Postnatal Development of the Human Nasal Septum and its Related Structures.

J. van Loosen

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An anatomical, radiological and histlogical study.

POSTNATALE ONTWIKKELING VAN HET MENSELIJKE NEUSTUSSENSCHOT EN AANVERWANTE STRUCTUREN.

Een anatomische, radiologische en histologische studie.

PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR
AAN DE ERASMUS UNIVERSITEIT ROTTERDAM.
OP GEZAG VAN DE RECTOR MAGNIFICUS
PROF. DR. P.W.C. AKKERMANS M.A.
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Supervisor:

Dr. H.L. Verwoerd-Verhoef

Institute for Otorhinolaryngology

Erasmus Universiteit Rotterdam

PROMOTIECOMMISSIE

Promotor:	Prof. Dr. C.D.A. Verwoerd
Overige leden:	Prof. Dr. F.W.J. Hazebroek
	Prof. Dr. S.E.R. Hovius
	Prof. Dr. J. Voogd
Co-promotores:	Dr. D. van Velzen
	Dr. H.L. Verwoerd-Verhoef

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Contents.

* Department of Otorhinolaryngology, Erasmus University, Rotterdam, The Netherlands

** Department Fetal and Infant Pathology, University of Liverpool, Liverpool, United Kingdom

*** Department of Pediatric Pathology, Dalhousie University, Halifax, Nova Scotia, Canada
Present: Department of Pathology, Westeinde Ziekenhuis, Den Haag, The Netherlands

**** Department of Radiology, Erasmus University, The Netherlands

1 Introduction.

The otorhinolaryngologist who is regularly confronted with nasal obstruction in children, finds himself supported by sophisticated diagnostic imaging (e.g. CT- and MRI-scanning) and makes use of similarly sophisticated surgical approaches and techniques.

It is the latter, which lies at the root of a tendency to carry out surgical interventions in the nasal region, inclusive of correction of nasal septum deviation, at an even younger age. This has raised the question for nasal surgery of the consequences for growth and development of the young and still rapidly developing midface.

The literature until the present, does not agree on the presence and extent of the effects of septal surgery for final outgrowth of the nose or midface (Pirsig, 1974, 1986; Huizing, 1979; Ortiz-Monasterio and Olmedo, 1981; Stucker et al., 1984; Healy, 1986; Jugo, 1987; Verwoerd et al., 1989; Walker et al., 1993; Potsic, 1997; Cotton and Myer 1999; Manning, Crysdale, Derkay, 1999).

In part inspired by van Limborgh (1970), as of the seventies, a considerable and coherent series of investigations has been carried out using the still rapidly growing septum of the young rabbit as model (Verwoerd et al., 1976, 1979 a,b, 1980, 1991; Nolst Trenité et al., 1987, 1988; Verwoerd-Verhoef et al., 1991). These demonstrated that the growing cartilaginous septum in the rabbit determines the final heighth and length of the whole of the nose by expansive growth. For longitudinal growth (in rabbits the anterior-posterior axis of the nose), continuity of the septal cartilage proved to be essential. The same applies to the growth in height (Verwoerd et al., 1979b). These findings are clinically important, as in surgical correction of septal deviation, the continuity of the septum is disrupted when deviated cartilaginous parts of the nasal septum are removed and repositioned.

Wound healing of the nasal septal perichondrium and cartilage in rabbits were studied (Verwoerd et al., 1991 a,b, Verwoerd-Verhoef et al. 1998). In contrast to the effects of partial septal resection in experimental animals, it was demonstrated that elevation of the muco-periochondrium, either on one or both sides, exerts no adverse effects on growth as long as there is no direct damage to the cartilaginous tissues.

Resection of, or injury to parts of the cartilaginous septum can modify the pattern of septal growth and thus indirectly cause malformations of the bony structures, even at some distance from the initial lesion (Nolst Trenité et al., 1987, 1988). The filling of cartilaginous defects by re-implantation of autologous cartilage may help to prevent septal perforation and the development of excessive scar tissue. This may slightly improve subsequent nasal growth however, this approach does not result in normalisation of growth as there remains, in many cases, a component of bending and dislocation of the implanted material relative to the non-mobilised parts of the septum (Verwoerd and Verwoerd-Verhoef, 1989; Verwoerd et al., 1991; Verwoerd-Verhoef et al., 1991; Verwoerd-Verhoef and Verwoerd, 1995).

The septal cartilage together with its bilateral triangular cartilages approximately forms a T-bar-like three-dimensional anatomic entity, cranially partially covered by the nasal bones. With regard to bone, perichondrium and the T-bar-shaped dorsoseptal cartilage (triangular cartilages), the basic morphology in children and rabbits show striking similarities (Verwoerd et al., 1989; Poublon et al.,1990).

During further growth the T-bar shaped cartilaginous structure is under permanent stress. (Verwoerd et al., 1989) Any kind of mechanical or surgical trauma, destroying this entity, initiates an irreversible deviation of the cartilage from its genetically determinated direction of growth.

In the newborn, the cartilaginous nasal skeleton is far more elaborate than in the adult and may be considered as an extension of the cartilaginous anlage of the anterior cranial base (Poublon et al., 1990).
The importance of the septolateral cartilage (T-bar structure) for midfacial growth was demonstrated by resection experiments in growing rabbits. The triangular cartilages proved to be necessary for the normal development of the nasal bones, the transverse expansion of the dorsal nasal meatus and the normal development of the nasal turbinates, (Poublon et al., 1990; Verwoerd-Verhoef and Verwoerd, 1995).

The cartilaginous septum also had influence on the developing nasal bones (Verwoerd-Verhoef and Verwoerd, 1995), on the (normal) development of the maxilla and, to a lesser extent, of other parts of the facial skull (Verwoerd et al., 1976, 1979).

However, the outgrowth of the midfacial skeleton (inclusive of the nose) of the rabbit differs in some aspects from the human midfacial development.

With the enlargement of the brain, especially of the frontal region, and the concomitant rotation of the eyes to the midline, there has been a relative decrease of the intra-orbital distance in humans compared to that in the rabbit (Enlow, 1990). This has resulted in a smaller region at the root of the nose and a shortening of the snout. Thus, humans have close-set eyes and short, narrow noses that do not interfere with binocular vision.

The growth of the frontal lobes have resulted in flexure of the cranial base (Enlow, 1990). This results in the increased height of the midface, typical for man and virtually absent in the rabbit (Takahashi, 1988, a,b).

These evolutionary changes have proforma effects on the final shape of the human septum (Verwoerd and Verwoerd-Verhoef, 1989).

In contrast to the extensive knowledge available with respect to the anatomy of the adult nasal septum in man (Lang, 1989; Tardy and Brown, 1990), little is still known about the cartilaginous nasal skeleton in the growing child.

Detailed knowledge of the fine structures of the midface and cartilaginous components thereof is especially important at young age. For it is during this period that the cartilaginously developed chondrocranium, of which the nasal septum is an integral part, shows initial a firm ossification as part of a process of rapid growth. As knowledge of this period is almost entirely based on animal data (rabbits), there is a need to detail the developmental anatomy of the human nasal septum and to assess possible species differences.

In view of the above the following overall questions were raised forming the aims of the studies reported subsequently in this thesis:

I. Which changes occur in the human nasal septum during the peri- and later postnatal period specifically of:

a. The anatomy

b. The dimensions

of the various components?

II. What are the possible consequences of the recorded characteristics of development for the application and interpretation of (imaging) diagnostic assesment of the nasofrontal region in the growing child?

III. What are the possible consequences of septal trauma and surgery for the recorded characteristics and for development of the nasal skeleton?

After an initial overview of the background literature on the antenatal anatomy and the available information on the anatomy of the human nasal septum in Chapter 2, Question I is dealt with in Chapter 3 to 8. Question II is addressed in Chapter 9, whereas the issues raised in Question III are addressed in Chapters 4 to 8. A general and integrating discussion of the findings is presented in Chapter 10.

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2

Postnatal development of the Human Nasal Skeleton. Literature Review.

2.1. Postnatal growth of the human nose

From birth to adulthood the nose, as part of the viscerocranium, grows and does so over a longer period than the neurocranium, transforming the baby face into the adult face with prominent nose and jaws. The neurocranium follows the growth of the brain, which reaches 90% of its adult volume at 6 years of age (Moore et al., 1974). The growth of the viscerocranium does not cease until 18 to 20 years of age (in fact, some growth may continue) and shows a number of changes in rate. In the first months after birth the growth rate is high and decreases slowly until the onset of sexual maturation in the early teens. The rate of growth then accelerates rapidly (the adolescent growth spurt), reaching a peak within a year or so and subsequently declining to approximately zero by about 20 years (Tanner, 1962; Moore et al., 1974). Consequently, it can take many years before the effects of trauma or surgery on nasal growth become evident. Thus, the follow-up of nasal growth after an injury at preschool age has to be continued until after the adolescent growth spurt. Apart from the extra growth of the viscerocranium, a change in rate of nasal growth around puberty contributes to the development of the adult profile. During infancy and childhood, the nose predominantly grows along the anterior-posterior axis. After puberty, however, the increase in height of the nose seems to be more important (Imai, 1953).

2.2. Specific anatomy of the infant nose

In the newborn the cartilaginous nasal skeleton is far more elaborate than in the adult and may be considered as an extension of the cartilaginous anlage of the anterior cranial base (Scott, 1953; Ford, 1958; Poublon et al. 1990). Except for the bony vomer, the neonatal septum is completely cartilaginous. Superiorly, it merges with the cartilage of the crista Galli; posteriorly, it reaches as far as the partly ossified sphenoid (Scott, 1953; anteriorly it is firmely attached to the anterior nasal spine (Latham, 1968).

The septal cartilage and upper lateral cartilages are no separate anatomical entities. They are parts of a T-bar-shaped structure (Poublon et al., 1990).

The upper lateral cartilages in the newborn are not triangular in shape, but look like elongated vaults (dorsolateral cartilages) on both sides of the supra-septal groove. They merge in cephalic direction with the cartilaginous cranial base and laterally terminate in the nasal wall. The lower alar cartilages are already found as separate structures. The nasal bones, formed by desmal ossification, cover the cranial half of the cartilaginous nasal roof (Poublon et al., 1990).

The only bony part of the septum at this age, the vomer, is a complex structure. The alae, formed by desmal ossification at either side of the inferior part of the septal cartilage (Mall, 1906; Fawcett, 1911; Augier, 1931; Norback 1944) are already well developed. The unpaired lower triangular part is the product of desmal ossification in the "space" between the mucous membranes lining both nasal fossae from the inferior edge of the septal cartilage to the bony palate. The median inferior part of the vomer is extremely thin in the neonate and the connection with the palate appears to be weak at dissection. Only anteriorly is the nasal septum firmly connected to the upper jaw by collagen fibers between the septal cartilage and the anterior nasal spine.

2.3. Postnatal changes in anatomy of the human nasal skeleton

At birth the cartilaginous nasal skeleton is a T-bar-like structure, extending from the skull base to the tip of the nose (Poublon et al, 1990). The later development of this cartilage is characterized by simultaneous processes of growth, ossification, regression, and remodelling. The cephalic parts of the dorsolateral cartilages gradually disappear, leaving the comparatively much smaller upper lateral cartilages in the adult stage. The variable degree of extension (7 to 20 mm) of the upper laterals under the nasal bones reported in literature (Straatsma and Straatsma, 1951; Hinderer, 1970) reflects differences in degree of regression. The rate and mode of regression of the upper lateral cartilages is not yet known. Incidental observations during surgery show that at the age of 3 years, the nasal bones are still supported over the full length by the underlying upper laterals cartilages.

The cartilaginous nasal septum shows growth and ossification at the same time. Small centers of ossification would be present in the superior part of the septal cartilage at birth and merge as the perpendicular plate, which extends in posterior-anterior direction (Schultz-Coulon and Eckermeier, 1976). When the latter reaches the bilateral alae of the bony vomer a posterior-inferior part of the septal cartilage is enclosed by bone (Scott, 1953; Moore et al., 1974; Takahashi, 1988). The cartilage in this vomeral tunnel will be replaced by bone or may partly survive to adulthood (sphenoid tail) (Melsen, 1977).

The septovomeral junction appears to be highly variable. The superior part of the vomer follows the frequently occurring deviation of the basal rim of the cartilaginous septum, whereas the insertion of the inferior part reflects the line of fusion of the palatal halves. This can result in an angle between the superior and inferior part of the vomer (Takahashi, 1988). Moreover, the ala vomeris on the convex side of the angle is often defective, so the septal cartilage will project sidewards.

Finally, the cartilaginous septum is reduced to the anterior half of the nose. The adult anatomy of the nasal septum, is summarised in figure 2.1.

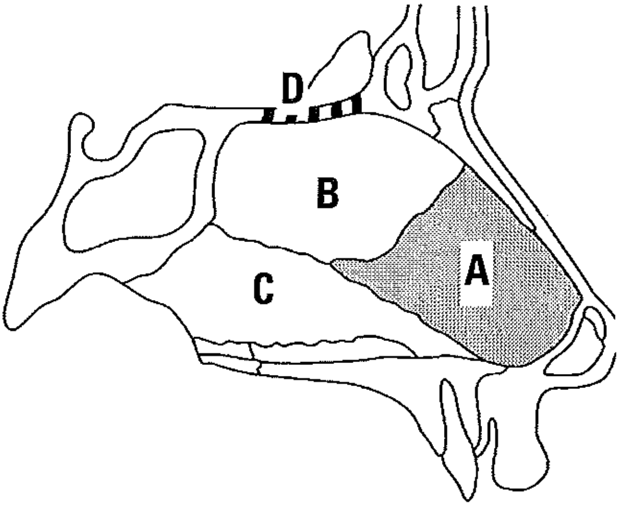

Figure 2.1. *The adult nasal septum: A septal cartilage, B perpendicular plate, C vomer, D crista Galli*

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3

The Nasal Septal Cartilage in the Newborn.

3.1 Introduction

In neonates and young children it is well known that the nasal septum is mainly cartilaginous (Cleland, 1861; Hillenbrand, 1933; Scott, 1953). However, the morphological and histological characteristics of this septal cartilage at a young age have scarcely been studied.

In rabbits it has been demonstrated that the cartilaginous septum shows a specific pattern of regional differences in thickness and histological differentiation (Meeuwis et al, 1985; Verwoerd et al, 1991).

The aim of the study was to investigate whether such a pattern of regional differences also occurs in human neonates.

3.2 Materials and Methods

The nasal septum of 3 normally developed human neonates without signs of congenital malformations and stillborn after a pregnancy of 36, 38 and 42 weeks respectively, were examined.

After block dissection described by Melsen (1977), including the nasal septum, part of the hard palate, the cribriform plate and the sphenoid bone, semi-serial sections (5 micron) were cut in the transverse and frontal plane and stained with haematoxylin and azophloxin. Using a photographic lateral view of the prepared septum (Figure 3.1), semi-serial 5 micron sections spaced at 1 mm, were used for a three-dimensional reconstruction (magnification factor 10 x).

The thickness measured in the cartilage is represented on a shading-coded diagram of the reconstruction (Figure 3.2).

3.3 Results

The thickness of the cartilage of each septum varies considerably: from 400 micron in the anterior area to 3500 micron in the posterior region (Figure 3.2). The cartilage increases in thickness from the anterior free ridge

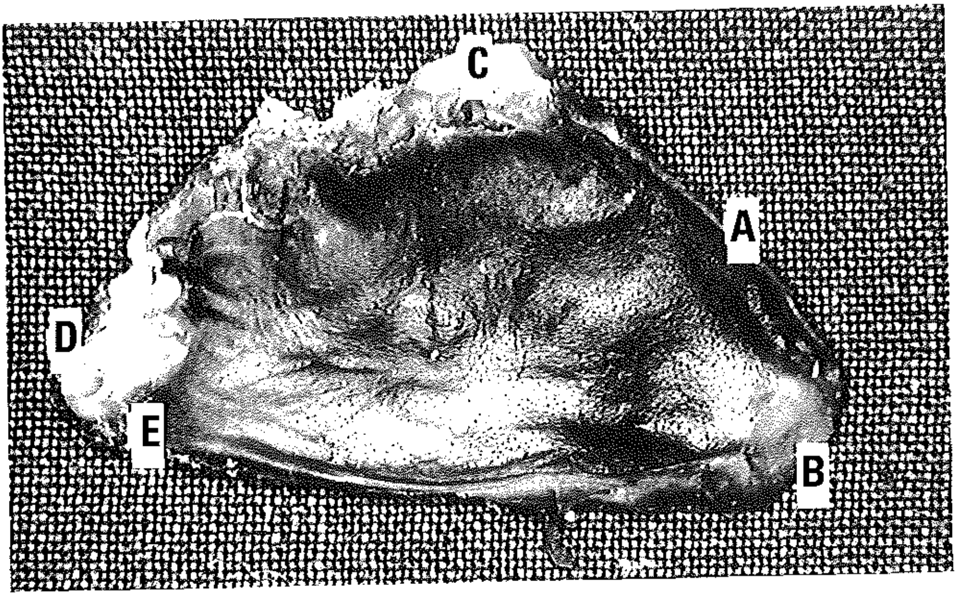

Figure 3.1. *The fully prepared septum of a 42 week-old-neonate. Nasal dorsum (A), columellar rim (B), crista Galli (C), sphenoid(D), choana (E).*

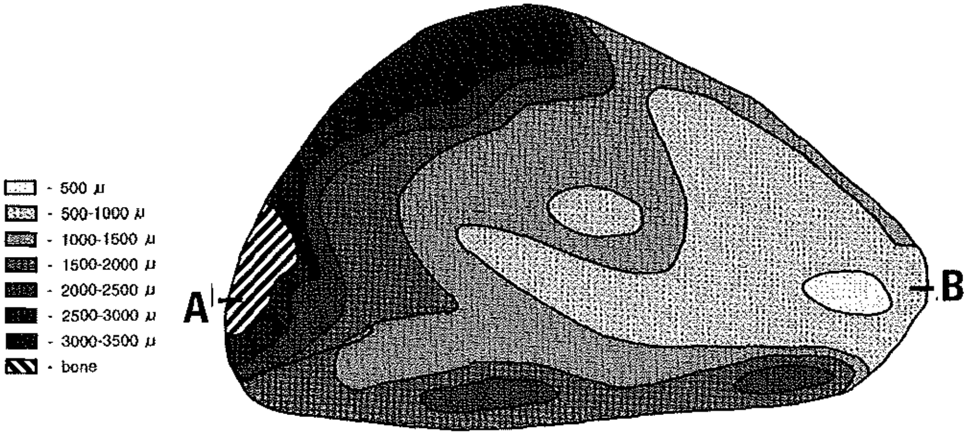

Figure 3.2 *Shading-coded diagram representing the thickness of the nasal septum. The anterior thin area on the left, the lamina cribrosa on top and the sphenoid on the right side.*
The thickest part is found at the lower rear end of the sphenoid and at the lamina cribrosa.
(A-B) Level of histologic section illustrated in Figure 3.6.

of the columella towards the posterior junction with the sphenoid rostrum (Figure 3.3).

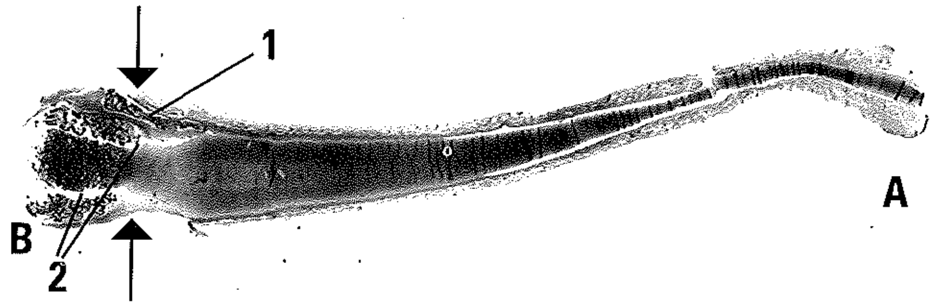

Figure 3.3Histological section of a 38-week-old human septum from anterior (A) to posterior (B). Spheno-septal junction (arrows) note the difference in thickness from posterior (B) to anterior (A). Level of section is indicated in Figure 3.2 (haematoxylin - azophloxin, x 5). 1 = vomer wing, 2 = artefact.

In all specimens there is a significant difference in histology between the thin part anteriorly and the remainder of the septal cartilage. The central, thin area consists of small, round chondroblasts with prominent dense nuclei, centrally located in the cells (Figures 3.4, 3.5).
The presence of "twin-cells" lying in one lacuna additionally indicates a proliferative activity.

The cellularity in the remainder of the nasal septum is characterized by hypertrophic chondrocytes with eccentric nuclei (Figures 3.6, 3.7).

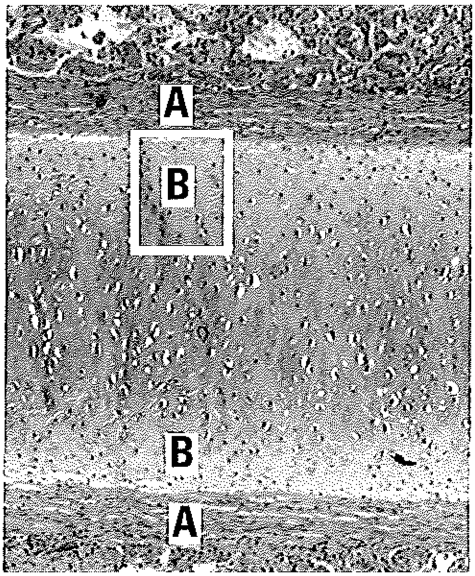

Figure 3.4 *The anterior thin part of the cartilaginous septum covered by a layer of perichondrium (A), adjacent to a peripheral zone with small, round chondroblasts (B) (haematoxylin - azophloxin, magnification x 10).*

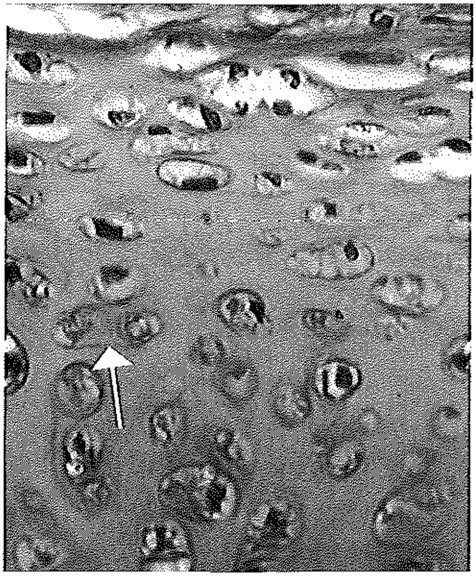

Figure 3.5 *Anterior thin part in higher magnification (Figure 3.4). Round chondroblasts with dense prominent nuclei, centrally located in the cells. The presence of "twin-cells" (arrow) demonstrates proliferative activity. (haematoxylin - azophloxin, x magnification x 50, Frame, Figure 3.4)*

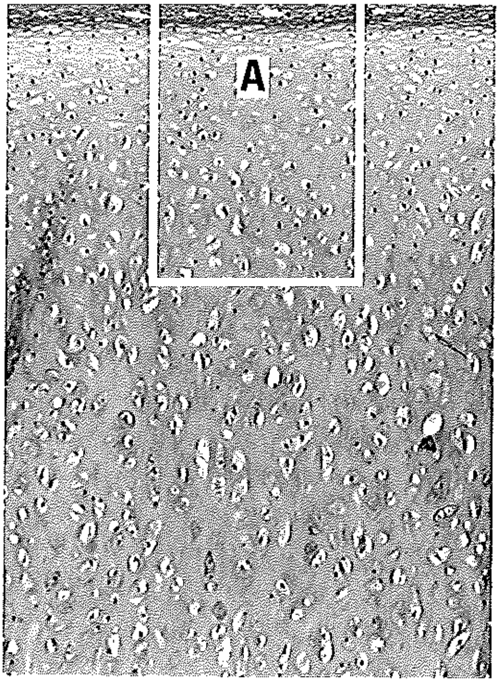

Figure 3.6 *Mid-septal zone with hypertrophic chondrocytes with eccentric nuclei (haematoxylin - azophloxin, x magnification x 10).*

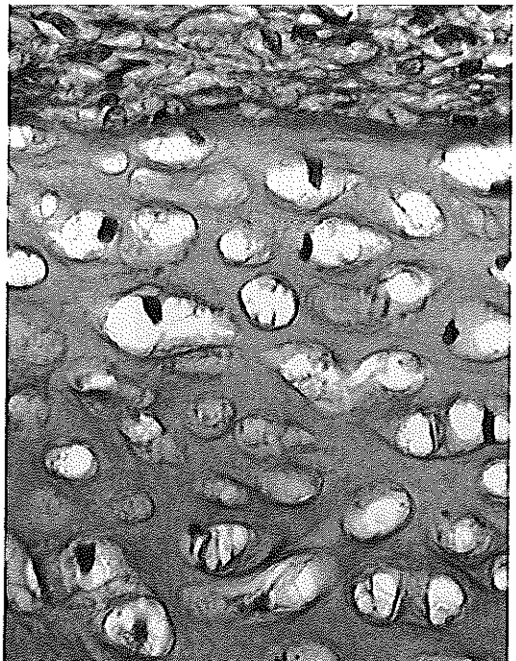

Figure 3.7 *Same mid-septal zone in higher magnification (haematoxylin - azophloxin, magnification x 50, Frame A, Figure 3.6)*

In the most dorsal region near the sphenoid, the process of beginning ossification is demonstrated by lacunae varying in size and matrix invasion. Bone marrow connective tissue, rich in bloodvessels grows into the matrix which is accompanied by deposition of bone (Figure 3.8).

