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Review Article

REVIEWING GENETICS IN ORTHODONTICS

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ABSTRACT

Orthodontics has gone through a series of conceptual changes based on the relative importance of heredity and the local environment in the etiology and treatment of malocclusion and dento-facial deformities. Article gives an overview of the basic concents of genetics and their implications as applied to the field of qrthodontics and dentofacialorthopaedics. Various studies have been reviewed, which establish a modern genomic basis for major improvements in the treatment of malocclusion and dentofacial deformities as well as many other areas of concern to orthodontists.

INTRODUCTION

The word genetics comes from a greek word, meaning "to generate". It was coined by william bateson[1]. Genetics is the science of heredity and variation. Heredity is the conservative factor in nature, which results from the transmission of similar physical elements/genes from parent to offspring.

Genetic variation, which is virtually always present among higher organisms, results from the transmission of changed or mutated genes or new combinations. The study of human inheritance is concerned with the existence of inborn characteristics of human beings. It deals with the similarities and dissimilarities of human characters, their causes and the way in which they are transmitted from generation to generation.

The problem of inheritance of craniofacial complex and malocclusion is of special interest to an orthodontist because he deals with their correction. The understanding of human inheritance is studied in 3 directions:

1. The study of population genetics.
2. Chemical nature of heredity material, the mutations and its damage an individuals.
3. Ways in which genes act within the living cells and organisms.
4. The main reason for problems in studying the role of genetics in malocclusion or in craniofacial complex are:
5. Multifactorial pattern of inheritance, where no single factor can be considered responsible.
6. All dentofacial characteristics are polygenic and continuously variable.

Chromosome Aberrations

The importance of chromosome aberrations was demonstrated in 1959 by Lejeune, Gautier and Turpin[2] with the discovery of trisomy 21, which is responsible for Down's syndrome. Trisomies or even greater multiples and deficient, transposed, broken, deleted or enlarged chromosome usually show abnormal development of the first branchial arch, which produces facial and oral cleft, oligodontia, facial asymmetry, micrognathia and malocclusion.

Trisomy 1 (Group-A) is characterized by subnormal height, cleft of lip and alveolar process, hypoplastic mandible and deformities of finger and toes.

Partial deletion of chromosome 4, in results in cleft lip, cleft palate, high arched palate, broad nasal base.

Trisomy 5 (Group-B) shows micro cephaly, hypertelorism, micro and retrognathism, small stature and submucous palatal clefts. Deletion of chromosome 5, (Group-B) produces catcry

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syndrome as described by Lejeune in 1964[3,4], which also includes microcephaly, micrognathia, hypertelorism, mental retardation, deep overbite and tooth crowding.

Trisomy 13, 14 and 15 (Group-D) show physical under development, mental retardation, deafness, cleft lip, cleft palate, small skull, micrognathia.

Trisomy 16, 17 and 18 (Group-E) present with elongated skull micrognathia, cleft lip, cleft palate, small stature, syndactyly. Deletion of chromosome 18 causes carp mouth as described by Valentine in 1969[5] as a small head, mandibular prognathism, retarded growth and no contact of vermilion centers with the lips in repose.

Trisomy 22 shows receding chin, under developed mandible, mental retardation and hypogonadism.

Other trisomies involving sex chromosomes

1. Trisomy XXX produces narrow dental arches, open bite, macroglossia, flat palate, delayed eruption, obtuse gonial angle, fissured enamel.
2. Trisomy XXY (Klinefelter's disease)[6,7]
3. Trisomy XYY
4. X0 (Turner's syndrome)[8]

Abnormalities related to chromosomes involving first and second branchial arches are:

1. Mandibulofacial dysostosis
2. Oculovertebral dysplasia
3. Pierre Robin syndrome
4. Oro-digito-facial dysostosis
5. Ectodermal dysplasia
6. Amelogenesis imperfect
7. Dentinogenesis imperfecta
8. Facial hemi atrophy
9. Cleft lip and palate
10. Cleidocranial dysostosis

Micro forms

According to Fogh-Andersen[9], micro forms present as submucous alveolar clefts or bone rarefactions in the alveolar process, at the base of pyriform opening of the nose, on the palate.

Mutations

Mutations are defined as a heritable alteration or change of the genetic material, which arises through exposure to mutagenic agents or errors in DNA replication and repair. Mutations may be (a) fixed or stable, which are transmitted unaltered (b) dynamic or unstable, which undergo alteration as they are transmitted in families.

