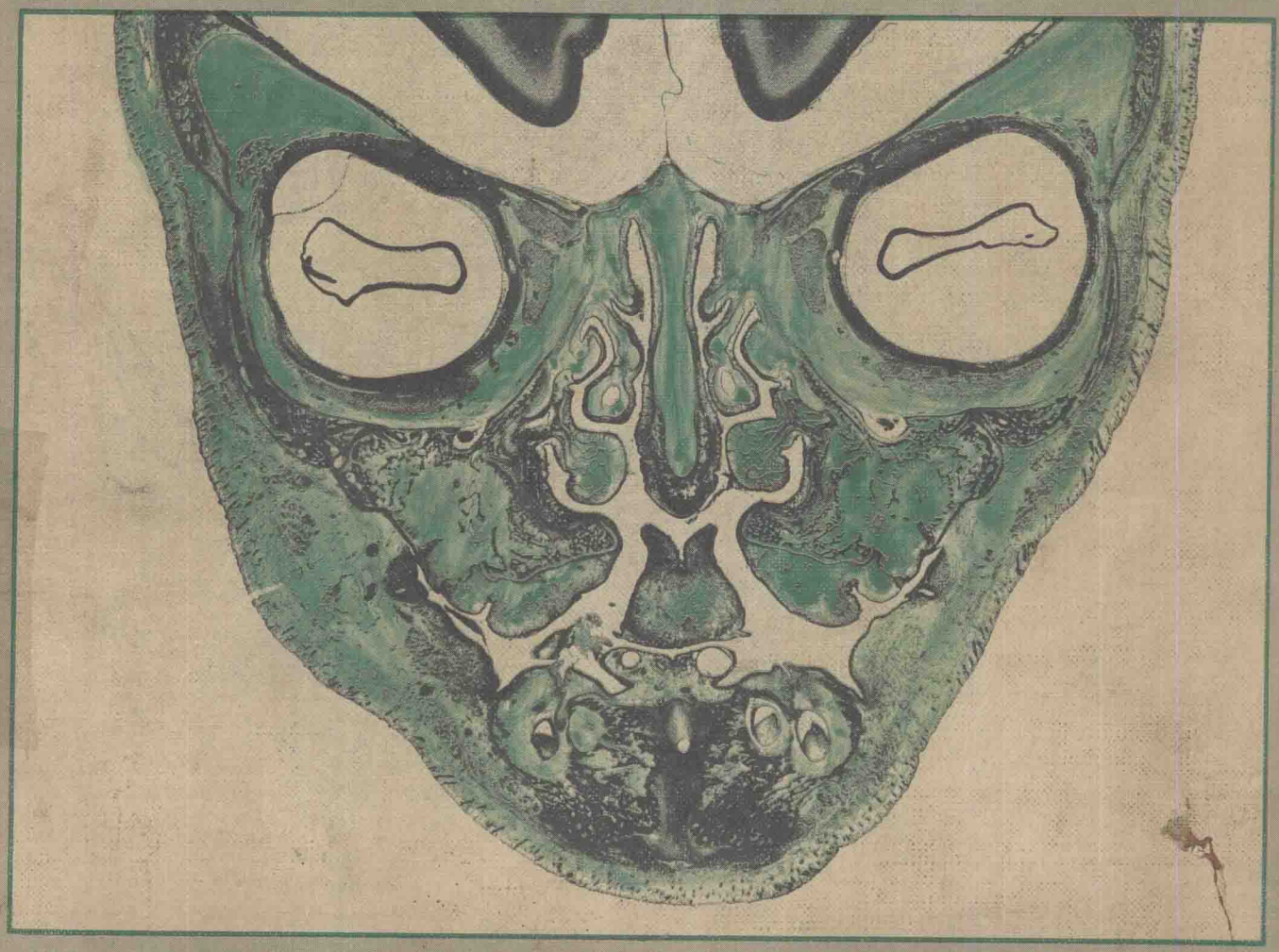
ATLAS OF DEVELOPMENTAL ANATOMY OF THE FACE

With special reference to normal and cleft lip and palate

BERTRAM S. KRAUS · HIRONORI KITAMURA · RALPH A. LATHAM



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Cover illustration: Coronal section through the head of a 17 week human fetus with Pierre Robin Syndrome. The section is near the juncture of the primary and secondary palates and shows the mandibular lateral incisor and cuspid buds in an early stage of calcification.

