CHAPTER 1

General Introduction

Variation

Teeth may vary in number, size, shape and position within the same species. Variation in number, size and shape tends to be of largely genetic origin or at least to involve genetic mechanisms; it used to be thought that this variation, which involves quantity of tooth material, was beyond the influence of environmental factors such as nutrition, but new evidence suggests that this is not so. Variation in position on the other hand is much influenced by environmental factors and, because tooth position depends on bone development and bone growth, is frequently secondary to conditions that affect growth.

Before considering the evidence that bears on the mechanisms that bring about these types of variation, which is one of the main purposes of this introductory chapter, it is necessary to discuss the term variation itself.

Variation in the biological sense comprises differences of every kind, morphological and other, that exist between individuals of the same species. Variation in the observable characteristics of an organism (phenotype) is the product of individual differences in genetic constitution (genotype) and of various environmental influences. Heritable variation is 'the material on which natural selection acts to bring about the evolution of species' (Bateson, 1894).

Variation implies deviation from a mean or norm; when the observed difference is slight, the term normal variation is sometimes applied. When the deviations are more gross and uncommon and amount to abnormalities, they may be said to constitute abnormal variation. The distinction between normal variation and abnormality is quite arbitrary, especially in con-

tinuous variation, that is variation in characters, like stature and tooth size, that can be measured against a continuous scale, even an ordinal one. Variation of tooth morphology is broadly continuous in the sense that it shows a great range in degree; not only is it hard to draw a distinction between variation and abnormality but, when frank abnormalities are grouped together, they form a more or less continuous spectrum of increasing disorganization of tooth form with tumour-like masses, odontomes, at the extreme end of the spectrum (see Chapter 25.)

Discrete or discontinuous variation is where there are no intermediate types; a character is either present or absent; for instance, blood types and primary sex characters where either an ovary or a testis is present. The terminology of variation is used with most rigour in the science of genetics in which another term, quasi-continuous variation, is employed for characters which are discrete, that is present or absent, but when present vary continuously in degree. Some dental variants, for example supernumerary cusps and absence of third molars (Grüneberg, 1951) in laboratory-bred animals, have been shown to exhibit quasi-continuous variation (Sofaer, 1975, 1976).

It is only possible to give here a condensed summary of the wealth of observation, terminology and concept which is relevant to systematic thinking about the processes that could have brought about the variation described in the various following sections. More extensive coverage of the early works is available in Gaunt and Miles (1967) and, for more recent concepts, we recommend J. W. Osborn (1978, 1981b, 1984) and Lumsden (1979). Sir Frank Colyer, in writing the first edition of this book, was influenced by the encyclopaedic authority of Bateson's classic work *Materials for the Study of Variation* (1894), which still deserves to be consulted, not only for the descriptions given of abnormalities of dentitions in various species, much of which Colyer incorporated into the present work, but also for Bateson's conceptual analyses. Bateson pointed out (pp. 195–198) that the tooth arches can be regarded, like the vertebral column, as a linear meristic series, that is a series of repeating parts; variation in the number, shape or size of the parts can be referred to as meristic variation. Bateson coined the term *homoeosis* (Gk. being alike) for where one part in a series assumes the shape characteristic of another part; for example, when a cervical vertebra possesses a rib element and thus resembles a vertebra in the thoracic region, or the sacralization of a lumbar vertebra. Homoeotic variation is a term that could be applied to a tooth in the canine region of the jaw which may, by virtue of cusps arising from its cingulum, partially resemble a premolar (see also Butler, 1967).

Morphogenetic fields

Our understanding of variation in size, number and shape and of position is greatly helped by the embryological concept of morphogenetic fields, whereby areas in the embryo develop the capacity to become organized in a particular way, provided that an evocator of appropriate strength acts upon them. Gradients of capacity have been postulated within such fields; capacity to react may be maximal at some point and fall off on either side of it, though not necessarily equally, so that a field can have eccentrically distributed gradients of capacity. Butler (1939, 1963, 1967, 1978b, 1982) was the first to adapt these field theory concepts to the mammalian dentition and to postulate that the dentition, or each quadrant of it, develops as a series of units within a continuous morphogenetic field. Each unit develops in a particular way according to its position in the field. The field has an antero-posterior axis with a morphogenetic capacity that differs qualitatively at each end. The field is also differentiated into regions corresponding to the incisor, canine and molar regions, and these may have some degree of independence, as when the canine is reduced or enhanced without a corresponding change in the rest of the dentition (Fig. 1.1).

In the dog, for example, the molarization influence can be said to be greatest in the region of the carnassial lower first molar and upper fourth premolar and becomes progressively weaker anteriorly through the premolars and posteriorly through the other molars.

The dentition is thus composed of a series of units which, although morphologically separate, arise from a morphogenetic field as a continuous system which may be altered by various processes as a whole, or at least as groups of teeth, rather than as single units. This concept has been widely used to describe the evolution of dentitions and the relation of one to another (Henderson and Greene, 1975) and also to explain in systematic terms variation in size and shape of groups of teeth. The concept of a morphogenetic field of odontogenic capacity also provides a basis for explanation of supernumerary teeth, and indeed for absence of teeth. Where there are supernumerary teeth, the capacity for tooth formation was abnormally strong and, where teeth are absent, the capacity, perhaps in a localized area and for reasons that may not be understood, did not develop.

