STUDIES IN THE CAUSES OF DENTAL ANOMALIES

W. G. DOWNS, JR.

*Department of Anatomy, Indiana University,
Bloomington, Indiana*

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In the studies basic to this paper, a large number of cases was included from the SOUTHERN INDIANA HOSPITAL FOR THE INSANE at Evansville, the INDIANA SCHOOL FOR FEEBLE-MINDED YOUTH at Fort Wayne, and the private practices of the author and his associates. Careful records were kept of both the dental and systemic findings for all of the patients, and where possible, records were obtained of the families of these patients. In the case of the School for the Feeble-Minded, in particular, these records were extremely complete and accurate, some of them extending back to the date of organization of the present institution—nearly thirty years ago; and many of them covering a period of ten years. A careful review of the literature, in its dental, endocrine and genetic phases, was made. Experiments were made with feeding and injecting dogs with the extracts of both the anterior and posterior lobes of the pituitary gland. Finally, experiments in feeding the extracts of both lobes of the pituitary gland are still in progress on a group of selected cases in the INDIANA SCHOOL FOR FEEBLE-MINDED YOUTH.

Six hundred and forty-seven clinical cases were studied. These were divided in accord with the endocrine diagnoses, as follows: cretins, mongols, dwarfs, giants, acromegalics, polyglandular dyscrasias, hermaphrodites, border-line cases, adiposo-genitalias, diplopias, goitres, microcephalics, macrocephalics, virilisms, infantilisms, myxoedemas and normals. The same group of cases was then divided according to the dental anomalies found, as follows: missing laterals, other teeth congenitally missing, peg-shaped laterals, super-numeraries, spaced uppers, bunched lowers, prognathisms, mesognathisms, and normals. The two classifications were then cross-consolidated to form table 1.

The purpose of this tabulation was to determine if certain types of dental anomalies occurred regularly in definite types of endocrine dyscrasias. It was felt that in order to determine this occurrence, either a certain type of dental anomaly must be found most frequently in cases of a certain type of endocrine dyscrasia, or that a majority of the cases of a

TABLE 1

GLANDULAR DYSCRASIAS	NORMALS (APPROX- IMATELY)	MISSING LATER- ALS	OTHERS MISSING	PEG- SHAPED LATER- ALS	SUPER- NUMER- ARIES	SPACED UPPERS	CROWDED LOWERS	PROG- NATH- ISM	MESOG- NATH- ISM	TOTALS
Cretins	17	4	0	2	0	1	2	2	1	29
Mongols	19	4	3	1	0	3	4	1	2	37
Dwarfs	5	1	1	1	2	3	3	2	1	19
Giants	5	0	1	1	2	5	3	5	1	22
Acromegalics	11	1	0	1	1	4	2	4	1	25
Polyglandulars	20	3	3	1	2	7	8	4	2	50
Hermaphrodites	4	1	0	1	0	1	2	0	1	10
Borderlines	41	4	3	2	2	12	17	7	4	92
Adiposo-gen.	3	1	1	1	0	2	2	0	1	11
Diplopias	6	0	0	1	1	2	3	0	1	14
Goitres	16	1	2	1	2	2	5	1	0	30
Microcephalics	1	1	0	0	0	0	1	0	1	4
Macrocephalics	2	0	0	0	1	1	0	1	0	5
Infantilisms	2	1	1	0	0	0	0	0	1	5
Virilisms	3	0	0	1	1	0	2	1	0	8
Myxoedemas	3	1	2	0	1	3	0	3	1	14
Normals	229	4	1	3	1	7	18	6	2	271
Totals	387	27	18	17	16	53	71	37	20	647

Explanation—Figures above refer to cases studied, the horizontal ones being the endocrine groups, divided vertically to demonstrate how these in turn fall into the groups of dental anomalies. Cases were assigned to definite endocrine groups, only if the clinical picture presented was clear-cut. If there was any grave doubt as to the proper grouping, they were classed as "borderline" or "polyglandular" cases. It was not attempted to group the various kinds of "goitre" cases. Very probably all of the cases listed as "giants" are not true pathological giants, nor are all of those classed as hermaphrodites true "mixed" sex cases. It may be readily seen that a definite diagnosis in such cases would require autopsy or at least operative procedure. Dentally, cases were only classed as "spaced," "bunched," "prognathic," etc., if it could be reasonably assured that the condition was not due to operative or traumatic causes. On the whole, it is felt that the above classification is as accurate as available clinical diagnostic methods could make it.

definite dyscrasia must likewise present a particular type of anomaly. Such was not found to be the case.

