Rhinosurgery in children: developmental and surgical aspects of the growing nose

Abstract

The anatomy of the nasal skeleton in newborns and adults are not alike. The complete cartilaginous framework of the neonatal nose becomes partly and gradually ossified during the years of growth and is more vulnerable to trauma in that period. Injury in early youth may have large consequences for development and may result in a nasal deformity which will increase during growth and reach its peak during and after the adolescent growth spurt.

To understand more of the underlying problems of nasal malformations and their surgical treatment (septorhinoplasty) these items became the focus of multiple animal studies in the last 40 years. The effects of surgery on the nasal septum varied considerably, seemingly depending on which experimental animal was used. In review, however, the very different techniques of the experimental surgery might be even more influential in this respect. Study of one of the larger series of experiments in young rabbits comprised skeletal measurements with statistical analysis, and microscopic observations of the tissues. The behaviour of hyaline cartilage of the human nose appeared to be comparable to that of other mammals. Cartilage, although resilient, can be easily fractured whereas its tendency to integrated healing is very low, even when the perichondrium has been saved. Also surgical procedures – like in septoplasty – may result in growth disturbances of the nasal skeleton like recurrent deviations or duplicature. Loss of cartilage, as might occur after a septum abscess, is never completely restored despite some cartilage regeneration. In this article experimental studies are reviewed and compared.

Still there remains a lack of consensus in the literature concerning the developmental effects of rhinosurgery in children.

Based on their observations in animals and a few clinical studies, mostly with small numbers of patients but with a long follow-up, the authors have compiled a list of guidelines to be considered before starting to perform surgery on the growing midface in children.

Keywords: nasal surgery in children, rhinosurgery in children, nasal fractures in children, septoplasty in children, nasal growth, midfacial development

1 Nasal development and clinical problems

1.1 Postnatal development of the facial profile

“Adults have more face and less brains, children more brains and less face” is an intriguing statement for medical students at their first anatomy course. The prominent development of brains and eyes before birth and during the first years of life may explain the relatively large dimensions of the brain skull in young children. After birth the higher growth rate of the facial skeleton – nose, maxilla, mandible – compared to the brain skull, will result in a gradual transformation of the profile of a baby face into the adult profile (Figure 1).
‘Developmental mechanics’ underlying the prominent growth of the midface (nose and maxilla) in children are clinically most relevant. They provide a biological basis for nasal surgery in children and for orthodontic and surgical treatment of clefts. Currently the cartilaginous nasal septum is considered to be a dominant growth center in the developing midface, interacting with sutural growth of the bony skeleton. Loss or lesions of the septodorsal cartilage may result in anomalies of the growing nose and maxilla.

1.2 Rhinosurgery in children

In children even a minor injury of the nasal skeleton may interfere with developmental processes, resulting in a progressive malformation of the nose. Traumata of the nose are quite common in children. Only in a minority of the cases, the child is presented at an emergency department or examined by a family doctor. Many injuries of the nasal skeleton, therefore, are initially neither diagnosed nor treated. Later, aesthetic and/or functional problems may become manifest and children are referred to a specialist, sometimes several years after the injury. Then, the decision has to be made whether a surgical intervention is indicated, at what age and which surgical technique should be preferred [1], [2], [3], [4]. In many cases a ‘wait and see’ policy might be preferable and surgery even postponed until after the adolescent growth spurt. Unfortunately evaluation of late effects of surgery on further development requires a (long) follow-up, including the adolescent growth spurt, which seldom appears to be possible.

1.3 Nasal growth: dimensional aspects

Recently a review was published of data on nasal growth and maturation age of healthy Caucasian individuals [5], [6], [7], [8], [9]. The findings may be summarized as follows: (1) The maximum growth velocity of the nose (adolescent growth spurt) in girls appeared to vary from before the age of 8 years until the age of 12 years, whereas boys generally demonstrate a maximum around the age of 13 years; (2) The average age at which the growth velocity curve has its steepest descending slope – predicting the end of the nasofacial growth spurt – was found to be 13.4 years for adolescent girls and 14.7 years for adolescent boys; (3) These authors further conclude that rhinoplasty can be “safely” performed after the age of 16 years in girls and after the age of 17 years in boys [5].

Another study in Denver (USA) demonstrated increments in nose height, depth and inclination to be essentially complete in girls by 16 years of age, while continuing to increase in males up to and beyond 18 years [10]. Different conclusions were drawn from a study in the Aegean region in Turkey, where nasal height and nasal bridge length reached full maturation in males at 15 years and in females at 12 years [11]. A large study in Switzerland including 2500 individuals of central European descent and between 0–97 years of age showed an increase of nasal length and nasal protrusion in males until the age of 25 years and in females until 20 years [7]. Some authors have shown minimal nasal growth to continue into advanced age, which seems not relevant from a surgical point of view [12], [13], [14].
1.4 Anatomy of the nose in children at different ages (surgical aspects)

Next to dimensional features of postnatal growth of the nose significant changes concern the anatomy of the growing nasal bony and cartilaginous skeleton. These are illustrated by comparing nasal anatomy in children with the “adult” anatomy as presented in most textbooks.