Fixed mutations

1. Substitution → Transition / Transversion
2. Deletion
3. Insertion

Developmental genetics

Homeobox (HOX) Genes[10,11]

Homeotic genes contain a 180 bp sequence known as homeobox, which encodes a 60 amino acids domain, which binds to DNA. Mutation in these genes result in major structural mutations.

- Mutations in HOXA13 causes hand foot-genital syndrome.
- Mutations in HOXD13 result in synpolydactyly.
- HOX genes are paralogous because family members from different clusters such as HOXA13 and HOXD13 are more similar than adjacent genes in same clusters.
- MSX2 and EMX2 also contain homeobox-like domain.
- Mutation in MSX2 can cause craniosynostosis.
- Mutation in EMS2 causes cerebral malformation.

Paired-Box (PAX) Genes[12]

This encodes for 130 amino-acids these genes play an important role in the development of nervous system and vertebral column, kidneys and eyes.

SRY-Type HMG Box (SOX) Genes[13]

SRY is the Y-linked gene, which plays a major role in male sex determination. SOX and SRY genes share 79 amino-acid domain known as HMG Box.

- SOX1, 2 and 3 are expressed in nervous system.
- SOX9 is expressed in the developing nervous system.
- Mutations in SOX10 genes on chromosome 22 causes Waardenburg's syndrome.

T-BOX (TBX) GENES[14]

Mutation in TBX5 causes congenital heart abnormalities.

ZINC FINGER GENES[15]

The term zinc finger refers to a finger like to loop projection, which is formed by a series of four amino acids, which forms a complex with a zinc ion. Mutation in GL13 causes cephalopolysyndactyly.

Prenatal diagnosis of genetic disease

Techniques used in prenatal diagnosis

1. Amniocentesis
2. Chorionic villus sampling
3. Ultrasound
4. Fetoscopy
5. Cordocentesis
6. Radiography
7. Maternal serum screening
8. Preimplantation genetic diagnosis
9. Detection of fetal cells in the maternal circulation

The human genome project

The concept of a map of the human genome was proposed as long ago as 1969 by Victor A. McKusick[16]. In a workshop held in Alta, under the auspices of the US Department of Energy

(DOE) in 1984, in which the causes of mutations in DNA and detection of mutations was discussed.

In 1986 United States Congress approved a 15-year US human genome project, which started in 1991. Other nations also joined and the individual national projects are coordinated by the human Genome Organization (HUGO). The US human Genome Project (HGP) is run jointly under the auspices of the National Institute of Health's National Center for Human Genome Research (NCHGR) and DOE.

Objectives of the human genome project

1. Human gene maps and mapping of human inherited diseases.
2. Development of new DNA technologies.
3. Sequencing of the human genome
4. Development of bioinformatics
5. Comparative genomics: Separate genome projects for different species.
6. Functional genomics

Treatment of genetic disease

Conventional approaches to treatment of genetic disease: This includes restriction of diet as in phenylketonuria, hormone replacement, as in congenital adrenal hyperplasia, supplementation with a vitamin or coenzyme as in homocystinuria.

Protein or enzyme replacement

- Replacement of deficient or defective enzyme like the use of factor 8 concentrates in the treatment of haemophilia A.
- Most of the inborn errors of metabolism.
- Recombinant DNA techniques are used to biosynthesize the missing or defective gene product. For the artificial delivery system, such as liposomes are used.

Drug treatment

Drug Therapy

- Aminocaproic acid-Angioneurotic oedema
- Penicillamine-Wilson's disease

Drug avoidance

- Sulphonamides-G6PD deficiency
- Barbiturates-Porphyria

Tissue removal or transplant

- Kidney transplantation- polycystic kidney disease
- Splenectomy-Hereditary spherocytosis

Gene Therapy

Gene therapy can be defined as the replacement of a deficient gene product or correction of an abnormal gene.

Methods of Gene therapy

1. Viral
2. Non-viral

Viral agents

Retroviruses: Retroviruses integrate into the host DNA by making a copy of their RNA molecule using the enzyme reverse transcriptase. The provirus so formed is the template for the production of the mRNAs for the various viral gene products and the new genomic RNA of the virus.

Adenoviruses

Advantages of adenoviruses is that these are stable, easily purified and can infect the non-dividing cells.

