

SPECIAL REVIEW

Marathon of eponyms: 15 Osler–Rendu–Weber disease (Hereditary haemorrhagic telangiectasia)

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The use of eponyms has long been contentious, but many remain in common use, as discussed elsewhere (Editorial: Oral Diseases. 2009; 15; 185). The use of eponyms in diseases of the head and neck is found mainly in specialties dealing with medically compromised individuals (paediatric dentistry, special care dentistry, oral and maxillofacial medicine, oral and maxillofacial pathology, oral and maxillofacial radiology and oral and maxillofacial surgery) and particularly by hospital-centred practitioners. This series has selected some of the more recognised relevant eponymous conditions and presents them alphabetically. The information is based largely on data available from MEDLINE and a number of internet websites as noted below: the authors would welcome any corrections. This document summarises data about Osler–Rendu–Weber disease.

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Also known as

Babington disease
Goldstein haematemesis
Goldstein heredofamilial angiomatosis
Goldstein syndrome
Hereditary haemorrhagic telangiectasia
Osler disease
Osler syndrome
Osler–Rendu–Weber syndrome
Rendu–Osler syndrome

The condition

Osler–Rendu–Weber disease (hereditary haemorrhagic telangiectasia: HHT) occurs mainly in white people

(1:5000). HHT is an autosomal dominant syndrome characterised by multiple telangiectasia of the skin, and of the oral, nasal, conjunctival and gastrointestinal mucous membranes. These manifest from childhood and are liable to ulcerate and bleed, and so epistaxis and gastrointestinal haemorrhages are common. Bleeding from the telangiectases may be recurrent, life-threatening and increases with aging. Arteriovenous fistula, especially of the lungs, liver and brain, is a variable component: high-output cardiac failure and cerebral abscesses may result. Recurrent complications are severe anaemia, stroke and portal and pulmonary hypertension.

The mechanism underlying the formation of the vascular malformations in HHT seems related to *transforming growth factor beta 1* (TGFB-1) signalling defects adversely affecting matrix and connective tissue production. TGF-beta signalling has a pivotal role in angiogenesis.

Several forms of HHT have been described:

- Hereditary haemorrhagic telangiectasia 1, which predisposes to pulmonary and cerebral arteriovenous fistulae and early oral and nose bleeds, is related to mutation of the endoglin gene (ENG). ENG is a receptor for transforming growth factor beta 1 and transforming growth factor beta 3.
- Hereditary haemorrhagic telangiectasia 2 dermal lesions and hepatic vascular malformations are more frequent and appear earlier in life with later nose bleeds, but with an increased risk of pulmonary hypertension: it is related to mutation in the alk1 gene. Activin receptor-like kinase 1 (Alk-1 or AC-VRL1) is a TGFβ1 receptor.
- Hereditary haemorrhagic telangiectasia 3 has not yet been linked to a defective gene.
- Juvenile polyposis/HHT syndrome is caused by mutations in the SMAD4 gene, which modulates TGF.
- Hereditary haemorrhagic telangiectasia 4 has now been identified.

The diagnostic criteria for HHT include:

1. Spontaneous recurrent epistaxis
2. Multiple telangiectasis

3. Proven visceral arteriovenous fistulae
4. First-degree family member with HHT.

If three or four of these criteria are met, a patient has *definite HHT*, while two gives a possible diagnosis.

There is no specific treatment for the condition. Anaemia due to bleeding may necessitate blood transfusions. AVMs in critical organs may necessitate surgery or embolisation under radiographical control. Infra-red laser coagulation is well suited to the treatment of telangiectases in the skin and/or mucosal surfaces.

Background to eponym

Reports describing the condition were published by Henry Gawen Sutton (1864), Benjamin Guy Babington (1865) and John Wickham Legg (1876). Rendu in 1896 described a 52-year-old man who suffered repeated nose bleeds and had multiple haemangiomatic spots on the skin of the face and trunk, and on the lips, tongue and palate, and he speculated that nose lesions were responsible for the epistaxes. Rendu noted a family history: the mother had experienced similar problems.

William Bart Osler in 1901 authored the first comprehensive description of the disease in three patients, and emphasised its familial nature. Fredrick Parkes Weber subsequently a few years later reported a further series of cases. A haemorrhagic telangiectasia syndrome has been called Jaccoud-Osler disease after the Swiss physician Sigismund Jaccoud.