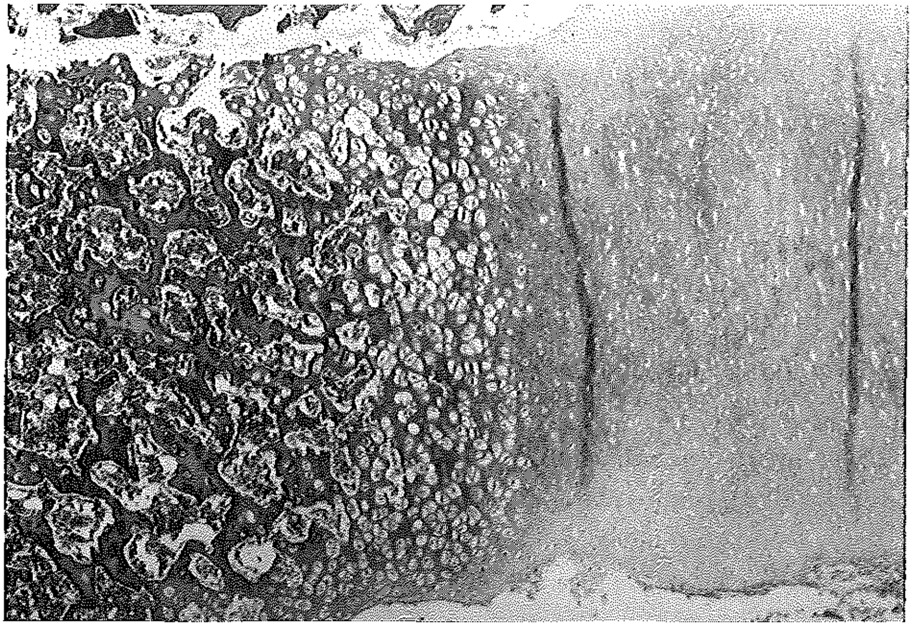

Figure 3.8 *Most posterior region of the septum showing the process of ossification. Lacunae varying in size, invaded by connective tissue rich in haemopoietic elements. Deposition of bone (haematoxylin - azophloxin, microscopical magnification x 10).*

3.4 Discussion

This study demonstrates that in the human neonate as well as in the young rabbit, the cartilaginous nasal septum varies considerably in thickness according to a specific pattern which is similar in both species. This similarity could be a significant factor in the assessment of the results of experimentation on the growing nasal septum in animals and suggests that more than only very restricted conclusions may be drawn, as was suggested by Vetter, Pirsig et al. (1984).

These findings in human neonates do not favour Delaire's and Precious' (1987) concept that the nasal septal cartilage is "a mass of pasta in a plastic bag, flattened by a roller to give it a uniform thickness". On the contrary, the characteristic differences in thickness seem to be connected with different biodynamic conditions in the various regions of the septum.

Comparison of the histological observations made in the young child and young rabbit suggested that in both species the anterior central, thin area shows the greatest proliferative activity. The dissimilarity between the various regions can be based on a difference in cell type or a process of "cell /tissue ripening". The latter means that in various specific sites the septal cartilage is developed to different stages of maturation / differentiation which then allows for differences in the role with respect to growth and/or support.

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4

Growth Characteristics of the Human Nasal Septum.

4.1 Introduction

Effective nasal surgery is highly dependent on a comprehensive knowledge of the anatomy, physiology, and biodynamics of the mid-facial skeleton. The influence of the nasal septum on the growth of the midfacial skeleton has been debated for more than a century. Recently, however, long-term follow-up studies in the rabbit have clearly demonstrated an important role of the dorsoseptal cartilage with respect to the normal development of the nasal bones, (pre-) maxilla and orbit, which is responsible for the postnatal changes of the facial profile (Verwoerd et al., 1995; Verwoerd-Verhoef et al., 1995). Although much has been published since the introduction of radiographic cephalometry by Broadbent (1931) and Hofrath (1931) on the postnatal development of the human cranium, very little is known of the growth and development of the human nasal septum.

Schultz-Coulon and Eckermeier (1976) studied the postnatal changes in the human nasal septum from the neonatal period to ten years of age. In this study they multiplied height with length to obtain the lateral surface area of the nasal septum. They demonstrated a rapid decrease of nasal septal growth after birth and an extensive ossification process during the first 10 years of life.

No growth features of the human nasal septum, however, have been described after the age of 10 years. In view of the fact that many surgeons prefer to postpone corrective nasal surgery until after the pubertal growth spurt, data on postpubertal growth are very important. Growth characteristics of the bony and cartilaginous part of the septum, respectively, are not available in the literature. The purpose of this study is to analyze the growth characteristics of the separate parts of the human nasal septum from birth until the post-adolescent period.

In the adult, the nasal septum is composed of three parts: (1) the cartilaginous septum; (2) the perpendicular plate; and (3) the vomer. The perpendicular plate is the product of endochondral ossification of the cartilaginous septum during childhood. The vomer is formed by intra-membranous ossification. In the neonate nearly all of the nasal septum is cartilaginous. The septal cartilage extends from the columella anteriorly to the sphenoid posteriorly, where it merges cranially with the cartilaginous "anlage" of the anterior cranial base.

The vomer is represented in the neonate by a thin bony lamella between the basal rim of the cartilaginous septum and palate. This inferior part of the vomer shows extensions on both sides of the cartilaginous septum. These "vomer blades" merge with the ossifying perpendicular plate (Verwoerd et al., 1989).

This study deals with the cartilaginous septum and the perpendicular plate and does not include the inferior part of the vomer which constitutes a minor, morphogenetically not related part of the septum. The immediate reason is that during preparation of the specimens a variable part remains fixed to the palate, whereas the other parts of the septum were obtained in their entirety.

4.2 Material and methods

Nasal septum specimens of 30 Caucasians, with normal facial development, varying in age from birth to 62 years, were obtained at routine post-mortem (Table 4.1). The specimens were acquired by a combined approach through the anterior cranial fossa and both nostrils (Van Loosen et al., 1988). After fixation in 4% formaldehyde in 0.1 M phosphate buffer (pH 7.4) for more than 24 hours, all specimens were decalcified before processing to paraffin by routine tissue processing. Specimens were sectioned semi-serially in a frontal plane. Sections (5 mm) were mounted and stained with haematoxylin and eosin. All specimens were recorded on Kodachrome slides together with two orthogonal calibration rulers defining the distances in the plane of the specimen (Figure 4.1). Most of the specimens (Table 4.1, Nos. 1-27) were also recorded on X-ray film, after direct placement of the specimen on top of the film-cassette and irradiation from a distance of 50 cm by a Senograph 500T (22 keV, focus at 0.3 mm; Figure 4.2; Verwoerd et al., 1989).

Table 4.1.

Overview of patient group and causes of death (n=30).

No.	Age/years	Sex	Cause of death
1	0	m	Solutio Placentae
2	0.6	m	Tuberculosis
3	1	m	Forensic case
4	1	f	Meningitis
5	1.5	m	Dehydration
6	2	f	Forensic case
7	2	m	Meningitis
8	2.5	m	Forensic case
9	2.5	f	Road Traffic Accident
10	3	f	Forensic case
11	3	m	Meningitis
12	3	m	Forensic case
13	4	f	Road Traffic Accident
14	4	m	Forensic case
15	8	f	Drowning
16	9	f	Road Traffic Accident
17	10	m	Forensic case
18	12	m	Road Traffic Accident
19	15	f	Road Traffic Accident
20	15	m	Forensic case
21	15	f	Septicemia
22	17	f	Accidental Death
23	17	m	Septicemia
24	17	m	Forensic case
25	18	m	Road Traffic Accident
26	20	m	Road Traffic Accident
27	30	f	Forensic case
28	40	m	Road Traffic Accident
29	58	m	Road Traffic Accident
30	62	m	Glioblastoma

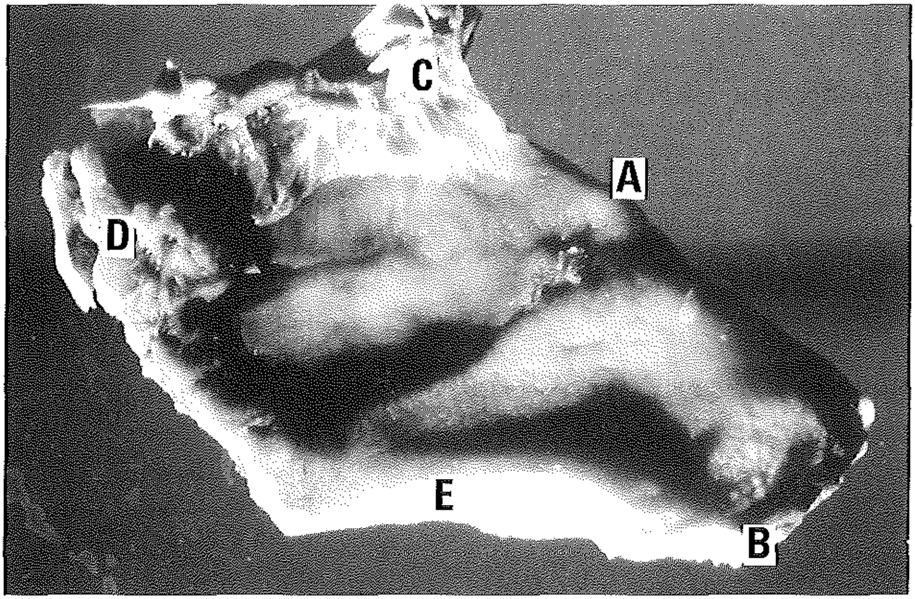

Figure 4.1. *Lateral aspect of fully prepared septum of a 30-year old male. A: nasal dorsum; B: columellar rim; C: crista Galli; D: sphenoid region; E: vomer bone region.*

The slides and X-ray images were projected on a digitizing tablet (Genius 1212B) connected to a personal computer. For each septum the circumferential outline was digitized from the slide as well as from the X-ray image. Areas were calculated in numbers of pixels applying the trapezium rule for integration (with help of a custom-made program). Using calibration rulers on the slide as a scaling factor, the number of pixels per cm^2 was calculated. The area of the preparation on the slide in number of pixels was divided by this scaling factor and by that converted to cm^2. Dividing this total preparation area (in cm^2) by its equivalent in pixels of the X-ray image projection, for each preparation an X-ray scaling factor was calculated. From the X-ray image the area fraction in numbers of pixels was measured of both the perpendicular plate (bony part) and the cartilaginous part, the latter including the cartilage between the vomer blades (Verwoerd et al., 1989) with exclusion of the sphenoid and pre

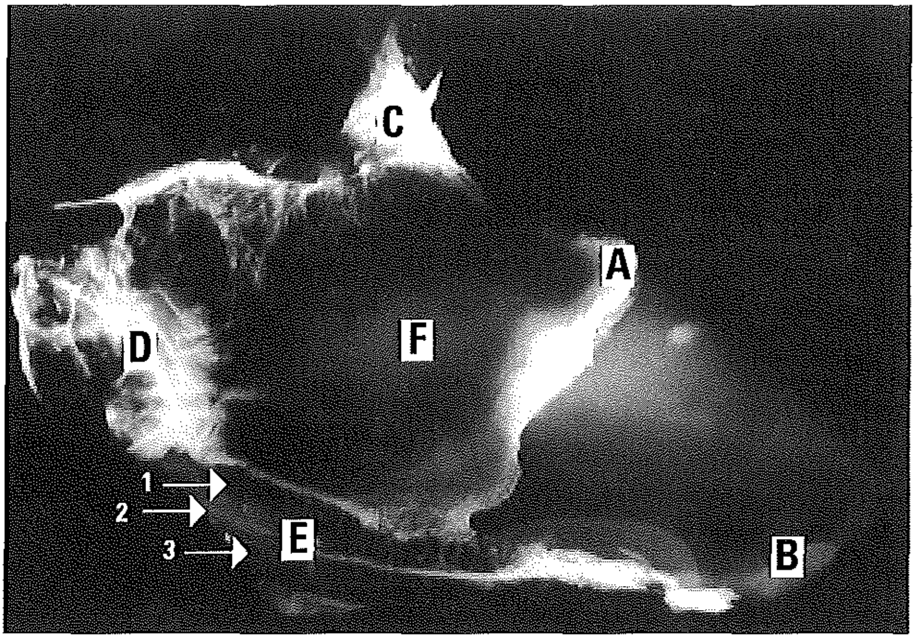

Figure 4.2. *Lateral X-ray of identical specimen (Figure 4.1)*
A: nasal dorsum; B: columellar rim; C: crista Galli; D: sphenoid region
E: vomer bone; F: perpendicular plate (Senograph 500t, film screen 22 keV, 0.3 m focus). 1 = vomer wing, 2 = fusion line, 3 = inferior part of vomer.

maxilla. The Relative Perpendicular Plate Area (RPPA) was calculated by dividing the two areas. The total area of the septum was defined as the sum of these two areas and, after conversion to cm^2, called the Total Area (TA). The absolute Perpendicular Plate Area (PPA) was calculated by multiplication of RPPA with TA. From repeated measurements it was calculated that the measurement error in TA was below 0.02 cm^2. TA was plotted against age in a scattergram and subsequently a "growth function" was fitted through the data (Slidewrite V5).

4.3 Results

The results of the measurements are summarized in Table 4.2. As is shown in Figures 4.3. and 4.4., the growth of the septal area (TA) diminishes continuously, more clearly so after the second year of life. A wide range of mathematical functions were tried, with help of a commercially available PC-program (SlideWrite Plus for Windows Version 3.00, Advance Graphics Software, Carlsbad, CA, USA) Curve fitting with this program includes linear regression for linear function fitting and Levenberg-Marquardt fitting algorithm for non-linear functions.

It appeared that total septum area data were described with the least amount of error by a summation of two similar simple growth functions, Y1 and Y2 in Figures 4.3. and 4.4.

The standard error of the fit is 0.8 cm^2. Given the much smaller error in the area measurements mentioned above, we conclude that the remaining spread of the data around the curve Y1+Y2 is due to interindividual anatomical variation and that the present data do not allow for assessment of more complex growth functions. The functions Y1 and Y2, as best fitting algorithms, to define the area growth of each of the separate parts of the septum. Y1 describes the growth of the cartilaginous part including the cartilaginous part between the vomer blades and concomitantly, Y2 that of the perpendicular plate. From the parameters of the Y1 function it could be surmised that the growth of the cartilaginous part starts at about -0.34 year, i.e. at about 4 months of gestation. Furthermore, the time-constant of cartilage growth is 0.72 year, which means that by 2.2 year the area has reached 95% of its final value. Similarly, from Y2 it can be concluded that growth of the bony part starts at about term (0.034 year) and has reached 95% of the final area at 36 years of age. An impression of the growth rate of the various areas is obtained by taking the derivative of function Y1 and Y2 (Figures 4.5. and 4.6.). Although similar in the pattern of age associated deceleration of growth, the overall capacity for growth of the cartilage is far greater than that for the ossified part of the septum.

Table 4.2.

Surface parameters of nasal septum components related to age (TA: total septum area, RPPA: relative perpendicular plate area; PPA: perpendicular plate area)

Study number	age years	total septum area cm^2 (TA)**	relative perpend. plate area. (%) (RPPA)	perp. plate area cm^2 (PPA)
1	0	3.68	0	0
2	0.6	5.99	2	0.12
3	1	8.15	12	0.98
4	1	8.46	11	0.93
5	1.5	9.73	16	1.56
6	2	11.29	15	1.69
7	2	12.37	14	1.73
8	2.5	11.39	16	1.82
9	2.5	11.34	21	2.38
10	3	11.63	32	3.72
11	3	12.30	26	3.20
12	3	9.97	27	2.69
13	4	13.30	39	5.19
14	4	13.38	29	3.88
15	8	14.04	39	5.48
16	9	15.90	43	6.84
17	10	16.29	36	5.86
18	12	18.08	54	9.76
19	15	17.17	49	8.41
20	15	17.78	46	8.18
21	15	17.90	55	9.85
22	17	18.36	51	9.63
23	17	18.07	48	8.67
24	17	18.91	44	8.32
25	18	20.42	56	11.44
26	20	19.21	55	10.57
27	30	19.39	63	12.22
28*	40	20.95*		
29*	58	21.08*		
30*	62	20.86*		

* : due to fragmentation no further (X-ray) quantification

** : Correction for premaxilla and inferior part of the vomer

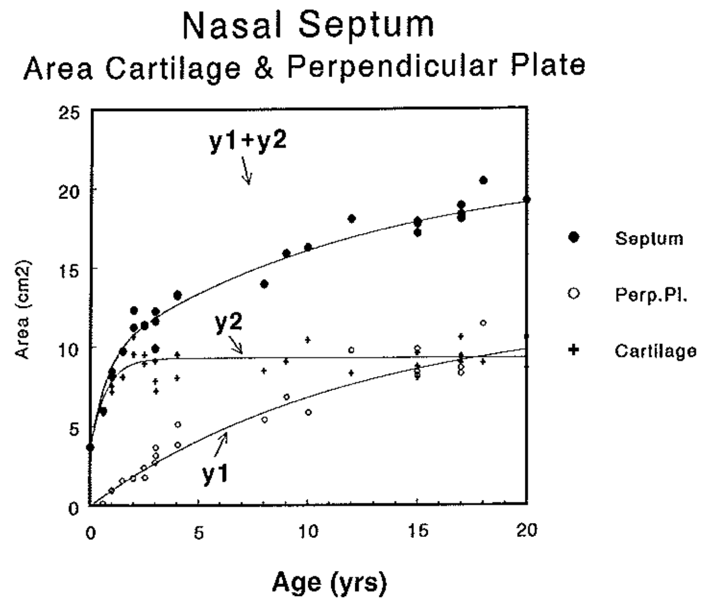

Figure 4. 3. *Area measurements of the total septum as a function of age (Y1+Y2) from 0-20 years. After mathematical analysis the curves for bone (Y1) and cartilage (Y2) are demonstrated.*

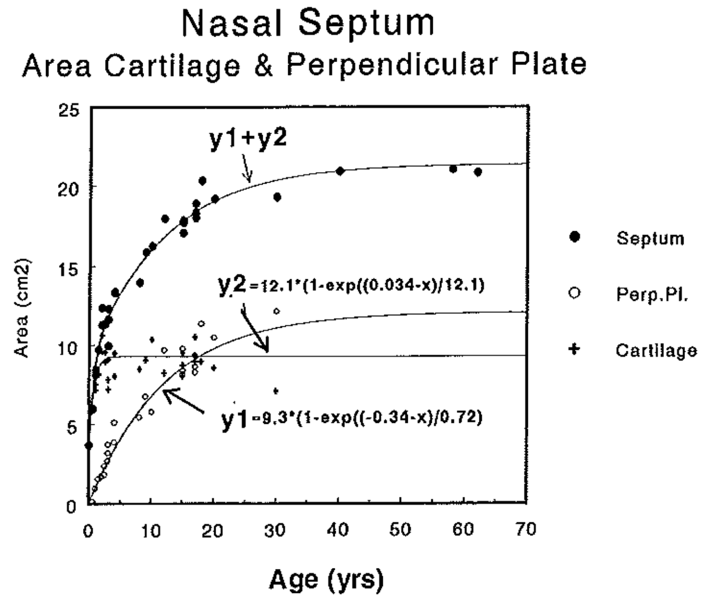

Figure 4.4. *Area measurements of the total septum as a function of age (Y1+Y2) from 0-62 years. After mathematical analysis the curves for bone (Y1) and cartilage (Y2) are demonstrated.*

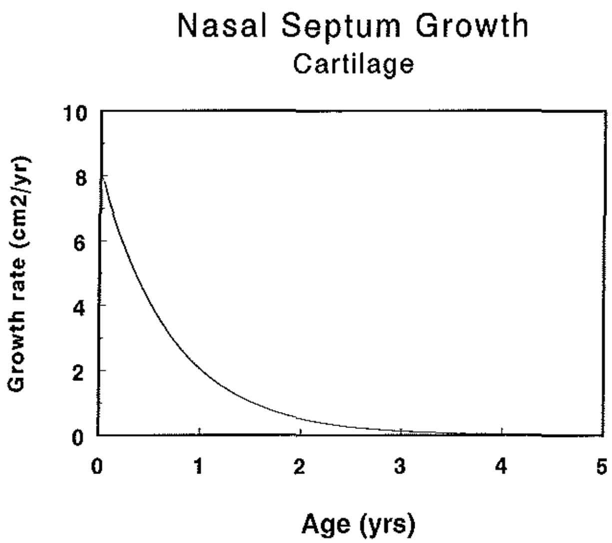

Figure 4.5. *Growth rate of the cartilaginous part of the septum as function of age. Note that the growth capacity of cartilage is much higher than that for the ossified part (compare vertical axis scaling between Figures 4.5. and 4.6.).*

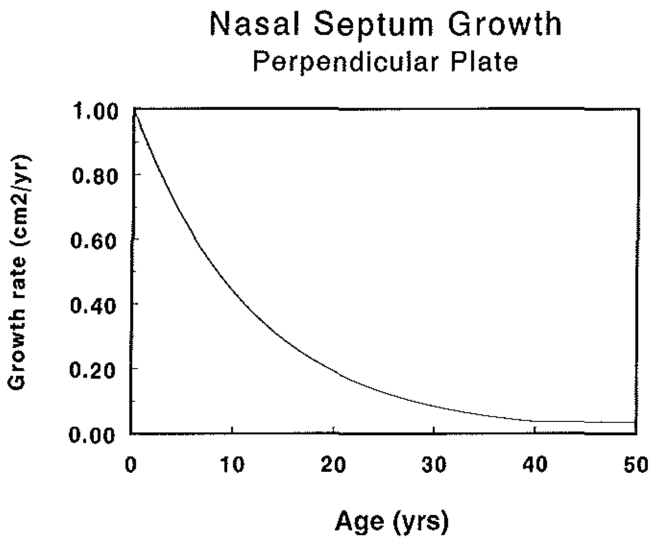

Figure 4.6. *Growth rate of the ossified part of the septum as function of age. Note that the growth capacity of ossified parts is much lower than that for cartilage (compare vertical axis scaling between Figures 4.5, and 4.6..*

4.4 Discussion

This study has been designed to evaluate postnatal growth of the human septum. The pattern of linear growth before birth (Bosma, 1986) is possibly continued into the first year of life (Figure 4.3.). After this, in contrast to before birth, there is continuous deceleration of growth. Our data on the septal area, as demonstrated in Table 4.2. and Figure 4.3., show (although the pattern of change is comparable) lower values for the period from birth to the age of 10 years than the findings of Schultz-Coulon and Eckermeier (1976). This could be explained by the fact that they multiplied height with length of the septum to assess the pattern of change of the total area and, thus, a systemic bias may have been introduced. Area measurements as performed in this study more accurately reflect the surface area of the irregularly shaped nasal septum. A second factor may be that we have excluded the variable inferior part of the vomer.