Variability, including differences between corresponding structures on the right and left sides of the body that constitute asymmetry, tends to be greatest in the later-developing teeth in each morphological class. Furthermore, heritability, the proportion of the observed variation due to additive genetic effects, tends to be lower in the later-developing teeth. These observations can be explained in terms of the field concept, or the clone concept to be described later, as due to the progressive exhaustion of the field substance responsible for initiating tooth development (Sofaer, 1977). There are some mouse mutants (Grüneberg, 1966; Sofaer, 1969) in which a supernumerary molar is sometimes associated with smallness of the true molars or absence of the third molar. Furthermore, if in a given morphological segment, e.g. the molar segment, the teeth which develop early are large, those that develop late tend to be small or absent or vice versa (Sofaer, MacLean and Bailit, 1972). There is some kind of competitive interaction between the tooth units within the segment. These phenomena can be explained in terms of a fixed potential for the total quantity of tooth material. Supernumerary teeth, to be dealt with in the next section, in general can be explained in terms of this concept or slight elaborations of it. For example, supernumerary teeth which are morphological duplications, or twins, can be thought of as resulting from a dichotomy of the tooth primordium. Even a simple conical (haplodont) supernumerary could be explained as the product of an unequal dichotomy.

The morphogenetic field concept has been elaborated by J. W. Osborn (1978, 1981b) to explain how individual teeth, each bearing some basic morphological resemblance to one another, may arise within the fields. The field influence, exerted from a generation point, can be assumed to be a field substance which diffuses through the tissues of the growing region. For purely physical reasons, there would be a gradient of concentration of the substance at increasing distances from the generation point but, in order to explain an eccentricity or peripheral limitation of the gradient, it is possible to postulate the destruction of the substance by the cells among which it is diffusing. To account for the production of tooth primordia at separate points in the field, it is necessary to postulate a further secondary field effect (Fig. 1.2), or a number of oscillations in field strength (Fig. 1.3), and inhibitory influences around the newly developing primordium. There are three primordial field areas in each jaw quadrant, the most anterior forming the incisors, the middle primordial area forming the canine, and the most posterior the cheek teeth. Each primordial field area is thought to give rise to a tooth, termed the stem

Fig. 1.1. A hypothesis concerning the nature of the differentiation of the dentition. (a) The dental lamina with undifferentiated rudiments. (b) The morphogenetic field which, acting upon the rudiments, determines them to develop in different ways. (c) The differentiated dentition that results. From Gaunt and Miles (1967), after Butler (1939).
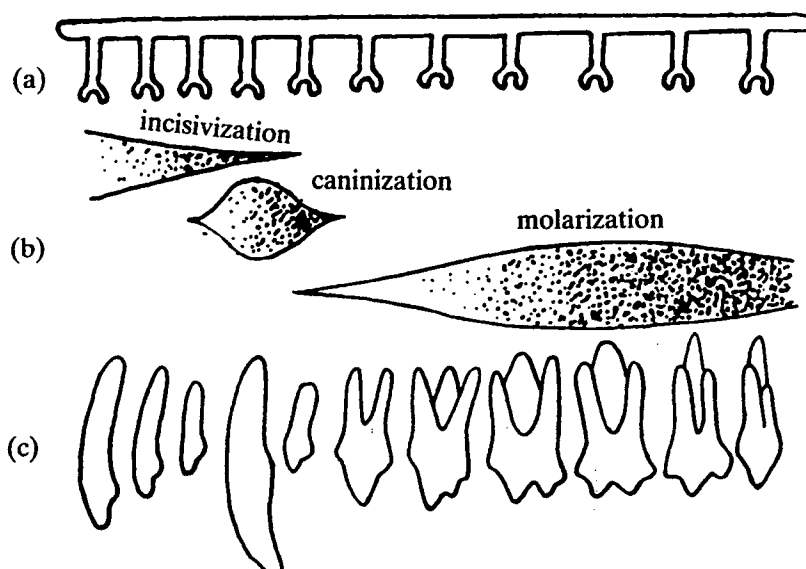
4   *Colyer's Variations and Diseases of the Teeth of Animals*

progenitor (Schwartz, 1984), which shows the charac-
teristics of its tooth class; for the molar field this, in
general, is the first permanent molar.

Osborn postulated a further idea, known as the
odontogenic clone concept, which has been elaborated
upon by Lumsden (1979). The concept postulates that
each primordium in a tooth field develops from a single
cell mass (clone) which initially consists perhaps of
only two cells, one for the mesodermal parts of the
tooth and one for the ectodermal cap (multiclone),
which after a certain number of cell divisions become
competent to initiate a primordium. Then, as the clone
grows and space becomes available, it gives rise to
further primordia (Fig. 1.4). Obviously this idea has to
incorporate concepts of local morphogenetic
thresholds and of inhibitory influences which develop
in the surrounding mesoderm or even within the

primordia themselves, otherwise a single enlarging
tooth mass would develop.