Atlas of Developmental Anatomy of the Face

To
Dorothy Simon Kraus

Preface

This atlas is designed to provide detailed, serial, and comparative data on the anatomy of the human face throughout the prenatal period of development. It is based upon an extensive sample selected from a collection of 25,000 aborted embryos and fetuses. These specimens were gathered over the past 12 years from some 250 hospitals in all sections of the United States and from several institutions in Japan. In this collection were found many kinds of abnormalities, including clefts of the lip and/or palate. The heads of many of these specimens were photographed, decalcified, embedded, serially sectioned, and stained, and selected histologic slides were in turn photographed. From this prepared sample 35 cleft and 47 non-cleft heads were carefully selected and photographed for this atlas.

To provide the broadest possible bases for comparisons between the normal and cleft specimens at every stage of fetal development, more than 1200 gross and microphotographs are included. They show the nature of the cleft, the status of external body development, and the histological details of the faces of both normal and cleft embryos and fetuses for each stage of maturation. The age range is from 33 days to full term. Three specimens are presented for every selected stage of normal development. For each normal and cleft specimen, sections are shown for the same six areas of the face. All histological sections are coronal. The atlas is arranged to afford easy comparison between the six selected areas of the face for both the normal and the cleft lip and palate specimens. In this way, the concept of normal anatomic variation is emphasized and continually reinforced.

In the course of studying cleft lip and palate in human embryos and fetuses, we were impressed with the number and variety of accompanying malformations, both external and internal. These, too, are illustrated in the atlas. Finally, certain details of palatal development not previously emphasized in the literature are presented in the final section of the atlas.

Thus we have tried to demonstrate:

1. Anatomic variation in facial development
2. Changes with age
3. Facial differences between cleft and non-cleft embryos and fetuses
4. Other malformations associated with cleft lip and/or palate
5. Special features related to palatal development.

The subject matter and organization of the atlas, based on these five goals, are described in detail in an introductory section, beginning on page 1.

We believe this volume is more than an atlas; rather it is a sourcebook of research material not ordinarily available to students and investigators. We hope it offers the means by which biologists and clinicians alike may gain better understanding of facial development, in both its normal and abnormal aspects, and may be stimulated toward the formulation of new research problems and the reformulation of old ones.

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Acknowledgments

The devotion, cooperation, and skills of many individuals were essential for the undertaking and completion of this atlas. Although space limitations prevent us from naming them, the authors wish to acknowledge with deep appreciation the invaluable help of their colleagues in pathology throughout the United States.

Many laboratory technicians have been engaged in the tedious and exacting task of preparing the hundreds of thousands of sections now accumulated. In particular the authors express their sincere gratitude to Karen Hill, Eleanor Oldham, Adelaide Guzanick, John Lowe, Eleanor Spence, Gretchen Luhman, Tamara Shiek, and Janis Stover.

The major photographic burden was carried by Richard L. Cole (assisted by Ben Goldberg) and by David Sullivan. In the early stages of the atlas' preparation a few of the cleft palate and malformation photographs were taken by Clifford Freehe. Lettering, drawings, and other illustrative features were the work of Virginia E. Brooks. To these competent medical illustrators the authors are greatly indebted.

The collection of specimens was begun at the University of Arizona, transferred to the University of Washington, and is now housed in the Cleft Palate Research Center at the University of Pittsburgh. To these institutions, which provided laboratory and storage facilities, the senior author in particular is deeply grateful.

Finally, no such sustained effort could have been possible without adequate funds. Much of the research during the past six years was supported by Grants DE-00910 and DE-01697 from the National Institute of Dental Research and by Grant HD-00707 from the National Institute of Child Growth and Human Development. This support is gratefully acknowledged.