Referring to table 1, it will be seen that in no case did there appear to be any typical coincidence of endocrine dyscrasia and dental anomaly. Missing laterals, peg-shaped laterals, crowded lower anteriors, cases of prognathism and the other anomalies all occurred with about equal frequency in the various endocrine dyscrasia types. It was found, however, that close to fifty percent of all of the cases of endocrine dyscrasias likewise had dental anomalies of one or the other types, while the larger group of normal cases showed only about seventeen percent of dental anomalies. Thus, while it was evident that dental anomalies are more frequent in endocrine cases, no conclusion of a positive nature could be drawn regard-

ing the regularity of occurrence of dental anomalies of a definite type in specific endocrine dyscrasias. It would, then, be difficult to understand how the appearance of a dental anomaly could be considered as pathognomonic of a particular type of endocrine dyscrasia.

While the literature in the endocrine, dental, and genetic fields bearing on the causation of dental anomalies is relatively scarce, its review was nevertheless productive of the finding of widely variant results and views. On the whole, its trend was toward a particular endocrine causation of specific dental abnormalities. KAPLAN (1917), WHEELON (1925), ENGELBACH and TIERNEY (1922), CEDERCREUTZ (1925), WARD (1925), TIMME (1918), PETZEL (1922), KRANZ (1912), GRAVES (1904), and HOWARD (1926) seemed to lean in varying degrees toward this view. HOWARD (1926) reports over six hundred cases studied and obtained results not coinciding with those included in this study. This was especially true in regard to the incidence of missing teeth in mongols. Inasmuch as it is extremely difficult to obtain accurate records of previous dental operations in patients of this type, it is at least possible that the findings in some of his cases were due to earlier extractions. In most of the cases reported in the literature, it is felt that there has not been a sufficiently large series of cases examined from this angle, or that the cases have not been carefully enough controlled to make the findings valid.

On the other hand, some workers have cited about an equal number and type of cases supporting the genetic origin of dental anomalies, rather than the endocrine. Among these latter are: LUCAS (1888), KEITH (1919), BEADLE (1926), PITTS (1922), THADANI (1921), and HOPSON (1920), while CASTLE (1916) is convinced that factors influencing dental development, like those concerned with the length and color of hair are undoubtedly genetic, and MAUD SLYE (1926) asserts that all regular types of variations from normal in any of the organs have a genetic origin.

In the feeding experiments, five litters of four puppies each were used, the average age for the entire series at the beginning of the experiments being four weeks, none being over six weeks of age. The animals were all about the same size, averaging about 2 kg in weight at the beginning of the experiments. No regard was paid to sex in these experiments¹. In each litter, one dog was fed the extract of the anterior lobe, one that of the posterior lobe, one that of the whole gland, and one, the control animal, was fed a normal diet only. Armour's tablets made from the dried ox-gland were used throughout. The dosage was computed so as to be approximately proportionate to the maximum dosage for a

¹ The animals used throughout were mongrels, so that although the blood was the same in all of those within a litter, the litters were not known to be homozygous for any character.

human of average weight, which was, in the case of the anterior lobe extract, .035 gm, of the posterior lobe extract, .0016 gm, and of the whole gland extract, .035 gm. The extract was administered regularly three times a day, each animal was given 4 gm of codliver oil (Mead-Johnson Company's) once a day, to offset any possibility of rickets, and all of the animals were wormed, when the need for it became evident.

Beginning four weeks from the start of the experiment, entire litters were killed at intervals of four weeks. Tissues were fixed in 10 percent formalin, decalcified in 5 percent HCl in 67 percent ethyl alcohol, and paraffin sections were made through the upper and lower maxillae at such an angle as to include the temporary teeth and the developing permanent ones.² These sections were then stained with chloral hemotoxylin and counterstained with eosin. The sections were carefully studied and compared, but no definite variations in placement, form or texture could be noted in either temporary or developing permanent teeth.