Herpes virus

These viruses are neurotropic i.e., infect the CNS they have a direct toxic effects on the nerve cells.

Other viruses

Influenza virus, vaccinia viruses can also be used.

Non-viral agents

Advantages of using non-viral agent are:

A. Non-eliciting of an immune response
B. Safer and simpler to use

1. Naked DNA
2. Liposome-mediated DNA transfer
3. Receptor-mediated endocytosis
4. Oligonucleotides

Future methods of gene therapy

1. Stem cell transplantation
2. Stem cell gene therapy
3. In utero fetal gene therapy

Role of Molecular Genetics and Genetic Engineering In Orthodontics

Orthodontics, has not escaped the ever-brewing controversy over the roles of heredity versus environment. In the normal course of events it is not unreasonable to assume that the offspring inherits quits a few attributes from his parents. These factors, or these attributes, may be modified by prenatal and postnatal environment, by physical entities, by pressures, abnormal habits, nutritional disturbances and idiopathic phenomena. We can say that there is a definite genetic determinant that influences the ultimate accomplishment of dentofacial morphology. The pattern of accomplishment (growth and development) has a strong hereditary component.
There are certain racial and familial characteristics that tend to recur. Since the offspring is a product of parents of dissimilar heredity, cognizance must be taken of the inheritance from both sources. This means possibilities of a recapitulation of a hereditary trait from either parent or a combination of traits from both patents to produce a modified characteristic. The end product may be quite harmonious, or it may be disharmonious. A child may have facial features that markedly resemble those of his father or mother, or the net result may be a combination of features from each parent. He may inherit tooth size and shape, jaw size, shape and relationship, and similar muscle and soft tissue configuration from the father or mother. But it is equally possible that he may inherit the tooth size and shape characteristics from one parent and the jaw size and shape from the other parent. The soft tissue draping may or may not

approximate the maternal or paternal pattern. Careful study of parents and previous siblings is also rewarding because it often provides clues of hereditary tendencies. In the complex interplay of chromosomes and genes, to recessive factors may combined become dominant characteristic or it may be offset by a genetic potential from the other parent, and the characteristic may disappear in the offspring.

Uviogenetics is an important basis for the diagnosis of malformations involving the dentofacial area and is destined to play an increasingly important role in orthodontic diagnosis.
Whenever the presence of dentofacial deformity and malocclusion of genetic etiology is suspected, cytogenetist is consulted for the assessment of patient's karyotype. Many diseases and malformations produced by chromosome disorders are accompanied by pathognomonic changes in the dermatoglyphics, the dermal ridge pattern of the fingertips. In 1970, Khorana and Associates[7] reported the complete synthesis of an artificial genes with 77 nucleotides.

Genetic engineering

Techniques of genetic engineering include amniocentesis, chromosome karyotyping, recognition of chromosome aberrations and their relation to specific dentofacial anomalies and malocclusion, the aborting of harmful genes, and the introduction of desirable genes into the early forming embryo. These techniques eventually will make possible the prevention of many antenatal, congenital, and postnatal genetically induced indeed dentofacial anomalies, including dental malocclusion. amniocentesis consists of tapping fluid containing cell from the amniotic sac in the pregnant women. The sex chromosomes are present in the 3 week-old embryo.
Sex determination of the patient is important in orthodontics for determining the group potential of the skeleton, time schedule of development of the dentition and body as a whole. In 1970 Edwards and Steptoe[17,18] were successful in re-implanting an ovum into the human uterus and using the human sperm to fertilize the ova in the test tube allowing them to subdivide to the blastocyst stage, when it becomes possible to determine the sex of the developing embryo[19]. In 1968, Jacobson[20] found that the presence of deleted or aberrant chromosome can be correlated to the potential for the occurrence of congenital and postnatal diseases and malformations.

Three types of genetic transmission of malocclusion and other dentofacial abnormalities are as follows:

1. Repetitive: The recurrence of a dentofacial deviation within an immediate family and in its progenitors.
2. Discontinuous: The recurrence of a malocclusal trait that reappears within the family background over several generations, but not continuously.
3. Variable: The occurrence of different but related types of malocclusion within several generations of the same family.

Aberrations in the morphology structures, such as dental malocclusions and dentofacial malformations, are highly polygenic. They are caused by multiple genes and vary widely, in their expressivity. Malocclusion is an incompletely autosomal dominant, with numerous heterozygous persons showing an absence of the inherited tendency.