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Atlas of Developmental Anatomy of the Face

List of Specimens by Age

Division II—Cleft Lip and/or Palate

Age	Specimen number	Type of Cleft	Page number*
41 days	X3636	Lip	**164**, 165
43 days	X436	Lip	**168**, 169
	X139	Lip	**172**, 173
47 days	W269	Palate	**176**, 177
	X2844	Palate	**180**, 181
	X1795	Lip and palate	**184**, 185
	X494	Lip	**188**, 189
	X491	Palate	**192**, 193
	X2769	Palate	**196**, 197
8 weeks	X2992	Palate	**200**, 201
	X2977	Palate	**204**, 205
9 weeks	W307	Lip and palate	**208**, 209
	X2337	Palate	**212**, 213
	W50	Lip and palate	**216**, 217
	X2647	Palate	**220**, 221
	X3079	Palate	**224**, 225
	X516	Palate	**228**, 229
10 weeks	X2993	Lip and palate	**232**, 233
	X2448	Lip	**236**, 237
	X104	Lip and palate	**240**, 241
	X498	Lip and palate	**244**, 245
12 weeks	X2336	Lip and palate	**248**, 249
	I29	Palate	**252**, 253
13–15 weeks	X3436	Lip and palate	**256**, 257
	X3688	Lip and palate	**260**, 261
16–18 weeks	X3881	Palate and micrognathia	**264**, 265
	X2812	Lip and palate	**268**, 269
	X2464	Lip	**272**, 273
	X2326	Palate	**276**, 277
	X478	Lip	**280**, 281
19–21 weeks	X193	Palate	**284**, 285
	W85	Lip and palate	**288**, 289
Newborn	X3726	Lip and palate	**292**, 293
	X3108	Palate	**296**, 297
	W92	Palate	**300**, 301

* Page numbers in boldface type refer to photograph of palate of each specimen.

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Subject Matter and Organization of the Atlas

As indicated in the Preface, this atlas has been designed to demonstrate

(1) anatomic variation,

(2) changes with age,

(3) differences between embryos and fetuses with cleft and with non-cleft lips and palates,

(4) other malformations associated with cleft lip and/or palate,

(5) special features related to palate development.

The organization of the atlas will be discussed in terms of these general subjects.

Variation

Perhaps the most important innovation is the attempt to convey the concept of variation. Seldom does an atlas present more than one specimen of a given age, sex, and condition. The result is that the student acquires almost unconsciously an attitude toward anatomy or histology that is rigid and non-biologic. The basic fact of biology, as Darwin emphasized over a hundred years ago, is variation. Some knowledge of the range within which any specific trait may vary and still not be deleterious to the organism is indispensable if defective or malformed structures are to be recognized. An attempt has been made in this atlas to depart from the idea of stereotype and to provide a feeling for variability by showing three specimens for each age grade in Division I, which presents the so-called normals or controls.

At this point a few words must be interjected to explain the use of the term "normal." Normality, in the statistical sense, refers to an arbitrarily selected area about the mean. In terms of pathology, however, normality includes any variations about the mean which do not prevent the organism (human, in this case) from functioning in his society and environment in a way that is recognized and accepted as normal behavior. A good example of the difference between the statistical and pathologic definitions is the case of malocclusion. Orthodontists report that 70 per cent of the United States population have some form of malocclusion. Statistically it could be maintained that malocclusion is thus a normal condition,

while excellent occlusion is relatively rare and, hence, an abnormal condition. On the other hand malocclusion in a child or young adult is often a source of social discomfiture and mental anguish, so that alleviation of the condition is sought. In this sense, malocclusion is an abnormal condition, since it interferes with the normal behavior of the individual. It does not matter if the discomfiture is manifest physically or mentally; its existence is a fact.