1.4.1 Nasal skeleton in a neonate

The nasal bones, are fibrously connected with the frontal and maxillary bones, and are supported by the upper lateral cartilages (Figure 2). At the caudal margin of the nasal bones the periosteum seems firmly connected with perichondrium of the underlying cartilage. The upper lateral cartilages extend under the full length of the nasal bones to merge with the cartilaginous anlage of the anterior cranial base [15]. Upper lateral cartilages and the nasal septum constitute the septodorsal cartilage. The cartilaginous septum is based on the sphenoid and reaching from sphenoid to columella. First indications of ossification of the septum cartilage may be found near the anterior skull base, representing the anlage of the perpendicular plate. Anteriorly the spinoseptal ligament is anchoring the cartilaginous septum to the anterior nasal spine of the maxilla.

The vomer is represented by a thin layer of bone – the vomeral wings – on each side of the basal rim of the cartilaginous septum. Inferiorly the vomeral wings are connected, with the anlage of the inferior (unpaired) part of the vomer. The latter is presented as ossifying mesenchym between the mucous membranes lining both nasal cavities [16].

1.4.2 Nasal skeleton: from neonate to adult

Differences between the nasal anatomy in neonates and adults in the first place refer to the septodorsal cartilage. In the adult stage a major part (60% or more) of the septum consists of osseous components as a result of chondral (perpendicular plate) and desmal (vomer) ossification (Figure 3a-c).

The cartilaginous septum loses its basis on the sphenoid to be mainly connected to and supported by the anterior rim of the perpendicular plate. Under the osa nasalia the extension of the upper lateral cartilages has been obviously reduced to 5–10 mm. Some aspects of the postnatal development of the nasal skeleton will be presented in the following paragraphs.

1.4.3 Developmental aspects of the nasal skeleton in growing children

As children become older the dimensions of the nasal skeleton increase and the relation between bony and cartilaginous parts of the nasal skeleton will change [17]. Consequently the age-specific anatomy should be appreciated by clinicians, both in diagnosis and treatment. A few aspects of the anatomical development in children may be summarized in the following paragraph.

Regressive changes. The intracranial parts of the dorsolateral cartilages show regression and are at the anterior skull base replaced by the osseous cribiform plate (Figure 2). Subsequent regression of the dorsolateral cartilages is gradually proceeding in anterior direction. Data concerning this process are scarce. In exploring nasal dorsum fistulae in 4-year old children the dorsolateral cartilages may still be found extending as far as the nasofrontal suture. Form and dimensions of the dorsolateral cartilages, remaining in the adult stage may vary substantially, in particular as far as the part covered by the nasal bones is concerned.

Progressive ossification. As a result of progressing ossification of the cartilaginous septum the perpendicular plate expands from an area near the anterior cranial base in caudoventral direction [18], [19], [20]. The ventral edge will gradually shift from intracranially in caudal direction under the nasal dorsum (Figure 3a-c). Consequently the ventral edge of the perpendicular plate may not be considered to be a reliable orientation point in relation to the anterior skull base during septum surgery in children.

The age at which the ossifying front of the perpendicular plate will reach the vomeral alae which develop on both sides of the septal cartilage seems to vary and may even...
The growth of the cartilaginous part of the septum and the bony part were measured in cm² (Figure 4). The growth rate of the nasal septum exclusive of the vomer is at its maximum in the newborn and slows gradually down to reach a plateau in the specimens of 20 years and older. The dimensions of the cartilaginous part demonstrate a rapid increase to a maximum at the age of 2. Later growth of the total septum is due to development of the perpendicular plate by ongoing ossification of septal cartilage at the septo-ethmoidal junction. Apparently the ossification is balanced by new formation of cartilage. Mitotic activity and expansion of the intercellular matrix contribute to compensating the loss of cartilage by ossification [27].

1.5.1 The nasal septum in identical twins

Grymer and Melsen [28], [29] studied 42 pairs of identical twins ranging from 18 to 22 years of age. In 74% of the individuals a deformity was found in the posterior (bony) part of the septum, whereas only in 22% deformities of the anterior (cartilaginous) septum could be demonstrated. The distribution of deformities within pairs suggests that the anterior malformation might be the effect of external trauma, although the adult patients could not remember an accident! The posterior deformities were considered to be part of a ‘normal’ developmental process of the maxillary complex where both genetic and epigenetic factors may play a role [24], [25]. In 11 adult twins of which only one of the two had a deformity of the anterior nasal septum; the nose of the affected sibling was found to be shorter than in the non-affected sibling and also the antero-posterior length of the maxilla seemed to be smaller (although not significant in cephalometry). From these observations the authors concluded that the nasal septum do influence the development of the nose and the antero-posterior dimensions of the maxilla.