- Deduction of diagnostic decisions from cephalometric measurements of a child in comparison that of parents with regard to genetic endoment is problematical because of continuing growth and of the effects of environmental factors. The angles and lines in the cephalometric tracings may be the result of environmental factors and not related at all to the genetic pattern endoment.
- Tongue thrusting and mandibular jaw posturing show a genetic background according to Shelton, Haskins and Bosma 1959[21].
- Wood and Green 1969[22] found monozygotic twin diagnosis, based on the regular left homolateral intrapair comparison of mandibular second premolar morphology plus genetically determined morphologic traits of other teeth.
- Each of the facial bones is developed according to its specific genes. However, the muscles are also dependent on the functional muscles attachment and nerves supply (Functional matrix of Moss)[23].
- Stein and Associates in 1956[24] showed genetic variation to be a strong factor in the etiology of malocclusion.
- Heredity is a more important factor in determining dental occlusal relationship of height dimensions than of depth dimensions.
- Heredity is an important factor in malocclusion related to bimaxillary protrusion, abnormal overjet, overbite, openbite, palatal width and interarch relation.
- Hunter in 1970[25] found genetic correlation to be strongest between father and children especially in mandibular dimensions.
- There is a significant relationship in facial height between mothers and their offspring.
- Facial skeletal structures are more frequently transmitted from mothers to sons than from mothers to daughter.

Hereditary control of teeth

The acceleration, retardation, shedding of deciduous dentition, order of eruption, number and size of individual teeth, tooth structure, form, colour are hereditarily determined. Alvesalo 1971[26] found tooth size to be related to the sex chromosomes.

- Agenesis of teeth appears to be simple dominant genetic origin (Gravely 1971)[27].
- Resemblance in caries experience is greater in mono ovular than biovular twins.
- According to Butler's Field Theory (1939)[28] the dental variability manifest itself in a distal than in a mesial direction from the more stable "Key" teeth. The three fields included those for molars premolars, incisors, and canines. Considering each quadrant separately, the molar/premolar field would consist of the first molar as the key tooth, the second and third molars on the distal end of the field, and the first and second premolars on the mesial end. The theory predicts that the third molar and first premolar would most variable in size and shape.
- The relationship and function of the oral soft tissue can be genetically influenced. The low position of tongue is found in the prognathic jaws while raised tongue occurs in disto-occlusion.

- Generalized gingival fibromatosis, an inherited autosomal dominant gene can produces malocclusion.
- The correlation for the mandibular plane angle is more highly significant between mothers and sons.

Influence of heredity in the etiology of malocclusion[24]
According to Brash[29], Salzmann[30], Strang[31] malocclusion of the teeth and jaws has been said to be the most common structural defect in man. The observations concerning in the role of heredity in etiology of malocclusion are:

Heredity racial influence: Dental Characteristics, Like facial characteristics, Show racial influence. In homogeneous racial groupings incidence of malocclusion seems relatively low. Where there has been a mixture of racial strains the incidence of jaw size discrepancies and occlusal disharmonies is significantly greater. May more class-II malocclusions with mandibular underdevelopment are seen than class-III malocclusions where there may be excessive mandibular size. Because the jaws the getting smaller, there is a greater frequency of impaction of third molar teeth, a greater incidence of congenital absence of certain teeth and a retrognathic tendency in man as he ascends the evolutionary scale.

Hereditary facial type: The facial type, if not the individual characteristics, of the offspring probably is heavily influenced by heredity. Facial typing is three dimensional. Different ethnic groups and mixtures of ethnic groups have differently shaped heads. There are three general types, the brachycephalic, or broad round heads; the dolichocephalic, or long narrow heads; and the mesocephalic, a shape in between the brachycephalic and the dolichocephalic. This is admittedly and arbitrary division and there are may gradations. With broad faces usually go broad cranial and facial bony building blocks and broad dental arches. With long narrow faces usually go harmonious bony structures that house narrow dental arches. Hasund and Sivertsen (1971)[32] point out the sex-lined nature of facial width and dental arch shape. Females demonstrate a positive correlation the wider the face, the wider the arch.

Hereditary influence of the growth and development pattern: Recognizing that the ultimate morphogenetic pattern has a strong hereditary component, it is reasonable to assume that the accomplishment of that pattern is also at least partially under the influence of heredity. For example, a child patient is very slow in losing his deciduous teeth and the eruption of permanent teeth is slow. The environmental influence can and do modify the hereditarily determined pattern. Onset of puberty varies with the different races and with geographic distributions. Maturation of females is confined to a narrower age range and begins earlier in girls than boys. To single out one factor and assess its precise role in practically impossible.

