AN INHERITED ANOMALY OF DENTITION.

By O. A. BEADLE.

(With One Plate and One Text-figure.)

Hereditary defects of dentition are rare and it is believed that these observations have an interesting bearing upon the problem of heredity in man, especially when considered in connection with certain similar cases reported in the literature.

The purely genetical interest is therefore offered as an apology for presenting the results of investigations unavoidably lacking the completeness which would be demanded by an odontologist.

With the hope of increasing the value of this communication, the few relevant cases in the literature are discussed in connection with these original observations.

Such information as has not been directly confirmed and extended by personal examination of the patients, is believed to be perfectly reliable, though often rather desultory. It is to be regretted that no radiograms were obtainable.

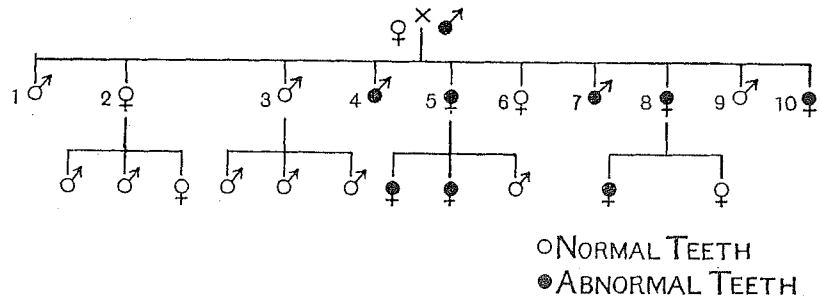

Fig. 1.

The essential anomaly in question is the sporadic absence of a varying number of teeth of both sets, which has been traced through three successive generations. There are also various irregularities in the age of eruption of the deciduous and permanent teeth.

The history begins with the two members of the parent generation (cf. Fig. 1). Of these the mother had normal teeth, but the father was deficient in certain teeth, the exact number not having been ascertained.

The F_1 generation consists of a family of ten, five of whom are de-

ficient in teeth in various ways. It has not been possible to examine many of these owing to their wide distribution over the globe. The ten children are as follows in order of age:

1. Male. Normal teeth; married but has no children.
2. Female. Normal teeth; married and has normal children.
3. Male. Normal teeth; married and has normal children.
4. Male. Abnormal dentition; died, no details forthcoming.
5. Female. Teeth abnormal; has three children, two of whom are deficient in teeth and one so far normal.
6. Female. Normal teeth; unmarried.
7. Male. Abnormal teeth; unmarried; not examined.
8. Female. Abnormal teeth; has two children, one of whom is deficient in teeth and the other normal.
9. Male. Normal teeth; unmarried.
10. Female. Abnormal teeth; unmarried.

Details of teeth deficiencies are not available except in a few cases which have been personally examined. This is so in the following, which includes both F_1 and F_2 generations.

1. 8th child: female. She lacks only the lower left central incisor. At the time of examination her two children were aged only three years and six weeks respectively, so it was too early to come to definite conclusions about the teeth; but the elder was almost certainly going to show abnormality of tooth development. The second, the mother thought, would be normal. These children are now six and three respectively and a recent letter states that the younger has the full complement of deciduous teeth, but that the elder has only sixteen teeth which are very widely spaced.

2. 5th child: female. She is very deficient in teeth and owing to the kindness of the Royal Dental Hospital, Leicester Square, I have been able to examine both her and her second child. Her dental formula is

	R.				L.		
0 0 0	1 0	1	0 1	1 0	1	0 0	1 1 1
0 0 1	1 1	1	0 0	0 0	1	1 0	0 0 0

The first child, a girl of 12 years old is also deficient in teeth. It is stated that she still has only her first set; but she has not been available for examination.

The second child, a girl of six years, has the following dental formula:

	R.					L.		
1	1 0	1	0 0	0 0	1	0 1		1
1	1 1	1	0 0	0 0	1	1 1		1

(Molars above and below the line are erupting.)

A photograph of her mouth was obtained.

The third child at the age of 12 months was normal; this is a male child.

3. 10th child: female. Lacks both lower central incisors and some back teeth, not determined.

In all these examinations allowance had to be made for extractions, and this was often difficult, but the above formulae are probably accurate in spite of this.

In many of these cases there has been great delay in the eruption of both deciduous and permanent teeth; this is markedly so in the eldest child of No. 5. Further, it should be noted that often the mother has been led to suspect the existence of an abnormality before the teeth have all appeared, from the spacing of the teeth and form of the jaw. In some cases, where the first set was deficient, the gaps were filled by the permanent teeth, but nevertheless gaps always remained in some places among the latter.

