

# Ectodermal Dysplasia: A Review

Achala Chokshi<sup>1</sup>, Krunal Chokshi<sup>2</sup>, Riddhi Chokshi<sup>3</sup>, Sanjana Mhambrey<sup>4</sup>

1- Senior lecturer, Dept of Oral pathology, Narsinhbhai Patel Dental College & Hospital, Visnagar, Gujarat. 2- Senior lecturer, Dept of Pedodontics and Preventive Dentistry, Ahmedabad Dental College And Hospital, Ahmedabad. 3- Post Graduate student, Dept of Periodontics, Narsinhbhai Patel Dental College & Hospital, Visnagar, Gujarat. 4- Sr. Lecturer, Dept of Pedodontics & Preventive Dentistry, Srinivas institute of Dental Sciences, Mukka Surathkal, Mangalore.

Correspondence to:

Dr Krunal Chokshi, Senior lecturer, Dept of Pedodontics and preventive dentistry, Ahmedabad dental college and hospital, Ahmedabad.

Contact Us: www.ijohmr.com

## ABSTRACT

Ectodermal dysplasia is a hereditary disease which shows characteristic congenital dysplasia of one or more ectodermal structure and other accessory appendages. The skin, hair, nails, exocrine glands, and teeth are the tissues which show primary defects. More than 170 different pathological clinical conditions have been recognised and defined as EDs in last decade, all sharing in common anomalies of the hair, teeth, nails, and sweat glands. Many are associated with anomalies in other organs and systems and, in some conditions, with mental retardation. The anomalies affecting the epidermis and epidermal appendages are exceptionally inconsistent and clinical overlap is present among the majority of EDs. Most EDs are defined by meticulous clinical signs. To date, few contributory genes have been identified for these diseases.

**KEYWORDS:** Ectodermal Dysplasia, Atrichosis, Hypotrichosis, Anodontia, Hypodontia, Anhidrosis, Hypohidrosis

## INTRODUCTION

Ectodermal dysplasias (EDs) are an inherited group of disorders that share in general developmental defects concerning minimum two of the major structures characteristically held to derive from embryonic ectoderm – hair, teeth, skin and sweat glands.<sup>1</sup>

### Definition and classification

As defined by Freire-Maia [1971, 1977] ED's are "congenital disorders characterized by alterations in two or more ectodermal structures, at least involving one in hair, teeth, nails, or sweat glands". It is essential to accentuate that an ED should have a genetic cause and that the four cited classical structures are affected in the following decreasing order of frequency: hair, teeth, nails, and sweat glands, associated or not with alterations in other ectodermal appendages. This order establishes the norm for the EDs classification as will be shown as follows.

According to Freire-Maia's classification, EDs are divided into two groups:

- Group A which consists of all the entities with defects in two or more of the standard structures, and
- Group B comprises of those with disturbances in only one of these structures plus another ectodermal defect.

11 subgroups have been included in Group A depending on the involved structures: 1-2-3-4 (*hair-teeth-nails-sweat glands*); 1-2-3 (*hair-teeth-nails*); 1-2-4 (*hair-teeth-sweat glands*); 1-3-4 (*hair-nails-sweat glands*); 2-3-4 (*teeth-nails-sweat glands*); 1-2 (*hair-teeth*); 1-3 (*hair-nails*); 1-4 (*hair-sweat glands*); 2-3 (*teeth nails*); 2-4 (*teeth-sweat glands*); 3-4 (*nails-sweat glands*). Similarly,

Group B is classified into four subgroups with number 5 added at the end, depicting that another ectodermal anomaly is present: 1-5, 2-5, 3-5, and 4-5. Other ectodermally derived structures like mammary glands, thyroid gland, thymus, anterior pituitary, adrenal medulla, central nervous system, external ear, melanocytes, cornea, conjunctiva, lacrimal gland and lacrimal duct that may also be involved in EDs.

"Pure ectodermal dysplasias" are the entities with disturbances only in ectodermally derived structures and structures that are not derived from other embryonic layers. In contrast, "syndromes of ectodermal dysplasia and malformation" presents not only ectodermal signs but also disturbances of another embryonic origin, such as cleft lip/palate.