Heredity and specific dentofacial morphologic characteristics: Lundstrom in 1949[33] made intensive analysis of the dentofacial morphologic characteristics in twins and concluded that heredity could be considered significant in determining the following characteristics: (1) Tooth size, (2) Width and length of the arch (3) Height of the palate, (4) Crowding and spacing of teeth, (5) Degree of sagittal overbite (overjet), (6) Position and conformation of perioral musculature to tongue size and shape, (7) Soft tissue peculiarities (character and texture of mucosa, frenum size, shape and position, etc.)

Heredity also plays of part

1. Congenital deformities.
2. Facial asymmetries.
3. Macrognathia and micrognathia.
4. Macrodontia and microdontia.
5. Oligodontia and anodontia.
6. Tooth shape variations (peg-shaped lateral incisors, Carabelli's cusps, mamelons, etc.)
7. Cleft palate and harelip.
8. Frenum diastemas.
9. Deep overbite.
10. Crowding and rotation of teeth.
11. Mandibular retrusion.
12. Mandibular prognathism.

Detlefsen (1928)[34] concluded that the tooth size and shape and arch size are determined by heredity. Schultz (1932)[35] identified hereditary tendency toward the elimination of upper lateral incisor, while Huskins (1933) stated it to be a sex linked recessive trait. Iwagaki (1938)[36] reported mandibular protrusion and edge-to-edge bite to be more prevalent to Japanese. Lebow and Sawin (1942)[37] published pedigrees indicating in heritance of human facial features. Moore and Hughes (1942)[38] observed that the incidence of asymmetry in the jaw size, in children with asymmetrical parents was 300 times as great as in children normal parents. Weininger (1953)[39] stated that diastema is a result of a sex linked dominant gene. Stein, Kelley (1956)[40] reported that Angle's class-II occlusion may be due to recessive factors. Asbell (1957)[41] did a study of the family line transmission of dental occlusion.

Genetics of tooth size

In the clinical literature statements are sometimes found suggesting that the size of teeth is basically an inherited trait-the environment has little or no effect. The "key" tooth in each morphologic class of teeth has the highest heritability. Sofaer (1971)[42] noted that with the lowest heritability erupt latest.

Bader (1965)[43] reported strong genetic contribution to the size of the first and second molars (66 percent) and somewhat less to the third molar (47 percent).

Genetics of tooth eruption

The studies of heritability of tooth eruption point to multiple genes with nutrition, diseases and other postnatal factors playing minor role.

Genetics of congenitally missing teeth

Grahnen (1956)[44] found that if either parent had one or more congenitally missing teeth, there was an increased likelihood that their children also would be affected. Genes also influence hypodontia. The congenital absence of teeth is a discontinuous anomaly.

Genetics of tooth morphology

The Cusp of Carabelli and shovel-shaped incisor are traits of polygenic origin with a discontinuous distribution.

Inheritances of the craniofacial complex and malocclusion

Studies have reveled that the Class-II, Division-I patient is much more similar to is own immediate family than to a

randomly selected set of unrelated Class-II individuals. Even the mesiodistal buccolingual tooth dimensions showed greater similarity among family members than among unrelated persons. If a patient with a moderate Class-II, Division-1 comes from a family with good occlusion the result are expected to be better. The Class-III malocclusion, on the other hand poses a special problem since this relationship appears to be the result of a complex polygenic model of inheritance.

Genetics Of Dental Caries

Finn (1963)[45] reported that expected that caries rates among relatives of caries-free subjects, confirming the familial nature of the disease. But association has been found between the chemical structure, anatomic contribution of the tooth, composition of saliva, dietary habits and fluoride content of enamel and caries rate.

Genetic of Periodontal Disease

Gorlin (1967)[46] in his family and twins studies concluded that genetic factors in periodontal disease are extremely complex and that the isolation of these factors is difficult. Degree of gingivitis was 6 to 13 percent more in children of first cousins than the control children.

Benjamin and Baer (1967)[47] reported periodontosis demonstrating a strong familial tendency.