The differences between various concepts are
subtle but important. Some can be tested by experi-
ment; for example, the validity of the odontogenic
clone concept received strong support from the work
of Lumsden (1979) who showed that early primordia of
the lower first molar tooth from mouse embryos
cultured in the anterior eye chambers of adult mice
generated the perfectly shaped and mineralized
crowns of the entire three-molar tooth row.

The concepts expressed here in a simple form are
undergoing rapid development and change; for
instance, Osborn (1984) has renamed the cell units
involved in tooth initiation, clades, in place of the
previous clones.

There is a great deal of other evidence that tooth

Fig. 1.2. An explanation, in stages I–V, in terms of morphogenetic fields for the development
of five structures of differing size and shape graded A–E. A field generator (heavy stipple) is
generated in I and produces a gradient of diffusing field substance (light stipple in II–V).
Primordia develop at points within the field by a secondary influence. All primordia (indicated
by crossed open boxes) initially have identical potential. Each primordium develops a size and
shape determined by the concentration of field substance. The differing sizes and shapes are
indicated by the height of each structure (black rectangles) which corresponds with the level
of concentration of field substance. Inhibitory influences around each primordium are
postulated.
From: Osborn, J.W. (1978).
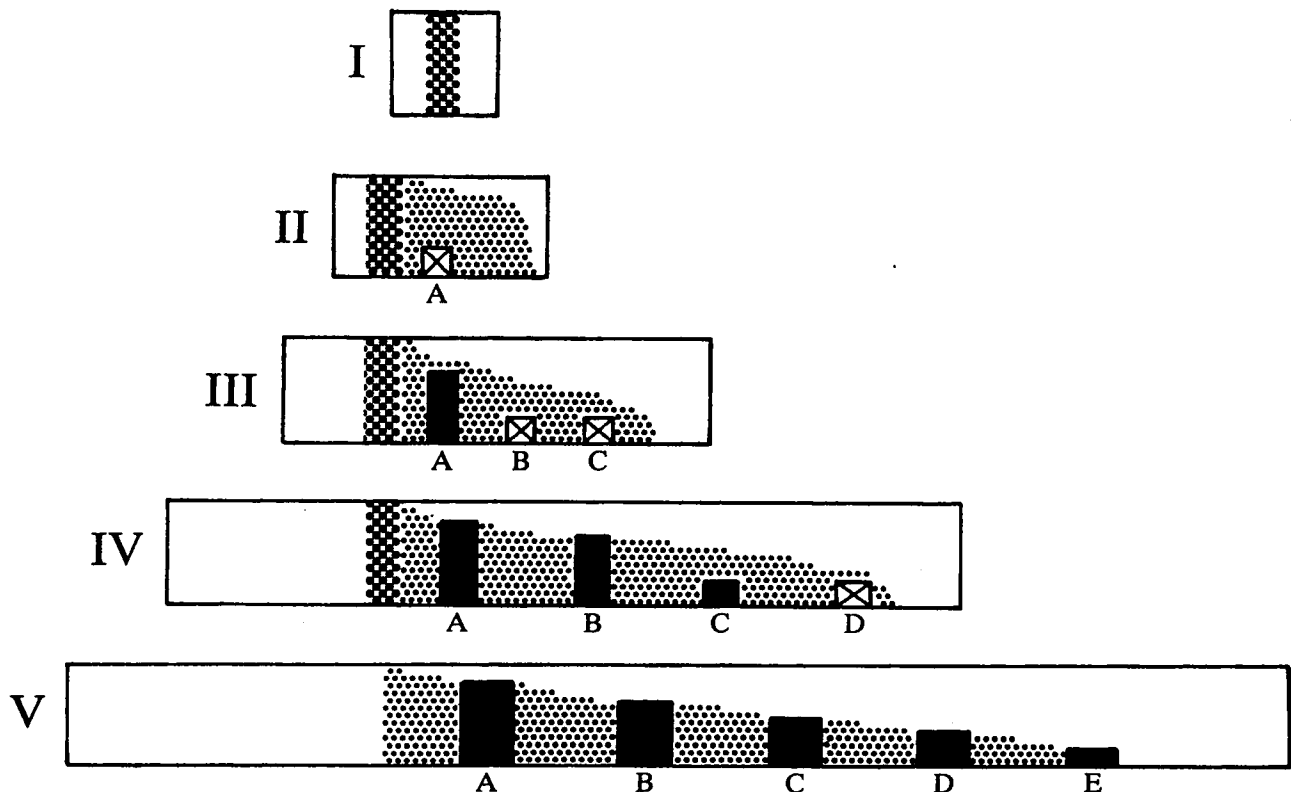
primordia acquire at an early stage the inherent capacity to form teeth of predetermined potential size and shape. For example, each half of a bisected rabbit molar tooth primordium explanted *in vitro* develops the full cusp pattern of a molar (Glasstone, 1952) though it remains much smaller than *in vivo*, presumably because *in vitro* it is not sufficiently nourished to develop its full size; in general, tooth primordia grow larger when cultured *in vivo*, as in the anterior chamber of the eye where a blood supply develops, than they do *in vitro* (Lumsden, 1978).

Of course, during the conversion of a primordium into a tooth, elaborate processes of differentiation of cell types and differential growth rates occur in various parts of the primordium or tooth germ, all under the control of between-cell influences (Slavkin, 1974). See also Reif (1980) on reversal of polarity in tooth germs referred to in the next section.