Particular attention is drawn to the following points:

(1) The abnormal dentition seems to behave perfectly as a Mendelian dominant, this dominant factor being present in the heterozygous state in the male parent. The F_1 offspring show 50 per cent. of the dominant abnormal and 50 per cent. of the recessive normal characteristic; further, in the two families of F_2 offspring examined and described above it is tempting to believe that a similar ratio has occurred, as expected, in spite of the small size of those families.

(2) Although pains have been taken where possible to find the exact nature of the tooth abnormality, the failure to do this in so many of the cases does not rob the observations of all their interest, since the most striking feature of the whole series, besides the regularity of inheritance according to Mendelian laws, is the great irregularity of the deformity itself. Any of the teeth may be affected as far as the data available indicate, except the canines.

(3) At the outset of the investigations a correlation was suspected

between tooth deficiency and dark hair colour. It was found however that there are three exceptions to this rule. In spite of this there is a very striking parallelism, at least fifteen cases conforming to the rule against the three exceptions. The father, four of the abnormal children (the fifth being fair), and all the abnormal grandchildren except one are dark, while all the rest of the family are fair; except one of the normals who is dark (2nd child of 8). Are we perhaps dealing with a case of linkage between two genes with a crossing-over value of about 10 per cent. in the male? The number of cases is insufficient to make this more than suggestive.

Discussion.

Although a Wassermann test has not been obtained in any of these cases, it is almost certainly not merely a case of transmitted syphilis; there is nothing to make one suspicious of this disease; the family is generally speaking a healthy one; moreover, absence of teeth due to congenital syphilis is apparently not reported. We are certainly dealing with a true hereditary factor. Is this an inherited general physiological abnormality of which the dental defect is only a part? Unfortunately there are no means of testing this. A history of idiopathic tetany or convulsions would have been interesting as suggesting some defect of calcium metabolism; but nothing of this kind is present. It seems more likely that we are dealing with a true genetic factor, a change or mutation, perhaps, in some gene which exerts its effect on the tooth germ itself, quite apart from any inherited general anomaly in the body as a whole.

This view is made still more probable when considered together with the extremely careful series of observations recently published by Wheelon. These cases all have reference to the lateral incisors only, which are apparently the most frequently missing of any teeth.

The three first cases show definite hereditary defects of the upper lateral incisors, transmitted through the female line in each instance. Case II is a patient with a congenitally absent right upper lateral incisor. The mother, maternal grandmother, three sisters, two brothers and a nephew all show a similar defect. Case III lacked the upper lateral incisors. A similar defect was possessed by the mother, maternal grandmother, four maternal aunts, one maternal uncle, one sister and this sister's daughter, *i.e.* four generations. Wheelon's cases all show various hereditary general disorders such as extreme nervousness, diabetes, menstrual disorders, etc.; but none of these showed a parallelism

with the tooth defects. He tries to bring all the patients described under the head of dyspituitarism, but the evidence given for this does not seem very convincing, and there does not seem more justification for explaining the tooth deficiencies as part of a general metabolic disturbance than in our own cases.

There is a greater uniformity among Wheelon's cases than our own, although there are variations; for instance, in Case II, where the rule is the absence of the right upper lateral incisor, one sister lacked the left upper lateral incisor. Again in Case III, which lacked usually both upper lateral incisors, one maternal aunt was minus a right upper lateral incisor and a sister with her daughter a left upper lateral incisor.

Our case is very irregular and is the only case so far discovered in the literature which involves the molars as well as the incisors. According to Pitts the third molar and lateral incisors are the most frequently absent of all the teeth.

Now this irregularity is in striking contrast to a further series of cases described.

The most instructive of these is that of Thadani, who describes a hereditary absence of all teeth in a race living in India. The toothless members, who are called Bhudas, are all males and transmit the defect through the female line only; in fact it is a case of ordinary sex-linked inheritance. Incidentally the toothlessness is associated with baldness and sensitiveness to heat.

Ovazza, again, reports in two families the hereditary absence of all incisors, behaving as a single dominant Mendelian character. This case is similar in genetic behaviour to ours, but unlike ours, is constant.

We would submit, therefore, that there are three types of congenital tooth defects.

I. Absence due to malnutrition after, or shortly before, birth and not inherited: *e.g.* Wheelon's fourth case. A good example of this is one given by Hopson, a Ghond with complete absence of both deciduous and permanent teeth, probably due to extreme malnutrition; there was no hereditary history. This may occur also in more than one member of the same generation of a family, probably through the same influences acting on all the members concerned, perhaps *in utero*. An example of this is a case of Pitts' of two brothers, both having an absence of deciduous and permanent central incisors and also of permanent lateral incisors.

These cases must not be confused, however, with true hereditary defects.

II. Inherited, but inconstant tooth defects; such are our own case and Wheelon's first three cases.

III. Inherited and very constant tooth defects behaving exactly like any other Mendelian characters. Such are Ovazza's and Thadani's cases.