It was noticed that growth of the septum continues, even after puberty, albeit slowly. This confirms earlier cephalometric studies by Thompson and Kendrick (1964) and Sarnas and Solow (1980), who showed that even after the age of 20 years, a significant overall growth of the midfacial structures occurred. Our data suggest that, at least for the septum after the age of 36 years, this process comes to a virtual halt and near-final values are reached.

Until the present, it has not been noted in the literature that the sum total area of the cartilaginous part of the septum remains constant after the age of two years. It seems that in compensation to the newly formed cartilage an equal amount is transformed into bone, and thus the total area remains constant in this way. At the same time the septal cartilage shows changes in form and gradually assumes a more inferial position. In the adult situation the cartilaginous part of the nasal septum has become more anteriorly localized. This is reflected in a more prominent nose when compared to the newborn. However, the question of whether the reducing nasolabial angle solely results from septal growth as proposed by Wissner (1970) remains. Wheras at later age atrophy of the alveolar ridge in particular may well contribute to this appearance (Pirsig and Haase, 1986). Using our measurements and calculations, neither adolescence-associated growth-spurt/acceleration (Hinderer, 1970) nor growth spurts at the ages of three, six or seven years and adolescence (Reichert, 1963) could be demonstrated for the human nasal septum. Being a transversal study, differences as small as those noted in optimalized longitudinal cephalometric investigations (Pirsig and Haase, 1986) cannot be detected, especially since such small accelerations are known to vary greatly in age of onset (Rosenberger, 1934; Bergersen, 1972). The study of such individual accelerations additionally should take into account besides sex, age-dependency differences (Riolo et al., 1974; Prahl-Andersen et al., 1979; Engel et al., 1994).

Thus, as this investigation was of the transversal type, it does not completely exclude the existence of growth spurts. However, the narrow spread of the data around the regression line makes it improbable that significant deviations from the average growth pattern exist. Interindividual variation in time of onset and in size may well have been obscured in the present data set. Therefore, a longitudinal study, with regularly-spaced metallic implants in the nasal septum of an experimental animal as used by Björk (1955) for human skull growth, may be required to finally clarify any remaining ambiguity.

In summary, the results of this study demonstrate that:

(1) the growth rate of the nasal septum is highest in the newborn and slows down continuously, more clearly after the second year of life, but continues even after puberty;

(2) the cartilaginous part of the nasal septum increases rapidly in sagittal dimensions during the first years of life. After the age of two years the total area of the cartilaginous septum remains constant;

(3) endochondral ossification of the cartilaginous septum, resulting in the formation of the perpendicular plate, starts after the first half-year of life. The expansion of the perpendicular plate in the sagittal plane continues until after puberty;

(4) the development of the cartilaginous nasal septum after the age of two years is characterized by: (a) a balance between new formation of cartilage and loss of cartilage by the process of endochondral ossification, and (b) a constant remodelling and gradual shift to a relatively more anterior position;

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5

The Significance of Regional Variations in Thickness of the Human Nasal Septum.

5.1 Introduction

The central role of the nasal septum, as a component of the load-bearing ability of the nasal pyramid, has been recognised by a number of authors as early as the fifth decade of this century (Riggs, 1953; Rubenstein, 1956; Luongo et al., 1958). The existence of interlocked stresses in the nasal septum was demonstrated ex-vivo by Fry (1966, 1967) and in-vivo by Verwoerd et al. (1989 a,b, 1991, 1998). The importance of the central strut in the resistance model was highlighted by Clarke (1967). It was later emphasized that the nasal septum and the upper lateral cartilages form a T-bar shaped structure, which supposedly has a greater mechanical strength than a 2-dimensional septum (Verwoerd et al., 1989b, 1998). At birth the cartilaginous nasal septum reaches from columella to sphenoid and anterior skull base. The perpendicular plate has not yet been formed.

Van Loosen et al. (1988) demonstrated the regional differences in thickness of the human cartilaginous nasal septum in the neonatal period. In this study it was shown that the thickness of cartilage varies considerably from 400 micron thickness in the anterior area to 3500 micron in the posterior region. These variations mimic the pattern previously observed in the rabbit (Tonneyck-Müller et al., 1984; Verwoerd et al., 1991). Variations in septal thickness are scarcely mentioned in literature and when available, show considerable differences amongst authors. For example Kowatscheff (1943) reported that the posterior segment of the septal cartilage in the newborn and at the age of three months are similarly dimensioned as in adults: 2.1 - 2.5 mm (2100 - 2500 micron). Zuckerkandl (1892) pictured the anterior-inferior part of the septum as an "expansion" of 4 - 8 mm (4000-8000 micron). Cottle et al. (1958) stated that 3 - 4 mm (3000-4000 micron) is the width of the septal cartilage over wide areas. Lang (1989) described the septal cartilage as a 3 - 4 mm (3000-4000 micron) thick structure, but showed in his frontal sections of the adult nasal septum more specific regional variations in thickness, without mentioning them. Delaire and Precious (1987) also considered the nasal septum as a segment of cartilage with a uniform thickness.

As yet, a detailed study of the possible presence and extent of regional variations in thickness between birth and adulthood is absent in literature.

Knowledge of this architecture of the cartilaginous septum would lead to a better understanding of biomechanical properties and growth of the septum.

Van Loosen et al. (1988) demonstrated that at birth the nasal septum, except for the vomer 'anlage', is completely cartilaginous. In the second half of the first year of life, the septum progressively ossifies in posterior-anterior direction by a process of endochondral ossification (Schultz-Coulon et al., 1976). Consequently, the cartilaginous structure changes into a partially osseous (perpendicular plate) and partially cartilaginous, composite structure. Each of the components may well have its own range of sagittal dimensions related to age and growth, as was reported earlier (van Loosen et al., 1996). Therefore, the aim of this study is:

1. To describe the development of the regional variations in thickness of the human cartilaginous nasal septum in relation to age.

2. To discuss the hypothetical effects of these differences in relation to growth of the nose.

5.2 Materials and methods

Human nasal septa were collected by block dissection at post-mortem from patients having died from intercurrent disease not affecting the nasal structures. Eight patients, varying in age from newborn (38 weeks gestation) to 42 years of age were included in the study.

The specimens were fixed in 0.1 M phosphate buffered, pH 7.4, 4% formaldehyde for a minimum of 2 x 24 hours. After decalcification, specimens were embedded in paraffin using routine tissue processing methods. Specimens were semi-serially sectioned in a frontal plane, and consecutive 5 micron sections, stained with Haematoxylin and Eosin, were prepared every 2.5 mm for the entire length of the block specimen.

Slides were projected using a standard slide projector on a paper screen after calibration. Three-dimensional representations were reconstructed as published previously (van Loosen et al., 1988). Camera lucida drawings at 1:200 magnification were used for the 3-dimensional reconstruction (magnification x10) of individual septa. The thickness measured in various areas of the septum were represented on a grid-coded diagram. The changes with age for the

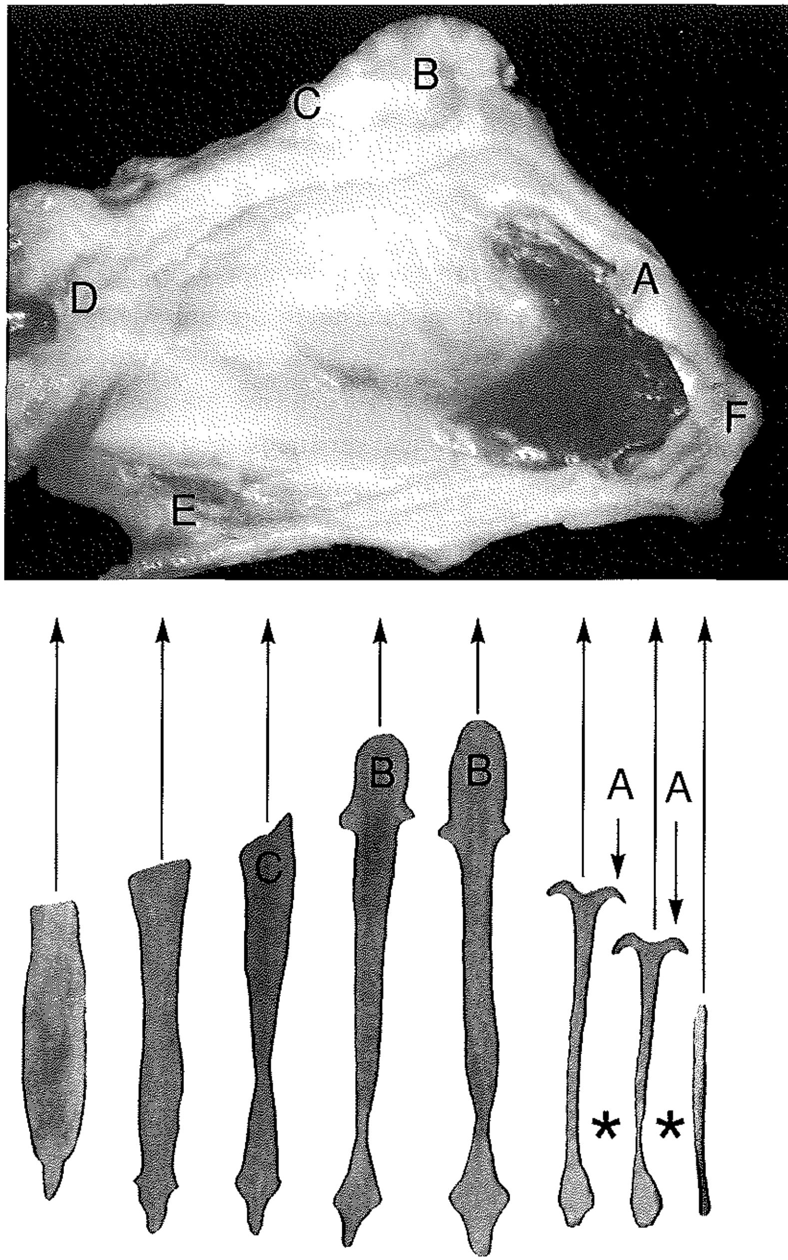


Figure 5.1 *Back-lit septal resection specimen of a 38-week-gestation neonate. Note the translucent anterior area. Other differences are obscured due to limited light transmission properties of cartilage. The regional characteristics at the frontal, central and more posterior area are illustrated by right angle sections below. A: upper lateral cartilage (transected); B: crista Galli; C: anterior skull base; D: sphenoid; E: vomer; F: columella.*

different regions were studied by systematic comparison of the results for each case (Figure 5.1).

5.3 Results

The terminology used in the description relates to the septum of the head in the upright position; thus there are anterior, posterior, inferior and superior parts.

The results of the study for each case are summarised in the diagrammatic representation of regional variations in thickness of the cartilaginous septum and presented in Figure 5.2 and 5.3.

In the neonate (0 years of age), the distribution in thickness is shown in Figure 5.2. A marked increase in thickness from 400 to 3500 micron, occurs from anterior to posterior. The most anterior part of the septum is thin, varying from 400 to 1000 micron. The thinnest part (minimally 400 micron) is noticed in the most anterior and premaxillary region.

Inferiorly the septum thickens up to 2500 micron. This thickened inferior part of the septum is located superiorly to the vomer anlage. It extends from the sphenoid rostrum posteriorly to the anterior nasal spine anteriorly. It is further referred to as the sphenospinal zone of cartilage.

Superiorly, extending from the sphenoid rostrum to the crista Galli and nasal dorsum, a zone of similarly thick cartilage to a maximum of 3500 micron, is found (sphenodorsal zone).

The widening of the septum adjacent to the nasal dorsum is related to the transition of the cartilaginous nasal septum into the bilateral upper lateral cartilages (Figure 5.1). No ossification was identified in this septum.

The results of the analysis of the septum of a 2.5 year old infant demonstrate that anteriorly and centrally the septal configuration strongly resembles that of the neonate (Figure 5.2). The septal cartilage is relatively thin and varies in thickness from 400 micron in the most anterior region to 1500 micron in the middle part of the septum. Again, here a more substantial inferior cartilaginous beam of up to 2500 micron in thickness can be recognised (sphenospinal zone). This beam is based on the sphenoid rostrum where the cartilage locally still

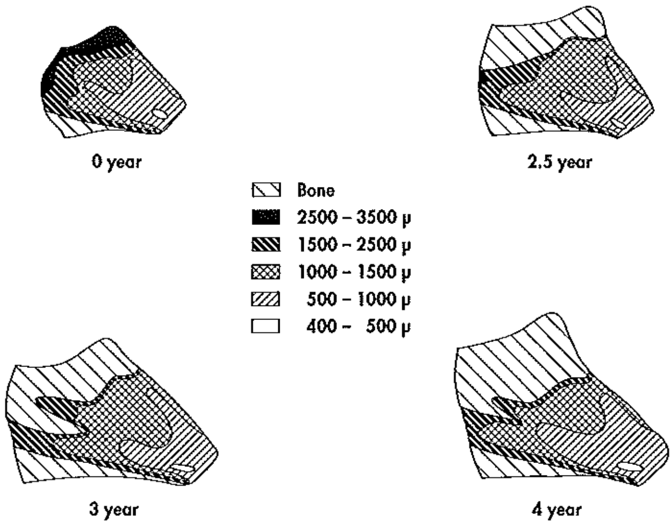


Figure 5.2 *Grid-coded diagrams illustrating regional variations in thickness of the cartilaginous part in 4 septal specimens of 0, 2.5, 3 and 4 years old, respectively. Diagrams are proportionate to each other. For anatomical oriëntation see Figure 5.1. The bony part is composed of the the perpendicular plate superiorly, and the vomer inferiorly.*

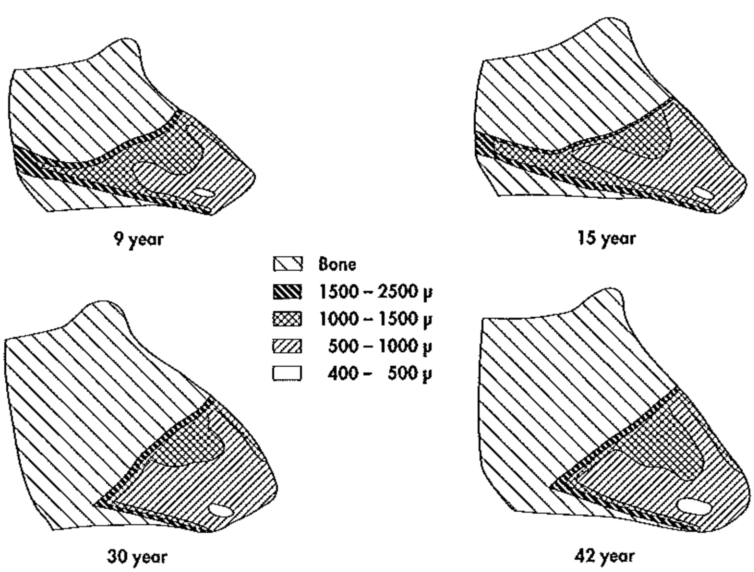


Figure 5.3 *Grid-coded diagrams illustrating regional variations in thickness of the cartilaginous part in 4 septal specimens of 9, 15, 30 and 42 years old, respectively. Diagrams are proportionate to each other, and to those of Figure 5.2. For anatomical orientation see Figure 5.1.*

reaches a maximal thickness of up to 3500 micron. In the posterior-superior region an ossification front has developed which is extending in an inferior-anterior direction. Along this front cartilage is found to be locally thickened to 2500 micron. This rim is orientated obliquely from the sphenoid to the more anterior and dorsal regions of the septum (sphenodorsal zone).

In the septum of a 3-year-old child further progress of the ossification front in inferior direction is noticeable, and associated with the loss of the very thick (up to 3500 micron) cartilage segment adjacent to the sphenoid rostrum. The relative proportions of the anterior and central part of the septum have been preserved. In addition, the inferior cartilaginous beam, related to the vomer border and supported by the sphenoid, is still present (sphenospinal zone).

In the periode from 4 - 15 years (Figure 5.2, 5.3), the situation, except for further progress of ossification, is not substantially different from the situation at the age of 3 years.

At the age of 9 years (Figure 5.3), the relative proportions in the remaining segments of the anterior and central region of the cartilaginous septum have been maintained. The thickened beam along the vomer margin and the thickened zone along the ossification front of the perpendicular plate (orientated from the inferior to the dorsal segment of the nasal septum) can be identified. The same situation is observed at the age of 15 years .

In the older specimens (30 and 42 years) the ossification process has implicated the inferior-posterior area of thick cartilage, interrupting the sphenodorsal and sphenospinal zones present at a younger age. The pattern of regional variations in thickness of the remaining anterior segment of the cartilaginous septum appears to be unaltered. Compared to the newborn, in the adult situation the septal cartilage has, for over 50% of its anatomical area, been replaced by the generally very thin (±200 micron) bony perpendicular plate (Figure 5.4). In contrast to the major part of the perpendicular plate (Figure 5.5), the anterior edge of the perpendicular plate is a thick bar of compact bone (Verwoerd et al., 1992). It is firmly and end-to-end connected with the cartilaginous septum (septo-ethmoidal junction).

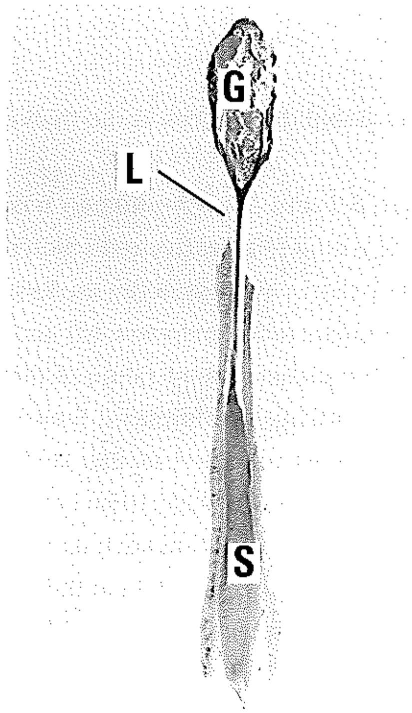


Figure 5.4 *Photograph of whole-mounted frontal section through the upper half of the central part of the nasal septum of the 9-year-old specimen. G: crista Galli; L: perpendicular plate; S: septal cartilage. The inferior edge of the lamina perpendicularis is relatively thin (compare with Figure 5.5)*

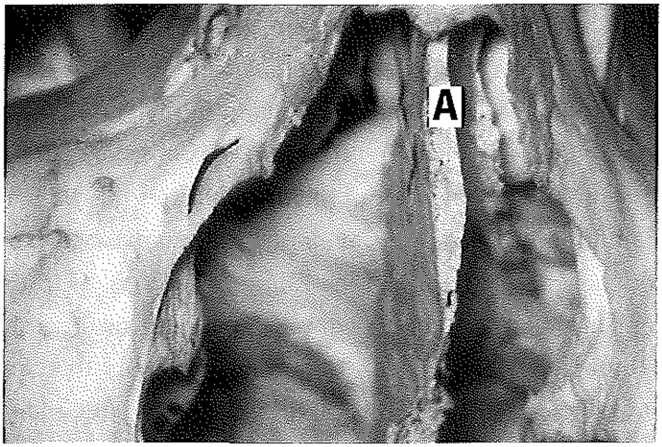


Figure 5.5 *Close-up of the anterior edge of the perpendicular plate in an adult skull. Note the thick and compact structure of the anterior rim (A), which supports the dorsal part of the cartilaginous septum.*

5.4 Discussion

This is the first study of regional differences in the thickness of cartilage in the human nasal septum.

As is evident from Figure 5.2 and 5.3, the human nasal septum after birth shows thickness ratios of 1:9, with a progressive reduction of these ratios in later life. This results mainly from progressive loss of the thickest, most posterior cartilage segments with final thickness ratios between 1:5 and 1:6. Anteriorly, both the overall architecture and the measurement range of the thick-thin segments are stable. In general, the previously referenced measurements all fall within the range of minima-maxima as recorded in this study. Since authors (Zuckerkandl, 1892; Kowatscheff, 1943; Cottle et al., 1958; Lang, 1989; Saunders et al., 1995) do not comment on any local variation such as was defined in this study, it may be assumed that differences between data in these publications are related to different locations of the measurements, and the age of the patients involved. The maximum thickness of the septal "expansion" as recorded by Zuckerkandl (1892) of up to 8 mm (8000 micron), is well outside our recorded range of dimensions and may have to be explained by measurements including the covering mucosa on both sides. As Saunders et al. (1995) also have demonstrated, this mucosa may locally be very substantial, up to 5 mm (Figure 5.6).

Previously the 3-dimensional architecture of the nasal septum was analysed in rabbits. In this species, at the age of 4 weeks a similar, complex pattern of regional differences in thickness was demonstrated (Verwoerd et al., 1991). Posteriorly, the septal cartilage adjacent to the sphenoid is at its thickest, whereas it reduces in anterior direction to a very thin anterior segment with a maximal ratio of 1:17 (50 as compared to 850 micron). Present at birth, this pattern is maintained throughout development to maturity (Tonneyck-Müller et al., 1982; Verwoerd et al., 1991). In the human newborn, as in the rabbit, a very thick segment of the cartilaginous septum is related to the sphenoid junction. Inferiorly in both species, the cartilaginous septum is thickened to a beam, whilst the anterior segment includes the thinnest cartilage area. Another zone of thick cartilage extends from sphenoid (posterior-inferior) to nasal dorsum (anterior-superior). Identical to the findings in man, the rabbit also features an ossification process, originating from the anterior skull base. However, the

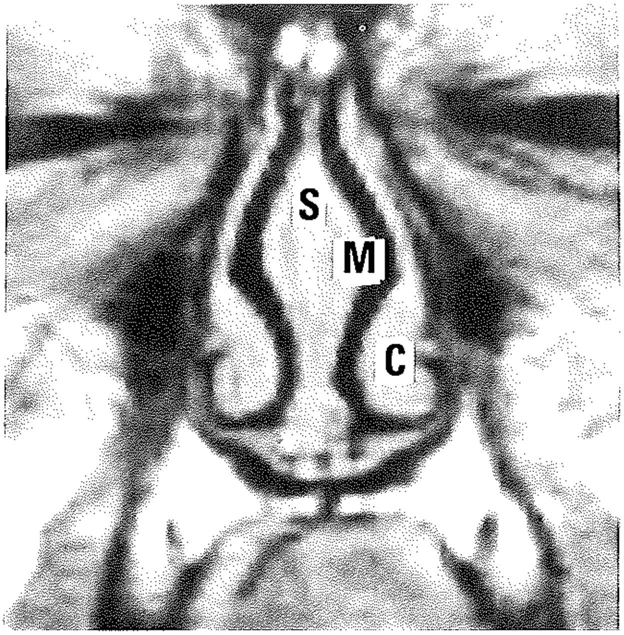


Figure 5.6 *Coronal MRI of nasal septum; T2-weighted image of a 2-year-old patient. S: septal cartilage; M: septal mucosa; C: concha inferior.*

extent of this process is limited in the rabbit and involves less than 10% of the total septal surface area (Takahashi, 1988a). In man it is much more extensive and the cartilaginous septum is ultimately replaced for more than 50% by bone (Takahashi, 1988a; van Loosen et al., 1996). In man the ossification eventually results in disruption of the original continuity of the sphenodorsal and sphenospinal zones, whereas in the rabbit the continuity of both is maintained through life.

In series of experiments in growing rabbits it was demonstrated that the increasing prominence (height) and lengthening of the nasal dorsum after birth is dependent on the growth of the sphenodorsal cartilaginous zone (Verwoerd et al.,1989a). Growth of the sphenospinal zone of septal cartilage provides lengthening of the upper jaw. On the basis of the morphologic similarity of the septum nasi in rabbit and man it is suggested that various types of post-traumatic maldevelopment observed in patients can be related to the loss of specific parts of the septal cartilage, as was earlier demonstrated in growing rabbits

(Verwoerd et al.,1980, Verwoerd-Verhoef et al., 1998). From clinical view according to these observations, three types of specific development of the nose after septal injury are discerned:

1. The underdevelopment of the nasal dorsum (too low, too short) with a retroposition of the anterior nasal spine and maxilla may be the result of a loss of septal cartilage involving both the sphenodorsal and sphenospinal zone (Figure 5.7a).