The definition of ED is used in sensu lato; EDs are simply groups of conditions presenting similar ectodermal signs: a subgroup includes conditions with defects in the same structures that may be affected in different ways. Conditions like pachyonychia congenita, incontinentia pigmenti, and dyskeratosis congenita lie within this broad definition are often excluded from ED classifications. However, there is no hindrance for a disturbance to belong to more than one clinical classification.

Other classifications include; *Lamartine classification* (2003) based on pathophysiologic defect such as; cell to cell communication and signaling; adhesion; development and other defects. Priolo and Lagana (2005) classify EDs based on defects in developmental regulation/epithelial - mesenchymal interaction and defects in cytoskeleton maintenance and cell stability.

How to cite this article:

Chokshi A, Chokshi K, Chokshi R, Mhambrey S. Ectodermal Dysplasia: A Review. *Int J Oral Health Med Res* 2015;2(1):101-104.

Priolo et al. (2000); Priolo and Lagana, (2001); Lamartine, (2003); Itin and Fistarol, (2004) classified EDs based molecular knowledge as the starting point.<sup>2,3,4</sup>

## DIAGNOSIS

An algorithm showing the approach to diagnosis has been described by Virginia P Sybert in Fitzpatrick's dermatology for general medicine. As described by the author, the first step in the algorithm is to determine presence or absence of sweating i.e. hidrotic/hypohidrotic or anhidrotic. The involvement of other ectodermally or non-ectodermally derived structures help in a further subdivision. Mode of inheritance may be different within an apparently uniform disorder group, and care must be taken in evaluating family members before providing recurrence risks(Fig No. 1).<sup>1</sup>

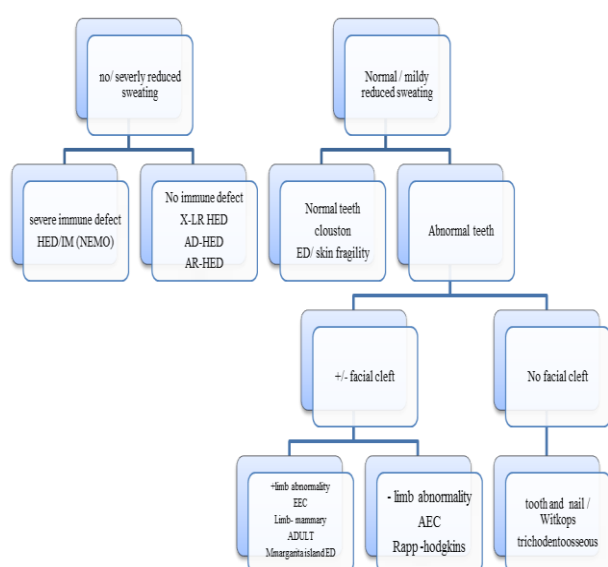


Fig No.1: Approach to the diagnosis of EDs. AD: autosomal dominant; ADULT: acro-dermato-ungual-lacrimal- tooth syndrome ; AEC: ankyloblepharon filliforme adantum- ectodermal dysplasia - cleft palate syndrome; AR:autosomal recessive; ED: ectodermal dysplasia; EEC:ectodactyly-ectodermal dysplasia- cleft lip/palate syndrome;HED hypohidrotic ectodermal dysplasia; IM: immune defects; X-LR: X-linked recessive

## HYPHIDROTIC ECTODERMAL DYSPLASIA

### CHRIST-SIEMENS-TOURAINÉ SYNDROME/ AHIDROTIC ECTODERMAL DYSPLASIA

Hypohidrotic ED / Christ-Siemens-Tourainé syndrome is the most common form of ED. It is caused by alterations in the gene *ectodysplasin* (EDA or EDA1) located at Xq12-13, this gene encodes for a transmembrane protein called *ectodysplasin* composed of 391 amino acids. A large number of mutations in this gene causing X-LHED have been identified. Till date, no proper link between the nature of the mutation and clinical features has been established. Mutations in the autosomal gene, EDAR mapped to 2q11-q13, have been implicated in an autosomal dominant and recessive form of hypohidrotic

ED that are clinically similar to X-LHED. EDAR acts as a receptor for ectodysplasin. Mutations in EDARADD gene have been recognized in the autosomal recessive form of HED. EDARADD is an intracellular adaptor protein that assists in transmitting signals from the activated EDA receptor to the nucleus of the cell. Certain cases show X-linked NEMO gene is found to cause HED and immune defects.<sup>1</sup>

**Clinical features:** The characteristic clinical features include skin, tooth, and sweating abnormalities. In the newborns, the diagnosis in the first days of life is difficult as the characteristic abnormalities are not prominent. Skin desquamation during the neonatal period is seen in Up to 70% of boys with X-linked HED and female carriers. Alopecia is generally the first noticeable clinical feature.