Although the matter cannot be fully discussed here, it is appropriate to mention that tooth germs, explanted at stages before they are likely to be contaminated with osteogenic cells of the jaw and cultured either *in vivo* or *in vitro*, often develop at least traces of an ensheathing periodontal ligament and alveolar bone. This finding seems to indicate that the periodontium, including alveolar bone, develops from, or under the influence of, the same ectomesenchymal primordium that gives rise to the teeth themselves (Ten Cate, 1972; Ten Cate and Mills, 1972; Lumsden, 1984). See also Chapter 9, p. 155.

Fig. 1.3. Gradient-field theory explanation for the formation of a 7-unit (4 deciduous molars and 3 molars) mandibular post-canine dentition in a hypothetical carnivore. Where oscillations in the field strength of a special substance produced by the field generator (Fg) rise above a certain threshold, indicated by the interrupted line, a tooth primordium (solid circle) is initiated. The field strength is greatest towards the centre where the primordium of M_1, the largest and most carnassial tooth, develops and it diminishes in strength both distally and mesially where teeth of diminishing size develop.

The open circles indicate hypothetical potential primordia that could arise if the field strength were sufficient or if some suppressive influence were lifted. Other (supernumerary) primordia could arise between the solid circles if for some reason an additional local area or oscillation of concentration of generator substance above the threshold occurred. If such a concentration arose at the expense of an adjacent oscillation, but was not sufficient to reduce it below the threshold, a supernumerary tooth associated with smallness or cusp deficiency in a tooth of the normal series would occur.
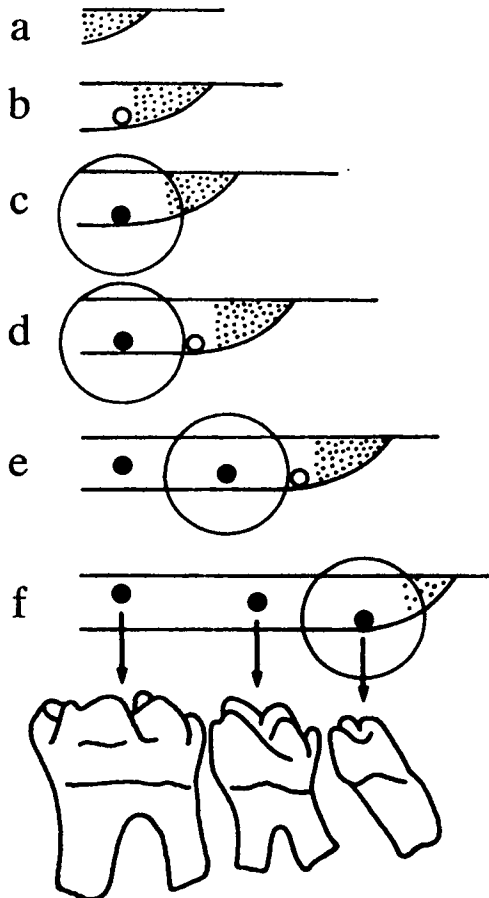Based on Lumsden, A.G.S. (1979).
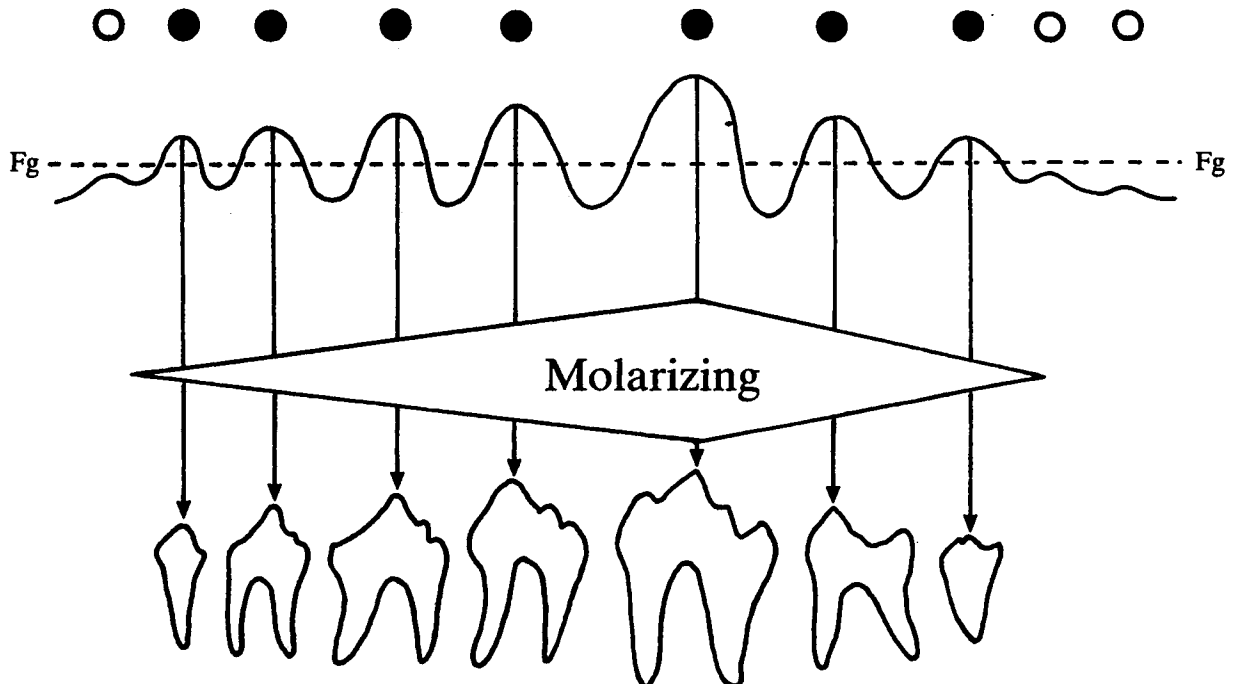
Supernumerary teeth