Although the specimens in Division I are labeled "controls" or "non-clefts," the point remains that the specimens used in this atlas represent a population of *aborted* human embryos and fetuses, that is, a population that failed, for one reason or another, to survive. Since a study such as this could hardly deal with a living population, and since an effort had to be made to establish anatomic norms for the various prenatal stages of development, it was decided to focus primarily on a dichotomy based upon the presence or absence of a cleft lip and/or palate. An embryo or fetus which exhibited no sign of cleft was examined for the presence of other malformations or anomalies. If the search was negative, the specimen's head was sectioned serially and stained. For any one age, sections from comparable areas from three of these specimens were examined simultaneously. The morphology of bones, cartilage, soft structures, and teeth was noted in particular. If the variation in these structures was relatively slight, it was then assumed (after examination of at least 30 such specimens for any age group) that the normal range of variation was being presented. There was no reason to make the *a priori* assumption that the fact that these fetuses were aborted was in itself *prima facie* evidence of abnormality in the facial anatomy. No doubt such abnormalities do occur in this population, but do they not also occur in the viable, successful fetus? The reader will find, among the normal specimens shown in Division I, occasional pathologic entities. It is emphasized, however, that the primary distinction, in terms of normal and abnormal, is between the cleft lip and/or palate on the one hand and the non-cleft (and presumably normal) palate on the other.

Age Changes

The course of prenatal growth and development can never be reconstructed with any validity from the study of adult specimens, a few fetuses of other species, or two or three specimens widely separated in age. Changes in form, from the tissue to the gross structure, take place continuously and often dramatically throughout the entire prenatal period. It would be most revealing if one could follow the same embryo throughout its ontogenesis, but failing this opportunity it is necessary to attempt to reconstruct development on a cross-sectional basis. This requires a large sample consisting of several specimens at each age level. The ages selected for the atlas, ranging from 35 days to full term, were judged to provide insight into critical periods of change in one or more facial structures, particularly with reference to the nasal and oral elements.

It is possible, therefore, for the student interested in any particular structure of the face to follow its development

from 35 days to birth, noting at each period the kind and range of variation that can occur. At the same time, the general increase of size can also be observed and roughly measured, since the magnification is indicated on each photograph.

For each three specimens in any age group a guide page is provided. This shows the general appearance of the body at this stage, offers a lateral and a frontal view of the head, and indicates on drawings of the head and palate where the sections that are represented are located. In addition, a photograph of the palate is presented in order to give an idea of the size and state of development of this structure at that particular age.

It will be noted that in both Division I (normal) and Division II (cleft) there are six sections (represented by letters A, B, C, D, E, F) presented for each specimen. The locations of these sections have been carefully chosen so that they are directly comparable not only between the specimens for any one age group but between those of different age groups. Thus area A for both the normal and cleft specimens between 41 and 49 days is uniformly a section through the primary palate. It is therefore possible to study the changes in the face that occur in the frontal plane of the primary palate from ages 41 through 49 days, with the variations present at each age. The other five selected areas in the frontal plane include B, the junction of primary and secondary palates; C, the center of the secondary palate; D, the end of the nasal cavity; E, the center of the soft palate; and F, the end of the palatal processes.

In both Divisions I and II, from 8 weeks (50 days) to full term, the selected areas differ somewhat. Area A represents the middle of the lip; B, the primary palate at the level of the lateral incisor; C, the posterior limit of the premaxillary portion of the bony palate; D, the anterior limit of the palatine bone; E, the posterior limit of the horizontal process of the palatine bone; and F, the center of the soft palate. Again, each of these areas can be followed from 8 weeks (50 days) to full term in order to observe the changes that take place.

Sections taken through the heads of specimens of 35 and 37 days (shown in Division I) were selected somewhat differently. In this group, area A represents the facial processes; B, the primary palate; C, the junction of primary and secondary palates; D, the primitive posterior nares; E, the center of the secondary palate; and F, the remnant of Rathke's pouch.

Comparison of Abnormal with Normal

In Division II, instead of a guide page before each age group as in Division I, a photograph of the palate is presented for each cleft specimen. It is thus easy not only to compare the cleft palate with the normal palate of the same age but to refer to the gross picture of the cleft from the various histologic sections and thus to locate approximately each of the six areas shown.