Children with hypohidrotic ED will have fine, scanty, light-coloured hair which thickens and darkens as patient grows up. The eyebrows and beard hair are also scant, but the hairs of eyelashes, armpit and pubic area might be normal. Hair from other body part is sparse or even absent.<sup>4</sup>

Tooth abnormalities may become apparent during lactation as hypoplasia of the alveolar crests. Within the families, same family or between the sexes a great degree of variation can be seen regarding the number of missing and malformed teeth. In comparison to the posterior teeth the anterior teeth will exhibit more morphologic discrepancies. Commonest example would be a tooth with cone or peg shaped crown.

The ability to perspire is either decreased or absent which leads to hyperthermia in patients. Recurrent idiopathic fever spikes are seen in more than 90% of younger patients during the first year of life. 6% of the children affected with X-linked HED will exhibit Febrile seizures.<sup>5,6</sup>

## HIDROTIC ECTODERMAL DYSPLASIA

### CLOUSTON SYNDROME

This was first described in French – Canadian kindred. The disorder is caused by a mutation in *connexin gene*, *GJB6* or *connexin – 30* this gene maps on the centromeric region of the long arm of *chromosome 13*. Hidrotic ED has a variable expression, and both males and females are affected equally.

Hair loss, nail dystrophy, and palmoplantar keratoderma are the 3 major characteristic features of the hidrotic ED's. Teeth and sebaceous gland function are normal in hidrotic EDs unlike in HED. Hair abnormalities are apparent as atrichia (absence of hair) or hypotrichosis (less hair), which may gradually get worse; the fine, slow-growing hair has a disorganized structure and reduced birefringence. Women are completely bald, whereas men show expression that varies from fair hair with focal alopecia to complete baldness. The eyebrows

and eyelashes are scant or absent, as is pubic and axillary hair. Nail disorders range from an almost normal appearance to micronychia or onychia; the nail plate may show thickening, desquamation, colour changes, striation, and onycholysis. Nail abnormalities in these patients may be reminiscent.<sup>7</sup>

## ECTODACTYLY-ECTODERMAL DYSPLASIA - CLEFT LIP/PALATE

### EEC SYNDROME

It is classified as multiple congenital anomaly syndrome because it has major involvement of structures other than ectodermally derived. Mutations in p63 a tumor suppressor gene located on chromosome 3q27. EEC is an autosomal dominant syndrome with variable expression and reduced penetrance. Intra and interfamilial difference in severity is observed.

The most frequent abnormalities are malformations of the limbs like ectodactyly and syndactyly, ED associated with sparse, hypo-pigmented or light coloured hair, absence of eyebrows and eyelashes, and alopecia, and oro-facial cleft, followed by tear duct abnormalities, genital malformations, and deafness, although the clinical manifestations vary greatly within and among families. The skin is usually fine, dry and of an atopic appearance while the nails are dystrophic and may appear pitted. Perioral lesions and angular cheilitis may be present in the oral commissures as a result of anatomic changes caused by reconstructive surgery for cleft lip/palate. Tooth abnormalities such as hypodontia or anodontia have also been reported, as well as a propensity to tooth decay due to defective enamel and changes in the salivary gland function.<sup>8,9</sup>

## ANKYLOBLEPHARON FILLIFORME ADNATUM – ECTODERMAL DYSPLASIA CLEFT PALATE SYNDROME

### HAY – WELLS SYNDROME

The disorder is caused by mutations in *tumor suppressor gene p63* that has been implicated in acro-dermatoungual-lacrimal- tooth or ADULT syndrome ectodactyly-ectodermal dysplasia- cleft lip/palate or EEC syndrome and other autosomal dominant forms of ED but the mutation causing each syndrome cluster in the different region of the gene.

