Oral Diseases (2009) 15, 434–436. doi:10.1111/j.1601-0825.2009.01536.x

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SPECIAL REVIEW

Marathon of eponyms: 4 Down syndrome

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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 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 recognized 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 paper summarizes data about Down syndrome.

Oral Diseases (2009) **15**, 434–436

Keywords: oral; eponyms; Down's syndrome; trisomy 21

Also known as

Morbus Langdon-Down
Langdon Down disease
Morbus Down
Mongolism (outmoded and politically incorrect term)

The condition

Down syndrome is the most frequent genetic cause of learning impairment, appearing in one out of 800 live births, in all races. An older mother is more likely to have a baby with Down syndrome, but, as older mothers have fewer babies, about 75% of babies with Down syndrome are born to younger women. The occurrence of Down syndrome per 1000 living births is approximately 0.5 for a woman under 25 years of age, 5 from 25–35 years, and 35 for mothers over the age of 45. Down syndrome affects many, if not most, organs and may result in multiple impairments and about one-third succumb in the first few years.

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Down syndrome is usually caused by an error in cell division that results in the presence of an additional third chromosome 21 (trisomy 21), in 88% derived from the mother. The resultant range of physical disabilities varies, depending on the proportion of cells carrying the additional chromosome 21. Down syndrome is usually because of a random event during formation of the ovum or sperm causing one of three genetic variants. In 92%, there is an extra chromosome 21 in all cells (*trisomy 21*). In 2–4% there is a *mosaic trisomy 21* – the extra chromosome 21 is present only in some cells. In approximately 3–4%, material from one chromosome 21 is translocated on to another chromosome (*translocation trisomy 21*), cells then have two normal chromosomes 21, but also have additional chromosome 21 material on the translocated chromosome, usually chromosome 14 or 15.

There may be an increased likelihood of Down syndrome in future pregnancies where the mother has had a child with translocation trisomy 21.

A range of chromosome 21 genes is implicated in Down syndrome including amyloid beta A4 precursor protein (APP), type 1 collagen (COL6A1), Crystallin, Alpha-A (CRYA1), Down Syndrome Critical Region Gene 1 (DSCR1), Tyrosine Phsphorylation-Regulated Kinase. (DYRK), Avian Erythroblastosis Virus E26 Oncogene Homologue 2 (ETS2), Interferon Alpha Receptor (IFNAR), and Superoxide Dismutase (SOD1). Genes involved in the mental changes appear to include DYRK1A and RCAN1. DYRK1A phosphorylates transcriptional factors, such as CREB and NFAT, endocytic complex proteins, and Alzheimer disease-linked gene products. RCAN1 is an inhibitor of calcineurin A, and is thought to cause neuronal malfunction in DS and Alzheimer disease.

The characteristic features of Down syndrome are short stature, learning impairment, and a typical facies with brachycephaly, widely spaced eyes, Brushfield's spots in the iris, and epicanthic folds. The hands show clinodactyly (short fifth finger) and simian (single) palmar creases. Approximately 50% have congenital cardiac disorders (atrial septal defect, mitral valve prolapse or, less often, atrioventricular and ventricular septal defect) and associated early onset of pulmonary hypertension. Mitral valve prolapse can lead to

arrhythmias, embolism or sudden death. If it causes a systolic murmur, it can predispose to infective endocarditis, particularly in older persons. Dementia, or memory loss and impaired judgment similar to that in Alzheimer disease patients, may develop. Seizure disorders affect between 5% and 13%, a 10-fold greater incidence than in the general population. There is susceptibility to transient myelodysplasia, and defective development of the spinal cord. Atlantoaxial instability can cause spinal cord compression if the neck is not handled gently. The external ear and the bones of the middle and inner ear may maldevelop and thus up to 90% have hearing loss of >15–20 decibels in at least one ear. Cataracts appear in approximately 3%.

Children with Down syndrome are 10–15 times more likely than other children to develop leukaemia. There is also a predisposition to testicular cancer.

Multiple immune defects mean that infections of the skin, gastrointestinal and respiratory tracts, and periodontal disease, are common: superoxide dismutase which has been shown to increase in Down syndrome may be implicated in the immune defect. Chronic respiratory infections include TB and recurrent middle ear, tonsil, nasal and sinus infections. There is a 12-fold higher mortality rate from infectious diseases, particularly pneumonia. The life expectancy for people with Down syndrome though low, has increased substantially to age 50 and beyond, particularly because infections are now more readily controlled and treated.