Supernumerary teeth can be loosely categorized morphologically into three kinds: (1) Supplemental teeth which resemble teeth of the normal series in both crown and root morphology though not always in size. They may sometimes resemble ones already in the arch so closely that it may be impossible to be sure which is the supernumerary element. (2) Haplodont supernumerary teeth have simple, usually conical, crowns and single roots. (3) Tuberculate supernumerary teeth have more complex crowns, and have what can be called an occlusal surface bearing several tubercles, often with deep indentations. Like haplodont supernumerary teeth, these tuberculate supernumeraries usually have single roots.

Supernumerary teeth usually develop more or less synchronously with the teeth adjacent to them but occasionally their development is out of step (Miles, 1954). For example, a supernumerary tooth in the incisor region may have a fully-formed root whereas the roots of the incisors are still forming; conversely the supernumerary may be in an earlier stage of development than the adjacent teeth. Obviously sometimes this asynchrony is explicable on the basis that the supernumerary tooth is associated with a different dentition, deciduous or permanent.

Reference has already been made (p. 2) to the explanation of the origin of supernumerary teeth in terms of the morphogenetic field theory; namely, that they are a manifestation of a localized excess of odontogenic capacity. There is some evidence that, in general, the prevalence of numerical variation is greatest at the peripheries of the tooth-class fields. The evidence is strongest in respect of the distal end of the molar field; for example, disto-molars, either larger or smaller than normal, and absence of third molars are particularly common in primates (Schwartz, 1984).

A further idea is that supernumerary teeth arise from the splitting or dichotomy of a tooth primordium (Bateson, 1894, p. 268; Sprawson, 1937; Wolsan, 1984c). Supplemental teeth would be explained on the basis of the primordium dividing into equal parts each with the capacity to form a tooth of normal morphology. Haplodont and tuberculate supernumerary teeth would be explained by division of the primordium into parts which, although having the capacity to form a complete tooth, did not have the full regulative capacity to form a tooth of normal morphology and size. Certain observations, such as the existence of tooth forms which strongly suggest partial dichotomy, and some *in-vitro* experiments lend plausibility to the idea of dichotomy. This evidence is elaborated on in the next section, Connate teeth.

Some observations made in sharks are of particular importance to the dichotomy hypothesis of origin of supernumerary teeth as well as to the mechanisms of control of tooth morphogenesis. Compagno (1967) described three abnormal dentitions in three different taxonomic families of sharks. The teeth are normally blade-like with a central cusp which is distinctly distally inclined. Other morphological details distinguish the mesial and distal surfaces of the teeth; for instance, in *Galeorhinus zyopterus* the distal margins of the central cusps are serrated. In the lower jaw of two and the upper jaw of the other of the three abnormal specimens, one tooth as well as all its successors were of

Fig. 1.4. Explanation in terms of clone theory for the formation of the mouse molar dentition. The stippled region represents the growing margin of the clone; the large circles represent zones of inhibition. The gradient of final form is related to the times at which the primordia (black dots) are initiated. Small circles represent tissues which have reached the critical mass to form a primordium (Lumsden, 1979).
From: Lumsden, A. G. S. (1979).

reversed morphology; that is, the central cusp was inclined mesially and the serrated edge faced mesially. In other words, at least superficially, the affected tooth families had the morphology of the teeth of the opposite side.

Reif (1980) described additional examples in other species of shark and noted that many were associated with evidence of trauma and of initial splitting of a tooth germ at a very early stage (protogerm), producing two teeth instead of one. He suggested that sometimes the mesio-distal polarity of one part of the divided germ undergoes reversal. Although the first generation of teeth derived from the divided germ would be smaller than normal, successive generations are larger until eventually only the tooth with reversed morphology would be recognizable. The dental lamina and newest generations of teeth in the elasmobranchs are susceptible to trauma because they are situated beneath the mucosa in the inner aspects of the cartilaginous jaws. An instance was illustrated by Andre (1784; see also Gudger, 1937) in a tiger shark (*Galeocerdo tigrinus*) in which a spine of a sting-ray had stuck in the lower jaw and produced a family of several generations of malformed teeth.

In the older literature on supernumerary teeth, suggestions are common that they may be examples of atavism, that is they represent the recurrence of a character possessed by an ancestral form which had apparently been lost in the process of evolution. Atavism, with the original authority of for example Bateson (1894), is a concept that now appears to be out of favour with geneticists in general, and is rarely discussed in the general literature on abnormal development. Atavism cannot for example be offered as an explanation for polydactyly because no ancestor of the mammals with more than five digits on each extremity has ever been postulated.

