical presentations of HHT
- Articulate treatment guidelines and referral options

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Nosebleeds

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Nosebleeds

- 60% lifetime incidence
- 6-10% of patients seek care
- 50% occurrence by age 10 yrs.
- 1 in 10 children report recurrent
- Supportive care management
- 22% worldwide prevalence
  < 10 yrs. and > 50 yrs.

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Passali, D. et al., 2020
Yan, T. & Goldman, R., 2021

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Nosebleeds

- Idiopathic
- Trauma
- Inflammation
- Medication
- Structural
- Systemic

Image by Creative Commons for Microsoft 365

Passali, D. et al., 2020
Seikaly, H., 2021

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Nosebleeds

- Remain calm
- Have supplies
- Pinch the lower third of the nose
- Pack nose

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What is HHT?

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History of HHT

HEREDITARY EPISTAXIS.
To the Editor of THE LANCET.

- Dr. B Babington, an English physician, first described familial epistaxis in 1865 in a letter to The Lancet editor,
  - 8-year-old boy and his mother

Reynolds, J.R. & Babington, B.G., 1865

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History of HHT

- Dr. Sir William Osler: noted the condition to be a blood vessel disorder versus bleeding disorder, reported characteristic lesions in the GI tract
- Dr. Frederick Weber: published > 1200 articles, series of cases
- Dr. Henri Rendu: observed skin and mucosal findings, differentiated HHT from hemophilia
- Osler-Weber-Rendu (OWR)

Curehht.org

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What is HHT?

- Rare
- 1: 5000
- Autosomal dominant blood vessel disease
- Alterations in TGFβ
- Equal gender expression
- Greater prevalence in Dutch Antilles (Curaçao and Bonaire) 1:1330
- Variable penetrance in the same family

Faughnan, M. et al., 2020

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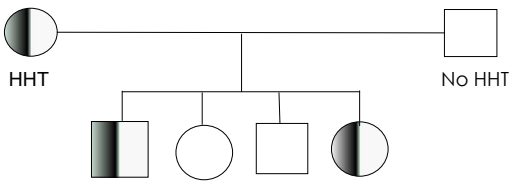
Diagnosing HHT

Autosomal dominant inheritance



50 % chance of HHT for each child

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Diagnosing HHT

- Curaçao Criteria
  - 4 criteria
  - If 3 are present, definite diagnosis
  - If 2 are present, possible diagnosis
  - If 1, unlikely diagnosis
- Genetic testing
  - Easier and more affordable than in the past

Shovlin, C., et al., 2000

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Curaçao Criteria

- Epistaxis
  - spontaneous and recurrent
- Telangiectasias in characteristic sites
  - lips, mouth, nose and fingers
  - gastrointestinal tract
- Visceral involvement
  - lungs (pulmonary arteriovenous malformation) PAVM
  - brain (brain arteriovenous malformation) BAVM or spine AVM
  - liver AVM
- First degree relative with HHT diagnosis

Shovlin, C., et al., 2000

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Genetic testing

- Genetic testing
  - Endoglin (HHT1)
  - ACLVR1 (HHT2)
  - SMAD4 (JPS)
  - RASA1
  - GDF2
  - EBPH4

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Nosebleed Phone Inquiries

- We would like to have our son screened because his father had nosebleeds all his life and just found out at age 37 yrs., that he has HHT.
- We were told by grandparents that there is a bleeding problem in the family and there isn't anything we can do about it. Is this true? Everyone has nosebleeds.
- My daughter has terrible nosebleeds and we have seen an ENT physician, and he believes that she may have this disease that I cannot pronounce; He called it HHT. Is this what she has?

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Nosebleeds

- Most common symptom of HHT
- 95% of patients by age 40 yrs.
  - most by age 12 yrs.
- Gush, ooze
- Daily or rarely
- Contribute to anemia
- Families consider symptom normal
- Most bothersome symptom of HHT

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Nosebleed Management

- Remain calm
- Have supplies
- Pinch the lower third of nose
- Pack nose
- Moisture
- Trim nails and behavior modification
- Topical therapy
  - Vasoconstrictors (oxymetazoline)
- Anemia

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Epistaxis Severity Screen : ESS

Answer each question about your symptoms as they have occurred over the past three months.

- How often do you TYPICALLY have nose bleeding?
- How long does your TYPICAL nose bleeding last?
- How would you describe your TYPICAL nose bleeding intensity?
- Have you sought medical attention for your nose bleeding?
- Are you anemic (low blood counts) currently?
- Have you received a red blood cell transfusion SPECIFICALLY for nose bleeding?

