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Experience of the Irish National Centre for hereditary haemorrhagic telangiectasia 2003–2008

C.F. Ni Bhuachalla [a], T.M. O' Connor [b,*], M. Murphy [a], N. Colwell [b], A. Brady [a]

[a] *Dept. of Radiology, National HHT Centre, Mercy University Hospital, Cork, Ireland*
[b] *Dept. of Respiratory Medicine, National HHT Centre, Mercy University Hospital, Grenville Place, Cork, Ireland*

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Embolisation

Summary
Hereditary haemorrhagic telangiectasia (HHT) is a group of autosomal dominant disorders of vascular structure. The Irish National Centre for HHT at the Mercy University Hospital, Cork, Ireland was founded in 2003. From 2003 to 2008, screening of 164 patients with contrast echocardiography, thoracic computerised tomography (CT) and cerebral magnetic resonance imaging (MRI) has identified 88 patients with definite HHT, 72 (82%) of whom had epistaxis, 70 (80%) had telangiectasia and 81 (92%) had a first-degree relative with HHT. We sought to describe the manifestations of HHT in an Irish population and to determine differences between internationally reported data.

The HHT patient database was analysed to describe demographics, clinical manifestations and interventional procedures performed in all referred patients.

Contrast echocardiography and/or CT were performed in 86 patients with definite HHT, identifying 27 patients (31%) with pulmonary arteriovenous malformations (pAVMs). Nineteen patients with single or multiple pAVMs had 28 embolisation procedures performed, with 1–6 pAVMs embolised per procedure. Cerebral MRI was performed in 78 (89%) patients and 2 (2.3%) had cerebral arteriovenous malformations (cAVMs).

HHT prevalence is thought to be 1 in 2500–8000, suggesting that there are many undiagnosed cases in Irish patients. Internationally published data suggest a prevalence of 15–35% for pAVMs and 10–23% for cAVMs in patients with HHT. While the prevalence of pAVMs in our group is consistent with these data, the prevalence of cAVMs is considerably lower, suggesting that Irish patients with HHT may differ genotypically and phenotypically from those in other countries.

* Corresponding author. Tel.: +353 21 4935325; fax: +353 21 4935350.
E-mail address: terryoconnor@eircom.net (T.M. O' Connor).

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Introduction

Hereditary haemorrhagic telangiectasia (HHT) is a group of autosomal dominant multisystem vascular dysplasias characterised by recurrent epistaxis with cutaneous and mucosal telangiectases (Fig. 1) and visceral arteriovenous malformations (AVMs).[1] It is historically known as Rendu-Osler-Weber syndrome, after three physicians who, in the late 19th and early 20th century, recognised this hereditary disorder involving nosebleeds and characteristic cutaneous and mucosal red spots. The title HHT was devised by Hanes in 1909.[1]

HHT affects 1 in 8000–10,000 individuals but is subject to ethnic and geographical variation, with prevalence reported as 1 in 2500 in some regions of France.[2] Penetrance and expressivity are also subject to variation, even within a single affected family,[2] that is, an affected individual with epistaxis, telangiectasia and pulmonary AVMs may have a sibling with epistaxis only. A number of HHT subtypes have been identified including HHT type 1, associated with an endoglin gene mutation (chromosome 9) and HHT type 2 associated with an ALK-1 (AC-VRL1) gene mutation (chromosome 12). Other chromosomes involved in HHT include chromosomes 5, 7 and 18 (MADH4 or SMAD4 gene).[2,3] These genes encode proteins expressed on vascular endothelial cells which are involved with signalling by the transforming growth factor-beta (TGF-β) family. TGF-β signalling affects cellular growth and differentiation. Thus abnormal angiogenesis in HHT is thought to occur due to aberrant TGF-β signalling caused by disturbed protein function from endoglin and ALK-1 genetic mutations.[4] Genetic testing may help to diagnose HHT in a patient with an affected relative who has a known HHT mutation.[5]

The understanding of HHT and its complications continues to evolve since this condition was first recognised. The Scientific Advisory Board of the HHT Foundation International established clinical criteria for the diagnosis of HHT (the Curaçao criteria) in 1998 (Table 1). HHT diagnosis is considered *definite* if three criteria are present, *possible* or *suspected* if two criteria are present and *unlikely* if fewer than two criteria are present.[6] More recently, international guidelines for the diagnosis and management of HHT have been published.[7]

HHT is a relatively common but under-recognised condition. The importance of screening for this disorder must be emphasised as up to 10% of affected individuals suffer disability or premature death as a result of complications associated with HHT.[5] These complications are often due to an AVM's increased likelihood of rupture when compared with a regular blood vessel. In the case of pulmonary AVMs (pAVMs) (Fig. 2) complications also arise from right-to-left shunting of blood leading to cerebrovascular accident or brain abscess due to bland or septic emboli entering the cerebral circulation.[8] Therefore, all patients with suspected or confirmed HHT, as well as first-degree relatives of definite cases, should be referred to a specialist centre for appropriate screening.[2]

The Irish National HHT Centre was established in the Mercy University Hospital (MUH) in Cork, Ireland in January 2003. This centre aims to identify patients with this condition, to identify all affected family members through screening, to identify the manifestations of HHT in each person affected and to manage these appropriately. Screening tests for visceral AVMs include contrast echocardiography, computerised tomography (CT) of thorax and magnetic resonance imaging (MRI) of brain. Interventions for epistaxis, pAVMs and cerebral AVMs (cAVMs) are carried out as necessary and include nasal cautery, nasal septal dermoplasty, nasal grafting and AVM embolisation. This paper reports the experience of the Irish National HHT centre from 2003 to 2008, with particular reference to the prevalence of AVMs in this patient population compared with other international data.

Methods

Patients referred to the Irish National HHT Centre were invited to attend for clinical history and physical examination; further investigations in those with clinical features of HHT

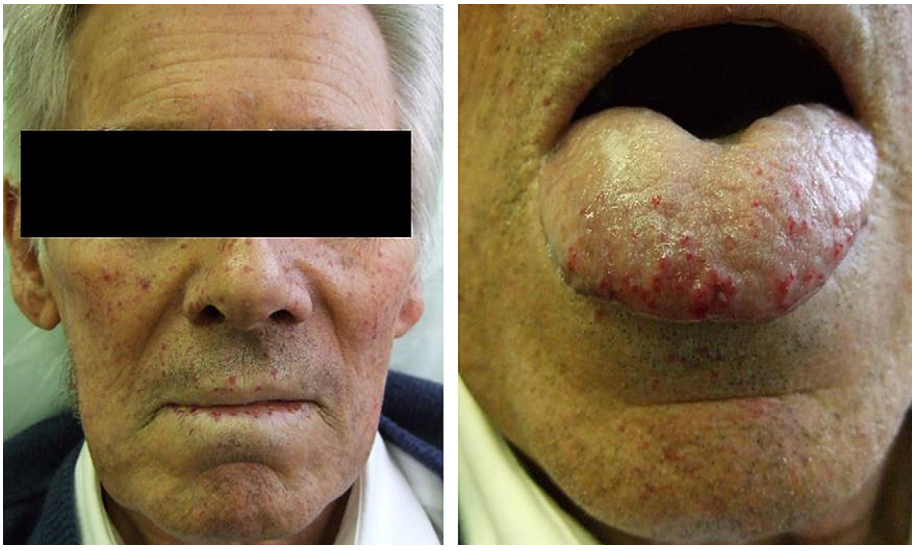

Figure 1 67 Year male with HHT and multiple mucocutaneous telangiectasia.