For the injection experiments, dogs likewise were used. The age of the animals was the same as that of those in the preceding experiments. Six litters of three puppies each were used. In each litter, during the first six weeks, one dog was injected with .18 cc of antuitrin (Parke, Davis and Company) twice daily, one dog received .18 cc of pituitrin (Parke, Davis and Company) twice daily, while one, the control animal, received a like amount of sterile water. Although no apparent untoward local or systemic effects were observed from this rather excessive dosage, six weeks after the beginning of the experiment, it was felt better to use a more nearly proportionate dosage and the amount was reduced to .06 cc twice daily, in each case.

As in the preceding series, litters were killed at intervals of four weeks from the beginning of the experiments, except in the case of the last litter, in which the death from spasms, of the animal receiving anterior lobe extract made it necessary to kill the remaining members of the litter two weeks earlier than had been contemplated. Sections were made of the maxillae of all of these animals and prepared in the same manner as in the preceding series.

While some very interesting and surprising systemic results were obtained, which will be discussed in a later paper, no definite changes in the placement, form or texture of the temporary or the unerupted permanent teeth could be demonstrated.

In none of the cases, in either the feeding or injecting experiments, were

² It was felt to be better to study the effect on the permanent dentition prior to eruption, as decalcification of an erupted tooth destroys the enamel completely, whereas if decalcified in its crypt, all of the structures remain intact.

there any apparent histological differences in the number, form, size or nuclei of the ameloblasts; the size, arrangement or form of the forming enamel rods; the number, size, arrangement or form of the dentinal tubules; or the number, size, form or nuclei of the odontoblasts or of the various pulpal cells. Neither was there any apparent interference in the form, size or placement of the erupted temporary teeth or of the unerupted permanent teeth. In short, neither type of medication, simulating in some degree over-secretions of the gland, seemed to influence to any extent the teeth of these animals.

In seven months of administration of the pituitary extracts, *per orum*, to the patients of the INDIANA SCHOOL FOR FEEBLE-MINDED YOUTH, no evidence of any effect on the dental mechanism has been noted. Considering the length of time required for the formation of the human dentition, no results could be expected in such a period. These experiments are still in progress.

From the above-detailed series of experimental studies, it is felt that certain tentative conclusions may be warranted. While the endocrines may, and judging from the literature, probably do, play an important part in calcium metabolism, they do not apparently act in such a way as to cause regular types of dental anomalies (see table 1).

In the cases studied clinically, it was noted how frequently the anomalies were found recurring in families. For this reason, a study was made of the possibility of the occurrence of a genetic factor in the production of dental anomalies. Seventy-one patients showing very typical anomalies were selected for this study, and the group was divided in accordance with

TABLE 2

DENTAL ANOMALIES	FAMILY HISTORIES OBTAINED		FAMILY HISTORIES NOT OBTAINABLE	TOTALS OF EACH TYPE
	Histories Positive	Histories Negative		
Missing Laterals	9	0	2	11
Others Missing	2	0	0	2
Peg-shaped Laterals	2	1	2	5
Supernumeraries	2	1	3	6
Spaced Uppers	10	1	5	16
Crowded Loweres	9	1	8	18
Prognathism	3	1	1	5
Mesognathism	3	1	1	5
Totals	40	6	22	68

Explanation—While the above figures refer to individuals studied, columns 1 and 2 likewise represent families, as where the history was obtained, the entire family was charted and studied. The series is divided into the different types of anomalies, only as a matter of secondary interest, to demonstrate the proportions found.

the type of anomalies presented. Of these seventy-one cases, forty-seven fairly complete family dental records could be obtained.

In twenty-four cases no family dental record was obtainable. Of the forty-seven cases in which a fairly complete family record was obtained, five showed no dental anomaly in other members of the family, while forty-two did show one or more other anomalous cases of a similar character in the family. The forty-two families showing positive results were then studied to determine what proportion of anomalies was found in each generation (see table 3).

TABLE 3

	TOTAL NUMBER INDIVIDUALS PER GENERATION	TOTAL NUMBER ANOMALOUS INDIVIDUALS PER GENERATION	TOTAL NUMBER NORMAL INDIVIDUALS PER GENERATION	RATIO ANOMALOUS INDIVIDUALS TO NORMAL INDIVIDUALS
Parental Generation	84	39	45	3.4:4
Filial 1 Generation	177	21	156	0.5:4
Filial 2 Generation	382	107	275	1.5:4
Filial 3 Generation	219	64	155	1.6:4
Filial 4 Generation	16	8	8	40 :4

Explanation—This table was made by taking the entire number of cases of each type from the totals in each generation of the forty-two positive cases for which histories were obtainable, from column 1 of table 2. Thus, the ratios are cross-sections of each generation of the entire forty-two families. There is a regularity which bespeaks adherence to some genetic system.

