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THE INHERITANCE PATTERN OF MISSING, PEG-SHAPED, AND STRONGLY MESIO-DISTALLY REDUCED UPPER LATERAL INCISORS

by

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INTRODUCTION

Many different models have been presented for the inheritance pattern of missing upper lateral incisors. Some authors maintain that this trait is inherited through an autosomal dominant gene (*Schultz*, 1932; *Montagu*, 1940; *Jöhr*, 1934; *Mandeville*, 1950; *Lysell*, 1953; *Grahnén*, 1956) while according to some other authors the inheritance pattern is autosomal but recessive (*Iltis*, 1948; *Thomsen*, 1955). Incomplete dominance has also been presented as a possible inheritance pattern (*Keeler & Short* 1934). Various limiting adjectives have often been linked to this genetic mechanism. It has been supposed to be sex-linked (*Huskins*, 1930) and/or to have incomplete penetrance and expressivity (*Huskins*, 1930; *Grahnén*, 1956). The penetrance has been supposed to be rather high (*Grahnén*, 1956), variable (*Huskins*, 1930; *Shultz*, 1932) or weak (*Mandeville*, 1950). The expressivity has generally been found to be variable (*Grahnén*, 1956; *Huskins*, 1930; *Shultz*, 1932; *Mandeville*, 1950).

The frequency of missing upper lateral incisors has been found to vary remarkably between different populations. In addition to the variation due to chance strong inbreeding and racial factors have been presented as most important causes for this variation. Limitations in investigation methods,

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e.g, lack of x-ray investigation, have most likely also influenced the results. The minimum frequency presented in the literature is 0.2 % in Chinese men (*Hrdlicka*, 1921), and the maximum frequency 21.5 % in an isolated Swiss population (*Jöhr*, 1934), while most frequencies vary between 1—3 %.

The inheritance of peg-shaped upper lateral incisors, i.e., teeth with reduced mesio-distal diameter and with proximal surfaces converging markedly in the incisal direction, has been rather commonly assumed to be associated with the genetic mechanism which causes the missing of upper lateral incisors. *Grahnén* (1956), for instance, claimed that peg-shaped incisors are a modified manifestation of the genotype that causes hypodontia. The variation in the frequency of peg-shaped upper lateral incisors is smaller than that of missing upper lateral incisors, the minimum being 0.8 % in a Swiss village (*Dietrich*, 1932) and the maximum 8.4 % in Chinese men (*Hrdlicka*, 1921), while most frequencies vary between 2—5 %. Generally speaking, the frequency of peg-shaped upper lateral incisors increases when the frequency of missing laterals decreases, and vice versa. If one of the frequencies is near the average, the other is approximately the same. No significant sexual differences in the frequencies have been found although the frequencies in the women are, on an average, slightly higher. However, a hypothesis of a hologynic inheritance of the trait has been presented (*Rostand & Tetry*, 1965).

The purpose of the present investigation was to attempt to explain the inheritance pattern of missing and peg-shaped upper lateral incisors, to discuss the inheritance of »borderline cases», and, in general, to try to elucidate the genetic relations between mesio-distally reduced and missing or peg-shaped upper lateral incisors. The »borderline cases» comprise upper lateral incisors, which are very small in their mesio-distal dimensions but whose proximal surfaces do not converge in incisal direction.

MATERIAL AND METHODS

The material of this study was collected during field investigations in the summers, 1966, —67 and —68 on the island Hailuoto, located off the western coast of Finland at the 65th parallel. The object was the whole population of the island, which numbers approximately 1300. The family lines of the inhabitants of the island, based on the parish registers, were investigated. A map of the family lines was made, including four to five generations. Of the population, 700 participated in the investigation, and 185 of them were edentulous (*Alvesalo & Ainamo*, 1968). It was possible to investigate the upper lateral incisors in 306 persons.

In the clinical examination missing, peg-shaped and strongly mesio-distally reduced upper lateral incisors were recorded. The findings of missing laterals were verified by x-ray examination. Clinical observations were later ascertained from plaster models, which were taken of all investigated dentulous individuals. The observations were limited to the permanent dentition. By interviewing and inspection it was ascertained that neither the propositus nor his sibs, parents or grandparents had illnesses which could lead to the missing, or peg-shaping of upper lateral incisors.