Nevertheless, geneticists do recognize in breeding experiments a process called reverse mutation in which the mutation appears to go back to what is called the wild-type. Furthermore, it is well established that the genome can carry genetic information in the form of recessive genes for many generations without the information being expressed; then, if the carrier of the recessive gene happens to be crossed with an individual that carries the same gene, the information gains expression in the offspring.

Horns occasionally appear in hornless breeds of domestic cattle and sheep whose ancestors were horned (Darwin, 1859, p. 454 and 1868, p. 315). An example in the dentition is the occasional occurrence of lower second molars, absent from the felid phylogeny since the Miocene (Kurtén, 1963). In such cases, it would seem to be legitimate to consider atavism,

especially if there was evidence that the condition was heritable (Wolsan, 1984c). Similarly, it is probably wise only to give serious consideration to atavism as a cause of supernumerary teeth where there is at least a probability that the condition is heritable or, in exceptional circumstances, such as the occurrence of a supernumerary tooth in the diastema in the Rodentia.

Although supernumerary teeth often appear to arise as spontaneous accidents of development, in the few instances where the familial relationships of the animals are known or where numerical variation within particular populations has been quantified, there is evidence that the supernumerary teeth tend to occur more frequently in isolated groups and particularly in some domesticates. The controlling mechanism then is almost certainly genetic drift and many instances will be mentioned in the relevant chapters.

Although true duplication of continuously-growing rodent incisors does occur (pp. 131, 133 and p. 134), that is the development of more than one incisor where there is normally only one, some conditions have been described in which apparently-extra incisors may erupt beside the normal ones during adult life; for example, following the administration to rats of drugs that interfere with cell proliferation (Vahlsing, Kim and Feringa, 1977), or carcinogenic drugs to hamsters (Edwards, 1980) or of ^{224}Ra to mice (Humphreys, Robins and Stones, 1985), and in aged mice (p. 405) (Robins and Rowlatt, 1971). In the rats described by Vahlsing *et al.*, the drug seems to have stopped the proliferation of the formative tissues at the base of the incisor and its eruption had slowed or ceased. However, in due course as the cytotoxic effect wore off, proliferation restarted and tooth formation recommenced. Because of the period of non-formation, the new portion of tooth was not in continuity with the old and erupting with normal vigour grew, like a new tooth, alongside the old tooth and eventually erupted beside it. In the instance described by Edwards, the carcinogen appeared to have caused a proliferative overgrowth of some of the formative tissues at the base of the incisor which gave rise to a complex mass of dysplastic dentine, cementum and enamel. It seems that part of this proliferative tissue budded off and, exhibiting a more properly regulated growth of dental formative tissue, formed as an incisiform structure alongside the parent tooth.

Connate teeth

There is a variety of tooth anomaly, bearing evidence of being composed of two or more tooth elements, for which terms such as gemination, double teeth (Miles, 1954, 1966) connation, incomplete dichotomy, fused

teeth, synodonty and odontopagy have been employed. We favour the term connation (developed or born together), which was employed in this context at least as early as the middle of last century (J. Tomes, 1859), because we agree with Hitchin and Morris (1966) that the term exactly describes the anomaly. Many of the alternative terms express one or other of two divergent views of the origin of the anomaly. According to one view, it arises from a process of fusion or joining up of tooth germs; according to the other, it arises from a partial splitting or dichotomy of a tooth primordium. Insufficient evidence is available to determine this question but there are a few observations which may be significant.

It may be that some anomalies arise from fusion and others from a process more like dichotomy. An occurrence that suggests that a process of dichotomy of a tooth germ can produce multiple teeth, and that likewise a process of partial dichotomy could produce connate teeth, is that of the multiple small tusks that sometimes arise in connection with physical injuries to

elephant tusks (p. 414 *et seq.*). The work of Glasstone (1952), who found that each half of a rabbit-molar tooth germ cut in two formed a rudimentary whole tooth when grown in tissue culture, also seems relevant to the mechanism of production of both connate and supernumerary teeth.

Most connate teeth show various degrees of separation of the crowns of the tooth elements whereas the roots are single as in Figure 1.5A, B. Examples with joined crowns and separate roots are rare (Fig. 1.5C). As it is the tips of the crowns that are formed first, this means that in the initial stages of development of the majority of connate teeth the elements must have had separate identities and union could only have occurred as development proceeded. This observation would appear to be more consistent with the theory of fusion rather than that of dichotomy. In many connate teeth, the separateness of the crown elements consists only of a notch and groove. There is no difficulty in envisaging such teeth as developing within a single tooth germ that showed only some