Hoag, J., 2010

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Nosebleed Management

- Surgical therapy
  - Cautery: laser preferred
  - Embolization: Sotradecol
  - Intralesional injection: Bevacizumab
  - Septal dermoplasty
  - Young's procedure
- Systemic therapy
  - Antibiotic: Doxycycline
  - Antifibrinolytics: Tranexamic acid
  - Antiangiogenic: Bevacizumab, IV and nasal,
    - Pazopanib : oral

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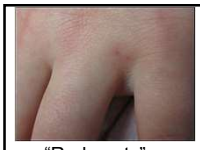

Telangiectasia

- "Red spots"
- Small dilated vessels
- Lips, face, oral cavity, fingers
- GI tract
- Hard to find
- Blanching
- Spider angioma-like

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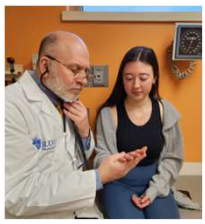
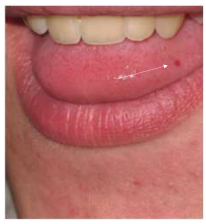
Telangiectasia



Careful physical examination

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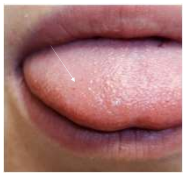
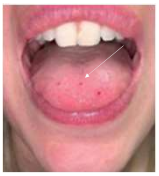
Telangiectasias

Small, 1-4 mm
Blanch

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Gastrointestinal Complications

- Upper and lower GI bleeding (50+)
- Most common sites are stomach and upper small intestine
- Difficult to treat
- Iron deficiency anemia
- Juvenile Polyposis Syndrome (SMAD4 or HHT3)
  - Endoscopy surveillance for polyp removal
- Liver AVMs
  - Increased prevalence in HHT2
  - Not screened for in children

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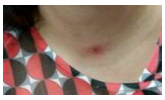
Patient case #1

- 8-year-old child seen by ENT for nosebleeds with history of electrocautery x3
- ENT noted a skin telangiectasia on mom
- Mother was diagnosed with ENG mutation.
- 50% of children had mutation
- PAVMs present, nosebleeds



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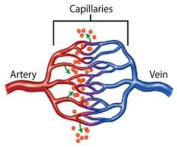
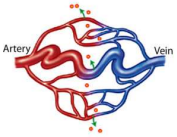
Arterial venous malformations



Normal



Abnormal

Curehht.org

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Pulmonary Arteriovenous malformations (PAVMs)

- 40-50% of patients will have PAVMs
- 60% of these will have multiple lesions
- PAVMs are rare without HHT
- 90% are simple AVM versus 10% that are complex
- Diffuse PAVMs may occur

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PAVMs

- Asymptomatic
- Cyanotic
- Exercise intolerance (short of breath)
- Hemoptysis
- Hypoxemia
- Migraine headache

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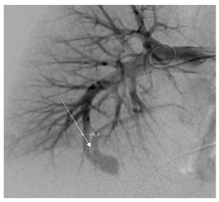
PAVMs

- Still many unknowns
- Might be present at birth
- May develop in childhood
- May develop throughout the lifespan
- Grow slowly



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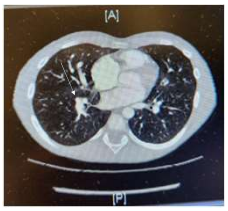
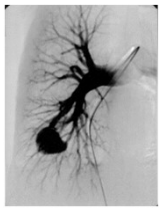
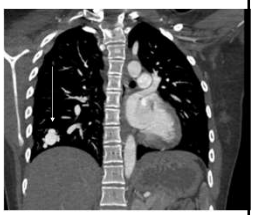
PAVMs







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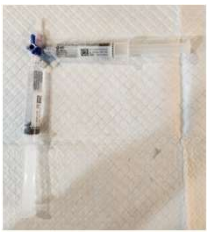
PAVM Screening



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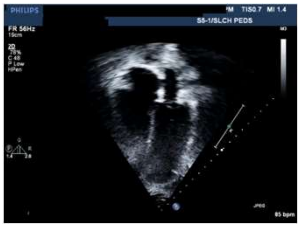
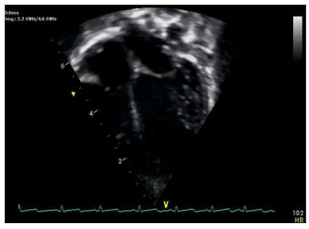
Contrast Echocardiogram





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PAVM Management

- Chest CTA after positive bubble echo

- Observation
- Endovascular embolization (2-3 mm)
- Surgical resection
- Antibiotic dental prophylaxis

Faughnan ME, et al., 2020

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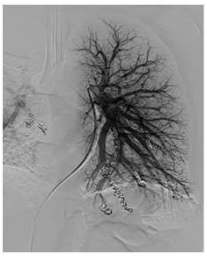
PAVM Management



Typical plugs and coils

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Patient Case #2

- 15-year-old boy in EU after skateboard accident
- Sp02 in the 80's
- Chest x-ray suspicious for PAVMs,
  - Chest CT confirmed PAVMs
- Positive family history of HHT,
  - No previous evaluation

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PAVMs Complications

- Asymptomatic
- Shortness of breath
- Hypoxia
- Heart failure / Pulmonary hypertension
- Brain abscess
- Stroke
- Death

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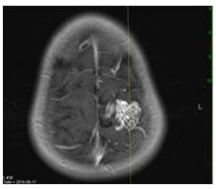
Brain Arteriovenous Malformations (BAVMs)