Table I.

List of the numbers of propositi, their phenotypes) and the number of pedigrees in which they are included.*

Propositus	Missing u. l. i.	Peg-shaped u. l. i.	Strongly mesio-distally reduced u. l. i.	Number of pedigree
110	+2+			1
112	+2+			1
162	+2+			4
166	+2+			4
346		2+		4
362		2+	+2	4
388			+2+	7
488	+2+			3
544			+2	
1072			+2+	5
1282			+2	3
1656			+2+	4
1692	+2	2+		—
1808	2+			3
1858	+2			5
1884		+2+		10
1920			2+	8
2114	+2	2+		3
2122	+2+			3
2124	+2+			3
2272			2+	9
2410		+2		6
2492	+2			2
2548	2+	+2		3

*) +2+ = bilaterally affected, +2 or 2+ = unilaterally affected

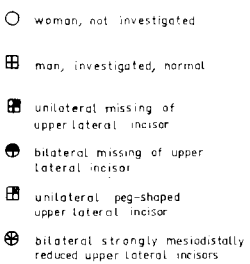
RESULTS

Among the 306 individuals investigated for lateral incisor anomaly 24 were affected. They are listed in Table I. There were 7 persons who missed both upper lateral incisors, three with one missing and one peg-shaped incisor, three with one missing and one normal incisor, one with bilateral peg-shaped incisors, one with one peg-shaped and one strongly mesio-distally reduced incisor, and two with only one peg-shaped incisor. In addition there were three persons whose both upper lateral incisors were strongly reduced mesio-distally, and four persons with one mesio-distally reduced incisor. All but two affected individuals were included in pedigrees; (numbers 1—10). (Figs. 1—10). Two persons were not in the pedigrees (numbers 544 and 1692); they were immigrants in the population and their pedigrees could not be found in the parish registers.

The frequencies of the various degrees of the trait were as follows:

missing at least one upper lateral incisor	4.25 %
having at least one peg-shaped upper lateral incisor	1.31 %
having at least one strongly mesio-distally reduced upper lateral incisor	2.29 %

From the pedigrees (Figs. 1—10) it can be found out that the missing and peg-shape of upper lateral incisors runs in families. Thus the trait is hereditary.



Explanation of the symbols used in the pedigrees.

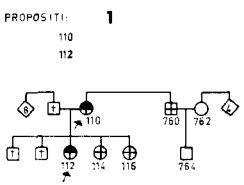


Fig. 1. Pedigree No. 1 (see Table I).

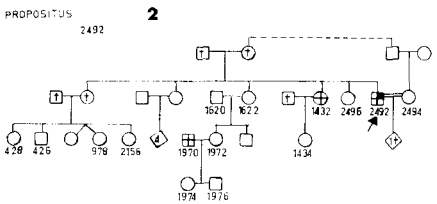


Fig. 2. Pedigree No. 2 (see Table I).

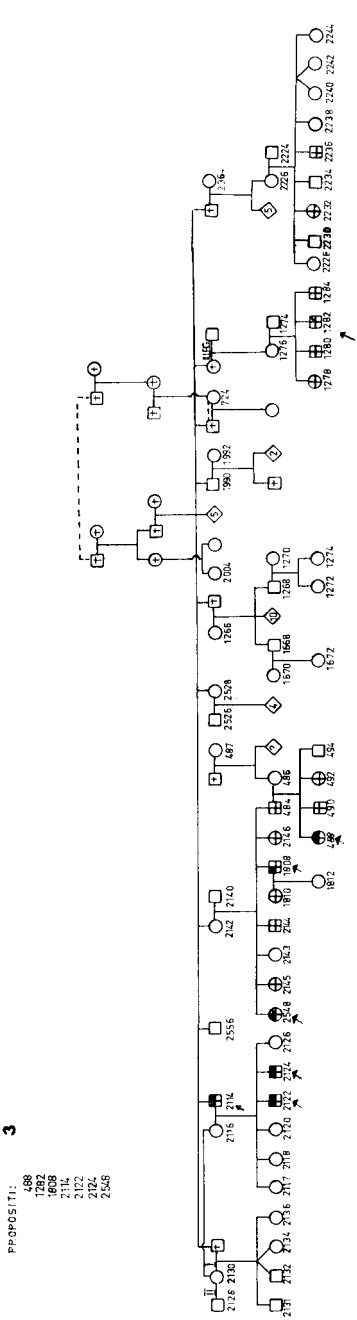


Fig. 3. Pedigree No. 3 (see text and Table I).