2. Partial loss of the sphenospinal cartilage leads to a retroposition of the anterior nasal spine. The lowering of the cartilaginous part of the nasal dorsum is the result of the underdevelopment of the maxilla (Figure 5.7b).

3. Loss of the thin anterior cartilaginous area is apparently of minor significance in view of the normal nose and upper jaw development after septal perforation in that region in early childhood (Figure 5.7c).

In the first years of life the superior-posterior part of the cartilaginous nasal septum is replaced by bone. When the ossification process interrupts the sphenodorsal zone of cartilage, the support of the nasal dorsum shifts to the thickened, anterior part of the perpendicular plate (Figure 5.3). Therefore, we recommend to leave this area untouched during surgery.

Even after puberty the sphenospinal zone of thick cartilage can regularly be identified, and then, is known as sphenoid tail. The presence of a sphenoid tail in adult patients depends on the degree of ossification. It only disappears when the endochondral ossification process has encroached the septal cartilage between the vomer blades.

From clinical experience, it is well known that the columellar rim of the septum has an additional supporting function for the cartilaginous nasal dorsum. Accordingly, this area is slightly thicker than the central-anterior, very thin area. Takahashi (1988b) suggested that this "vertical support" of the anterior part of the nasal dorsum is more important in adults than in young children.

Taking into account the local differences in thickness and their consequences for the mechanical properties of the cartilaginous nasal septum, some of the observed septal deformities can be explained. In particular the thinner and weaker parts of the septum may be expected to be more vulnerable in case of external trauma. In the newborn, deviation of the anterior part of the

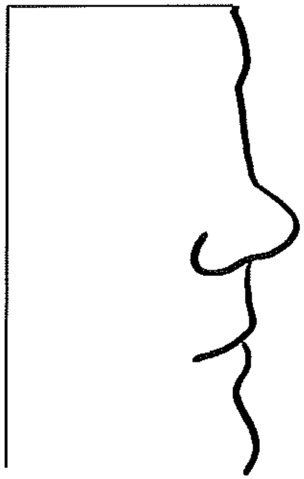
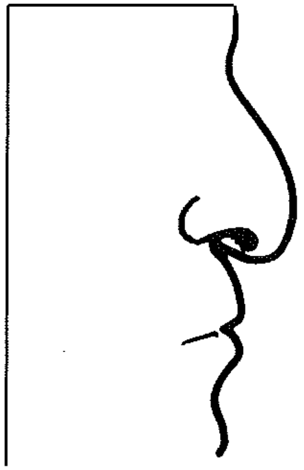
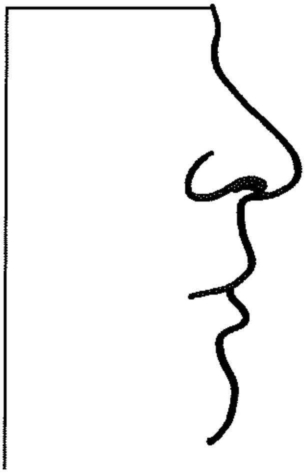


Figure 5.7
Outline of facial profile illustrating the development of nose and jaws after loss of major parts of the septal cartilage (after Verwoerd and Verwoerd-Verhoef, 1998).

a) loss of sphenodorsal and sphenospinal zone during early childhood: low and broad nasal dorsum, retroposition of anterior nasal spine, underdevelopment of maxilla.



b) loss of sphenospinal zone during infancy: normal prominence of the bony nasal dorsum. Underdevelopment of the maxilla is indirectly responsible for lowering the cartilaginous nasal skeleton.



c) loss of cartilage in central thin area with septal perforation: normal nose and jaw development.

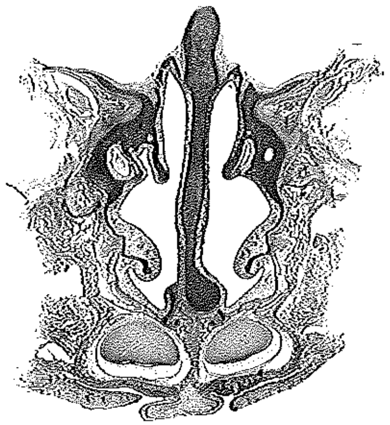


Figure 5.8 *Septal deflection in the thin anterior part of a neonatal septum (frontal section).*

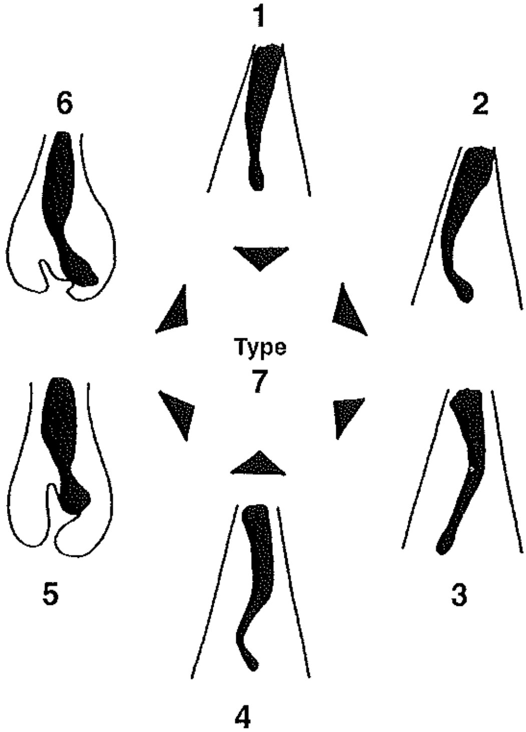


Figure 5.9 *Simplified classification of pathological neonatal septal deformities. The first 4 types are presented from a cranio-caudal view. Types 5 and 6 are presented from a anterior-posterior section. Type 7 represents a combination of the previous 6 types. (After Mladina, 1987).*

septum has been well described (Gray, 1974; Jazbi, 1977; Kent et al., 1988; Brain, 1992). In this septal deformity, the deflection takes place, during labour, in the thin anterior part (Figure 5.8).

Mladina (Mladina, 1987; Mladina et al.,1989, 1990) has divided septal deformities in 7 basic types (Figure 5.9). In most patients the bending of the septal cartilage occurs in the thin or relatively thinner areas as described, for the first time, in the present study. The types 1, 2 and 4 are noted as a vertical ridge due to bending or fracture at various sites in the anterior thin area (Mladina, 1987). The horizontal bending takes place in the thin part just above the basal rim. At anterior rhinoscopy, the horizontal types of deviation (type 5 and 6) appear as a single basal crest, which can reach the posterior part of the lateral nasal wall (type 5). The crest is formed by the thick basal cartilaginous rim located above the vomer bone. Another horizontal septal deviation (type 6) is characterised by a deep gutter on one side of the septum (Figure 5.9).

In conclusion this study has demonstrated that:

1. The human cartilaginous nasal septum is characterised by a specific 3-dimensional architecture with thicker and thinner zones varying with a factor of 1:9 at birth to 1:6 in adults. This pattern, maintained from birth to adulthood, is similar to that previously demonstrated in rabbits.
2. The thickness in the various zones of the septal cartilage hardly increases during further growth of the child. The nose develops in size by its sagittal dimensions through a process of simultaneous cartilage growth and endochondral ossification.
3. In young children the nasal dorsum is primarily based on the sphenoid via a zone of thick cartilage; later in life it is based on the thickened part of the anterior border of the perpendicular plate.
4. Various types of maldevelopment of nose and upper jaw in patients after an injury in early childhood, can be explained by the loss of specific parts of the septal cartilage, e.g. sphenodorsal and sphenospinal zone; loss of the extremely thin anterior area of septal cartilage seems not to be important for nasal growth.
5. The 3-dimensional architecture of the nasal septum is important for understanding the etiology of septal deviations, the origin of preferred fracture lines and the risks of surgery for nasal development.

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Persistent Pattern of Variations in Thickness of the Human Nasal Septum: Implications for Stress and Trauma as Illustrated by a Complex Fracture in a 4-Year-old Boy.

6.1 Introduction

For surgical intervention after nasal trauma, it is desirable to be able to predict at least to some extent the distribution of nasal fracture lines.

Harrison (1979) found reproducible patterns of fractures, beginning just posterior to the nasal spine 2-3 mm above the boundary with the bony vomer and extension posteriorly to the perpendicular plate of the ethmoid. Crossing this boundary it angles to cranially, sequestering a 1 cm wide strip of the plate. Before reaching the cribriform plate a second anterior angling results in a re-crossing of the boundary. Continuing in ventral direction the cartilage is followed, leaving a narrow rim attached to the base of the skull. This pattern was not described as age dependent although the experiments were limited to adults with a fractured nose and 15 cadavers without any age indication. For prediction of fractures in children there seems as yet no emperical study. Additionally there is no theoretical basis, which would predict the pattern as found by Harrison (1979) since the models are either limited by the use of a perspex plate of single thickness, or of 2 dimensions representing the bony and cartilaginous component in an attempt to take into account the differences in elasticity of perpendicular plate and the cartilaginous septum proper (Murray, 1987). Still the consistent pattern of a complex C-shaped fracture, opening in anterior direction can not be explained by these models.

Anatomical studies which would provide an alternative basis for the experimental findings were until recent of conflicting nature with wide ranges for nasal septal thickness being recorded in the literature. Zuckerkandl (1892) gave the most extreme at 4-8 mm, while Kowatscheff (1943), Cottle et al (1958) and Lang (1989) all presented different results of measurements ranging from 2 mm (Kowatscheff, 1943) to 4 mm (Lang, 1989). However these measurements do not take into account the considerable regional variations in thickness, which appear in a consistent pattern with age as presented by van Loosen et al., (1996). The latter study however extends from the paediatric age range to adulthood (0-42 years). If the findings of van Loosen et al (1996) were to be consistent with the consistent pattern of fractures as recorded by Harrison (1979), predictability of fractures might then be extended into childhood.

6.2 Materials and methods

A 4-year-old, previously healthy, male infant without congenital craniofacial defects, with multiple trauma inclusive trauma of the face and skull, deceased within 24 hours of the initial incident. The nasal septum was removed at postmortem with preparation of the specimen from the anterior skull base as was earlier described (van Loosen et al, 1988).

The specimen was photographed in back-lit mode after removal of mucosa and soft tissues (Figure 6.1).

Previously published diagrams, recording the 3-dimensional pattern of variations in thickness, were used for the study of the position of the fracture of the index case and those described by Harrison (1979) in relation to potential areas of less resistance / greatest vulnerability.

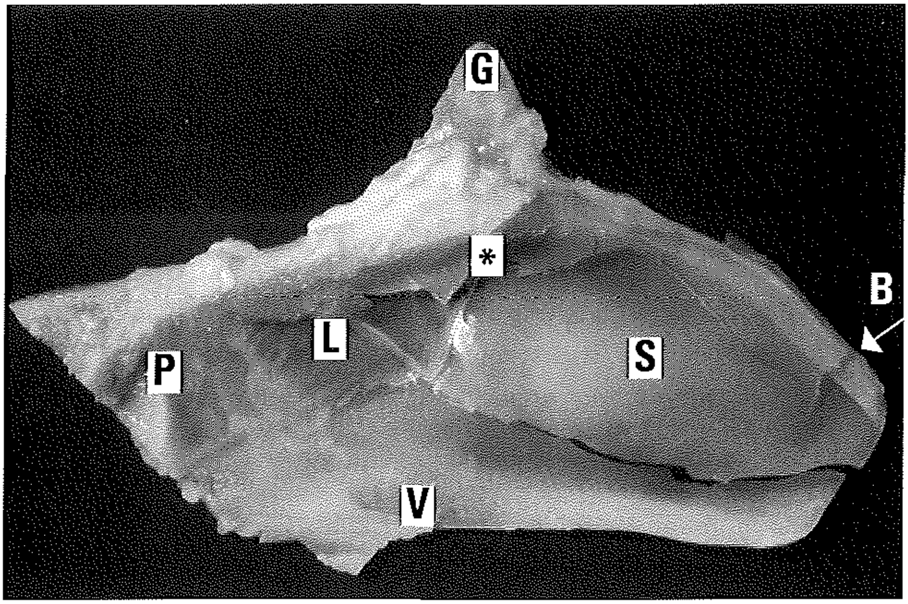

Figure 6.1. *Back-lit postmortem septal resection specimen of fractured, combined osseous and cartilaginous nasal septum of a 4-year-old boy. Note inverted C-shaped fracture line (asterisk). V: vomer, G: crista Galli, P: sphenoid margin, S: cartilaginous septum, L: perpendicular plate, B = second fracture line.*

6.3 Results

The fracture complex in the septal structures of the 4-year-old boy (Figure 6.1), consists of two separate groups. The main and longest fractureline begins directly posterior to the nasal spine, 2-3 mm above the boundary with the bony vomer, for the full caudal length of the cartilaginous septum. The fracture extends posteriorly to the perpendicular plate of the ethmoid. Crossing the boundary of the endochondral ossification zone, it extends into the thin perpendicular plate. The fracture then angles sharply in cranial direction, running parallel to the slightly curved ossification zone, thereby sequestering a 2-3 mm. wide strip of the plate which remains attached (through the zone of endochondral ossification) to the central part of the cartilaginous septum. Before reaching the cribriform plate, a second sharp angling in the anterior direction occurs, orienting the fracture back on a line parallel to its first segment in the cartilaginous septum. This then results in recrossing of the boundary between bone of the perpendicular plate and the cartilaginous septum, i.e. the ossification front. Continuing in ventral direction, the cartilage is followed, leaving a narrow rim attached to the base of the skull. There is a second small fractureline anteriorly running from the junction to the base of the frontal skull and extending partially into the cartilaginous septum, but not traversing to the vomer bone.

In Figure 6.2 a grid-coded diagram is shown detailing the regional distribution of differences in thickness of a nasal septum resection specimen of a 4-year-old human, obtained at post-mortem (Van Loosen et al., 1996). There was no medical history or findings at postmortem to the contrary, of craniofacial malformations or previous trauma or surgical intervention to the (mid) facial regions. From this diagram it is evident that the septum at this age has an overall wedge-shaped form, gradually increasing its thickness from 400-1000 microns anteriorly up to 2500 microns posteriorly at the junction of the perpendicular plate. However a number of features occurs which are of interest to the fracture described above. Inferiorly the septum thickens at the margin to form a "beam" up to 2000 micron thick which extends along almost of the whole of the caudal margin and forms the junction to the vomer groove or rim. This extends to the ossification zone posteriorly at the sphenoidal end.

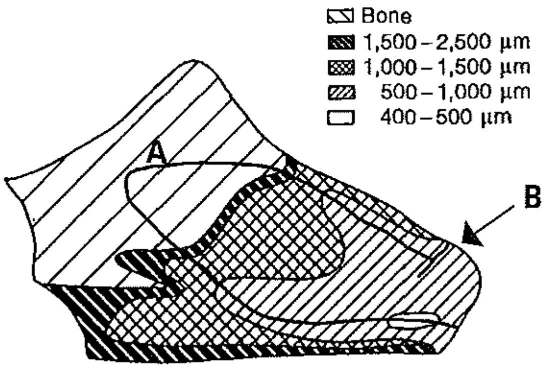

Figure 6.2. *Grid-coded diagram of a 4-year-old case study, illustrating the constistent pattern of regional variations in thickness (van Loosen et al., 1997).* **A**. *Fracture line.* **B**. *Second fracture line.*

6.4 Discussion

As we have shown previously for the neonatal period in man (van Loosen et al., 1988), a similarly complex architecture exists as that recorded in Harrison's (1979) studies for adults. With respect to the interpretation of its mechanical properties it is of interest that, the reproducibility of fractures in these experiments is high. The main features in children and adults are a posterior thick and anterior thin plate with a superior and inferior "beam" of thicker cartilage. The central segment in man is replaced by a thin perpendicular plate (up to 400 micron). Aside from overall dimensional growth, the remaining fraction of the cartilaginous septum, at least during the first four decades of life, maintains the same overall pattern of thick and thin areas. Also the vulnerability to mechanical forces may therefore similarly not change significantly with age.

6.5 Conclusions

In summary our previous studies demonstrate a consistent pattern of regional variations in thickness of the human nasal septum. The case as presented for the first time here shows a pattern of nasal septal fracture similar to the lines appreciated in the study by Harrison (1979). Now it can be predicted in children on the basis of the retained overall architecture, described first at birth (van Loosen et al., 1988) and which, with the exception of posterior replacement through endochondral ossification, is maintained throughout life.

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7

Interstitial Growth of Nasal Septal Cartilage Assessed by Automated Computer Assisted Image Analysis.

7.1 Introduction

Surgical intervention in the nasal septum requires a detailed understanding of the development of the nasal septum with age, since trauma to areas of growth may result in the development of deformities. Knowledge with respect to the presence and distribution of "vulnerable" growth areas of the nose is as yet not complete (Pirsig, 1986a,b, 1992; Verwoerd and Verwoerd-Verhoef,1989) and quantitative studies are lacking. Literature on septal dimensions related to age exist (Pirsig 1975; Vetter et al., 1983,1984a,b) and investigations of the nasal septum have concentrated primarily on the ossification zone (Schultz-Coulon and Eckermeier, 1976). In the neonate the nasal septum is completely cartilaginous. The anterior thin area shows mainly small, round chondroblasts, with the presence of "twin cells" whereas the remainder of the septum contains more hypertrophic chondrocytes. In the most posterior region, near the sphenoid rostrum endochondral ossification is recognised (van Loosen et al., 1988).

During further growth of the nasal septum two processes can be observed:

1. Cartilaginous septal growth by appositional and interstitial growth.
(Appositional growth: increase of the overall septal dimensions by external deposition of neocartilage by cells descendent from the subperichondrial cartilage. Interstitial growth: the increase of overall septal dimensions by production of intercellular substance, and to a lesser degree by an increase in cell size)
2. An intensive ossification process responsible for the perpendicular plate.

Vetter et al., (1983, 1984 a,b), described the metabolic activity of septal cartilage in humans. Their studies, however do not include patients below the age of 5 years. In this period the largest proportional increase in size of the septum occurs (van Loosen et al, 1996). In the nasal septum of the rabbit, a relationship between the variations in thickness and quantitative observations on the relationship between cells and intercellular substance have been found (Tonneyck-Müller and van der Werf, 1982; Tonneyck-Müller, 1984).

The aim of this study is to investigate the interstitial growth of the nasal septal cartilage in relation to: a) age; b) locations.

7.2 Materials and methods

7.2.1. Study set:

Nasal septum specimens of thirteen Caucasians, with normal facial development, varying in age from birth to 35 years, were obtained at routine post-mortem (Tables 7.1).

7.2.2. Sample preparation:

Specimens were fixed in 4% formaldehyde, sectioned after decalcification prior to routine tissue processing. Five micron sections were stained with Alcian Blue/PAS method.

7.2.3. Sample locations:

In each section the septum was assessed along a central axis, located midheight at 3 locations: the anterior, middle and posterior part of the septum. In addition the anterior thin part was also evaluated. Quantitation was carried out for all regions (figure 7.1).

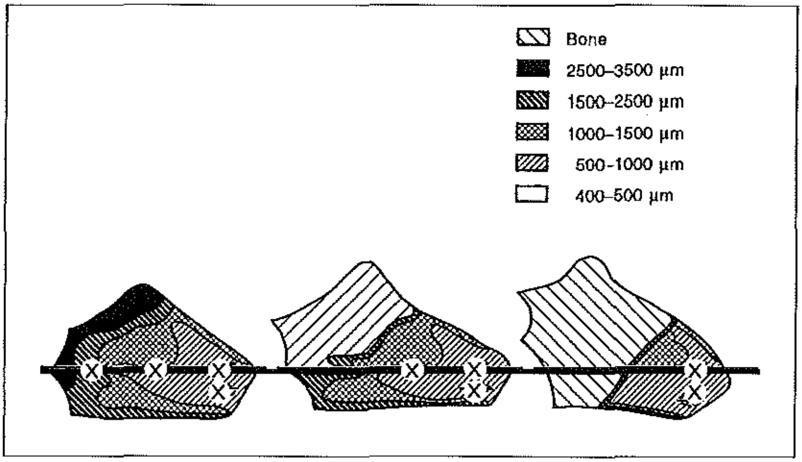


Figure 7.1. *Diagram of variations in thickness of the nasal septum of a neonate. Measurements along a central axis are marked. Note that the very thin area in the anterior inferior segment is separately assessed in this study.*

Table 7.1. Cause of death

Patient No.	*Age*	
1	*15 days*	*septicemia*
2	*1.5 months*	*forensic case*
3	*7 months*	*tuberculosis*
4	*1.5 years*	*dehydration*
5	*2 years*	*forensic case*
6	*3 years*	*forensic case*
7	*4 years*	*road accident*
8	*9 years*	*road accident*
9	*10 years*	*septicemia*
10	*20 years*	*road accident*
11	*27 years*	*forensic case*
12	*30 years*	*forensic case*
13	*35 years*	*road accident*

7.2.4. Subsampling routine:

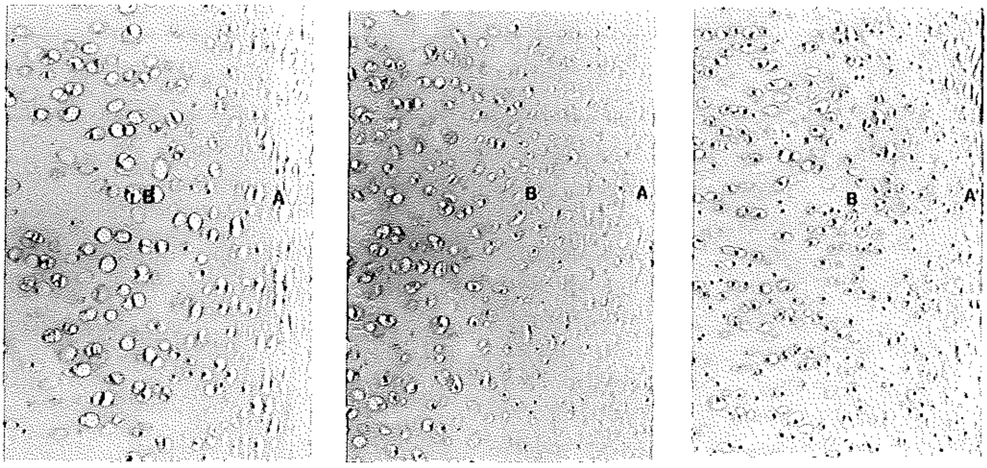
At each location measurements of the subperichondrial and central cartilage tissue was performed separately (figures 7.2, 7.4, location A/B). The central measurement was determined by placing the centre of the measurement frame of 180 x 240 micron in the centre of the septum, with the longest axis of the frame parallel to the septum. To position the subperichondrial measurement area, the longest margin of the counting frame was placed as close as possible to the fibrous perichondrium without accepting any actual overlap.

7.2.5. Imaging:

Digitised images of histological sections were acquired using the 40 x oil (N.A. 0.95) objective and a further 10 x photo-occular magnification using a Sony CCD-D Black and White camera.

7.2.6. Image processing and analysis:

Images were collected from the microscopical system and analysed on line after normalisation (calibration of the brightest as compared to the darkest area of each image on a 100 step scale) using the Fenestra (Confocal Technologies Ltd, Liverpool) software package.



a *b* *c*

Figure 7.2 *Microphotograph of 5-μm sections with subperichondrial (A) and septal center cartilage (B) at three different locations as illustrated in Figure 7.1: posterior (a); middle (b) and anterior (c) in a 15-day-old specimen. PAS/Alcian blue stain. x 10.*

7.2.7. Sample area:

Using the programme software an area of 180 x 240 micron as defined by a single pixel line frame, was used for all measurements throughout the study. The size of area was chosen to ensure the presence of minimally 100 to 120 cell profiles per image resulting in the required precision of calculated parameters.

7.2.8. Study parameters, definitions:

Image processing included on-line measurements of:

7.2.8.a. the total number of cartilage cell profiles: (any section, large or small, through a cartilage cell varying from very small cell caps without a nucleus to full size mid-nuclear through sections) in each 180 x 240 micron sample area. This measurement uses a protection against bias resulting from changes in cellular size between samples through the use of the edge rule (any profiles intersected by the left and upper boundary are to be included, any profiles intersected the right and lower boundary are to be excluded from the sample).