The main persons

William Osler was born on 12 July 1849, the son of an immigrant Cornish missionary, at Bond Head, Tecumseth, Canada.

He started to study arts at Trinity College, Toronto, but changed to study Medicine at Toronto Medical School in 1868. He subsequently transferred to McGill University in Montreal, Quebec, where he qualified in 1872. He then visited a number of medical centres in London, Berlin, Leipzig and Vienna, travelling with Harvey Cushing. They spent the longest period at University College, London, where Osler was the first to see platelets. Osler returned to Canada to undertake general practice in Dundas, Ontario; was appointed lecturer in the Institutes of Medicine at McGill and became Professor in 1875 at a young age of 26. A year later, he became pathologist to the Montreal General Hospital and, in 1878, a physician there. He was invited to occupy the Chair of clinical medicine at the University of Pennsylvania, Philadelphia, in 1884, and became a founding member of the Association of American Physicians. In 1888/1889, Osler accepted an invitation to be the first Professor of medicine at the Johns Hopkins University Medical School, Baltimore. Osler published his book 'Principles and Practice of Medicine' in 1892. This textbook

spread his fame throughout the world and inspired the philanthropist and businessman Frederick T. Gates to advise John D. Rockefeller, philanthropist, to direct his foundation towards medical research and to establish the Rockefeller Institute of Medical Research in New York.

In 1904, while visiting the UK, Osler was invited to, and accepted, the Regius Chair of Medicine at the University of Oxford. He was elected a fellow of the Royal College of Physicians of London in 1884 and a fellow of the Royal Society in 1898. In 1911 he was made a baronet. William Osler died from bronchopneumonia and empyema on 29 December 1919, in Oxford.

Osler wrote some of the early descriptions of platelets and classical papers on hereditary telangiectasia, lupus erythematosus and polycythaemia vera.

Other eponymous conditions associated with Osler include: Osler nodes – cutaneous nodules in subacute bacterial endocarditis – described in 1885, and Osler-Vaquez disease – polycythaemia vera – described in 1903.

Henri Jules Louis Marie Rendu was born on 24 July 1844, in Saint-Germain-des Prés, Paris, France. He spent 2 years at the Rennes Agronomic School and later gained a doctorate in geology. He started studying Medicine in 1865, in Paris and, in 1868 became interne at the Hôpital Saint-Antoine working under Jules Guyot, Adolphe-Marie Gubler, Ernest Henri Besnier, Henri Louis Roger and Pierre Charles Édouard Potain, one of France's leading clinicians.

In 1870, after the start of the Franco-Prussian war, Rendu was appointed an army surgeon. On his return to Paris, he was appointed again at the Hôpital Saint-Louis where in 1873 he was awarded the Médaille d'Or of internship. He then spent a year at the Hôpital Necker with Potain. In 1874, he received the Médaille d'Argent for his thesis 'Paralyses related to tuberculous meningitis in children'. In 1877, Rendu received the degree of hospital physician – Médecin des Hôpitaux – and the next year finally achieved Professeur agrégé with a thesis 'Comparative study of chronic nephritis'.

He then worked in the Hôpital Tenon, and in 1885 returned to the Hôpital Necker as Head of the Department of Medicine, where he spent the rest of his career. In 1897, he received the ultimate accolade of election to membership of Academy of Medicine. Rendu died on 16 April 1902.

Frederick Parkes Weber was born on 8 May 1863, in London. He was educated at Charterhouse School, Cambridge University and Medicine at St. Bartholomew's Hospital, London, as well as in Cambridge, Paris and Vienna. Weber obtained his doctorate at Cambridge in 1892 and then worked at St. Bartholomew's Hospital and at the Brompton Hospital for Chest Diseases, before being appointed honorary physician to the German Hospital, Queen Square, London (1894). He worked there until the age of 80 years. He was also physician at the North London

Hospital for Consumption and assistant physician, then physician at Mount Vernon Hospital. He died in 1962.

Associated persons

Benjamin Guy Babington
Hyman Isaac Goldstein
Sir William Osler, Baronet
Henri Jules Louis Marie Rendu
Frederick Parkes Weber

Source internet sites (accessed 21 February 2009) and further reading

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