Fig. 4. Pedigree No. 4 (see Table I).

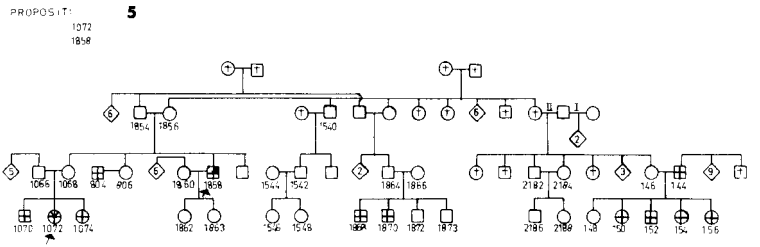


Fig. 5. Pedigree No. 5 (see Table I).

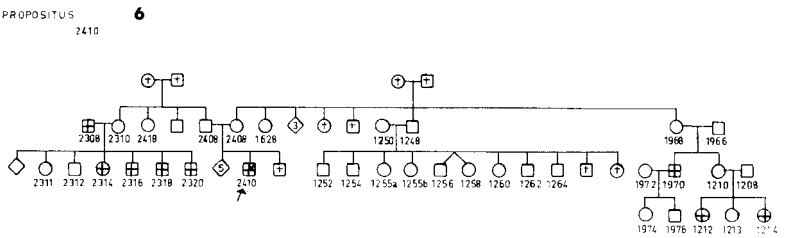
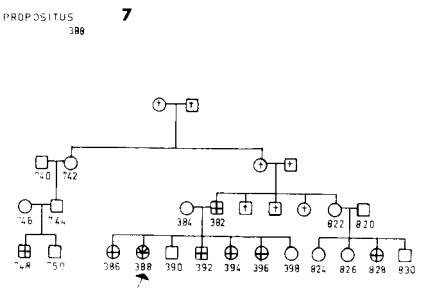


Fig. 6. Pedigree No. 6 (see Table I).



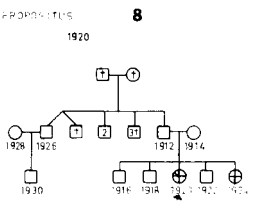
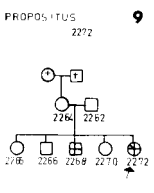


Fig. 7. Pedigree No. 7 (see Table I).

Fig. 8. Pedigree No. 8 (see Table I).



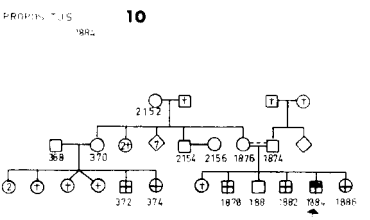


Fig. 9. Pedigree No. 9 (see Table I).

Fig. 10. Pedigree No. 10 (see Table I).

The question arises whether peg-shaped and mesio-distally reduced incisors are determined by the same gene as the missing of these teeth.

Of the 7 persons who had one peg-shaped upper lateral incisor, three were also missing the other incisor. Of the rest of the group one could conceivably have the gene causing the missing of incisors since one lateral was missing in one of her relatives; the remaining three persons had no relatives with missing upper lateral incisors. The total percentage of persons having peg-shaped incisors was 1.31 %. On the other hand, the percentage of the four persons with peg-shaped teeth, having relatives with missing teeth among their investigated relatives was 11.11 %. This is significantly greater than the former value ($t = 3.68$, $P < 0.1$ %). Considering this and the fact that nearly half (42.9 %) of the persons having a peg-shaped incisor also had a missing incisor it may be concluded that peg-shape is a weaker expression of the gene which causes the missing of upper lateral incisors.