The Genetics of Cleft Lip And Cleft Palate[48]

The genetic evidence comes from family studies in which it can be shown that the siblings of patients with cleft lip (with or without cleft palate) have an increased frequency of cleft lip (with or without cleft palate) but not of isolated cleft palate, and that siblings of patients with isolated cleft palate have an increased frequency of isolated cleft palate but not of cleft lip. This was pointed out by Fogh-Andersen (1942)[49] and confirmed by several others. The concordance rate of cleft or palate is expected to be higher in monozygotic twins than in dizygotic pairs. In the case of CL (P), the risk for siblings born of unaffected parents increases from about 4% after one affected child to 9% after two-affected (Curtis *et al*., 1961)[50]**.**

Genetics of Mandibular Asymmetry[51]

The pedigrees of families suggests that the unilateral mandibular prognathism may be autosomal and dominants with a variable expressivity. Whether a causal connection exists between the unilateral and bilateral prognathism, or whether they are transmitted as separate traits, is not known.

Congenital Tooth Anomalies and Malocclusion - A Genetic Link[52]

- Studies on class-III subjects show a high of correlation with congenital tooth anomalies.
- Markovic (1992)[53] and Mossey (1999)[54] reported the heritable class-II Div-2 malocclusion to be related with small teeth.
- Dermaut (1986)[55] reported the relation of tooth agenesis to anteroposterior and vertical growth characteristics.
- Stellzig *et al* (1994)[56] related maxillary canine impaction to horizontal growth characteristics.

Genetic Study of Class-Iii Malocclusion[57]

They found class-III malocclusion to be inherited as an autosomal recessive trait. The incidence of the affected offspring in the situation were one parent was affected and the other carrier was found to be 50%.

A Study of Occlusion and Arch Width In Families[58]

- Variation in tooth position i.e. crowding, rotations and occlusal relation are due to non-genetic causes.
- Occlusal relation are similar among siblings but because of intrafamilial environment.
- Maternal environment is not responsible for arch width and shape variables.
- Chung[59] detected maternal effect on malalignment but not on lingual cross bite.
- Genetic influence is more for overjet, less for overbite, least for molar relationship.

CONCLUSION

A permanent interaction between genetic and environmental factors, both of a continually altering nature, determine the dentofacial morphology. We know now, that the underlying biology of an individual may be just as important as the malocclusion in the development of a treatment plan.

The influence of genetic factors on treatment outcome must be studied and understood in quantitative terms.

References

1. Bateson W: Mendel's Principles of Heredity.Cambridge University Press; 1909.
2. Lejeune J, Gautier M and Turpin R.: Le mongolisme premier exemple d'aberration autosomique humaine. *Ann. Genete*, 1959;1-41-49.
3. Lejeune J, Lafourcade J, Berger R, *et al*. Trios cas de deletion partielle du bras court d'un chromosome 5. C R *Acad Sci(Paris),* 1963;257:3098-102.
4. Lejeune J, Lafourcade J, de Grouchy J, *et al*. Deletion partielle du bras court du chromosome 5. Individualisation d'un nouvel etat morbide. *Sem Hop Paris*: 1964;18:1069-79.
5. Valentine D W, Bridges K W: High incidence of deformities in the serranid fish, Parulabrax nebulifer, from Southern California. *Copeia* 1969: 637-638.
6. Klinefelter H F, Reifenstein E C, Albright F: Syndrome characterized by gynecomastia aspermatogenes without A-Leydigism and increased excretion of follicle stimulating hormone. *J Clin Endocrinol Metab*. 1942, 2: 615-627.
7. Jacobs PA, Strong JA: A case of human intersexuality having possible XXY sex-determining mechanism. *Nature*. 1959, 2: 164-167.
8. Turner HH: A syndrome of infantilism, congenital webbed neck, and cubitus valgus. *Endocrinology*, 1938;23:566-574
9. Shields, E D, Bixler D, Fogh-Andersen P: Cleft palate: A genetic and epidemiologic investigation. *Clinical Genetics,* 1981; 20: 13-24. doi:10.1111/j.1399-0004.1981.tb01800.x

