Clinical aspects of Hereditary Haemorrhagic Telangiectasia (HHT)

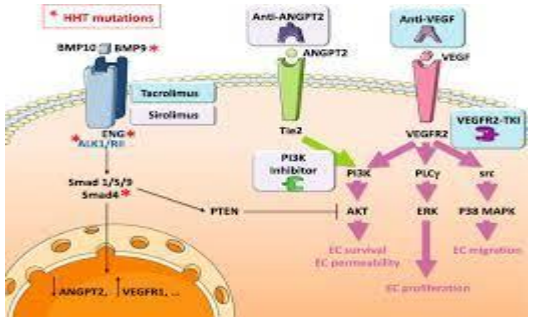
- Autosomal dominant condition with a prevalence of 1/5000
- National HHT Centre led by Dr Adrian Brady / Professor Terry O'Connor based in Mercy University Hospital Cork
- Between 2003 and January 2022, 688 patients attended the service
- 63.3% of patients had a CT Thorax (following a positive contrast echocardiogram), of which 31.3% were positive for pulmonary arteriovenous malformations (pAVMs).
- 65 patients have had a total of 202 pAVMs embolised.
- 92.9% of patients had a contrast-enhanced MRI Brain. 7.2 % were positive for cerebral arteriovenous malformations (cAVMs).
- 52.6% of patients were identified as having definite HHT (based on the presence of 3 or more Curacao criteria and/or positive genetic testing).

When should HHT be considered

The Curaçao Diagnostic Criteria for HHT

•If a doctor determines that at least three of these criteria are met, the patient is categorised as **definite HHT**.
•If two of the criteria are met, the patient is categorised as **possible HHT**.
•If fewer than two of these criteria apply, the patient is categorised as **unlikely to have HHT**.

1. Recurrent and spontaneous nosebleeds (epistaxis), which may be mild to severe.
2. Multiple telangiectases on the skin of the hands, lips, face, or inside of the nose or mouth. Telangiectases are small red spots that disappear when pressed upon.
3. Arteriovenous malformations (AVMs) or telangiectases in one or more of the internal organs, including the lungs, brain, liver, intestines, stomach, and spinal cord.
4. A family history of HHT (i.e. first-degree relative who meets these same criteria for definite HHT or has been genetically diagnosed).



Emerging Therapies HHT

Tacrolimus
BMPR2 activator in HHT
Decreases incidence of AVMs in mouse models

Bevacizumab
Antibody directed to VEGF, inhibiting neoangiogenesis

Octreotides
Inhibit GH and ILGF1
Clinical trials underway

Thalidomide
Reduces epistaxis by promoting vessel maturation

Pulmonary AVMS	Genetic factors in HHT	Complications
pAVMs are present in 15–45% of patients with HHT and HHT is the underlying cause in at least 80% of PAVMs. Adults with untreated PAVMs are at risk for stroke and brain abscess (due to paradoxical embolisation) and life-threatening haemorrhage. Contrast echocardiography is the screening test of choice, with a sensitivity of >90% . Computed tomography (CT) thorax (non-contrast) is the current accepted diagnostic gold standard and is used to confirm and measure the size of pAVMs in patients with positive contrast echocardiography. **Treatment** Transcatheter embolotherapy is the current standard treatment for PAVMs with feeding arteries > 2.5mm.	• Endoglin mutations - HHT 1 • Increased risk of pulmonary (58%) and cerebral AVMs (x 3-6) • ACVRL1 mutations – HHT 2 • pAVMs in 18% • Hepatic AVMs (x 3-6) • SMAD 4 mutations – HHT-Juvenile polyposis syndrome • GDF2 mutations – HHT 5 • A negative genetic test does not completely exclude HHT. 15% of people with HHT have mutations in genes that have not yet been identified as being associated with HHT	Brain abscess (pAVMs). Hemorrhagic or ischemic stroke (pAVMs & cAVMs). High-output congestive heart failure (liver AVMs). Chronic GI bleeding and anemia (GI telangiectasia). Cirrhosis, portal hypertension with esophageal varices (liver AVMs). Pulmonary hemorrhage (pAVMs). Antibiotic prophylaxis for bacteraemic procedures (esp. dental work) is recommended to prevent cerebral abscess When using IV access in patients with HHT, take extra care to avoid IV air Patients with pAVMs should avoid SCUBA diving

PAVM embolization - outcomes

- Technical success 88-100%
- Follow up CT at 6 months, to look for shrinkage of nidus
  - CT thereafter at 5 year intervals
- Immediate improvements in oxygenation (if pAVMs large)
- Reduced risk of brain abscess, stroke