Craniofacial features include brachycephaly, hypoplastic midface, anterior open bite, posterior crossbite and other types of malocclusion, tongue which may be absolutely or relatively large (macroglossia) and is often fissured, more especially after the age of about 4 years. The circumvallate papillae enlarge but the filiform papillae may be absent. The lips tend to be thick, dry and fissured. Poor anterior oral seal and also a strong tongue thrust may be seen. The palate often appears to be high, with horizontal palatal shelves (the omega palate), but a short palate is more characteristic. There is also a higher incidence of bifid uvula, cleft lip and cleft palate.

The first dentition may begin to appear only after 9 months and may take 5 years to complete, if ever. The deciduous molars may erupt before the deciduous incisors and deciduous lateral incisors are absent in about 15%. The eruption of the permanent teeth is often also irregular. Missing teeth are common: the third molars and lateral incisors are most often absent. Up to 30% have morphological abnormalities in both dentitions, particularly teeth with short, small crowns and roots. The occlusal surfaces of the deciduous molars may be hypoplastic and both dentitions may be hypocalcified.

Severe early onset periodontal disease may be partly because of poor oral hygiene, but may be the result of impaired cell-mediated and humoral immunity and a deficient phagocytic system. Acute ulcerative gingivitis may also be seen.

Background to the eponym

The first descriptions were in 1838 by Jean Etienne Dominique Esquirol (1772–1840), and by Édouard Séguin (1812–1880) in 1844. Langdon Down published a more elaborate description in 1866.

The main person

John Langdon Haydon Down was born in 1828, at Torpoint, Cornwall. He left school at the age of 13 to assist his apothecary father and then at 18 moved to London, working for a surgeon in the Whitechapel Road, where he had the opportunity to practice tooth extraction and venepuncture. In 1847, he began work at the Pharmaceutical Society in Bloomsbury Square, in the laboratory and subsequently became assistant to Professor Redwood and then to Michael Faraday (1791–1867). When he fell ill he returned to the West Country and spent 3 years recuperating on Dartmoor. His father died in 1853, when Down entered the London Hospital Medical School, graduating in 1858 with top marks, and soon was elected to the Royal College of Surgeons. He took a post as resident physician and subsequently as medical superintendent at the Earlswood Asylum for Idiots in Redhill, Surrey (subsequently the Royal Earlswood Hospital). He was soon elected assistant physician to the London Hospital (1859) and was conferred Doctor of Medicine, and for 10 years worked between Earlswood and his London practice in Harley Street. Down became a lecturer on materia medica and therapeutics, and then in the principles and practice of medicine at the London Hospital Medical College. He later founded Normansfield Mental Hospital, naming it after his friend Norman Wilkinson.

Down published on the classification of mental disease and became a fellow of the Royal College of Physicians (FRCP) in 1869. Down's original paper on the condition which now bears his name but was termed by him ''mongolism'', was in the London Hospital Reports, 1866, 3: 259–262 and his monograph Mental Affections of Childhood and Youth, published in 1887, contained a fuller description. He also described Frohlich Syndrome (adiposogenital dystrophy) 40 years before Frohlich. He died on 7 October 1896, in Normansfield, Hampton Wick.

Associated persons

Édouard Séguin
Jean Etienne Dominique Esquirol
John Langdon Down

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

Desai SS (1997). Down syndrome: a review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **84:** 279–285.

Dixon N, Kishnani PS, Zimmerman S (2006). Clinical manifestations of hematologic and oncologic disorders in patients with Down syndrome. *Am J Med Genet C Semin Med Genet* **142C:** 149–157.

Lourie J (1982). *Medical eponyms: who was Coude?* Pitman: London.

Park J, Oh Y, Chung KC (2009). Two key genes closely implicated with the neuropathological characteristics in Down syndrome: DYRK1A and RCAN1. *BMB Rep* **42:** 6–15.

Scully C, Langdon J, Evans J (2009). Editorial. *Oral Dis* **15:** 185–186.

http://www.whonamedit.com, http://rarediseases.about.com/

http://medcosmos.blogspot.com/2008/09/1000-eponyms-in-medicine.html

http://insidesurgery.com/index.php?itemid = 264

http://en.wikipedia.org/wiki/List_of_eponyms