7.2.8.b. the profile density:

The fraction of total area (180 x 240 micron) taken in by the total number of cell profiles in the sample, and

7.2.8.c. the mean profile area:

The average profile area (in micron) of the cartilage cell profiles selected in a given 180 x 240 micron area sample. This parameter is calculated from the total area taken in by cartilage cell profiles in a given 180 x 240 micron frame (in absolute square micron) divided by the total number of profiles found cell per frame resulting from the image segmentation).

7.2.9. Sample calibration:

As magnification for all histological sections was the same throughout the study, and as we carried out a comparative study between samples for age related changes, a software based unit of image area in pixels was used (Arbitrary Units of area: A.U.) as input in all trend analyses and statistical procedures.

7.2.10. Sample size definition:

Using the progressive (or running) mean method (an "on-line" facility of Fenestra), the number of samples required for a precise measurement in each area was studied. We found that for each area of the nasal septum studied, a "mean value" for each parameter within 5% of the final value (as may be determined by using an inifinite number of local samples) was achieved using 4-5 areas of 180 x 240 microns per location in all cases.

7.2.11. Graphic and statistical analysis:

Values listed in the tables 7.2 and 7.3 were graphically displayed with help of a commercially available programme (SlideWrite Plus for Windows Version 3.00, Advance Graphics Software, Carlsbad, CA, USA).
For the indication of trends in the data against age curve fitting was done with the same program. This includes linear regression for linear function fitting and Levenberg-Marquardt fitting algorithm for non-linear functions. As a relevant trend the function with the highest overall correlation with the experimental data was chosen without assigning any meaning to the mathematical form of the selected function. Interestingly, in most of the trends the function selected

indicated a proportionality to the natural logarithm of age.

7.2.12. Statistical analysis:

Differences between locations were tested for statistical significane with the Wilcoxon Matched-Pairs Signed-Ranks test using the SPSS programme, Version 8.0 for Windows. With help of this programme also the statistical significance of the relations between the cell profile aspects and age was tested (2-tailed) parametrically using Pearson correlation coefficients and nonparametrically by Spearman correlation coefficients.

7.2.13. Quality control and reproducibility studies:

All samples were analyzed twice by a non-medical scientific officer in a strictly randomised and blinded fashion. Randomisation included intra-septal location and subperichondrial versus central measurements.

Using randomisation 25 % of all samples / areas were re-measured by a second observer for the purpose of inter-observer reproducibility assessment. Reproducibility for the profile density and the mean profile area measurements were better than 90% for inter- and better than 95% for intra-observer reproducibility.

7.3 Results

The studied specimens vary in age from neonate to 32-year-old adult. In the neonate nearly the total nasal septum is cartilaginous. The first signs of endochondral ossification become manifest between 1 and 2 years of age. Ossification starts adjacent to the anterior skull base and sphenoid. The ossifying front expands in anterior-inferior direction. This results in a gradual loss of cartilage and simultaneously, in formation of the perpendicular plate. Finally, more than half of the adult nasal septum is composed of bone (perpendicular plate). As a consequence of ossification the cartilage in the posterior and midseptal area could be studied only in the younger specimens. The results are summarised in table 7.2 (profile area) and 7.3 (profile density), and illustrated in Figure 7.3-7.6; the statistical analyses are presented in table 7.4.-7.6.

Table 7.2. Mean profile area (in AU pixels)

		Septal center				Subperichondrial			
Patient No.	Age	posterior	midseptal	anterior	thin anterior	posterior	midseptal	anterior	thin anterior
1	15 days	197	86	62	56	79	44	41	45
2	1.5 months	205	125	70	59	79	49	45	47
3	7 months	158	112	81	57	70	57	43	43
4	1.5 years	216	137	78	48	93	85	40	41
5	2 years	205	150	87	49	71	82	48	37
6	3 years	200	166	89	61	64	75	39	45
7	4 years	200	137	84	54	85	86	51	39
8	9 years		218	138	66		72	77	58
9	10 years		121	123	73		88	84	69
10	20 years			147	86			88	78
11	27 years			138	112			94	83
12	30 years			124	118			84	91
13	35 years			194	121			117	96

Table 7.3. Mean profile density (in % area)

		Septal center				Subperichondrial			
Patient No.	Age	posterior	midseptal	anterior	thin anterior	posterior	midseptal	anterior	thin anterior
1	15 days	4,5	4,8	1,4	5,3	8,3	9,7	9,0	9,2
2	1.5 months	5,3	7,4	1,5	7,1	9,1	7,7	7,1	8,1
3	7 months	6,2	4,2	1,9	5,1	8,8	8,1	7,2	7,3
4	1.5 years	4,9	6,2	2,4	6,3	8,9	9,5	6,7	7,1
5	2 years	5,0	5,7	2,9	4,6	10,0	10,0	4,0	5,7
6	3 years	4,8	4,1	1,1	4,1	8,1	8,8	4,0	5,3
7	4 years	4,7	3,3	1,4	5,1	11,3	8,4	5,3	5,6
8	9 years		3,7	3,2	3,9		6,3	5,2	5,0
9	10 years		2,1	1,5	4,1		5,9	4,5	4,8
10	20 years			1,3	3,6			4,4	4,6
11	27 years			1,1	3,4			3,3	4,1
12	30 years			0,7	3,1			3,6	3,9
13	35 years			1,1	2,2			2,5	3,1

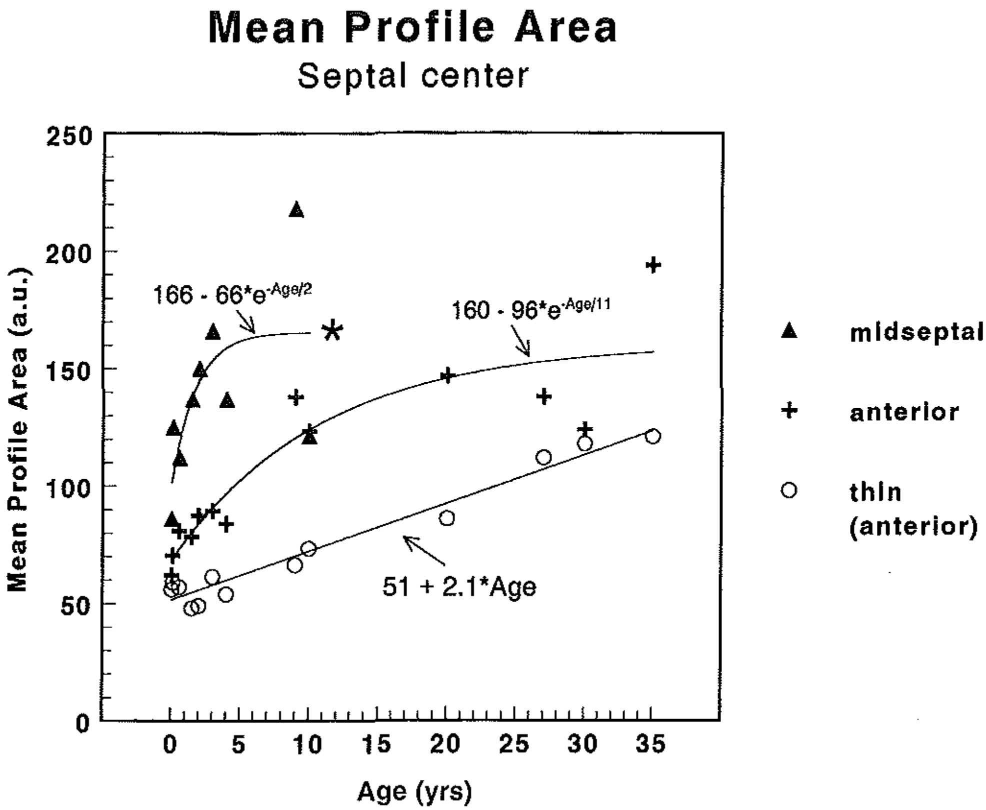


Figure 7.3. *Diagram showing results of septum center mean profile area measurements in the relevant anterior, midseptal, posterior and thin ventrocaudal area of 13 septa between birth and 35 years. Absent values are the result of progressive, age-related ossification of the midseptal, segment. Linear Y-scale in AU (pixels), linear X-scale in years of age.*

** Onset of endochondral ossification*

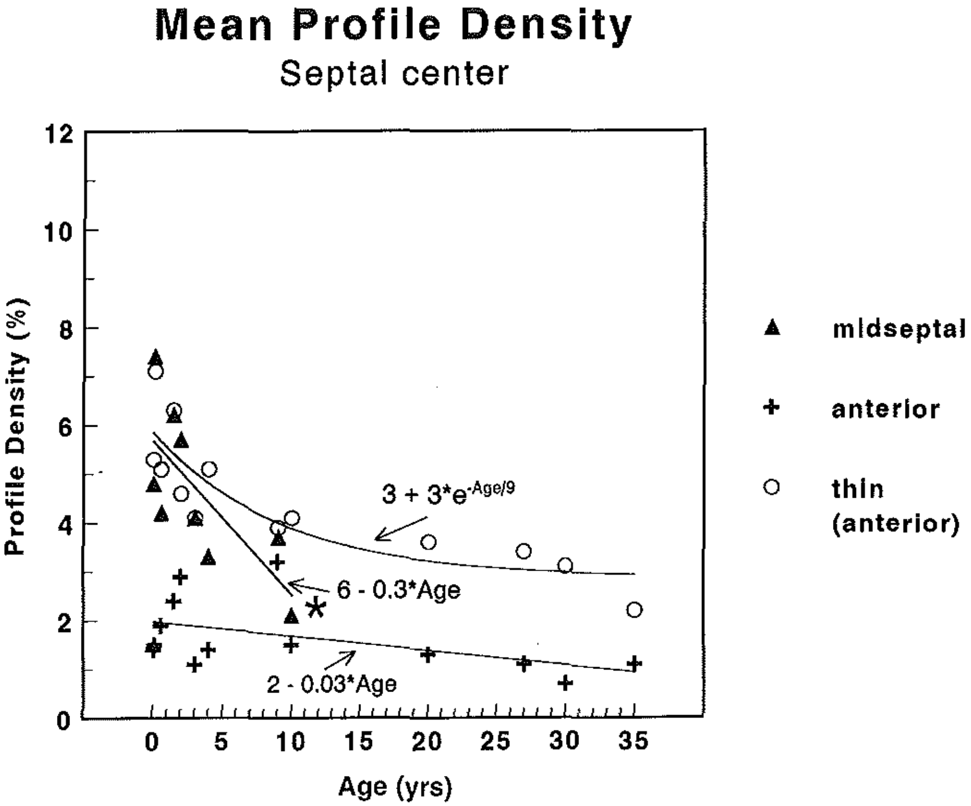


Figure 7.4. *Diagram showing results of profile density measurements in the anterior, midseptal, posterior and thin, ventrocaudal area of 13 septa (center) between birth and 35 years.*
Absent values are the result of progressivc, age-related ossification of the midseptal segment. Linear Y-scale in percent (pixels), linear X-scale in years of age.
* *Onset of endochondral ossification*

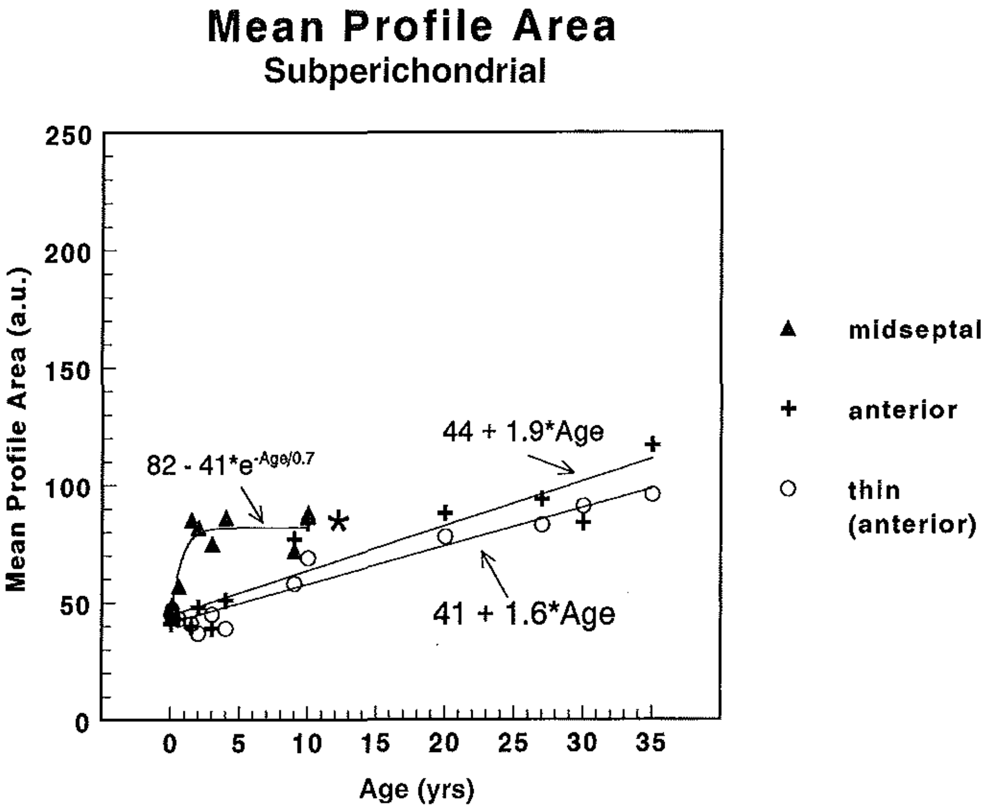


Figure 7.5. *Diagram showing results of subperichondrial mean profile area measurements in the anterior, midseptal, posterior and thin ventrocaudal area of 13 septa between birth and 35 years. Absent values are the result of progressive, age-related ossification of the midseptal segment. Linear Y-scale in AU (pixels), linear X-scale in years of age.*
** Onset of endochondral ossification*

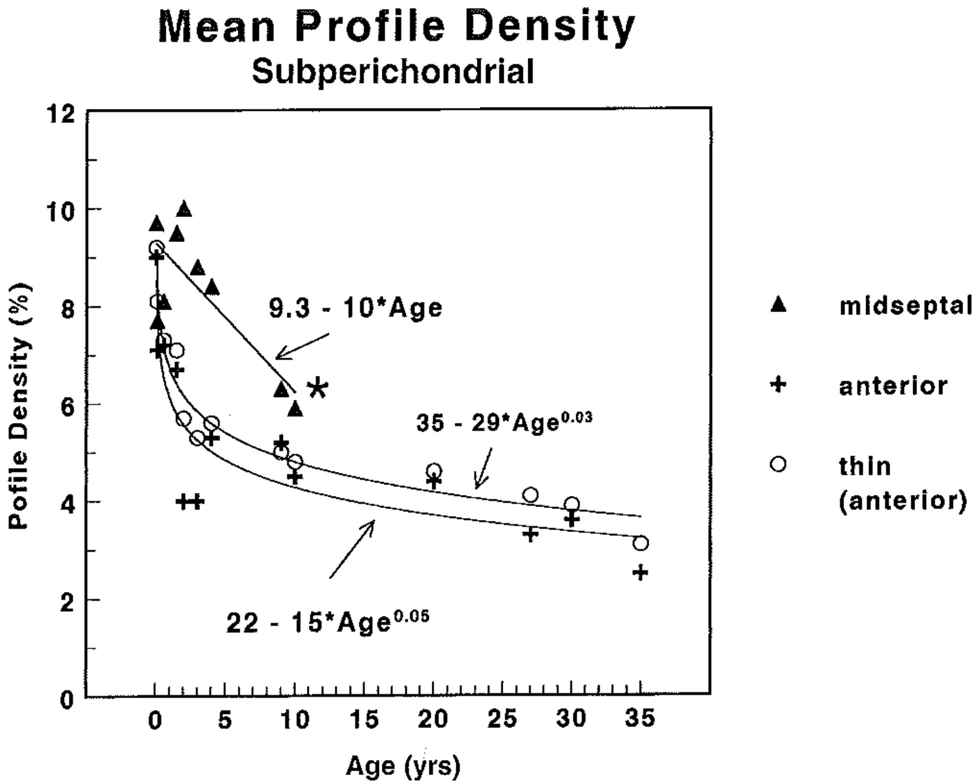


Figure 7.6. *Diagram showing results of subperichondrial profile density measurements in the anterior, midseptal, posterior and thin ventrocaudal areas of 13 septa between birth and 35 years. Absent values are the result of progressive, age-related ossification of the midseptal, segment. Linear Y-scale in percent (pixels), linear X-scale in years of age.*

** Onset of endochondral ossification*

Location	anterior		anterior thin		midseptal		posterior	
anterior			>	0.003	>	0.008	....	0.028
thin anterior	<	0.001			>	0.011	....	0.028
midseptal	<	0.008	....	0.208			....	0.598
posterior	<	0.018	....	0.496	....	0.933		

Table 7.4. *Comparison of cell profile densities between different locations in the anterior-posterior direction. In the upper right triangle of the table the densities at the subperichondrial positions are compared. In the lower left triangle the same is done for the central positions. Comparisons should be read from column entry to row. For instance: the subperichondrial cell profile density at the thin(anterior) location is significantly higher than at the anterior location, with a (2-tailed) significance level p=0.003 using the Wilcoxon Matched-Pairs Signed-Ranks test. Given the low number of pairs in the comparisons (13, 9 or 7, Table 7.2) only p-values below 0.02 were considered to indicate significant differences. Gray shaded entries show non-significant correlations.*

Location	anterior		thin(anterior)		midseptal		posterior	
anterior			....	0.041	....	0.028	>	0.018
thin anterior	>	0.001			>	0.011	>	0.018
midseptal	<	0.011	<	0.008			....	0.310
posterior	<	0.018	<	0.018	<	0.018		

Table 7.5: *Comparison of cell profile areas between different locations in the anterior-posterior direction (table lay out similar to Table 7.4)*

Cell Profile aspect		Density			Area		
Correlation Type		Parametric		Non Par	Parametric		Non Par
X-variable		LogAge	Age		LogAge	Age	
Position	Location	Significance of correlation (p-values)					
Subperichondrial	anterior	0.000	0.004	0.000	0.001	0.000	0.000
	thin anterior	0.000	0.000	0.000	0.004	0.000	0.003
	midseptal	0.187	0.011	0.170	0.002	0.109	0.016
	posterior	0.281	0.170	0.432	0.883	0.963	0.908
Septal Center	anterior	0.513	0.083	0.045	0.000	0.000	0.000
	thin anterior	0.001	0.000	0.000	0.006	0.000	0.013
	midseptal	0.076	0.023	0.010	0.046	0.134	0.130
	posterior	0.937	0.412	0.702	0.778	0.596	0.696

Table 7.6: Statistical significance (p-value) of the correlation of the cell profile aspects either tested parametrically against the logaritm of age and against age itself or tested nonparametrically against age. Gray shaded entries show non-significant correlations.

Central zone of septal cartilage: cell profile area

At all ages the largest cells are found in the posterior cartilage, the more anterior the smaller the chondrocytes. The large cells present in the posterior part of the newborn, show no further increase in size prior to ossification. Midseptal ossification is preceded by an marked increase in cell profile. The mean profile area in the other parts of the septal cartilage gradually increases with age.

The statistical analysis for the central cell profile area (Table 7.2 and Fig. 7.3) showed that:

1. a significant ($p<0.02$) larger area exists at the posterior location compared with the other three locations;

2. a significant ($p<0.02$) larger area exists at the midseptal location compared with the Anterior and the thin(anterior) locations;

3. a significant ($p<0.02$) smaller area exists at the thin(anterior) location compared with the anterior location.

Central zone of septal cartilage: cell profile density

In the specimens of 4 years and younger, the density in the posterior and midseptal area is much higher than anteriorly. No further changes of density are noted in the posterior cartilage. The midseptal cartilage density, however, seems to decrease in the specimens from 0 to 10 years of age (non significant). The density in the anterior cartilage is only slightly (non significant) decreasing from the neonatal to the adult stage. In all specimens the densitiy in the anterior thin area is larger than in the anterior cartilage which nearly equals that of the posterior cartilage.

This analysis for the central cell profile densities (Table 7.3 and Fig 7.4) showed only a significantly ($p<0.02$) lower density at the anterior location compared with the other three locations.

Subperichondrial cartilage: cell profile area

At birth the highest value for the cell profile area is found posteriorly, and it remains unchanged until the onset of ossification. The midseptal cartilage shows a rapid increase during the first year of life to reach, prior to ossification, a plateau at the same level as observed in the posterior cartilage. Both the anterior and the anterior thin area demonstrate a gradual increase of cell profile from birth to 35 years of life (oldest specimen). They finally reach a maximum comparable to the values found in the midseptal and posterior regions.

From the statistical analysis (Wilcoxon) on differences in subperichondrial cell profile areas between the locations in the anterior-posterior direction (Table 7.2 and Fig. 7.5) it was shown that:

1. a significant ($p<0.02$) larger area exists at the posterior location compared with the anterior and the thin(anterior) locations, but not with the midseptal location;

2. a significant ($p<0.02$) larger area exists at the midseptal location compared with the Thin(anterior) location, but not with the anterior location;

3. no significant difference exists between the thin(anterior) location and the anterior location.

Subperichondrial cartilage: cell profile density

At birth the density is relatively high in all areas. The midseptal region shows a downward tendency with age. The anterior and anterior thin cartilage demonstrate a very rapid decrease of density in the first 4 years of life, which is slowing down after that period. In older specimens only a slight further decrease of density was noted.

From the statistical analysis (Wilcoxon) on differences in subperichondrial cell profile densities between the locations in the anterior-posterior direction (Table 7.3 and Fig. 7.6) it was shown that:

1. no signicant difference exists between the posterior location and the other three locations;

2. a significant ($p<0.02$) higher density exists at the midseptal location compared with the anterior; thin(anterior) location,

3. a significant ($p<0.02$) higher density exists at the thin(anterior) compared with the anterior location.

7.4 Discussion

Dimensional aspects of the postnatal development of the human nasal septum were previously reported (Verwoerd et al, 1989, Van Loosen et al., 1996). An interesting finding was that after birth the cartilaginous septum rapidly expands to its maximal size at the age of 2 years. Further growth of the septum appeared to be due to enlargement of the bony perpendicular plate (Van Loosen et al., 1996).
The present study deals with two features of the cartilaginous part of the developing nasal septum, (1) the mean cell profile area, reflecting cell size, and (2) the mean cell profile density, reflecting the relation between the cellular component and the combined cellular and extra-cellular tissue components.

In literature no data on mitotic activity nor quantative histometric data concerning evolution of cell size or intercellular volume could be found for the human septum. These aspects, however, were studied in the cartilage of the growing rabbit cricoid (Verwoerd-Verhoef et al., 1997).
In that study it was concluded that a high mitotic activity at birth, in both cartilage and perichondrium, slows down in a few weeks. After the age of 8 weeks no mitotic figures could be demonstrated and increase of cell size and/or matrix components appeared responsible for further growth. It could suggest that also in the nasal septum proliferation of cartilage cells is restricted to the first period of postnatal life.

From our analysis of the series of human specimens of different ages, it is evident that most changes occur during the first 10 years of life. Afterwards only moderate and gradual changes were observed. Unfortunately, no specimens were available in the age range from 10 to 20 years, the period in which the adolescent growth spurt is known to take place. The evolution of the measured values, before the age of 10 and after the age of 20, does not give any indication of biological phenomena in the cartilage to be associated with a growth spurt of the nasal septum.

The various parts of the cartilaginous septum show as far as profile area and profile density are concerned, specific patterns of development. This regionalisation coinciding with previously described regional differences in septal thickness stresses that the nasal septum is not a homogeneous structure with uniform properties. (van Loosen et al, 1999). This conclusion is particularly relevant for surgical interventions like partial resection, and transposition of resected, eventually crushed, cartilage parts which all would interfere with the functional 3-dimensional organisation of the septal cartilage.

An intriguing question is how this region-specific development is programmed, and whether perichondrium and cartilage would play different roles in this process. Regionalisation of the septal cartilage is not a unique human phenomenon, as was demonstrated in a series of rabbit experiments (Verwoerd et al., 1989, 1991; Verwoerd-Verhoef et al., 1991, 1995). Detailed studies on these questions, probably on a molecular biological level have not yet been published, but are certenly needed for further illucidation.