- Present in 10-20% of patients with HHT
- BAVMs can be singular or multiple
- 1% chance of hemorrhage per BAVM per year
- Spinal AVMs may be present

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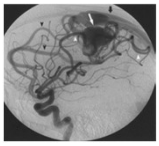
BAVM Management



- Brain MRI
- MRA with known BAVM
- Sedation
- Management
  - Gamma Knife (stereotactic radiosurgery)
  - Surgical resection
  - Observation

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BAVMs Complications

- Intracranial hemorrhage
  - Stroke
  - Seizure
  - Death
- CNS complications
  - Lifelong complications

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The Curaçao Criteria and Children

- Pahl, K., et al., 2018
  - 290 patients with a family history of HHT,
  - 4 age groups, 0-5, 6-10, 11-15, and 16-21 years
  - Multicenter chart review
  - Genetic testing, (considered the gold standard) was compared to the Curaçao Criteria
- Conclusions:
  - Curaçao Criteria is reliable to diagnose HHT in children who meet 3-4 criteria. Genetic testing is recommended for patients with 1-2 criteria.
  - Sensitivity lowest in 0-5 and highest in 16-21

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HHT Referral

- CureHHT Centers of Excellence (CoE)
- Proactively manage the care of patients with HHT
- Review and plan with HHT specialist
- Multidisciplinary team of experts
- HHT specialists work closely with an HHT coordinator
- Subspecialties include cardiology, neurology, neurosurgery, radiology, hematology and others

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HHT Referral

- Comprehensive phone intake by coordinator
- Obtain and review records
- Family and facility confirm insurance
- Plan evaluation with CoE or specialist

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International Pediatric Guidelines

The expert panel recommends....	Quality of Evidence (Agreement %)	Strength of Recommendation (Agreement %)
E1: that diagnostic genetic testing be offered for asymptomatic children of a parent with HHT.	High (96%)	Strong (94%)
E2: screening for pulmonary AVMs in asymptomatic children with HHT or at risk for HHT at the time of presentation / diagnosis.	Moderate (94%)	Strong (94%)
E3: that large pulmonary AVMs and pulmonary AVMs associated with reduced oxygen saturation be treated in children to avoid serious complications.	Moderate (98%)	Strong (98%)
E4: repeating pulmonary AVM screening in asymptomatic children with HHT or at risk for HHT; typically at 5 year intervals.	Low (92%)	Strong (86%)
E5: screening for brain VM in asymptomatic children with HHT, or at risk for HHT, at the time of presentation / diagnosis.	Low (86%)	Strong (86%)
E6: that brain VMs with high risk features be treated.	Low (100%)	Strong (98%)

Faughnan ME, et al., *Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia.* Ann Intern Med. 2020 Dec 15;173(12):989-1001. PMID: 32894695

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HHT Screening

Patient has HHT Familial Mutation → Consultation and clinical screening tests

Patient does not know their genetic mutation → Consultation and Genetic testing

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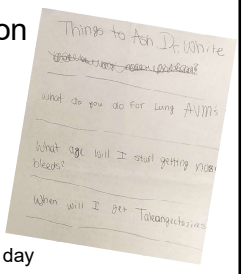
HHT Consultation

- History and physical examination
- Pulse oximetry
- Bubble echocardiogram
- Brain MRI
- Genetic testing
- Other specialty appointments as needed
- Review of all tests, plans at the end of the day



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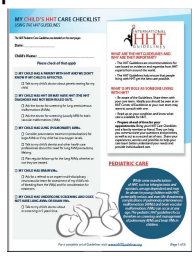
HHT Follow up

- Education and guidance
- Individualized appointment follow up
  - Months-5 years
  - PRN
- No scuba diving
- Limit NSAID use, avoid Aspirin
- Visit HHT CoE at least once



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Patient Case #2

- Summary of HHT center consultation:
  - Sp02 88% on room air at presentation
  - Nosebleeds, telangiectasias, clubbing of nailbeds
  - Positive genetic marker in ENG (HHT1)
  - Embolization of 3 PAVMs, feeding vessel was 5 mms

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Patient Case #3

- 4-year-old asymptomatic boy presents to HHT center for evaluation, Dad with ENG mutation
- Patient tests positive for ENG
- Brain MRI reveals right parietal occipital AVM (12mm)
- Craniotomy for removal of AVM
- Positive bubble echocardiogram

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Delay in Diagnosis

- Underdiagnosed
- Long diagnostic delay
- Pierucci, P. et al., 2012
  - 233 participants, 88 patients received Dx at first visit
  - Clinical signs at age 14 yrs., referral at age 29
  - Dx at 40 yrs. with lag time of 25.7 yrs.
  - 22 pts suffered severe complications during interval

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Case presentation

- 5-year-old boy found unconscious at his home
  - EMS arrived within 10 minutes
  - Transferred to hospital
  - Family history of HHT
  - Asymptomatic
  - Never evaluated

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Living with HHT

- No Cure
- Uncertainty
- Denial
- Family support
- Advocacy
- Research

Palmer, S. 2017

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Thank you!

HHT patients and families
Dr. Andrew J. White
Dr. Katheryne Amba
Curehht.org
HHT providers
Researchers
SPN

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