These last two types of inherited characters suggest certain considerations with regard to the nature of the hereditary unit, which are briefly discussed here.

The striking parallelism between the distribution of chromosomes among the progeny of a pair of individuals and that of certain morphological or physiological characteristics has given rise to the most fruitful conception of the gene.

Now it has hardly been sufficiently emphasised that the recognition in the first instance of the Mendelian unit, as a concrete entity depended upon two important conditions which are by no means always satisfied.

(1) In an often complex combination of morphological differences inherited together as a single unit, there is sometimes one which meets the eye at once and gives the unit its name (eye colour, abnormal wings, etc.), but this is usually only part of a complex whole.

(2) In spite of the existence of segregation and recombination of other units not under observation, in accordance with Mendel's Second Law, there are many unit characters of such potency that they retain their distinctive form unchanged.

These facts enabled the idea of the hereditary unit as a thing of constant value and calculable history to be evolved.

After this had been grasped and Mendel's Second Law was established it was shown that many characters superficially of a like kind, though not inherited as a single unit, but apparently unstable, could be explained as the result of the mutual influence of two or more pairs of units upon one another, each pair however being distributed by exactly the same mechanism as the single pair of characters first studied.

But the recognition of this single unit would have been prevented, or at any rate delayed, were it not for the development by some such units of so great a potency that they determine certain salient characters, as part of a whole which is ignored, and moreover are not at the mercy of influences from other units associated with them in all sorts of combinations as a result of Mendel's Law of independent assortment.

Briefly stated, a single gene often determines characters which are constant in visible form in spite of the various permutations and combinations of other genes with which it coexists.

This suggests the idea of a variable ascendancy of some genes over the potential influence of coexisting genes. Potency of this kind might, of course, involve only one definite element of the complex of characters it determines. Now a change in a gene could have little evolutionary value until it had become potent enough over other genes to maintain a stable change in some one morphological or physiological character.

There is a further type of stability needed, namely an ability to resist modification in the interaction with environmental influences during embryonic development.

That such modification occurs we know from the famous experiments of Morgan on *Drosophila melanogaster*, in which the physical condition of the culture medium greatly changed the end result of certain genes.

The value of a change in a given locus in a chromosome will depend, then, partly upon its potency to maintain a stable change in some structural character regardless of the two influences tending to make it inconstant:

(*a*) Its genetic environment as we might express it, *i.e.* the associated genes which in various combinations are tending to modify its result.

(*b*) The subtle, incalculable influences of environment with which it co-operates to produce its end result.

These theoretical considerations are given because it is believed that the foregoing observations of tooth anomalies help to lend them interest.

It is suggested that we see here two degrees of stability of the hereditary unit.

In our own cases we are certainly dealing with a change in a single gene which is severely influenced by indeterminable changes either in general genetic constitution or in environmental interaction, or both; we cannot say which is the predominant factor.

In the cases of Thadani and Ovazza quoted, however, the change has sufficient inherent potency to give a constant result even in spite of the varying conditions under which it is placed. It is changes of this type, we would urge, that alone can have any importance for the theory of evolution by Mutation. If it is objected that we are dealing merely with a transmitted "weakness of the germ plasm," as has been argued in the experiments of Stockard and others on the inherited effects of poisons, the answer is that a "weakness" is only a change in a factor whose result is possibly or actually detrimental to the organism. Surely such a weakness might equally well be the origin of a useful character, in which case it would need only a sufficient stability in the face of almost overwhelming modifying forces, to be of evolutionary significance.

If these armchair speculations, appended to such slender observational data, need an apology, this must be that they are based upon the enormous mass of experimental results which has been collected in recent years by the brilliant researches of Morgan and the galaxy of other investigators who owe their inspiration to him.

Acknowledgment is gratefully made to those friends whose assistance in various directions has enabled this paper to be got together; in particular to Prof. J. S. Huxley at whose suggestion the enquiry into this family history was undertaken.

REFERENCES.

WHEELON, H. (1925). *Endocrinology*, Vol. IX. pp. 35–60.
PITTS, A. T. (1922–3). *Proc. Roy. Soc. Med. Sec. Stud. Child. Dis.* Vol. XVI.
THADANI, K. I. (1921). *Journ. Hered.* Vol. XII. p. 87.
OVAZZA, V. E. (1922). *La Stomatol.* Vol. XX. pp. 21–23.
HOPSON, M. F. (1920–1). *Proc. Roy. Soc. Med. Sec. Odont.* Vol. XIV. pp. 23–6.
LUCAS (1888). *Tr. Clin. Soc.* Vol. XXI. p. 64.

EXPLANATION OF PLATE XVI.

Views of dentition of upper and under jaws of second daughter of ♀ No. 5 in pedigree.