Reviewing the specimens between 0 and 10 years of age, it is evident there is a difference between the parts of the cartilaginous septum, which will be involved in endochondral posterior and midseptal ossification and those which remain cartilaginous (anterior and anterior thin).
Prior to ossification the cartilage is characterised by a large cell profile. The mean cell profile area in the anterior region changes from 60 AU to 120 AU.Cell profile increases with a factor 2, whereas in the same period the cell density hardly changes. Assuming that no cells are lost by apoptosis, a 100% increase of the intercellular component may be concluded. Thus, the volume of cartilage also increases with a factor 2. As the size of the cartilaginous septum does not

alter after the age of 2 years, the expansion of the cartilage is balanced by loss of cartilage at the progressing front of ossification (Van Loosen et al., 1996).

At birth the mean profile area in the subperichondrial and central zone is the same for the anterior and anterior thin region. Cellular maturation of the central zone explains the later increased cell profile in the anterior region. A similar phenomenon is however to a lesser extent, observed in the anterior thin region. where the subperichondrial character of the cells prevail.

In the period between 10-35 years of age, both in the anterior and the anterior thin region the cell profile shows a gradual increase, the cell density a minimal decrease. It is interesting that the anterior and anterior thin region demonstrate permanent and consistent differences in cell profile and cell density. The thin area is characterised by smaller cells and less intercellular matrix in comparison to the anterior cartilage. This could relate to their different biomechanical function.
The anterior area is considered to contribute to the support of the nasal dorsum, in contrast to the anterior thin area, which has most probably no 'load bearing' function.

7.5 Conclusions

1. The results of this study demonstrate the dynamic nature of the cartilaginous septum during childhood. Increase in cell size, production of intercellular matrix and transformation into bone follow region-specific patterns. The growing cartilaginous septum demonstrates an obvious three-dimensional organisation in morphology and development. These biological features warn the surgeon not to treat the nasal septum in children as just a supporting element. Actually, better knowledge of the dynamic nature of the growing cartilage should improve surgical strategies.

2. With increase of age, interstitional growth due to increase of cell size and/or volume of intercellular substance shifts from mainly posterior to the more anterior parts.

3. No signs for adolescence growth spurt of the nasal septum were

observed, but cannot completely be excluded.

4. As the absolute size of the septal cartilage reaches its maximal size at the age of two, the later marked growth activity is most probably balanced by endochondral ossification, resulting in the formation of the perpendicular plate.

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8

Surgical Aspects of the Anatomy of the Vomer in Children and Adults.

8.1 Introduction

In most publications on septal surgery hardly any attention is paid to the exact anatomy of the vomer and certainly not to the developmental changes during childhood. Recently, Takahashi (1988) reviewed his anatomical studies of the (isolated) vomer of dried human skulls together with many other aspects of the septal development in various animal species.

The nasal septum is cartilaginous up to the 8th month of intra-uterine life. Peter (1913); Hillenbrand (1933) and Schultz-Coulon and Eckermeier (1976) described the development of the perpendicular plate by endochondral ossification. The first anlage of the vomer is a bilateral centre of desmal ossification just lateral to the basal rim of the septal cartilage (Fawcett, 1911). Both centres fuse on the inferior side to form a bony gutter. The inferior part of the vomer is the result of desmal ossification located between the mucous membranes lining both nasal fossae.

The perpendicular plate reaches the vomer between the 4th and 7th year after birth (Hillenbrand, 1933) but according to Schultz-Coulon and Eckermeier (1976), this may even occur after the age of 10 years. Thus, the most postero-inferior part of the cartilaginous septum ("sphenoid tail") is enclosed in a bony tunnel (vomerine tunnel) and will ultimately ossify in most individuals (Scott 1953; Melsen 1977).

Developmental variations at the junction of vomer and perpendicular plate are very common. A symmetrical development of the vomer is exception rather than rule. In case only one vomeral ala is formed, during surgery the cartilaginous sphenoid tail can be found extending along side the "vomeral bone", actually the other ala. Often this situation is combined with a spina vomeri.

To our knowledge reports describing the development of the nasal septum radiographically have not been published. In this paper a radiographic evaluation of the development of the vomer from birth to the age of 30 is presented. Additionally, a short comment will be given on the anatomical features of the vomer in skulls with facial clefts.

8.2 Material and methods

Postmortem specimens of the nasal septum of 22 Indian patients, with apparently normal facial structures, where examined radiographically. The specimens were collected in the Department of Pathology, Grant Medical Collega, Bombay, India (head: Prof. Dr. U.L. Wagholikar). The ages ranged from birth to 30 years. The specimens were obtained by block dissection and included the nasal septum, part of the hard palate, the cribriform plate and the sphenoid bone (van Loosen, 1988). Lateral radiographs were obtained on a mammography unit (Senograph 500t, film screen, 22 keV, 0.3 mm focus and magnification). Frontal CT-scans were made of a few specimens.

The skulls presented here are part of the collection of the Museum of Vrolik, Anatomical Institute, University of Amsterdam.

8.2.1 Observations in nasal septa

0-1 year of age; N= 4, (Figure 8.1, Figure 8.2).

In radiographs the cartilaginous septum shows no signs of ossification: a perpendicular plate has not yet been formed. The ala vomeris is well demonstrated. The zone of fusion of both alae, inferior to the basal rim of the cartilaginous septum, is demonstrated as a contrasting line (Figure 8.1F). The inferior part of the vomer has a triangular shape and extends between the superior line of the fused vomerine alae and the inferior palate; posteriorly it has a free edge at the level of the choana. The lower part of the vomer consists of a very thin bony plate between the mucosa on both sides.

1-10 years of age; N= 13, (Figure 8.3).

The earliest centre of endochondral ossification is seen annex the anterior skull base.

This primordium of the perpendicular plate enlarges gradually in antero-inferior direction as a result of replacement of cartilage by bone. The rim of the perpendicular plate always shows more contrast, because of a greater thickness compared to the central area.

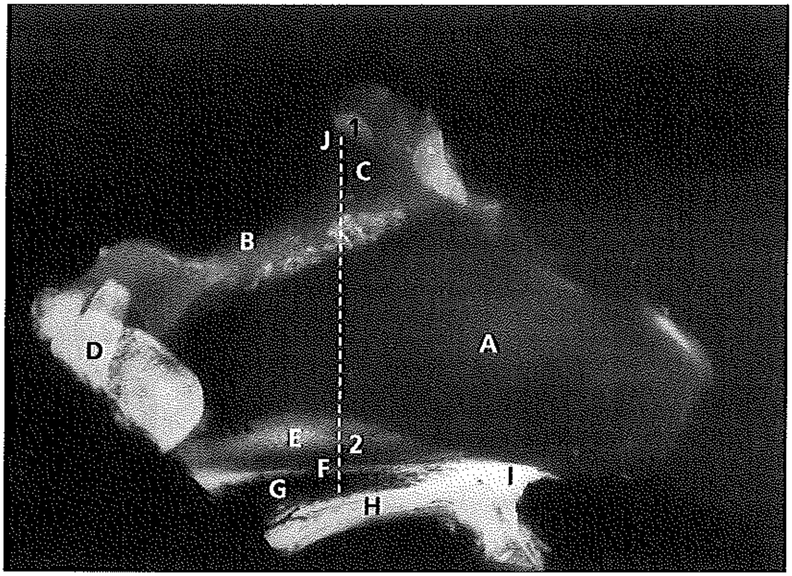

Figure 8.1 *Lateral X-ray picture of nasal septum, neonate. A= cartilaginous nasal septum, B=anterior skull base with overprojection of bony lateral ethmoid region, C=crista Galli, D=sphenoid bone, E=ala vomeris, F=fusion line of both alae vomeri, G=inferior part of vomer, H=palate, I=anteriornasal spine, J=level of frontal CT-scan (1-2) represented in CT picture (Figure 8.2).*

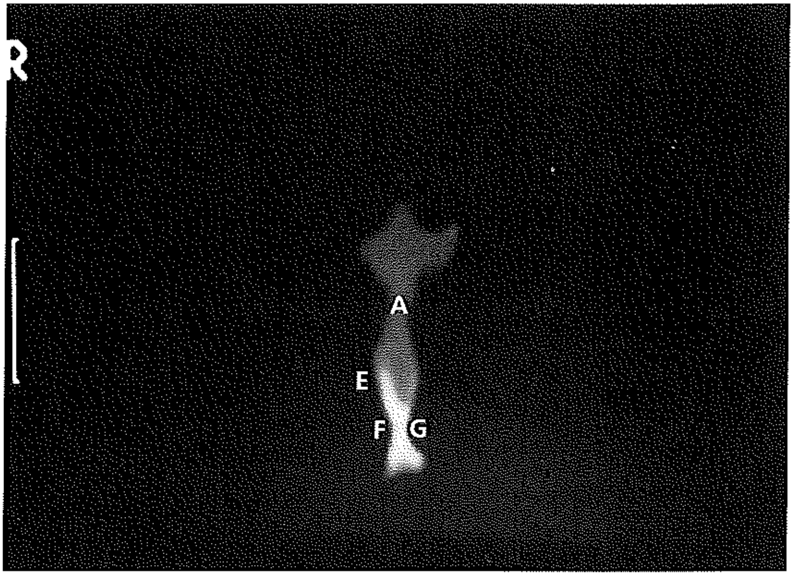

Figure 8.2 *CT-scan frontal plane (line A-B Figure 8.1) of nasal septum. A= cartilaginous nasal septum, E=ala vomeris, F=fusion of both alae vomeris, G=inferior part of vomer.*

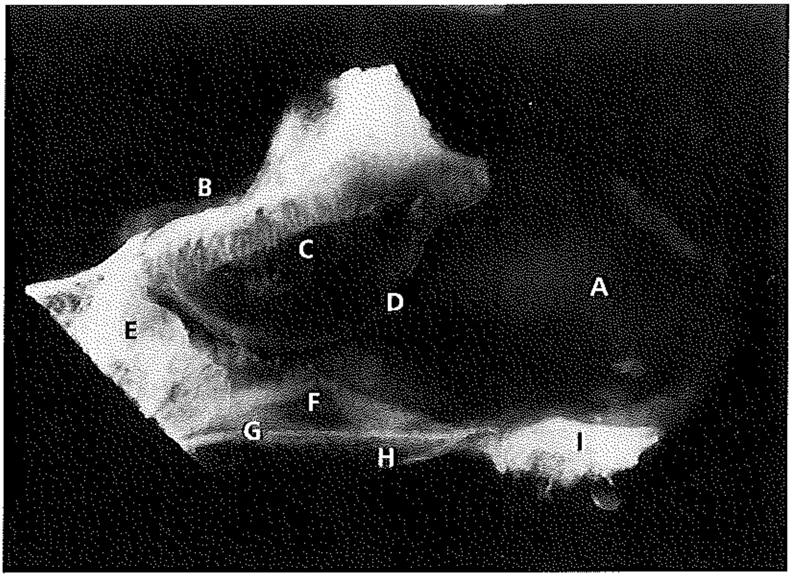

Figure 8.3 *Lateral X-ray picture of nasal septum, age 10 years. A= cartilaginous nasal septem, B=anterior skull base, C=perpendicular plate, ventral thin area. D=thickened rim of perpendicular plate, E=sphenoid bone, F=ala vomeris, G=fusion line of both alae vomeris, H=palate, I=maxilla with anterior nasal spine.*

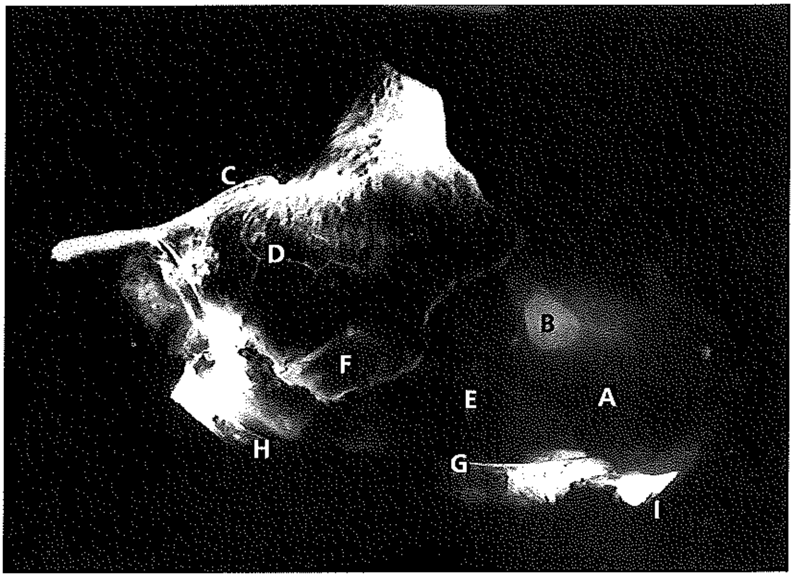

Figure 8.4 *Lateral X-ray picture of nasal septum, age 17 years. A= cartilaginous nasal septem, B=artefact, C=anterior skull base, D=perpendicular plate, E=ala vomeris, F=overlapping perpendicular plate and alae vomeris, G=line of fusion of alae vomeris, H=inferior part of vomer, I=anterior nasal spine.*

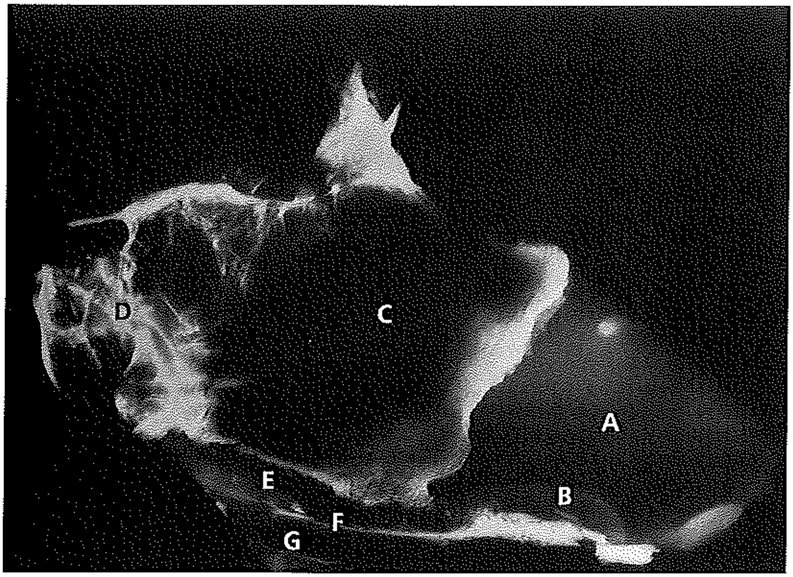

Figure 8.5 *Lateral X-ray picture of nasal septum, age 30 years. A= cartilaginous nasal septum, B=artefact, C=perpendicular plate, D=sphenoid bone, E=vomerine tunnel with sphenoid tail (?), F=line of fusion of alae vomeris, G=inferior part of the vomer.*

The age at which the perpendicular plate reaches the vomerine alae was found to be highly variable: in our material between 3 and 10 years after birth.

10-17 years of age.; N= 7, (Figure 8.4).

The progressive expansion of the median perpendicular plate and the extension in cranial direction of the bilateral vomeral ala results in an overlap.

17-30 years of age; N= 6, (Figure 8.5, tabel 4.1).

Even in this age group the enlargement of the perpendicular plate continues, whereas at the same time the cartilaginous nasal septum becomes proportionally smaller. The overlap between vomer and perpendicular plate can no longer be demonstrated, probably because of a bony integration of both structures. Between the thickened rim of the perpendicular plate and the line of fusion of both alae vomeris a remnant of the septal cartilage -the sphenoid tail- was often present in a vomerine tunnel as in the previous age group.

8.3 Discussion

With respect to the morphological development the vomer can be divided into two parts. First, the superior part, composed of the partly fused alae vomeris and secondly, the inferior part which is extending as far as the palate.

In animal experiments it was demonstrated (Poublon, 1987) that the position of the superior part of the vomerine gutter is determined by the cartilaginous septum, i.e. cartilage dominates bone (Verwoerd and Verwoerd-Verhoef, 1989). The morphology of the inferior part is probably further determined by the line of fusion of the palatal halves. This hypothesis could be tested by studying skulls with facial clefts. In these anomalies the relation between the basal rim of the septum is abnormal as a result of underdevelopment of one or both palatal halves.

Van Limborg (1964) described the development of the maxilla in a series of human skulls with facial clefts. It was possible to reinvestigate part of his material which today is still present in the museum Vrolik, but now with special interest in the nasal skeleton.

8.3.1 Observations in skulls with unilateral cleft of alveolus and palate

(Figure 8.6, 8.7, 8.8).

All the 4 adult skulls with this type of cleft showed identical features. The perpendicular plate is deviated to the cleft side and its basal rim is sharply bended in lateral direction. The ala vomeris on the cleft side has not developed. The imprint of a sphenoid tail in the remaining ala, although no cartilage remains present in these skulls, is evident and extending as far as the vomeral spine. Instead of vertical, the position of the inferior part of the vomer, deviated to the cleft side is almost horizontal. The transverse diameter of the floor of the nasal fossa looks extraordinary broad.

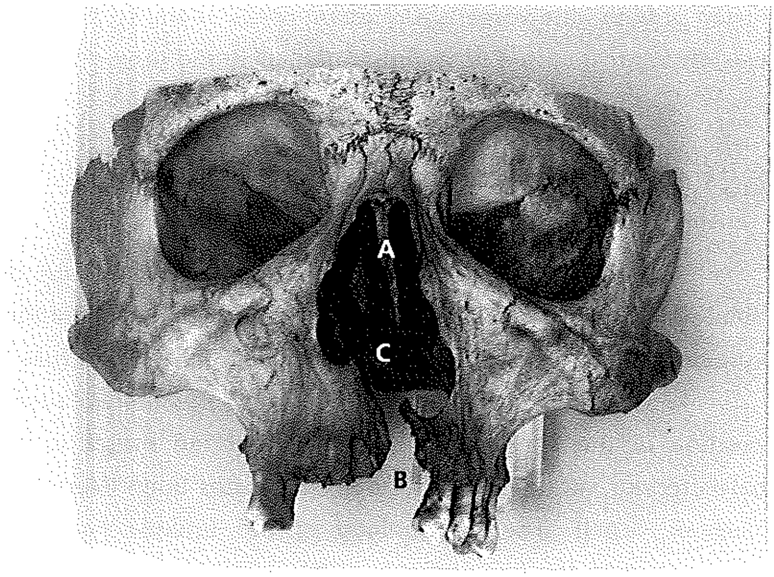

Figure 8.6 *Adult skull with left-sided cleft of alveolus and palate. Frontal view. A= perpendicular plate, diviated to the affected side, B=cleft in alveolus and palate, C=vomer: 'horizontal' position, broadening nasal floor*

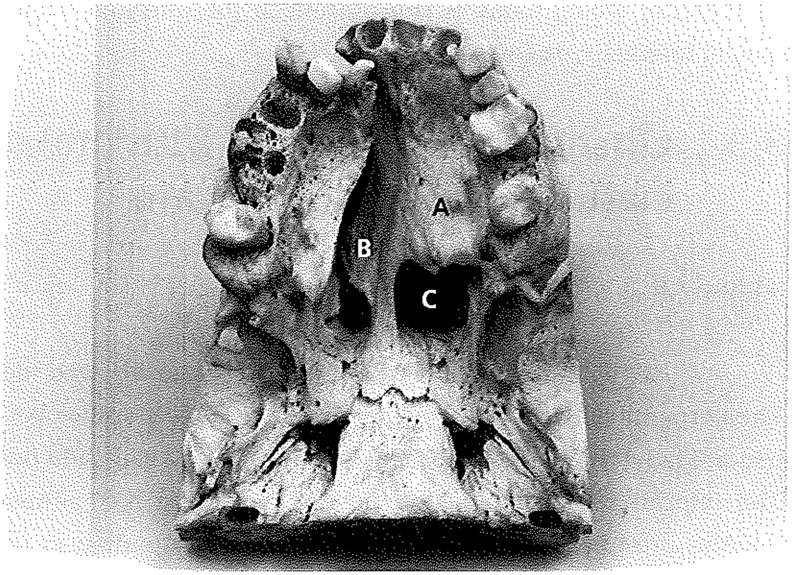

Figure 8.7 *Adult skull with right-sided cleft of alveolus and palate. Palatal view. A= cleft of alveolus and palate, B=vomer, connected to palatal half, C=choana*

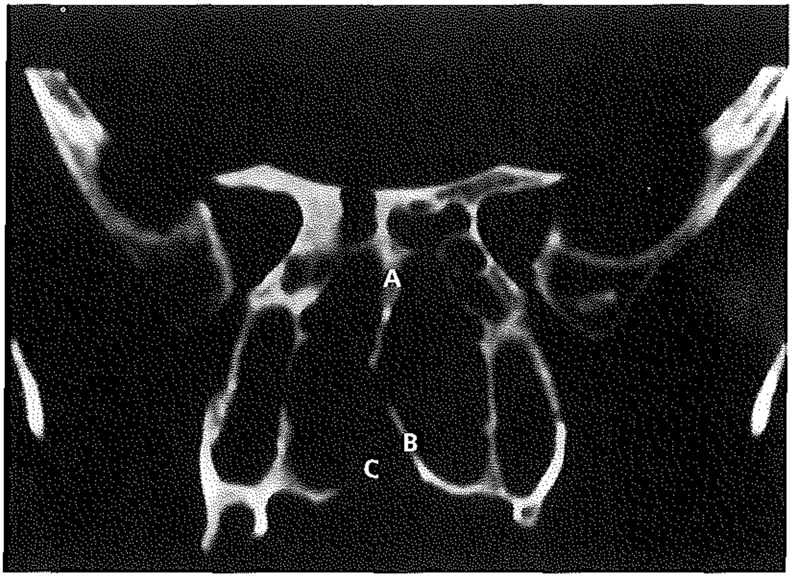

Figure 8.8 *Adult skull with unilateral right-sided cleft of alveolus and palate. CT-scan, frontal plane. A=perpendicular plate, B=vomer 'horizontal' position, broadening nasal floor, C=cleft*

This, however, is not the result of a broadening of the palatal part but caused by 'horizontalization' in this way contributory to the nasal floor of the inferior part of the vomer.

8.4 Conclusions

1. At birth the inferior part of the vomer is composed of an extremely thin plate of bone.
It may not be considered to support the cartilaginous nasal septum. It seems that resection of this part of the vomer will not interfere with later nasal development. Evaluating acquired or congenital deviations of the nose in infants, one should realise that the nasal septum is not firmly connected to the palate.
2. In skulls with unilateral clefts of alveolus and palate the vomer is malformed. The inferior part can assume an almost horizontal position and then, contribute

to the broadening of the nasal floor on the non-cleft side. Thus, planning a septal correction the anatomy of the nasal floor has also to be considered.

Acknowledgements

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9

Computed Tomography of the Human Developing Anterior Skull Base.

9.1 Introduction

Computed tomography (CT) is now widely used to investigate the abnormalities of the anterior skull base. However, little attention has been given to the different manifestations of the developing and ossifying anterior skull base and to problems in the interpretation of CT in the first years of life.

Parts of the anterior skull base are formed by membranous ossification of fibrous tissue, whereas the anlage of other medial parts is cartilaginous (Schaeffer, 1920; Mugnier, 1964; Hamilton, 1972) including the nasal septum and crista Galli (van Loosen and van Velzen, 1989). The replacement of this cartilage by bone is not complete at birth and continues during childhood. The whole of the complex, consisting of the nasal septum, crista Galli, lamina cribrosa (cribriform plate) and lateral ethmoids, initially develops as a cartilaginous structure (Fawcett, 1911; De Beer, 1937; Scott, 1953). In the neonate the nasal septum is still cartilaginous (van Loosen et al, 1988) and the upper lateral cartilages extend into the anterior base of the skull (Poublon et al., 1990). During further development of the infant, between the first and sixth year of life, ossification of the lamina cribrosa begins by fusion of the ossifying nasal septum and the lateral ethmoid (Scott, 1953; Ford, 1958; Krimpotic-Nemanic, 1977; Fairbanks, 1983).

This study was carried out to evaluate the CT pattern of ossifying structures in humans.