Fig. 1.5. Three examples of connate teeth.
A and B: *Canis familiaris* (dog). Left and right sides of jaw (from Bateson 1894, p. 211). The left upper canine is bifid (A). In the right upper canine (B), the disturbance of development is similar; however not only is the crown bifid but an axial groove extends on to the root. These teeth are remarkably similar to those of a fox shown in Figure 4.49. Both these specimens support, or are consistent with, the hypothesis of dichotomy of tooth germs.
C: *Cercopithecus aethiops tantalus* (tantalus monkey). ♂. Captive. RCS Odonto. Mus., G 13.4. Mandible. A much more uncommon type of connation in which, although the incisive edges are bifid, each crown element has a separate root; a specimen which favours the idea of fusion for a time of two elements which were separate at an extremely early stage of development.
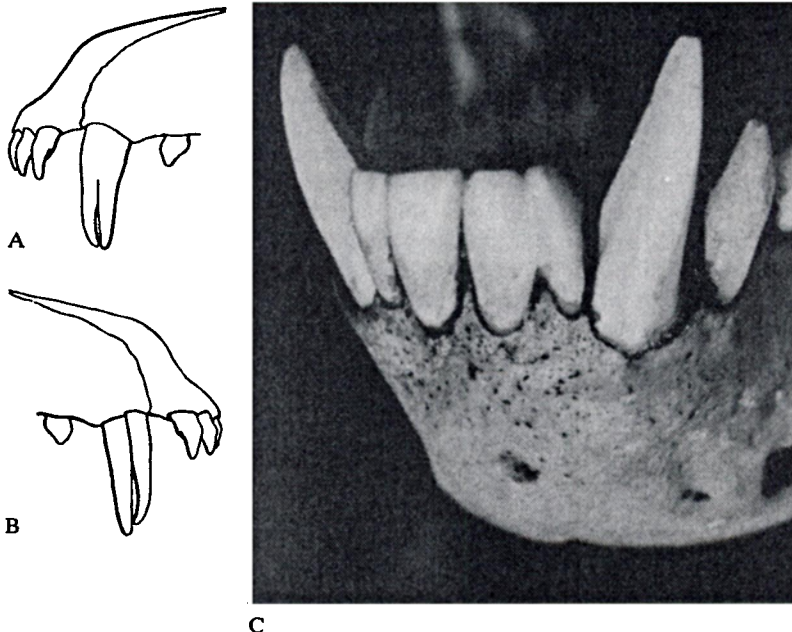
degree of division into elements in its internal structure. However, connate teeth occasionally occur which consist of more than one crown springing from a single root element and the distance is so great between the tips of the crowns, where tooth formation is initiated, that it is inconceivable that the whole connate tooth was formed from a single germ. It must have developed from two separate germs which later united. A close study of some connate teeth shows a ridge of tissue at the point of junction of the two elements producing an appearance suggestive of distortion by pressure.

It seems reasonable to conclude that not all connate teeth arise in the same way; some may arise by dichotomy and others by a process of fusion of tooth germs or primordia. It must be borne in mind that a quite different kind of tooth fusion can also occur, caused by the overgrowth of cementum after tooth formation is complete. This can happen when the roots of adjacent teeth are in contact and the cementum of the roots undergoes hyperplasia as a result of some chronic inflammatory process.

Connation of teeth occurs sporadically in many species; it has been observed in the median egg-teeth in the viper, *Vipera berus* (Smith, Bellairs and Miles, 1953).

Many examples of connation are described in later sections of the book. Whether any of these are heritable can only be determined by studies of families or controlled breeding experiments. Certainly some are; for example, Hitchin and Morris (1966) noted that connated upper incisors turned up in some Lakeland Terrier dogs being bred for show. Connation was then deliberately bred for over several generations, mostly by sire-daughter matings. Connate incisors, mostly in the upper jaw and often bilaterally, occurred commonly in these terriers and eventually occasionally in the mandible also. Connation in the deciduous dentition was often repeated in the permanent successors. The heritability in this instance was amply demonstrated but the exact mode of inheritance was unclear.

These experiments produced suitable material for the study of the embryonic stages in the development of the anomaly. In normal development, tooth germs arise along the course of a continuous two-layered epithelial tooth band; the parts of the band between the germs normally degenerate and disappear, but it seems that, where connate teeth are to be formed, the band persists. Then, as the formation of the originally-separate adjacent teeth proceeds and they become contiguous, stellate reticulum spreads from the enamel organs of both tooth germs between the two layers of the persistent band. Gradually not only does the stellate reticulum become continuous but so does the

ameloblast layer. Although amelogenesis may cease at the point of contact of the two tooth germs, differentiation of odontoblasts continues, the two odontoblast layers join and then proceed to form the dentine of what is now a single connate tooth.

The morphology of the connate tooth, whether for instance it is simply a large incisor with a deep notch at the incisive edge, or has two separate crowns joined only at the cervices to a single root, depends on how much of the originally separate teeth has been formed before the stellate reticulum grows across within the persistent tooth band.

Connation, both of an upper incisor with a supernumerary incisor and of a first permanent molar with a mesially-situated supernumerary molar, is common in the mutant tabby-mouse (Sofaer, 1969). The histology of the early stages of tooth development in these mice tended to be similar to that just described. Crowding together of the tooth germs, as when supernumerary teeth appear, seemed conducive to what must be called a process of fusion. Appearances suggestive of dichotomy were not met with.