10. McGinnis,W., Levine,M., Hafen,E., Kuroiwa,A. and Gehring,W.J. A conserved DNA sequence in homoeotic genes of the Drosophila Antennapedia and bithorax complexes.: Nature, March 1984;308, 428 - 433 (29)
11. Scott MP, Weiner A: Structural relationships among genes that control development: sequence homology between the Antennapedia, Ultrabithorax, and fushi tarazu loci of Drosophila.: Proc. Natl. Acad. Sci. USA, 1984;81,4115-4119.
12. Marcus Noll: Evolution and role of Pax genes. Current Opinion in Genetics & Development. Volume 3, Issue 4, 1993, Pages 595-605
13. Larysa H Pevny , Robin Lovell-Badge: Sox genes find their feet Current Opinion in Genetics & Development.: Volume 7, Issue 3, June 1997, Pages 338-344
14. Virginia E. Papaioannou: The T-box gene family: emerging roles in development, stem cells and cancer.: Development. 2014 Oct; 141(20): 3819-3833.
15. Klug A.:The discovery of zinc fingers and their applications in gene regulation and genome manipulation. Annu Rev Biochem. 2010;79:213-31
16. Victor A. McKusick: Human Genetics: Prentice-Hall, 1969.
17. Steptoe, Patrick C., and Robert G. Edwards, "Laparoscopic Recovery of Preovulatory Human Oocytes after Priming of Ovaries with Gonadotrophins," *The Lancet* 295 (1970): 683-89.
18. Steptoe, Patrick C. and Robert G. Edwards, "Reimplantation of a Human Embryo with Subsequent Tubal Pregnancy," *The Lancet* 307 (1976): 880-82.
19. Jiang, Lijing, "Robert Geoffrey Edwards and Patrick Christopher Steptoe's Clinical Research in Human in vitro Fertilization and Embryo Transfer, 1969-1980". Embryo Project Encyclopedia (2011-05-12). ISSN: 1940-5030 http://embryo.asu.edu/handle/10776/2279.
20. Harold A. Mitty, Murray G. Baron, and Julius H. Jacobson, II Pelvic Arteriovenous Malformations American *Journal of Roentgenology* 1968 102:2, 424-430
21. Shelton, R.L. , JR., Bosma, J.F., and Haskins, R.C. Tongue Thrusting in One of Monozygotic Twins , J. *Speech Dis.,* 24:105-17, 1959.
22. Barry F. Wood, Larry J. Green: Second Premolar Morphologic Trait Similarities in Twins: *Journal of Dental Research*, 48, 1:74-78, 1969.
23. Melvin L. Moss: A theoretical analysis of the Functional matrix: *Acta Biotheoretica*, March 1968, Volume 18, Issue 1-4, pp 195-202
24. Kathryn F.Stein, Thomas J.Kelley, Eunice Wood : Influence of heredity in the etiology of malocclusion,: *American Journal of Orthodontics,* Volume 42, Issue 2, February 1956, Pages 125-141
25. Hunter WS. A study of the inheritance of craniofacial characteristics as seen in lateral cephalograms of 72 like sexed twins. *European Orthodontic Society Report of Congress.* 1970; 41:59-70.
26. Alvesalo L. The influence of sex-chromosome genes on tooth size in man. A genetic and quantitative study. Suom Hammaslaak Toim. 1971; 67(1):3-54.
27. Gravely J.F and Johnson D.B : Variation in the expression of hypodontia in monozygotic twins Dent Pract 1971;21:212
28. BUTLER, P. M. (1939), Studies of the Mammalian Dentition.-Differentiation of the Post-canine Dentition. Proceedings of the Zoological Society of London, B109: 1-36. doi:10.1111/j.1469-7998.1939.tb00021.x
29. Brash, J.C. The Etiology of Irregularity and Malocclusion of the Teeth. Dental Board of the United Kingdom, London; 1929.
30. Salzmann, J.A. Principles of Orthodontics. J. B. Lippincott Company, Philadelphia; 1943.
31. Strang, R.H.W. in: Textbook of Orthodontia. Lea & Febiger, Philadelphia; 1943.
32. HASUND and R. SIVERTSEN (1971) Dental Arch Space and Facial Type. The Angle Orthodontist: April 1971, Vol. 41, No. 2, pp. 140-145.
33. Lundström, A. Tooth Size and Occlusion in Twins. *Am. J. Orthodontics.* 1949; 35:878-879.
34. Detlefsen, J.A. Intrinsic or Hereditary Factors Versus Extrinsic or Environmental Factors in the Determination of Tooth and Oral Peculiarities. *J. D. Res*. 1928; 8:419.
35. Schultz, Adolph H. The Hereditary Tendency to Eliminate the Upper Lateral Incisors. *Human Biol.* 1932; 4:34.
36. Iwagaki, H. Hereditary Influence of Malocclusion: Statistical Studies of the Heredity of Progenia. *Am. J. Orthodontics and Oral Surg*. 1938; 24:328.
37. Lebow, M.R., Sawin, P.B. Inheritance of Human Facial Features. *J. Hered.* 1941; 32:127.
38. Hughes, Byron O., Moore, George R. Heredity, Growth and the Dento-Facial Complex. *Angle Orthodontist*. 1941; 11:217.
39. Weininger, Margarete. The Inheritance of Widely-spaced Incisors. Ztschr. Morphol. u. Anthropol. 1953; 32:367.
40. Stein, Kathryn F., Kelley, Thomas J., Wood, Eunice. Influence of Heredity in the Etiology of Malocclusion. *Am. J. Orthodontics*. 1956; 42:125.
41. Milton B Asbell: A study of the family-line transmission of dental occlusion. *Am. J. Orthodontics*.1957; 43; 4:265-285.
42. Sofaer, J. A., Bailit, H. L. and MacLean, C. J. (1971), A Developmental Basis For Differential Tooth Reduction During Hominid Evolution. *Evolution*, 25: 509-517. doi:10.1111/j.1558-5646.1971.tb01910.x
43. Bader, R. S. (1965), Heritability of Dental Characters In The House Mouse. *Evolution*, 19: 378-384. doi:10.1111/j.1558-5646.1965.tb01729.x
44. Grahnen, H. (1956) Hypodontia in the Permanent Dentition. A Clinical and Genetical Investigation. *Odontologisk Revy,* 7, 1-100.
45. Finn, S.B., Caldwell, R.C. Dental caries in twins. I. A comparison of the caries experience of monozygotic twins and unrelated children. *Arch Oral Biol*. 1963; 8:571-585.
46. R. J. Gorlin, R. E. Stallard, B. L. Shapiro: Genetics and Periodontal Disease. *Journal of Periodontology*. January-February 1967, Vol. 38, No. 1, Pages 5-10