Of the persons who had strongly mesio-distally reduced upper lateral incisors, one had a peg-shaped tooth. None of the other 7 persons with strongly mesio-distally reduced incisors had missing or peg-shaped incisors. Three of them could carry the same gene which causes the missing of upper lateral incisors in some other persons, whereas four could not. These three people represent 6.38 % of their 47 investigated relatives. This is not significantly greater than the average probability (2.29 %) of having strongly mesio-distally reduced incisors ($t = 1.57$, $P > 10$ %). Thus strongly mesio-distally reduced teeth are evidently not a weaker expression of the gene which causes the missing of upper lateral incisors, but are obviously caused by some other factors.

Because missing and peg-shaped upper lateral incisors are expressions of the same gene, one may speak of only one trait. Thus the total frequency of this trait in the population investigated was 5.56 %. The trait shows in all families an inheritance pattern of a single, autosomal, dominant gene with incomplete penetrance.

In calculating the degree of the penetrance the maximum likelihood method as described by *Mather* (1957) has been used. The symbol q denotes thus the degree of the penetrance and p the probability of a person having the gene. Thus the probability of being a person who expresses the trait is qp and the probability of a normal person is $1-p + p(1-q)$. In a sibship where there is at least one affected person, $p = 1/2$. The probability of affected *(a)* and normal *(b)* individuals in the sibships of this kind is thus

$$P = (q/2)^a \cdot ((1-q)/2)^b \cdot (a+b)!/a! \cdot b!$$

The logarithm of this expression is

$$L = a \log (q/2) + b \log ((1-q)/2) + C$$

Differentiating and equation to zero lead to the equation of estimation

$$\frac{dL}{dq} = \frac{a}{q} - \frac{b}{2-q} = 0, \text{ which gives } q = 2a/(a+b)$$

In the sibships of the present material where there were both affected (at least one missing or peg-shaped upper lateral incisor) and normal persons, there were altogether 9 affected and 16 normal individuals which give $q = 2 \cdot 9/(9+16) = 0.72$ or 72 %. This is the degree of the penetrance of the gene. The material is too small for analyzing whether penetrance is greater in women than in men. However, the material does not at all support the view of hologynic inheritance.

The percentages of the various degrees of the expression of the gene are as follows:

Bilateral missing of upper lateral incisors	29.65 %
One missing and one peg-shaped u.l. incisor	12.71 %
Unilateral missing of upper lateral incisor	12.71 %
Bilateral peg-shaped upper lateral incisors	4.23 %
Unilateral peg-shaped upper lateral incisor	12.71 %
No expression	28.80 %

In the present material there were only four cases in which it was possible to investigate the degree of the expression of the gene in subsequent generations. There were two cases (propositi 110 and 112, mother and daughter, and 162 and 166, father and son) in which the expression was complete in both generations. In one case the father (nr. 2114) had almost complete expression and his two sons (nrs. 2122, 2124) had complete expression. In one case the daughter (nr. 488) had full expression while her father (nr. 484), as a carrier of the gene, had none; the sibs of the father (nrs. 1808 and 2548) showed rather strong expression. Because exactly the same gene, as in pedigree nr. 3, can cause almost all degrees of expression, it may be concluded that the degree of the expression is not a character of the gene but the expression is determined by modifying factors.

DISCUSSION

The frequency of missing upper lateral incisors in the Hailuoto population was 4.25 %. This is somewhat higher than the average and very much higher than in Finnish undergraduates where it was 1 % (*Rantanen*, 1955).

The frequency of peg-shaped upper lateral incisors in Hailuoto was 1.31%. This is lower than the average values but higher than the frequency in Fin-

nish undergraduates, in which the frequency of peg-shaped upper lateral incisors was 1 % (*Rantanen*, 1955).

When comparing the frequencies in Hailuoto with other values one must first take into account whether other values are taken from random sample populations or natural breeding (Mendelian) populations. In random populations one gets the average frequency of the gene but in natural populations severals factors affect the frequency when all individuals are scored. Because the individuals are more or less relatives with each other the same genes will be registered in several individuals, in other words, more than once. Inbreeding and genetic drift will affect the gene frequencies, too, especially in small populations. All these factors may be causes of the differences between the average frequencies and the values from Hailuoto.