Sofaer and Shaw (1971) noted that connate molars and supernumerary molars occurred sporadically in a colony of rice rats (*Oryzomys palustris*). Selection of animals for the presence of these abnormalities produced a strain with a high incidence of fusion of the first and second molars, and even of the third molar as well, to produce a molar of giant size. Although rudimentary supernumerary molars occurred sometimes, in this instance crowding of the teeth did not appear to be a factor in the connation. The autogenetic mechanism appeared to be as described above. The mode of inheritance appeared to be by a single autosomal recessive gene with variable penetrance in homozygotes.

Knudsen (1965, 1966*a*, *b*) reported many varieties of tooth fusion associated with exancephaly in mice induced by teratogenic agencies, mainly maternal hypervitaminosis A. There were even bizarre examples of fusion of upper molar germs with lower molar germs on the same side. Ritter (1963) induced fusion of the lower incisors in mice with X-radiation. In these cases, it was argued that the underlying cause is a deficiency of the growth of the connective tissue which normally separates individual tooth germs during development.

Genetic and environmental causes of variation

It used to be thought that tooth size is genetically determined and is not at all influenced by environment. However, evidence (reviewed by M. L. Moss,

1978) now suggests that the size of the crowns of teeth may be affected by the maternal diet; for instance Holloway, Shaw and Sweeney (1961) found that, in the offspring of rats fed on a diet deficient in protein, the crowns of the molar teeth were smaller than those of offspring of rats on a normal diet. By appropriate measurements, they established that the smaller size was due to the dentine cores of the crowns being smaller, rather than due to the enamel covering being thinner. This is extremely important because the size of the crown of a tooth is determined primarily by the size of the dentine part of it which, once formed, cannot be added to externally and therefore cannot increase in size; the ultimate size of the crown is then determined secondarily by the thickness of enamel laid down upon the dentine core which depends upon the rate and duration of amelogenesis, both of which could be affected by environmental factors such as nutrition and hormone levels. M. L. Moss (1978) adduced evidence that male-female differences in the duration of amelogenesis may be responsible at least in part for the larger tooth crowns so often found in the male. Similarly, minor sex differences in tooth crown morphology could be produced by sexually different rates or durations of amelogenesis affecting localized areas of the crowns.

The discovery in 1944 that maternal infection with the rubella virus in the early months of pregnancy leads to various human birth defects (Kraus, Ames and Clark, 1969; Smith, Soskolne and Ornoy, 1978) gave impetus to experimental work on laboratory animals which has now provided ample evidence that a wide variety of conditions, such as vitamin deficiencies or the presence of noxious substances, can disturb embryonic development (Robens, 1970). One of the commonest malformations is cleft palate in which the development of the teeth on either side of the cleft is also disturbed (Shah, 1979). However, malformed teeth and absence of teeth (anodontia), in the absence of cleft palate, have been described as products of experiments that disturb pregnancy (Miles, 1954).

There is now a vast literature on experimental teratogenesis, or abnormal development, stimulated by the discovery that maternal administration of many new drugs during the early stages of pregnancy have a teratogenic side-effect. In such experiments, developmental anomalies show a marked tendency to be multiple, as indeed do those that occur spontaneously; for instance anencephaly and lesser abnormalities of development of the head region such as cleft palate are commonly associated with polydactyly and failure of the caudal end of the neural tube to close (spina bifida).

The genetic potential and influence of the general environment would be expected to be the same on both sides of the body; hence, when an abnormally high level of asymmetry occurs between paired structures, it is regarded as an indicator of developmental instability resulting either from poor genetic control or from unusually large local environmental differences between sides. Thus inbreeding, which is known to increase sensitivity to environmental variation, is associated with a tendency for abnormally high levels of asymmetry of tooth-crown size (Bader, 1965; Sofaer, 1978); a similar increase in asymmetry of teeth and limb bones has been observed in rats and mice following disturbance of their prenatal and perinatal environment by noise, heat, cold or protein deprivation (Sciulli, *et al*, 1979). When populations are available for study, data on dental symmetry can throw light on the relative contributions of genetic and environmental sources of instability of the developmental processes (Sofaer, 1975, 1976).

Many examples of the high incidence of dental anomalies in isolated populations and on islands are given in the text. Such characters can be produced by the processes known as genetic drift and founder effect. Genetic drift is the fluctuation of gene frequencies resulting from random combinations of alleles from generation to generation. In a large population, its effect is small compared with that of selection, but in an isolated, finite population its effect may be more marked, leading to the appearance of characters that may have no selective advantage. In founder effect, a population is initiated from a small number of individuals as when a few animals are introduced on to an island. Genetic drift and the absence of some alleles present in the parent population may produce genetic change in the island population (Hedrick, 1983).

Large mammals on islands tend to be smaller than in the parent population on the mainland (Foster, 1964; Sondaar, 1977; M. Williamson, 1981). The extent to which this is genetically or environmentally determined is uncertain, but it may be related to founder effect and to the absence of predators whose activities would result in the selection of larger individuals, as well as to the exhaustion of preferred food plants. Teeth seem to diminish in size more slowly than the jaws; thus such isolation may encourage tooth crowding. The process of domestication (which entails the isolation of a small segment of the wild population) may have a similar effect, resulting in small size in many domestic animals; in canids, small size and tooth crowding are characters that can be used to distinguish the sub-fossil dog (*Canis familiaris*) from the ancestral