AEC syndrome is an autosomal dominant disorder with complete penetrance and variable expression.

Ankyloblepharon is adhesion of eyelids due to formation of fibrous bands between them, which hinders the opening or moving of eyelids normally. In addition to the ectodermal abnormalities seen in other forms of EDs, skin erosions can be observed on the scalp, head, skin folds, palms, neck, and soles. Superinfection and poor

healing of these erosions are not uncommon.<sup>10</sup>

## RAPP – HODGKINS SYNDROME

It is an autosomal dominant syndrome that shares its feature with Hay Wells syndrome cleft palate with or without the cleft lip. This form of ED is caused due to a mutation in the *p63 gene*.

## TOOTH AND NAIL SYNDROME

### WITKOP SYNDROME / HYPODONTIA WITH WITH NAIL DYSGENESIS

Witkops syndrome is an autosomal dominant syndrome with variable expression and intrafamilial variability. This syndrome is caused due to mutation in *msx1* gene which plays an important role in the formation of certain teeth (premolars, first molars, and third molars) and nails, by determining the integrity and thickness of the nail plate. Nail dysplasia and hypodontia are characteristic clinical features of Witkops syndrome.<sup>11</sup>

## CONCLUSION

In conclusion, ectodermal dysplasias are a diverse group of inherited disorders that have many overlapping features and it is difficult to classify them. Biomolecular findings from recent studies have helped us to understand the usefulness of clinical-functional classification in clinical practice. The clinical manifestations of ED cause significant social problems in affected individuals. It affects both oral functions and normal body functions of the patients. A prompt diagnosis & rehabilitation by the multidisciplinary approach is the key to successfully manage ectodermal dysplasia.

## REFERENCES

1. Klaus Wolff, Lowell A. Goldsmith, Stephan I. Katz, Barbara A. Gilchrist, Amy, S. Paller, David J. Leffell. Fitzpatrick's Dermatology in General Medicine. Seventh edition United States: McGraw-Hill, 2008
2. Freire Maia N. 1971. Ectodermal dysplasias. Hum Hered 21:309-312. Freire Maia N. 1977. Ectodermal dysplasias revisited. Acta Genet Med Gemellol 26:121-131.
3. Visinoni AF, Lisboa-Costa T, Pagnan NAB, Chautard-Freire-Maia EA. 2009. Ectodermal dysplasias: Clinical and molecular review. Am J Med Genet Part A 149A:1980-2002.
4. Lamartine J. Towards new classification of ectodermal dysplasia. Clin Exp Dermatol. 2003;28:351.
5. Lu PD, Schaffer JV. Hypohidrotic ectodermal dysplasia. Dermatol Online J. 2008;14:22.
6. Blüschke G, Nüsken KD, Schneider H. Prevalence and prevention of severe complications of hypohidrotic ectodermal dysplasia in infancy. Early Hum Dev. 2010;86:397-9.
7. García-Martín P, et al. Ectodermal Dysplasias: A Clinical and Molecular Review. Actas Dermosifiliogr. 2013;104:451-70.
8. Jan AY, Amin S, Ratajczak P, Richard G, Sybert P. Genetic heterogeneity of KID syndrome: identification of a Cx30 gene (GJB6) mutation in a patient with KID syndrome and congenital atrichia. J Invest Dermatol.

- 2004;122:1108-13.
9. Pierre-Louis M, Byer-Parsons T, Burkhart CN, Morrell DS. Perioral lesions in ectrodactyly, ectodermal dysplasia, clefting syndrome. *Pediatr Dermatol.* 2010;27:658-60.
  10. León-Mateos A, Monteagudo B, Rodríguez L. Patient with «lobster-claw» hands and feet: ectrodactyly-ectodermal dysplasia-clefting syndrome. *Actas Dermosifiliogr.* 2008;99:822-3
  11. Fete M, van Bokhoven H, Clements SE, Mc Keon F, Roop DR, Koster MI, et al. International Research Symposium on Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate (AEC) syndrome. *Am J Med Genet A.* 2009;149A:1885-93.
  12. Fitzpatrick Memarpour M, Shafiei F. Witkop tooth and nail syndrome: a report of three cases in a family. *Pediatr Dermatol.* 2011;28:281-5.

Source of Support: Nil  
Conflict of Interest: Nil