For each of the six areas shown there are two magnifications presented. The top pictures throughout the two divisions are taken at low power and show

the entire face. The ones directly below concentrate upon the nasal septum and the palatal area. Since much the same areas are presented for the cleft lip and/or palate specimens, it is possible to examine in detail both cleft and non-cleft histologic features in the region of the palate for any given age and to trace the course of both normal and abnormal development of this structure. In addition, the low-power microphotographs enable the reader to determine what other features of the face show abnormal development in association with the cleft. The selection of areas in the cleft specimens (Division II) to correspond with those in the non-cleft group (Division I) was rendered somewhat difficult by the widespread disturbance of the facial anatomy in the former. Various landmarks were chosen, then rejected when each proved unstable in the cleft specimens. In some cases, therefore, a choice was made based upon the best judgment of the three authors.

With so many interesting specimens available and so many of the serial sections affording the opportunity of following a structure from its anterior to its posterior limits, it became apparent that the principal task was to make the decision on what must be omitted from the atlas. This was done reluctantly and with full realization that the particular needs of specialists in some of the craniofacial areas might not be accommodated. However, the material that is presented does provide an adequate idea of the nature of the data now on file at the Cleft Palate Research Center. These data may be examined at the center by qualified investigators upon request.

Associated Malformations

A third division of the atlas was planned to afford the reader an opportunity to see the numerous other external and internal malformations and defects that accompany the cleft lip and/or palate in the human fetus. The cleft specimens are presented in chronologic order. Of the 35 cleft specimens illustrated in Division II, 19 are shown in Division III with associated malformations. For a preliminary report on the nature and prevalence of such malformations the reader is referred to papers by Kraus, Kitamura, and Ooé (1963) and Kitamura and Kraus (1964).

Special Problems

In the course of examining serial sections of many specimens, both cleft and non-cleft, it is inevitable that a number of new problems present themselves and questions arise that could only be asked after viewing the actual anatomy of facial development. Some of these problems are extremely pertinent to a full understanding of the nature of cleft formation, and answers to some of the questions must be forthcoming before research into the etiology of cleft lip and palate can be adequately and validly designed.

It was tempting, throughout the production of the atlas, to interject some of the authors' own speculations and hypotheses. It was felt, however, that these could best and more properly be presented in separate papers and that they should not be incorporated in a book that purports to illustrate, not to convert. It is acknowledged, nonethe-

less, that in the very selection of material for inclusion in the atlas a certain amount of bias and inclination toward the authors' own concepts is possible.

Division IV devotes a great deal of space to the subject of epithelial pearls, a subject that has received very little attention since the work of Bergengruen in 1909. The first portion of this division illustrates the development of these pearls in the normal palate; the second portion shows how such pearls form at the junction of the primary and secondary palates. Pearls of nasopalatine duct and midline origin are illustrated. The third portion demonstrates the development of dental pearls. Finally, the distribution of epithelial pearls in cleft palate fetuses is pictured in a few selected specimens, and the reader is left to his own speculations as to the significance of this material.

Other special topics concern the nature of the epithelium on the nasal and oral aspects of the palatal shelves, the matter of dental anomalies in cleft palate fetuses, details on the development of the nose and primary palate, and some drawings which sum up the authors' findings regarding the pattern and chronology of palatal fusion in man. One of the specimens used in the section on nasal and primary palatal development represents a 33 day stage. Those interested in an earlier phase of development than the 35 day stage shown in Division I can consult specimen X1777 (pp. 361–364). For the story of the development of the bony palate, the reader is referred to the articles by Woo (1949) and Kraus (1960).

A special chapter reviews the laboratory procedures used in preparing, sectioning, and staining the specimens and the special problems presented by the age, state of preservation, and size of the embryos and fetuses. It will be noted that the low-power photomicrographs of one specimen in each of the age groups of Division I (normals) contain numbers identifying the various anatomic landmarks. The code for these numbers is to be found at the beginning of this division. It was not deemed essential to provide these identifications for all three specimens in each age group.

Finally, at the end of this volume, there is a bibliography which attempts to bring together most of the significant literature pertaining to the prenatal development of the face and particularly to the subject of cleft lip and palate. This list will at least give the prospective researcher in the field of orofacial development a good beginning. A catalogue of both control and cleft embryos and fetuses used in the atlas is provided. This gives estimated age in days or weeks, specimen number, crown-rump length (C.R.) in millimeters, weight in grams, estimated fertilization age, fixative used, type of stains, and type of cleft.