9.2 Materials and Methods

9.2.1 Fetal material

16 human fetuses, referred to our laboratory for pathological examination after spontaneous abortion, evenly distributed between 18 and 32 weeks gestational age were studied after routine fixation in 0.1 M phosphate-buffered formaldehyde 4%, pH 7.4.

9.2.2 Infant material

Midfacial CT images were available in 3 children, (1, 2 and 6 years of age respectively), who had been assessed for neurological symptoms.
The midfacial block specimen from the youngest child was also available for histology.

9.2.3 Computed Tomography

CT of all fetal skulls was performed in coronal sections using a Philips Tomoscan 350 with contiguous 1.5 mm slices.

In children only those CT scans were used, which were primarily acquired in a coronal plane with identical slice thickness and spacing, to avoid differences in resolution due to the method of data-acquisition.

9.2.4 Magnetic Resonance Imaging (MRI)

For the documentation of the non-osseous cartilaginous structures, 6 representative fetal skulls were available. They were analysed in a previous collaborative study using MRI (Dyna scan, 4.2 Tesla MRI Zentralforschungs Institut, CIBA-GEIGY Basel), in the same plane (van Loosen and van Velzen, 1989; Allegrini et al, 1990).

9.2.5 Tissue processing and histology

All midfacial blocks were decalcified and embedded in paraffin. 5 mu semiserial sections were cut in a frontal plane and stained with combined Alcian Blue / PAS Stain.

9.3 Results

9.3.1 Fetal age group

In all stages histological analysis demonstrated that the medial part (nasal septum) of the anterior skullbase was fully cartilaginous, whereas the greater lateral part of the anterior skullbase consisted of bone (Figure 9.1).

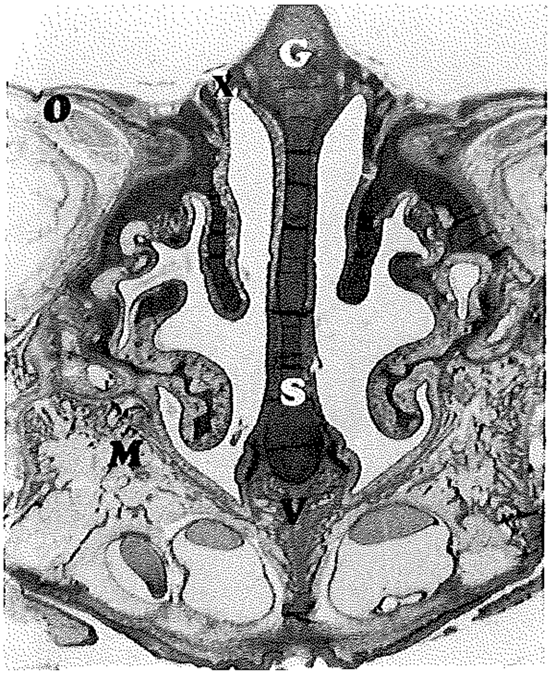

Figure 9.1 *Photomicrograph of a histological frontal section of a 28-week-old fetus. X: Lamina cribrosa, G: Crista Galli, S: Nasal septum, W: Lateral wall, V: Vomer, O: Orbital roof, M: Maxilla. (5 mum. paraffin section, Alcian Blue / PAS stain).*

MRI showed the early cartilage as an intermediate signal layer between the cerebral hemispheres and the mucosa lining on both sides of the nasal cavities (Figure 9.2).

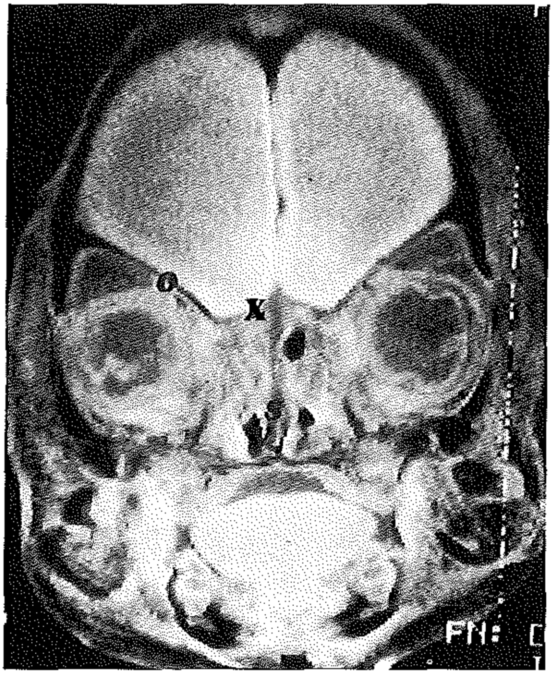

Figure 9.2 *MRI of the same 28-week-old human fetus as in Fig. 9.1. Fixed 0,1 M, phosphate buffered formaldehyde, pH 7,4. X: Lamina cribrosa, S: Nasal septum, V: Vomer, O: Orbital roof. Note the cartilaginous (intermediate) continuity of the lamina cribrosa where a "defect" is given in the CT-scan image. Here the nasal fossa is partly filled with meconium and fixation fluid, which has been removed in the histological section in Fig. 9.1. (Dyna scan, CIBA-GEIGY, Zentralforschungs Instituut, Basel, 4.2. Tesla, section thickness 2 mm, T2 weighted image, TR: 2560 ms, TE: 60ms)*

On the other hand, CT showed no density difference between the cartilage and the soft tissues. This resulted in a defect-like discontinuity in the medial part of the anterior skull base (Figure 9.3).

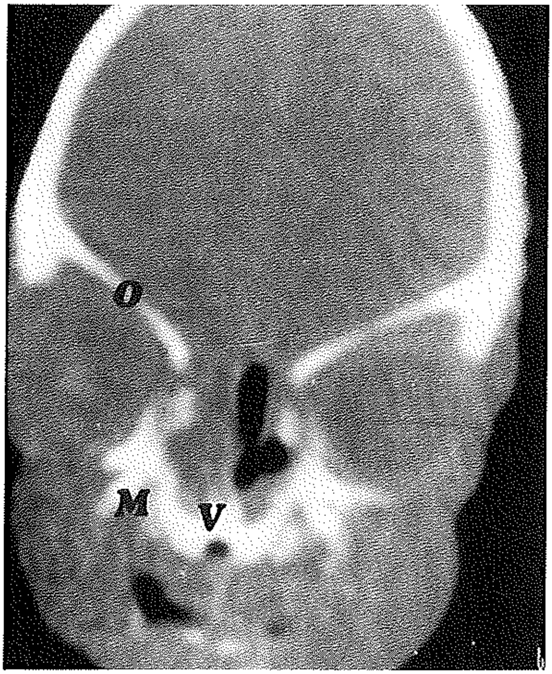

Figure 9.3. *Coronal CT-scan of the human fetus of Fig. 9.1 and 2. Fixed in 0,1 M, phosphate buffered formaldehyde, pH 7.4. V: Vomer, M: Maxilla, O: Orbital roof. Note the "defect" in the base of the skull in the anterior fossa. The right nasal fossa is filled with meconium. (Philips Tomoscan 350, section thickness 1,5 mm)*

9.3.2 Postnatal age group

A "defect" as described above is still present on CT of the anterior skull base in a 1-year-old and 2-year-old (Figure 9.4) infant. It was not observed on CT of a 6 year old child (Figure 9.5).

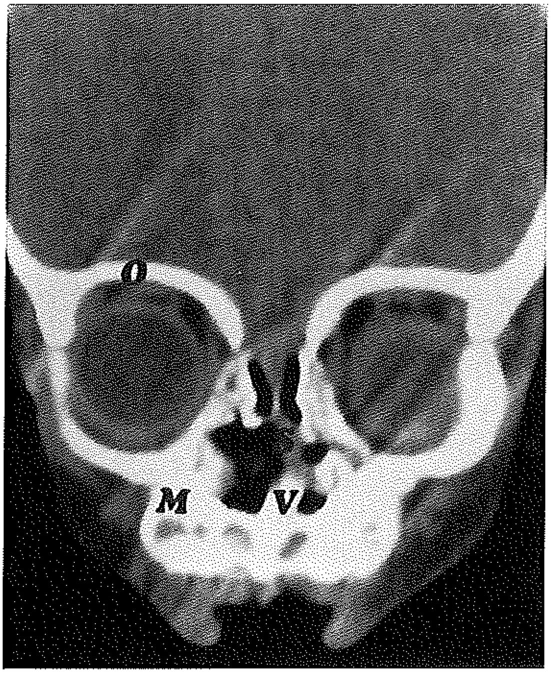

Figure 9.4 *CT of a 2-year-old infant. S: Nasal septum (deviated), V: Vomer, M: Maxilla, O: Orbital roof. Note persistent "defect" in lamina cribrosa. (Philips Tomoscan 350, section thickness 1,5 mm*

Histological analysis of the base of the skull of the 1-year-old child showed the medial part of the anterior skull base still to be cartilaginous without the presence of any structural defect.

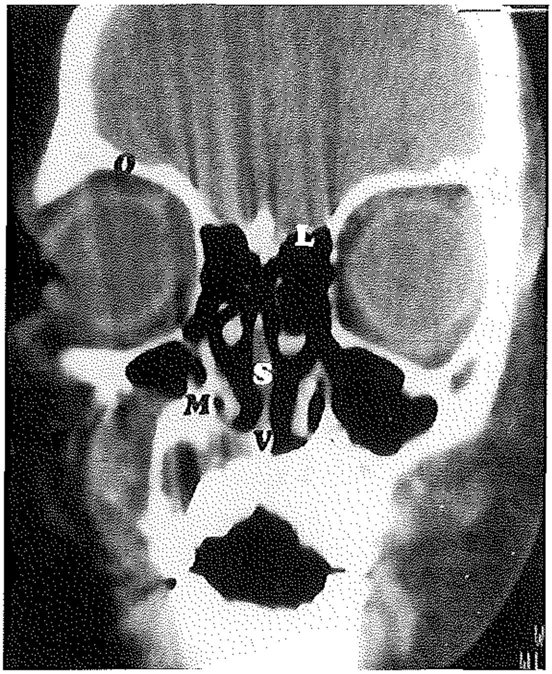

Figure 9.5 *CT of a 6 year old infant. L: Bony lamina cribrosa, S: Nasal septum, V: Vomer, M: Maxilla, O: Orbital roof Note osseous continuity of base of the skull. (Philips Tomoscan 350, section thickness 1,5 mm)*

9.4 Discussion

During the first years of life the observations show that CT does not represent the true nature of structures in the anterior base of the skull. The images obtained are easily misinterpreted and the false assumption made of a "defect" where actually a cartilaginous continuity is present. Prior to reconstructive surgery of congenital and anatomical or posttraumatic defects, additional investigations are necessary for proper evaluation. Perhaps MRI, considering its capability for demonstrating cartilage and soft tissues, will become a better modality method of supplying this additional information, especially as it collects and displays its data in very comparable modes.

The finding that the ossification of the lamina cribrosa in this, albeit limited, material takes places between the second and sixth year of life, has not been reported before. Detailed studies of the process of ossification of the different contributing components of the base of the skull are warranted.

9.5 Acknowledgements

The authors are indebted to Dr. P.R. Allegrini and Dr. G.R. Bullock (Zentralforschungs Institut, CIBA-Geigy Basel) for the use of MRI scan findings derived from a previous collaborative study reported on separately (Allegrini et al, 1990) and to Dr. H.L. Verwoerd-Verhoef for her suggestions.

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10

Summary and Concluding Remarks.

The introduction of this thesis (chapter 1) culminated in three questions with respect to anatomical and surgical aspects of growth and development of the cartilaginous human nasal septum:

I. What changes do occur in the human nasal septum during the peri- and postnatal period, specifically with regard to a) the anatomy, and b) the dimensions of the various anatomical components?

II. What are the consequences of the recorded characteristics for possible vulnerability of the cartilaginous septal structures as they relate to trauma or surgical interventions which involve the nasal septum?

III. What are the possible consequences of the described anatomy for the application and interpretation of diagnostic imaging assessment of the naso-frontal region in the growing child?

After survey of the literature (chapter 2) these questions were addressed by detailed studies into the dimensional and microscopical development of the various septal components in a combined approach consisting of:

1. an anatomical and histological study of the neonatal nasal septum.
2. a quantitative study of the sagittal dimensions of the human nasal septum during postnatal growth.
3. a study of the regional variations in nasal septum thickness by a 3-dimensional reconstruction for the postnatal period.
4. a study of the implication of variations in thickness, demonstrated in a facial trauma case of a 4-year-old boy.
5. a quantitative study of septal cartilage growth in the postnatal period, assessed by automated computer-assisted image analysis.
6. an anatomical and radiological study of the ossifying nasal septum and vomer in children and adults.
7. a CT-study of the anterior skull-base (cribriform region) and its consequences for diagnostic imaging.

The results and conclusions of the various chapters will be summarised and briefly discussed.

The nasal septum in the neonate (chapter 3)

In most textbooks of anatomy the nasal septum is described to consist of

three parts: the cartilaginous septum and two ossified components, the perpendicular plate and the vomer. In the neonate, the perpendicular plate has not yet been formed and except for a vomer 'anlage' of small dimensions, the septum is a cartilaginous structure, reaching from columella to anterior skull base and sphenoid. As was demonstrated for the first time in the present study, the neonatal septum has a 3-dimensional architecture, characterized by a specific pattern of regional differences in thickness and histological appearance. The thinnest cartilage (400 micron) is found in the central-anterior area. The thickest zones (3500 micron) are observed posteriorly, between sphenoid and nasal dorsum, and inferiorly as a thickened basal rim from sphenoid to the anterior nasal spine of the (pre)maxilla. These observations are in striking contrast to the definition of the septum as one uniform plate of cartilage, as reported by Delaire and Precious (1987).
The newly established anatomical features in the human are similar to those earlier described for young rabbits (Tonneyck-Müller et al, 1982; Verwoerd et al, 1989). To our knowledge data on other species are not available. Postnatal development of the nasal septum comprises growth of the cartilage in sagittal dimensions and partial ossification of the posterior part.

Postnatal growth of the cartilaginous nasal septum and the perpendicular plate (chapter 4)

The sagittal dimensions of the nasal septum increase rapidly as of birth to the end of the second year of life. Continuous deceleration of the growth rate results in a plateau for final size, which is reached around the age of 40. An unexpected finding was that the cartilaginous component has already reached its final size at the age of 2 years. Subsequent growth of the septum is mainly due to the increasing dimensions of the bony component, the perpendicular plate. Persistent growth of septal cartilage is balanced by simultaneous loss of cartilage at the zone of advancing ossification. This confirms and supplements the report of Schultz-Coulon and Eckermeier (1976) describing the process of endochondral ossification at the sphenoid rostrum in children from 0-10 years of age.

An adolescence-related growth spurt could not be demonstrated in this study of the human nasal septum. This seems in contrast to the manifest changes of the outer contour of the nose which can be observed during puberty. The facial profile in that period is characterised by an increasing prominence and the lengthening of the nasal dorsum, and a decrease in nasolabial angle. To explain the apparent difference between the dimensional increase of the nasal septum and the development of the facial profile, the following items should be considered:

1. Small variations in growth rate, as demonstrated in longitudinal cephalometric studies may not be detected in a transversal study, like the present one.

2. The puberty-related changes in facial profile might be ascribed to a dissociation between growth of the maxillary area and the nose. In a separate study (van Loosen et al, 1997) it was demonstrated that height and length of the nose chamber as demarcated by the skeletal borders, hardly undergo any changes after puberty whereas the nasal septum continues to grow for several years although at a decreasing growth rate. The subsequent change of facial profile consequently occurs in a relatively short period, mimicking an adolescent growth spurt of the nose.

In our view the combined structure of the perpendicular plate-cartilaginous septum can be seen as a one-sided synchondrosis, with replacement of cartilage by bone. Consequently, a posterior chondrotomy would cause a dissociation of the septal cartilage from the perpendicular plate, at the septo-ethmoidal junction, which bears the risk of growth disturbances and loss of support of the nasal dorsum. Although Potsic et al. (1997) advocate to renounce septoplasty in children younger than 4 to 5 years of age, the vertical incisions these authors advise to perform after that age, still have the disadvantage of injuring the septo-ethmoidal junction.

In our opinion surgical trauma to this junction which contributes to the sagittal enlargement of the nose should be avoided until after puberty.

Postnatal evolution of the regional variations of the cartilaginous nasal septum (chapter 5)

By 3-dimensional reconstruction, based on histological sections, the regional variations of the thickness of the human nasal septum were studied in 8 complete nasal septa, varying between 0 and 42 years of age. Except for ossification of the posterior part of the cartilaginous nasal septum, the pattern of thinner and thicker areas as found in the neonate remains unaltered and is equally observed in adult specimens. This phenomenon has not yet been described in man, although it can be accidentally observed in some illustrations in former publications (McNamara, 1977; Lang, 1989). The endochondral ossification starts in the first year after birth and will result in a gradual replacement of the thickest posterior segment of the cartilaginous septum by a thin perpendicular plate. Consequently, the maximal transverse diameter of the cartilaginous septum is gradually reduced from 3500 micron in the neonate to 2500 micron in older children. As a result of formation of the perpendicular plate, the support of the sphenodorsal zone of thick cartilage shifts from the sphenoid to the equally thickened caudal edge of the perpendicular plate.

The anatomy of the nasal septum, not only in the neonate but also at a later age shows similarities between man and rabbit. In the latter species, a similar persistence of the 3-dimensional organisation of the septal cartilage from birth up to adulthood has been previously described (Verwoerd et al., 1989). The role of various parts of the nasal septum in the rabbit has been analysed in animal experiments (Mastenbroek 1978, Tonneck-Müller, 1982; Nolst Trenité 1984, Nijdam 1985; Poublon 1987; Meeuwis 1988). The sphenodorsal – later ethmoidodorsal – zone of thick cartilage is supporting the nasal dorsum. Growth in this area is held responsible for the increasing prominence and lengthening of the nasal dorsum. The thick basal rim (sphenospinal zone) is supposed to contribute to the forward outgrowth of the maxilla and, in particular, the position of the anterior nasal spine. Loss of septal cartilage, in most cases due to a septal abcess involving both sphenodorsal and sphenospinal zones, would lead to an underdevelopment of nose and upper jaw, as often is observed after a nasal trauma in infancy. When only the sphenospinal zone is traumatised, retroposition of the anterior nasal spine will occur. Since the columellar cartilage is fixed to the anterior nasal spine, retroposition of the latter will lead to a lowering of the distal part of the nasal dorsum. The developmental (and mechanical) function of the thinnest part of the septum is thought to be modest. It is conceivable, therefore, that children with a perforation of the thinnest part of the nasal septum show a normal development of the nose.

As illustrated above, the specific morphogenetic role of various parts of the septal cartilage can explain the thus far not understood observation of various types of facial (mal)development occurring after traumatic loss of septal cartilage. Although differing opinions are put forward in publications about the relationship between septal perforation and nasal development (Pirsig, 1992), it is evident that a perforation will affect nasal growth depending on the exact localisation of the defect in the septum, or not.

Post-mortem study of the fractured septum in a 4-year-old child (chapter 6)

The fracture in this patient involved both the cartilaginous septum and the perpendicular plate.

The fracture line can be characterized as a "C". The vertical part is situated in the thin central area of the perpendicular plate. The inferior extension crosses the septo-ethmoidal junction and follows the thinner zone of septal cartilage just superior to the thickened basal rim. The superior extension of the -C- also crosses the anterior edge of the perpendicular plate and runs into the thinner zone just under the nasal dorsum. Our observation is in contrast with the recent publication of Shapiro (1996) in which he stated that -C-shaped fractures, common in adults, do not exist in children. Harrison (1979) was the first to describe the C-shaped septal fracture in adults without giving any biological explanation. Actually, we demonstrated that the C-shape fracture line tends to follow the thinnest, most vulnerable, parts of the septum.

Developmental aspects of septal deviations (chapter 5 and 6)

The regional differences in thickness of the human nasal septum can also help to understand the preferred sites of septal deviations, as they were described by Mladina (Mladina, 1987; Mladina and Krajina, 1989). Their observations were confirmed by Gi-Min et al. (1995) in a nationwide survey in Korea, including more than 9000 persons, on the prevalence and risks of septal deformities. Both authors considered most deviations to develop after trauma in early childhood, but were not aware of the regional differences in the structure of the nasal septum. The preference of septal deviations and angulations for the anterior site, as reported by Mladina (category 1 and 2), seems to coincide with the thinner parts of the nasal septum, as recorded in our study.. The fracture pattern as described in chapter 6, would develop in more complex types of septal deviations involving both the cartilaginous and bony septum, like the types 3 – 7 as classified by Mladina (1987, 1989).

It may be assumed that the thinner areas of the septum are less resistent to mechanical forces and tend to fracture more easily. Mapping of thinner and thicker areas (with different elasticity and plasticity modus) contribute to understanding some mechanical aspects of nasal fracturing due to external trauma in childhood.

Interstitial growth of nasal septal cartilage (chapter 7)

The interstitial growth of the nasal septal cartilage expressed in the mean cell profile area and the mean cell profile density was studied for 4 different areas and 2 different locations, using an automated Computer Assisted Image Analysis Technique. The results for the posterior, middle, anterior and anterior thin area in central and subperichondrial regions were plotted against age.

It was demonstrated that the cartilaginous part of the human nasal septum has a specific 3-dimensional organization with regard to local differences of cell size and the proportionate amount of intercellular matrix in relation to location within the septum. These data are in agreement with histochemical studies of Vetter et al. (1983, 1984a, b), who demonstrated that the human nasal cartilage is built up from different areas displaying partial age dependency, strict local distribution and predominance of either matrix synthesis or cell replication and proliferative activity. The latter studies, however, do not differentiate between subperichondrial and central parts of the septum, and give no specific definition of the exact location (Pirsig, 1986).

The quantative histometric approach of our study images the complete cartilaginous septum, and revealed that from birth till its endochondral ossification at the age of 4 years, the posterior region demonstrates no changes in cell size nor cell cell density. It can be concluded that the cartilage in the posterior area shows no signs of interstitial growth until it becomes ossified around 4 years of age. In the midseptal zone there is a rapid increase of cell profile area for both locations, central and subperichondrial, till the age of 2 years. The cell density decreases linear and rapidly till the age of 10 years: the time of endochondral ossification of central and subperichondrial regions in that area. In conclusion, the interstitial growth in the midseptal area is fast and continues until the ossification process encroaches the cartilage. In the anterior part of the septum, the cell profile area in central as well as subperichondrial region enlarges

gradually but over a long period, at least far into adulthood. Simultaneously, the cell density shows a marked decrease, indicating a continuous production of intercellular substance.
Interstitial growth of the septal cartilage up to the adult age can play an important role in the formation of angulation or overlap of septal fragments after traumatic fracturing, and can explain the increase in dimensions of these septal anomalies, even in adult patients.

Developmental anomalies of the vomer (chapter 8)

During rhinosurgery, malformations of the septovomeral junction and the ethmoidovomeral junction are often observed. X-ray pictures (lateral projection) of nasal septum specimens from ages between 0 and 42 years have brought new information about the occurrence of anatomical variations. The anlage of the vomer is complex. The inferior part is a plate consisting of a existing of bony lamella between the basal rim of the septal cartilage and the superior surface of the palate. In the neonate, the bone of the inferior part is so fragile that it is possible to mobilize the palate versus the cartilaginous septum of the nose. The superior part of the vomer is formed by ossification on both sides of the basal rim of the septal cartilage (vomer wings). Superior and inferior parts together form a Y-shaped bony gutter enclosing the cartilaginous rim. The junction between perpendicular plate and vomer frequently shows anatomical variations. The ossifying front of the perpendicular plate can reach the bottom of the vomeral groove or save a strip of cartilage between the vomeral wings. These wings often develop asymmetrically. A local deviation of the basal rim of the septum to one side, in combination with underdevelopment of the vomeral wing on the same side, is a common finding. Such a spina vomeris is in most cases accompanied by a persistent posterior part of the septal cartilage, the sphenoid tail. Then the sphenoid tail extends in posterior direction, along the unilaterally formed vomeral wing.