Hailuoto is nowadays an isolated population with a rather high number of inhabitants. The inbreeding in the population is of minor importance, as proved by calculating the frequency of consanguinity in the population (*Alvesalo*, 1969). The effect of inbreeding through increased homozygosity and genetic drift must be a minor one. Another question is how strong the inbreeding has been in former times. The population has been isolated probably during its whole existence, which has lasted for four or five centuries. The gene frequencies have probably been composed in those early days and have been in equilibrium since then.

Another interesting problem is the relationship between the frequencies of missing and peg-shaped upper lateral incisors. It may be concluded in general that when one value is higher than the average the other is lower, and vice versa, or both are approximately the same and near the average. This goes back to the conclusion that missing and peg-shaped upper lateral incisors are different experssions of the same gene. Thus, besides, the variation in gene frequency there exists a variation in its expressivity, too. When both frequencies are added, the value from Hailuoto does not differ much from the average values anymore. The total frequency in Hailuoto was 5.56 % and in other populations it varies from 1.5 % to 9.0 %, the very high value, 27.0 %, from an isolated Swiss village being excluded (*Jöhr* (1934).

On the basis of this it may be concluded that the variation in the expressivity of the gene is more important than the variation of the gene frequency itself as a cause of phenotypical variation between populations.

The variation in the expressivity of the gene is probably caused by modifying genes. Their frequencies determine strongly the frequency of both phenotypes in different populations. For example, in Tristan da Cunha, which is also an isolated island population, the total frequency of the trait was 5.7 % (*Thomsen*, 1955), i.e., practically the same as in Hailuoto. The

frequencies of the modifying genes have, however, evolved in Tristan da Cunha in a different direction than in Hailuoto; the frequency of missing upper lateral incisors in Tristan da Cunha was 0.7 % and that of the peg-shaped ones was 5.0 %. The situation in Hailuoto was thus quite the opposite.

Most authors hold the view that the missing of upper lateral incisors is caused by a single dominant autosomal gene. The present material supports this view. Some authors, however, have proposed that the gene is recessive. This can be due to the existence of modifying genes, which in some cases can lead to an inheritance pattern of the trait resembling that caused by a recessive gene. *Iltis* (1948), for example, favored the view of a recessive gene, based on the fact that the missing of upper lateral incisors in his material occurred mostly in the offspring of consanguineous marriages. The explanation to this, however, can be that although neither of the parents expresses the trait, their children could do it because of the accumulation of negative modifying genes.

The present material supports the view that general mesio-distal reduction of upper lateral incisors is not caused by the same gene as the missing or peg-shaping of these teeth. This is especially interesting from the evolutionary point of view. Both of these traits are reflections of the same evolutionary trend, namely the decreasing of the size and number of teeth in the evolution of Primates. It is therefore interesting that the genetic mechanism behind them is probably different. If it is true that the difference between mesio-distally reduced teeth and the peg-shaping or absence of teeth is a qualitative one, there is an important mutational bound between strongly mesio-distally reduced and completely missing or peg-shaped upper lateral incisors. The etiology of peg-shaped teeth is probably such that they have only one (medial) lobe instead of three. There exists probably a major gene which determines whether the incisor has three or only one (or none) lobes. However, the modifying genes which determine how large the lobes are may always be the same. When the wild type of the major gene is present, high coincidence of negative modifying genes leads to a reduction in the size of the tooth but cannot cause its complete absence. In the presence of a mutated major gene the same arrangement of modifying genes causes absence of the incisor. On the other hand, high coincidence of positive modifying genes produces a peg-shaped incisor in the presence of the mutated gene or may even cause the absence of its manifestation.

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SUMMARY

The occurrence of missing, peg-shaped and strongly mesio-distally reduced upper lateral incisors was examined in an island population of c. 1300 persons. The frequencies in 306 persons were investigated and they were as follows: Missing at least one upper lateral incisor 4.25 %, having at least one peg-shaped upper lateral incisor 1.31 %, and having at least one strongly mesiodistally reduced upper lateral incisor 2.29 %.