47. Benjamin, S.D., Baer, P.N. Familial Patterns of Advanced Alveolar Bone Loss in Adolescence (Periodontosis). *Periodontics*. 1967; 5:82-88.
48. F C Fraser.: The genetics of cleft lip and cleft palate. *Am J Hum Genet*. 1970 May; 22(3): 336-352.
49. Fogh-Andersen, P., Inheritance of Harelip and Cleft Palate. Copenhagen: Munksgaard, 1942.
50. CURTIS, E.; FRASER, F. C.; and WARBURTON, D. 1961. Congenital cleft lip and palate: risk figures for counseling. *Amer. J. Dis. Child*. 102:853-857.
51. Maurits Persson: Mandibular asymmetry of hereditary origin. AJO-DO. January 1973Volume 63, Issue 1, Pages 1-11
52. Efthimia K. Basdra Magdalini N. Kiokpasoglou Gerda Komposch: Congenital tooth anomalies and malocclusions: a genetic link? *European Journal of Orthodontics,* Volume 23, Issue 2, 1 April 2001, Pages 145-152
53. Markovic M D: At the crossroads of orofacial genetics. *European Journal of Orthodontics* , 1992;14: 469-481
54. Mossey P A: The heritability of malocclusion: part 2. The influence of genetics in malocclusion. *British Journal of Orthodontics*, 1999; 26:195-203
55. Dermaut L R, Goeffers K R, De Smit A A: Prevalence of tooth agenesis correlated with jaw relationship and dental crowding. AJO-DO, 1986; 90:204-210.
56. Stellzig A, Basdra E K, Komposch G: Zur Atiology der Eckzahnverlagerung. Fortschritte der Kieferorthopadie, 1994; 55: 97-103.
57. Stephen F. Litton, Leonard V. Ackermann, Robert J. Isaacson, Burton L. Shapiro: A genetic study of class III malocclusion. AJO-DO, 1970; 58; 6:565-577.
58. Edward F. Harris, Richard J. Smith:A study of occlusion and arch widths in families. AJO-DO, 1980; 78;2:155-163.
59. Chung, C.S., Niswander, J.D., Runck, D.W., Bilben, S.E., Kau, M.C.W. Genetic and epidemiologic studies of oral characteristics in Hawaii's schoolchildren. II. Malocclusion. *Am. J. Hum. Genet*. 1971; 23:471-495.

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