It was felt that the constant recurrence of a certain type of anomaly within a given family, offered of itself, considerable evidence of a genetic causative factor. If, however, in addition to this, some regular formulae or ratios, describing these occurrences could be found, it would certainly lend strength to the original evidence offered. In determining these ratios, the first generation obtainable in each family was classed as the Parental, the next as the Filial 1, etc. The total numbers of individuals through each complete generation of the entire forty-two families was then divided into those showing a familial anomaly and those not showing it, classed as normals. The results of this tabulation (see table 3) showed eighty-four individuals in the Parental generation, of which thirty-nine had the anomaly which was found appearing in their respective families, while forty-five showed no evidence of it. This gave, in the Parental generation, a ratio of 3.4:4.0. In the next, or Filial 1 generation, of a total

FIGURE 1.—Explanation—Figures containing an x (⊗ 9, etc.) represent individuals having the anomaly—in this case, a very distinctive type of marked prognathism. Plain figures merely do not show it or at least, not characteristically. It is probable that those who do show it are homozygous recessives, but it is difficult to determine the genetic character of these who do not show it.

FIGURE 2.—Explanation—Explanation of figure 1 likewise applies to this, except that the anomaly in this case consists of missing laterals. No individual in this chart including the collateral lines, has laterals sufficiently large and well-formed to be considered fully normal, which, of course, makes it more difficult of even a tentative interpretation.

of one hundred and seventy-seven individuals, twenty-one exhibited the familial anomaly, while one hundred and fifty-six did not. The ratio yielded in this case, then, was .5:4.0. The Filial 2 generation, having a total of three hundred and eighty-two individuals, had one hundred and seven with their respective familial anomalies and two hundred and seventy-five without it. The ratio in this case, then, was 1.5:4.0. A total of two hundred and nineteen individuals of the Filial 3 generation disclosed sixty-four having the anomaly as against one hundred and fifty-five not having it, showing a slightly augmented ratio of 1.6:4.0. It was only possible to obtain Filial 4 family records in five cases, which yielded a total of sixteen individuals of this generation, of which exactly one-half showed the family anomaly and one-half did not, resulting in a balanced ratio of 1.0:1.0.

Where positively complete family dental records were obtainable, in a few instances the families were genetically charted as in figures 1 and 2.

Hypothetical genetic characters were given to the various individuals in the family, temporary charts were constructed, were corrected, new hypotheses were attempted and again corrected, until apparently probable schema were obtained. Figures 1 and 2 show the results in two of these cases. In one especially noticeable case, which is in the same family as that shown in figure 1, the anomalous individuals showed such exactly similar conditions in the different generations that one case was selected from each living generation, casts made, and photographs of these casts were taken. (Figures 3 to 5.)

While the results of the genetic tabulations do not yield Mendelian ratios, it will be remembered that in dealing with human genetics, so many factors enter into a given result that the probable error is enormous. Considering this, there is a regularity in the ratios in the sequence shown, which bespeaks adherence to some sort of a genetic system. It is probable, but undetermined, that the dental anomalies are simple recessive characters (CASTLE 1916). In any event, the appearance of these anomalies within given families is so regular that the hereditary influence seems more than likely.

In summary, the conclusions from the above-detailed series of investigations are fairly obvious. Although it is possible that dental anomalies may sometimes appear as the result of endocrine dyscrasias, just as may be the case with vitamin deficiencies or other developmental interference, it is very unlikely that there is any regularity about such appearance.

Dental anomalies probably cannot be considered as pathognomonic of any definite type of endocrine dyscrasia.

It would seem to be fairly certain that anomalies in dentition are recurrent in families as the result of the operation of genetic or hereditary factors.

FIGURE 3.—Cast of the mouth of individual 8 from figure 1 (Generation F1, Age 53).

FIGURE 4.—Cast of the mouth of individual 14 from figure 1 (Generation F2, Age 39).

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FIGURE 5.—Cast of the mouth of individual 20 from figure 1 (Generation F3, Age 6—temporary teeth). Note the regularity in type of these three cases. Other individuals from this family show, as nearly as is possible, an identical condition.

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