The material suggests that missing and peg-shaping of upper lateral incisors are different expressions of one dominant autosomal gene, whose penetrance is 72 %. On the other hand, mesio-distal reduction of upper lateral incisors has possibly another basis; it is evidently not a weaker expression of the gene which causes missing of these teeth.

It is concluded that phenotypical variation between populations is caused by differences in the frequency of the gene and, what is more important, by differences in its expressivity, which is probably caused by modifying genes. The role of these modifying genes in the evolution of teeth size and number reduction in relation to the major gene, which causes the presence or absence of upper lateral incisors, is discussed.

RÉSUMÉ

TRANSMISSION HÉRÉDITAIRE DE L'ABSENCE DES INCISIVES LATÉRALES ET DE LEURS ANOMALIES DE FORME: FORME COÏNOÏDE, FORTE RÉDUCTION DU DIAMÈTRE MÉSIO-DISTAL

Les caractères suivants ont été recherchés dans une population insulaire d'environ 1300 personnes: absence de l'incisive latérale supérieure et anomalies de forme de cette dent: forme conoïde et forte réduction du diamètre mésio-distal. Les fréquences ont été étudiées chez 306 de ces personnes et se répartissaient ainsi: absence d'au moins une incisive latérale supérieure, 4,25 %, présence d'au moins une latérale de forme conoïde, 1,31 %, et présence d'au moins une latérale de diamètre mésio-distal fortement réduit, 2,29 %.

D'après le matériel étudié, l'absence des latérales supérieures et leur forme conoïde sont des expressions différentes d'un gène autosomique dominant, dont la pénétrance est de 72 %. D'autre part, la réduction du diamètre mésio-distal des latérales supérieures repose sur un mécanisme d'un autre ordre; il ne s'agit pas d'une expression plus faible du gène causant l'absence de ces dents.

Les auteurs concluent que les variations phénotypiques existant entre

les populations sont causées par des différences dans la fréquence du gène, et, ce qui est plus important, des différences dans son expression, qui est probablement due à des gènes modificateurs. Ils présentent une discussion du rôle de ces gènes modificateurs dans l'évolution de la réduction de la grandeur et du nombre des dents, par rapport au gène principal déterminant la présence ou l'absence des incisives latérales supérieures.

ZUSAMMENFASSUNG

HEREDITÄT DER FEHLENDEN, ZAPFENFÖRMIGEN ODER IN IHRER MESIODISTALEN DIMENSION STARK VERKLEINERTEN LATERALEN INZIZIVE IM OBERKIEFER

Fehlen der lateralen vorderen Zähne im Oberkiefer samt zapfenförmigen und in ihrer mesio-distalen Dimension stark verkleinerte Forme entsprechenden Zahnes wurden unter der Bevölkerung d.h. unter 1,300 Individien in Hailuoto Insel untersucht.

Bei 306 untersuchten Individien kamen folgende Frequenzzahlen vor: bei 4,25 % fehlt wenigstens ein lateraler Inziziv, bei 1,31 % ist wenigstens ein lateraler Inziziv zaptenförmig und bei 2,29 % ist wenigsten ein lateraler Inziziv in seiner mesio-distalen Dimension verkleinert.

Aus dem Material ergibt sich, dass das Fehlen und die Zapfenartigkeit verschiedene Expressionen des dominanten autosomalen Genes sind. Die Penetranz dieses Genes beträgt 72 %. Andererseits wurde festgestellt, dass die mesio-distale Reduktion des lateralen Inzizivs anderer Herkunft ist; sie ist nicht eine schwächere Expression des Genes, das das Fehlen verursacht. Es wird gefolgert, dass eine phenotypische Variation zwischen den Populationen aus Verschiedenheiten in der Frequenz des Genes entsteht und, was noch wichtiger, aus Verschiedenheiten in der Expressivität des Genes, die vermutlich durch modifizierende Gene hervorgerufen wird. Es werden Schlussfolgerungen gezogen über den Anteil jener modifizierenden Gene an die Evolution der Grösse der Zähne und an die Reduktion der Zahl im Verhältnis zu dem sog- »major gen», das das Dasein oder Fehlen des lateralen Inzizivs bestimmt.

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