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Archives of Dentistry Editorial

The Dental and Oral Significance of Hutchinson-Gilford Progeria Syndrome

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Introduction

Like many other healthcare professionals who have contributed so much to the healing arts and sciences, Dr. Jonathan Hutchinson was a keen and astute observer of the human condition. Dr. Hutchinson was a 19th century surgeon who practiced in London. Hutchinson also served as president of the Royal College of Surgeons [1].

Hutchinson's writings were prodigious and were surpassed by virtually no other author of his time as his bibliography contains almost 1,200 items [2].

In 1886, Hutchinson published "Case of congenital absence of hair, with atrophic condition of the skin and its appendages". In this article, Hutchinson first described the genetic disorder which now bears his name-Hutchinson-Gilford progeria syndrome (HGPS) [3]. This syndrome was also later described by Gilford in 1904 [4].

HGPS is an extremely rare genetic disorder which is characterized by a series of signs and symptoms often associated with the elderly. In most cases, the genotypic basis for HGPS is a change in one nucleotide out of the three billion in the human genome [1].

Fortunately, there have been some recent advances in our understanding of HGPS but, the quantity of HGPS awareness and research must be increased to provide more substantial treatments for HGPS patients and, ultimately, a cure.

At any given time there are an estimated 200-250 individuals living throughout the world with HGPS [5]. It is a very rare disease with a birth prevalence of one in four million [5,6].

At birth the infant appears healthy [5]. Physical features and ailments most often associated with the elderly start to develop in the first few years of life [5]. Multiple organs and tissues replicate phenotypes which are associated with normal aging [5,7]. Physical signs and symptoms include prominent scalp veins, a beaked-nose and a loss of subcutaneous fat. Individuals with HGPS usually succumb to the disease in their early teenage years due to cardiovascular issues [8]. The cause of HGPS is genetic. In most cases, glycine GGC changes into glycine GGT in codon 608 of the lamin A (*LMNA*) gene. This activates a cryptic splice donor site to produce abnormal lamin A. This, in turn, disrupts the nuclear membrane. The result is an alteration in transcription. The abnormal lamin A protein is known as progerin which makes the nucleus unstable leading to premature aging and disease [9].

Presently, there is a test for HGPS. Previously, a diagnosis had to be made on physical symptoms alone. These symptoms usually did not present themselves until the first or second year of the child's life [10]. The diagnostic test is genetic in nature and tests for an *LMNA* mutation and thus confirms a suspected diagnosis of HGPS [11].

There is presently no cure for HGPS but, there are new drugs on the horizon which provide a hopeful outlook. These drugs aim to treat the underlying genetic cause of the syndrome while providing an increased life expectancy for individuals with HGPS [12].

Cardiovascular conditions are closely monitored. Oftentimes, a low-dose aspirin therapy is recommended [13].

Lonafarnib, a Farnesyl Transferase inhibitor, has exhibited some limited success in improving the various

conditions associated with HGPS [14,15].

Another very interesting and promising recent research development is that the anti-diabetic drug metformin has been demonstrated to reduce progerin expression thus alleviating pathological phenotypes of HGPS [16].

The dentist plays a vital role in the medical team for HGPS as there are many traits of the syndrome which are of a dental and/or head and neck origin. Micrognathia is often present [17]. This can lead to overcrowding and a delayed loss of deciduous teeth.

Oftentimes, a high caries incidence is present in individuals with HGPS. As such, these patients must have frequent recall visits for both a re-examination of the teeth and associated hard and soft tissues of the oral cavity. Oral hygiene instructions must be reviewed at each dental visit with the patient and caregiver. The importance of meticulous oral hygiene must be continuously stressed. The dentist should incorporate fluoride therapies into the preventive protocol for HGPS patients. Of course, there are many fluoride therapies to choose from including fluoride varnishes, self-applied fluorides (toothpastes, gels, mouth rinses) and professionally applied topical fluorides (higher-strength rinses, gels, foams). It is important to also stress that many bottled waters do not have optimal levels of fluoride [18].

HGPS patients typically experience a delayed eruption of teeth and root development. This is most likely due to the retrognathic position of the maxilla and mandible and insufficient jaw growth [19]. Orthodontic therapy may therefore be indicated as there are no limitations in providing dental treatment to HGPS patients [20]. It might be beneficial for any tooth movement to work in conjunction with an oral surgeon in order to ensure the efficacious and a traumatic removal of any over retained primary teeth which are in need of extraction.

Individuals with progeria are very special people on many different levels. This relatively small group of individuals deserves the support of researchers, healthcare practitioners and government agencies globally.

I call on the medical communities and funding agencies throughout the world to dramatically increase funding for HGPS research. Insurance companies and federal agencies must also act accordingly in a manner in which additional funds would be allotted for the treatment of HGPS and the enhancement of the quality of life for HGPS patients and their families. Corporate attention may be garnered by the very feasible hypothesis that HGPS accelerates a subset of the pathological changes [20] which is responsible for the normal aging process thus providing almost limitless research opportunities for researchers.

Indeed, I believe that these HGPS patients do hold the keys, within their mortal bodies, to the eternal mysteries of aging as they provide us with a rare and precious glimpse of the accelerated processes of natural aging. However, this should not be the primary reason we as healthcare providers and researchers and, more importantly, as merciful and benevolent human beings, must champion the cause of these brave children who suffer in silence.

Box 1-Dental manifestations [21,22]

- Anodontia
- Secondary incisors located lingually and palatally
- Incomplete formation of roots of primary molars
- Palatal pseudocleft
- Tooth size/arch length discrepancies
- Delay in calcification of the crowns of the permanent teeth
- Delayed tooth eruption of primary and secondary dentition
- Calcification along the nerve fibers and the vascular walls
- Abnormal tooth formation
- Reticular atrophy of the pulp
- Hypodontia
- Irregularity in calcification of the crowns of the permanent teeth
- Agenesis of permanent teeth especially second premolars
- Permanent molars often located in the ramus
- Narrow pulp chambers
- High caries incidence
- Gingivitis
- Discoloration
- Severe crowding
- Malocclusion
- Ankyloglossia

Box 2-Craniofacial manifestation[23,24]

- Alopecia
- Prominent scalp veins
- Craniofacial disproportion
- Perioral cyanosis
- Convex profile
- Limited range of motion
- Hypoplastic maxilla and mandible
- Micrognathia
- Retrognathic maxilla and mandible
- Class II skeletal malocclusion

- Small maxillary arch
- Comparative paucity of vertical growth
- Hypoplastic mandible
- Atrophy of alveolar process
- Small mouth
- Sparse to absent eyebrows and eyelashes
- Delayed closure of fontanelles and sutures
- No subcutaneous fat
- Relatively large tongue
- Sculpted beaked nose
- Prominent eyes
- Narrow and high palatal vault
- Short mandibular ramus
- Obtuse mandibular angle
- Prominent forehead and frontal bossing
- Large cranium.

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