In patients with a unilateral cleft of alveolus and palate, the nasal floor on the non-cleft side is malformed. In these cases the basal rim of the septal cartilage and the perpendicular plate are deviated to the cleft side. At the same time, the inferior part of the vomer extending from the palatal half on the non-cleft side to the deviated basal rim of the septum, shifts into an almost horizontal position, thereby broadening the nasal floor on the non-cleft side. The consequence is an angle between the inferior part of the vomer and the superior part, which is fused with the perpendicular plate.

Ossification of the anterior skull base (chapter 9)

In the neonate the skeleton of the nose and the middle part of the anterior skull base from one cartilaginous complex. In particular, the cribriform plate area has been studied by computed tomography (CT) and histopathology. It was demonstrated that at a young age also the anterior paramedian skull base still is completely cartilaginous. Ossification of this structure takes place between the second and the sixth year of life. During the first years of life, the cartilaginous preformation of the anterior skull base creates a "pseudo defect" on CT in the coronal plane. Early presence of ossified segments in the cribriform area, as reported by Bosma (1986), could not be identified.

In a recent publication on the maturation processes of the skull base and midface, Naidich et al., (1996) suggest that in a small part of the population, ossification may commence very early after birth. In other individuals ossification may not be complete even as late as the sixth year of life. From the reviewed literature, it is not always clear whether the CT- sampling is sufficiently representative. A considerable variability seems to, or at least may, exist concerning this segment of the base of the skull. The introduction of MRI, providing sufficient resolution through the efficient use of T1 and T2 weighted images, produced an opportunity for high contrast representation of cartilaginous structures. Furthermore, it even allows for functional assessment of cartilage through its principal ability to differentiate between proliferating and resting e.g. immature and mature cartilage due to the differences in water-binding properties of the more or less sulphated glycosaminoglycans of the matrix (Allegrini et al., 1990).

In contrast to CT-scanning, the representation of the soft/bony tissue-to-air interface remains a problem in MRI (Zinreich et al., 1996). Nevertheless, this imaging technique seems for now to be the essential replenishment of diagnostic imaging for the anterior skull base, in the first years of life.

Conclusion

The last decades brought an innovation of nasal surgery in adult patients. New instruments were introduced, new surgical methods were defined, based on better understanding of the anatomy. This study has demonstrated that the morphology of the nose in children is different, and has stressed the dynamic nature of the cartilaginous nasal skeleton during postnatal growth. In view of the potential benefits of modern surgical interventions further exploration of the mechanisms in development and wound healing of cartilage remains a challenge.

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11

Samenvatting en Conclusies.

In de laatste twee decennia is vooral door de Rotterdamse Pediatrische KNO Groep experimenteel onderzoek gedaan naar de postnatale groei van de neus en de invloed daarop van beschadiging of defecten van het kraakbenige neustussenschot. Hierbij bleek dat chirurgische of traumatische interventies aan het neustussenschot specifieke stoornissen kunnen geven van de uitgroei van neus en soms ook van bovenkaak en orbita.

Als men poogt de resultaten van deze experimenten te extrapoleren naar de mens blijkt dat in de literatuur bijzonder weinig bekend is over het nog snel groeiende neustussenschot op de kinderleeftijd.

Deze constatering heeft geleid tot drie vragen (Hoofdstuk 1):

I. Welke ontwikkelingen vinden in het humane neustussenschot plaats gedurende de postnatale periode met betrekking tot:

a. de anatomie

b. de ontwikkeling van de verschillende delen (lamina perpendicularis, kraakbenige neustussenschot en vomer)?

II. Welke zijn de mogelijke consequenties van deze ontwikkelingen voor de eventuele vulnerabiliteit van het neustussenschot in relatie tot trauma en chirurgische interventies?

III. Welke consequenties heeft deze anatomische ontwikkeling voor de interpretatie bij beeldvormende diagnostiek van de nasofrontale regio in het jonge kind?

Na een literatuurstudie (Hoofdstuk 2) werden deze vragen beantwoord door macroscopisch en microscopisch onderzoek naar de ontwikkeling van de verschillende componenten van het humane neusseptum.

Dit onderzoek bestaat uit de volgende onderdelen:

1. Een anatomische en histologische studie van het neonatale neustussenschot (Hoofdstuk 3).

2. Een kwantitatieve studie van de groei van het humane neustussenschot gedurende de postnatale periode (Hoofdstuk 4).

3. Een studie van de regionale dikteverschillen in het humane neustussenschot met behulp van een 3-dimensionale reconstructie (Hoofdstuk 5).

4. De consequenties van deze dikteverschillen met betrekking tot fracturen in het humane neustussenschot aan de hand van de beschrijving van het aangezichtsletsel bij een 4-jarig kind (Hoofdstuk 6).

5. Een kwantitatieve studie naar de interstitiële groei van het kraakbenig neustussenschot (Hoofdstuk 7).

6. Een anatomische en radiologische studie van het neustussenschot en vomer bij kinderen en volwassenen (Hoofdstuk 8).

7. Een morfologische studie van ontwikkelingen in de voorste schedelgroeve en de consequenties voor de beeldvormende diagnostiek (Hoofdstuk 9).

De resultaten en de conclusies van de verschillende hoofdstukken worden samengevat en kort bediscussiëerd.

Het neustussenschot van de pasgeborene (Hoofdstuk 3)

In de meeste anatomische leerboeken wordt het neustussenschot beschreven als bestaande uit een kraakbenig deel en twee benige componenten, de lamina perpendicularis en het vomer. Bij de pasgeborene is de lamina perpendicularis nog niet, en het vomer nauwelijks gevormd.
Het neustussenschot is vrijwel geheel kraakbenig en reikt van columella tot voorste schedelgroeve en sphenoid.

In dit onderzoek wordt voor het eerst aangetoond dat het neustussenschot van de pasgeborene een specifieke 3-dimensionale opbouw heeft, gekarakteriseerd door een patroon van regionale dikteverschillen en histologische beelden. Het dunste kraakbeen (400 micron) bevindt zich in het anterieure deel van het septum. De dikste gebieden (3500 micron) worden aangetroffen posterieur tussen het sphenoid en het neusdorsum en inferieur als een verdikte

kraakbenige zone verlopend van het sphenoid naar de spina nasalis anterior van de maxilla.
Deze waarnemingen zijn in tegenspraak met een eerdere publicatie waarin het neustussenschot wordt beschreven als een structuur zonder dikteverschillen (Delaire and Precious, 1987).

Een vergelijkbare bouw van het neustussenschot werd eerder beschreven voor het jonge konijn (Tonneijk-Müller et al, 1982; Verwoerd et al, 1989).
Voor zover ons bekend zijn er geen gegevens van deze aard bij andere diersoorten beschikbaar.

Postnatale groei van het kraakbenige neustussenschot en de lamina perpendicularis (Hoofdstuk 4)

Het neustussenschot neemt in lengte en hoogte zeer snel toe vanaf de geboorte tot aan het einde van het tweede levensjaar. Hierna resulteert een aanvankelijk snel en later geleidelijk afnemende groeisnelheid uiteindelijk in een "plateau" waarbij de maximale omvang in het mediane vlak is bereikt rond het 40e levensjaar. Een onverwachte bevinding is dat het cartilagineuze deel reeds op 2-jarige leeftijd zijn maximale omvang heeft. Hieruit valt te concluderen dat de groei van het totale septum (exclusief het onderste deel van het vomer) na deze periode is toe te schrijven aan uitbreiding van de benige lamina perpendicularis als gevolg van doorgaande enchondrale verbening van het neustussenschot.
Het daarmee gepaard gaande verlies van kraakbeen wordt kennelijk gecompenseerd door groei elders in het kraakbenige septum. De bevindingen in dit onderzoek bevestigen en vullen het onderzoek van Schultz-Coulon en Eckermeier (1976) aan, die het proces van enchondrale verbening ter plaatse van het sphenoid beschreven bij kinderen jonger dan 10 jaar.

Door een posterieure chondrotomie zoals toegepast wordt in de septumchirurgie worden het septale kraakbeen en de lamina perpendicularis van elkaar gescheiden, met als risico dat het verbeningsproces en hiermee de groei en de ondersteuning van het neusdorsum worden verstoord. Dit risico is niet

beperkt tot kinderen beneden de leeftijd van 4 tot 5 jaar zoals Potsic et al (1997) aannemen.
Naar onze mening dient chirurgie van deze regio welke bijdraagt tot de uitgroei van de neus bij, voorkeur vermeden te worden tot na de puberteit.

Aanwijzingen voor een puberteitsgroeispurt werden in deze studie voor het humane neustussenschot niet gevonden. Dit kan verklaard worden doordat kleine variaties in groeisnelheid, zoals in sommige longitudinale studies waargenomen, in een transversale studie zoals deze niet aangetoond kunnen worden. Het niet vaststellen van een puberteitsgroeispurt lijkt ook in tegenspraak met de verandering van het profiel van het aangezicht en de neus in het bijzonder, die kan worden waargenomen tijdens en na de puberteit. Wat de neus betreft gaat het dan om toename van de lengte van de neusrug en de hoogte van de neus ten opzichte van de bovenkaak en tenslotte om een verkleining van de nasolabiale hoek.
Deze veranderingen van het aangezichtsprofiel behoeven niet per se op een groeispurt van de neus te wijzen, maar zouden ook kunnen worden toegeschreven aan een verschil in groeisnelheid tussen het maxillaire gebied en het neustussenschot tijdens deze periode.

In een separate studie (Van Loosen et al, 1997) werd aangetoond dat de hoogte en lengte van de benige neuskamer nauwelijks enige veranderingen tijdens en na de puberteit ondergaan, terwijl het neustussenschot (en de neus) dan nog een aantal jaren, zij het met afnemende snelheid, doorgroeit. Dit kan verantwoordelijk zijn voor een ogenschijnlijke puberteitsgroeispurt van de neus.

Postnatale ontwikkeling van regionale dikteverschillen van het kraakbenige neustussenschot (Hoofdstuk 5)

Door middel van 3-dimensionale reconstructies gebaseerd op histologische coupes werden de regionale dikteverschillen bestudeerd in 8 humane neustus- senschotten, variërend in leeftijd van 0 tot 42 jaar. Afgezien van het verlies van het posterieure gedeelte van het kraakbenige neustussenschot als gevolg van verbening blijven de dikke en dunne gebieden, zoals deze werden

gevonden bij de pasgeborene (Hoofdstuk 3), tot op de volwassen leeftijd aanwezig. Dit is – merkwaardig genoeg – niet eerder bij de mens beschreven. Toch kan dit fenomeen in enkele illustraties van eerdere publicaties duidelijk worden herkend (McNamara, 1977; Lang, 1989).
De enchondrale verbening van het kraakbenige neustussenschot start gedurende het eerste levensjaar met als resultaat dat het dikste posterieur gelegen kraakbeen wordt vervangen door de benige lamina perpendicularis.
Zodoende wordt de maximale dikte van het overblijvende septale kraakbeen gereduceerd van 3500 micron bij de pasgeborene tot 2500 micron bij oudere kinderen. Het dikke kraakbeen wordt nog steeds gevonden in de twee eerder beschreven zones: (1) tussen sphenoid (later voorrand lamina perpendicularis) en neusdorsum (2) tussen sphenoid en spina nasalis anterior.

Bij het konijn is eenzelfde 3-dimensionale opbouw van het septale kraakbeen beschreven (Verwoerd et al, 1989). De rol van verschillende - dikkere en dunnere - delen van het neustussenschot voor de uitgroei van de neus, werden bij dit proefdier bestudeerd (Mastenbroek, 1978; Nolst Trenité, 1984; Nijdam, 1985; Poublon 1987; Meeuwis 1988).
Groei in het sphenodorsale – later ethmoidodorsale – gebied van dik kraakbeen bleek verantwoordelijk voor een verhoging en verlenging van het neusdorsum. De dikke basale zone (sphenospinale zone) stimuleert de voorwaartse uitgroei van de maxilla. Wanneer de experimenteel aangetoonde morfogenetische rol van de diverse delen van het septum nasi ook mag worden toegekend aan de overeenkomstige delen van het humane neustussenschot, is de verscheidenheid in gestoorde neusuitgroei na een partiëel verlies van het septale kraakbeen te begrijpen. Omvat het verlies zowel de sphenodorsale als de sphenospinale zone, dan leidt dit tot een onderontwikkeling van de neus en soms ook van de bovenkaak. Dit laatste wordt vaak beschreven na een neustrauma gedurende de vroege kinderjaren. Een traumatisch defect van de sphenospinale zone leidt later tot een retropositie van de spina nasalis anterior. Omdat het septale kraakbeen in de columella verbonden is met de geretroponeerde spina nasalis anterior, gaat dit gepaard met een verlaging van het kraakbenige neusdorsum.

Het dunne gedeelte van het cartilagineuze septum heeft een bescheiden functie ten aanzien van ontwikkeling en steun. Dit verklaart waarom kinderen met een perforatie van het centrale dunne gedeelte van het kraakbenige septum een normale uitgroei van de neus vertonen.

Verschillende theorieën omtrent de relatie tussen septumperforatie en ontwikkeling van de neus zijn beschreven door Pirsig (1992). Het is nu duidelijk geworden dat de vraag of een perforatie al of niet interfereert met de groei van de neus, afhankelijk is van de exacte localisatie van het defect in het neustussenschot.

Een postmortem studie van een gefractureerd neustussenschot bij een 4-jarig kind (Hoofdstuk 6)

De fractuurlijn heeft een C-vormig verloop. Het verticale deel is gelocaliseerd in het centrale dunne deel van de lamina perpendicularis. De inferieure uitbreiding passeert de grens tussen de lamina perpendicularis en het septale kraakbeen en volgt de dunne zone van het septale kraakbeen net boven de zich verdikkende basale zone. De uitbreiding naar boven van de C-fractuur gaat door de verbinding van lamina perpendicularis en het kraakbenige neustussenschot en verloopt in een dunne zone juist onder het neusdorsum. Deze observatie is in tegenspraak met recente publicaties van Shapiro (1996) waarin hij stelt dat C-vormige fracturen, welke bij volwassenen regelmatig gevonden worden, bij kinderen niet bestaan. Harrison (1979) beschreef als eerste het frequente voorkomen van de C-vormige fractuur bij volwassenen zonder daarvoor een biomechanische uitleg te geven. Dit onderzoek toont aan dat de C-vormige fractuur samenvalt met de dunne, meest vulnerabele delen van het neustussenschot.

Ontstaan van septumdeviaties (Hoofdstuk 5 en 6)

Mladina (1987) en Mladina en Krajina (1989) waren de eersten, die beschreven dat septumdeviaties bij voorkeur op bepaalde plaatsen voorkomen. Hun observaties werden bevestigd door Gi-Min et al (1995) in een landelijk onderzoek in Korea bij 9000 personen. Beide groepen van auteurs beschouwen de meeste septumdeviaties als het gevolg van trauma in de vroege jeugd. Toch waren beide zich niet bewust van de achterliggende oorzaak van de voorkeurstrajecten. Het voorkomen van de meeste septumdeviaties en verbuigingen in het anterieure gedeelte, zoals beschreven door Mladina (categorie 1 en 2) lijkt gerelateerd aan het dunnere gedeelte van het neustussenschot, zoals beschreven in hoofdstuk 5. Het fractuurpatroon, zoals beschreven in hoofdstuk 6, zou bij verdere uitgroei kunnen leiden tot een meer complex type van septumdeviatie waarbij zowel het kraakbenige en benige gedeelte van het neustussenschot betrokken zijn. Dergelijke complexe deviaties komen overeen met de types 3-7 volgen de klassificatie van Mladina (1987, 1989). Het lijkt aannemelijk dat de dunne gedeelten van het septum minder resistent zijn tegen mechanische belasting en daardoor eerder de neiging hebben tot fractuurvorming. Het in kaart brengen van dunnere en dikkere delen (met verschillende elasticiteit en plasticiteit) draagt bij tot een beter begrip van de mechanische aspecten van septumfracturen als gevolg van extern trauma op de kinderleeftijd.

Interstitiële groei van het kraakbenige neustussenschot (Hoofdstuk 7)

De dikte van het kraakbenige neustussenschot neemt na de geboorte niet toe. Daarentegen neemt de omvang in het sagittale vlak gedurende de eerste 2 levensjaren snel toe. Later wordt de veronderstelde groei van het kraakbenige septum volledig "gecompenseerd" door enchondrale verbening ter plaatse van de voorrand van de lamina perpendicularis. Over groei door proliferatie van cellen is niets bekend met betrekking tot het septale kraakbeen. In dit onderzoek werd voor het eerst de interstitiuele groei (door toename van celvolume en hoeveelheid celtussenstof) globaal in kaart gebracht.

Interstitiële groei bleek prominent aanwezig en vertoonde bovendien regionale verschillen, zoals eerder voor de septale dikte waren gevonden.
Interessant is dat in eerdere histochemische studies (Vetter et al, 1983, 1984 a,b, Pirsig 1986) vergelijkbare regionale verschillen in matrixsynthese en proliferatie capaciteit werden vastgesteld. Interstitiële groei van het septale kraakbeen speelt een belangrijke rol in de vorming van overlap en deviaties van septumfragmenten na trauma en kan tevens de toename van deze afwijkingen zelfs bij volwassen patiënten verklaren.

Chirurgische aspecten van het vomer (Hoofdstuk 8)

Röntgenfoto's van geïsoleerde neussepta met leeftijden tussen 0 en 42 jaar brachten nieuwe informatie aan het licht met betrekking tot het voorkomen van anatomische variaties.

De ontwikkeling van het vomer is complex. Het inferieure gedeelte is een benige plaat bestaande uit benige lamellen tussen de onderrand van het septale kraakbeen en de bovenzijde van het palatum. Bij de pasgeborene is het bot van het inferieure gedeelte zo fragiel dat het mogelijk is het palatum versus het kraakbenige neustussenschot te mobiliseren. Het superieure gedeelte van het vomer wordt gevormd door desmale verbening aan de beide zijden van de onderrand van het kraakbenige septum (vomervleugels). De superieur en inferieur gelegen delen vormen tesamen een Y-vormige benige goot die de kraakbenige onderrand van het neustussenschot omvat. De verbinding tussen de lamina perpendicularis en vomer vertoont regelmatig anatomische variaties. De ossificatiezone van de lamina perpendicularis kan de bodem van de vomergroeve bereiken of juist een strook kraakbeen tussen de vomervleugels laten bestaan.
De vomervleugels ontwikkelen zich vaak asymmetrisch. Een plaatselijke deviatie van de onderkant van het septum naar één zijde in combinatie met onderontwikkeling van de vomervleugel aan dezelfde zijde is een regelmatige bevinding. Deze spina vomeris wordt in de meeste gevallen vergezeld door een persisterend kraakbenig gedeelte aan de onderzijde van het septum: de "sphenoid tail". Deze sphenoid tail breidt zich uit in posterieure richting langs de unilateraal gevormde vomervleugel.
Bij patiënten met een unilaterale spleet van alveolus en palatum blijkt de neusbodem aan de niet-spleetzijde gedeformeerd. In deze gevallen is de onderrand van het septale kraakbeen en de lamina perpendicularis gedevieerd naar de spleetzijde. Tegelijkertijd strekt het inferieure gedeelte van het vomer zich uit tussen de onderrand van het kraakbenige septum en het palatum aan de niet-spleetzijde. Het resultaat is een vrijwel horizontale positie van dit vomerdeel. Daardoor lijkt de neusbodem aan de niet-spleetzijde verbreed. De consequentie is een hoek tussen het inferieure vomerdeel en het superieure deel dat op den duur is gefuseerd met de lamina perpendicularis. Bij een septumcorrectie in

aanwezigheid van een unilaterale gehemeltespleet dient men hierop bedacht te zijn.

Verbening van de voorste schedelgroeve (Hoofdstuk 9)

Bij de pasgeborene vormt het skelet van de neus en het middengedeelte van de voorste schedelgroeve één kraakbenig complex. In het bijzonder de lamina cribrosa werd bestudeerd met behulp van computertomografie (CT) en histologische technieken. Hierdoor kwam vast te staan dat op jonge leeftijd de voorste schedelbasis zowel mediaan als paramediaan nog steeds volledig kraakbenig is. Verbening vindt plaats tussen het 2e en het 6e jaar.
In de eerste levensjaren wordt deze kraakbenige voorloper van de benige voorste schedelgroeve weergegeven als een "pseudodefect" op de coronale CT-scan. De vroege aanwezigheid van verbeningskernen in dit gebied, zoals door Bosma (1986) beschreven, konden niet worden aangetoond.

Naidich et al (1996) suggereerden dat bij een klein gedeelte van de populatie de ossificatie in dit gebied vlak na de geboorte kan beginnen. In andere individuen zou deze ossificatie op het 6e levensjaar nog niet compleet zijn.

Door de introductie van de MRI, is er voldoende resolutie, bij efficiënt gebruik van T1 en T2 gewogen beelden, om deze kraakbenige structuren te visualiseren en defecten uit te sluiten of aan te tonen. Met hogere magneetveldsterkte is het zelfs mogelijk te differentiëren tussen rijp en onrijp kraakbeen, gebruik makend van de verschillen in waterbindende capaciteit van meer of minder gesulfateerde glycosaminoglycanen van de kraakbeen matrix (Allegrini et al, 1990). In tegenstelling tot de CT-scan, blijft de beeldvorming van de luchthoudende weke delen/benige overgang, een probleem voor de MRI-scan (Zinreich et al, 1996). Toch moet deze MRI-scan, gezien de voornamelijk kraakbenige structuur van de voorste schedelgroeve gedurende de eerste levensjaren, als een zeer belangrijk diagnostisch instrument worden gezien.

Conclusie

De neuschirurgie bij volwassen patiënten is de laatste decennia verrijkt met nieuwe concepten, nieuwe technieken en verfijnder instrumentarium. Voor de pediatrisch gerichte KNO-arts is de verleiding groot deze innovatie ook toe te passen bij kinderen en de traditionele terughoudendheid voor chirurgisch ingrijpen op deze leeftijd te laten varen.

De biologische basis voor de chirurgie van het neustussenschot tijdens de groei is nog zeer onvolledig. Het in dit proefschrift beschreven onderzoek beoogt bij te dragen aan het opvullen van enkele van de vele lacunes.

Met betrekking tot het neustussenschot op de kinderleeftijd werden (voor het eerst) beschreven:

a. de specifieke bouw bij de pasgeborene, en de veranderingen tijdens de kinderjaren;

b. de dimensionele groei;

c. de evolutie van het kraakbenige septum met enerzijds afbraak van kraakbeen, anderzijds interstitiële groei en tegelijkertijd behoud van de kenmerkende 3-dimensionale organisatie;

d. het verloop van fractuurlijnen in het septum.

Ook werden hypothesen geformuleerd met betrekking tot :

a. de gevolgen van partiëel verlies van septaal kraakbeen voor de verdere groei van de neus;

b. de biomechanische achtergrond van de voorkeurslocalisaties van fracturen en septumdeviaties.

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Curriculum Vitae.

De auteur van het proefschrift werd op 7 februari 1957 geboren in Vlissingen. Na het eindexamen VWO (B-richting) aan de Rijksscholengemeenschap "Scheldemond" te Vlissingen begon hij in 1976 met de studie geneeskunde aan de Erasmus Universiteit te Rotterdam.
Het arts-examen werd in 1983 behaald. In hetzelfde jaar werd aangevangen met de studie tandheelkunde aan de Universtiteit van Amsterdam (later ACTCA) en in 1984 werd het doctoraal examen eerste fase behaald.
Aansluitend startte de auteur een assistentschap op de afdeling keel-, neus-, en oorheelkunde in de KNO-kliniek van het Academisch Ziekenhuis Dijkzigt te Rotterdam.
In 1985 begon hij daadwerkelijk met de opleiding tot KNO-arts. De auteur werd op 1 februari 1989 als KNO-arts in het specialisten register ingeschreven.
Van 1989-1990 was de auteur als staflid werkzaam in het Academisch Ziekenhuis Dijkzigt.
In 1990-1993 was hij als senior staflid werkzaam in het Sophia Kinderziekenhuis te Rotterdam (samen met het Dijkzigt ziekenhuis vormt deze instelling het Academisch Ziekenhuis Rotterdam).
Sinds 1 december 1993 is de auteur werkzaam als KNO-arts in het Antonius Ziekenhuis te Sneek.
Per 1 november 1998 is de auteur benoemd tot Fellow of the Royal Society of Medicine (FRSM) te Londen, Groot Britannie.