In 1997 Grymer and Bosch documented facial growth for a period of 10 years of a patient – one of a twin – suffering septal destruction due to a septal abscess at the age of seven [30]. Drainage of the abscess was followed by an immediate implantation of homologous septal cartilage from a tissue bank. Nevertheless the patient developed a saddle nose, an upward displacement of the anterior part of the maxilla, diminished vertical development of the nasal cavity and a retrognatically positioned maxilla due to decreased anteroposterior maxillary growth com-
pared to the healthy sibling. This case report also pointed to the cartilaginous septum as an important factor which has an impact on vertical and sagittal growth of the nose and maxilla.

1.5.2 Cartilaginous nasal septum: thicker zones, thinner parts

In newborns the septum cartilage, reaching from sphenoid to columella, demonstrates a specific morphological organization of thicker and thinner parts [31], [32]. The transverse diameter may vary from 0.4 to 3.5 mm. The thickest cartilage is found near the junction with the sphenoid rostrum to decrease in more anterior parts (Figure 5a).

In addition two zones of thicker cartilage may be seen extending into the anterior part of the septum, the lower one being the basal rim of the cartilaginous septum reaching from sphenoid to the anterior nasal spine, the more dorsal one extending from the sphenoid to, and supporting, the nasal dorsum (Figure 5b). The thinnest cartilage is found between the sphenospinal and sphenodorsal zone and the slightly thickened caudal rim of the septum. Despite the progressive ossification of the nasal septum this pattern is still recognized in the remaining cartilaginous part of the adult nasal septum.

Each of these 2 zones of the cartilaginous nasal septum plays, as was demonstrated in animal experiments, a specific role in postnatal development of the nose and upper jaw [33].
1.6 Nasal septum fractures and deviations

As a result of the poor wound healing capacity of cartilage fractures will not heal and further growth will result in deviations of the separated parts [34]. Consequently preferred fracture sites may be associated with frequent types of septal deviation developing in children and ascribed to previous septal fractures [35], [36], [37].

1.6.1 Preferred fracture lines

The regional differences in thickness of the human nasal septum may explain the preference for specific fracture lines through the nasal septum. Harrison was the first to describe C-shaped septal fractures in adults without giving any biological explanation [38]. Later a similar fracture was reported in a 4-year old child [39]. The vertical part of the ‘C’ was found to be situated in the thin central area of the perpendicular plate. The inferior extension did cross the septo-ethmoidal junction and followed the thinner zone of septal cartilage just superior to the thickened basal rim. The superior extension of the ‘C’ passed the anterior edge of the perpendicular plate and did run into the thinner zone just under the nasal dorsum. Actually the C-shaped fracture line tends to follow the thinnest most vulnerable parts of the septum (Figure 6).

![Figure 6: Nasal septum of 4-year-old boy (post-mortem after traffic accident) with C-fracture. Fracture line runs through thinner area superior and parallel to sphenospinal (basal) zone extending into perpendicular plate and reappearing more dorsally under nasal dorsum; partial fracture of the septum parallel to the caudal rim, directly adjacent to the junction with the upper lateral cartilage.](image)

In case of dislocation of the caudal end of the septum – another common deformity in children – the fracture line is located in the area of thin cartilage, cephalic and semi-parallel to the caudal rim and just anterior to the connection between upper lateral cartilages and septum. Multiple and irregular fractures of the septum may be the effect of a mid-frontal trauma. Further non-coordinated growth of smaller or larger parts of the septum cartilage will result in a highly distorted septum which fails to push forward the nasal dorsum in the sagittal plane (Figure 7a).

1.6.2 Late effects of nasal fractures on the growing nasal skeleton

In young children traumata of the nose seem to occur rather frequently, sometimes resulting in septum fractures with or without associated fractures of the bony nasal pyramid. A relative small number of those children are seen by family doctors and an even smaller number by ORL-specialists. Long-term follow-up of facial development in these patients is no routine and late effects on further nasal growth have been seldom reported, only when the adult patient pays a visit to the office to ask advice of the ORL-specialist for his/her crooked or bad-functioning nose.

An example is the evolution of the nasal dorsum after nasal trauma in a 4-year old girl, demonstrated by photographs made at different ages (Figure 8a-c). Treatment included a closed reduction of the dislocated bony pyramid and fractured parts of the septum. One year later the nasal dorsum appeared to be normal! However in the following years further growth resulted in a progressive deviation of the nasal septum and dorsum at the age of 8 with a further increasing deformity during the adolescent growth spurt.

1.7 Facial development after loss of septum cartilage

In 1984 Pirsig reported on 3 patients, each patient being 16 years of age but with a different history of facial injury at a young age [40]. Loss of cartilage of the septum at the age of 3 years completely impeded the ‘extra growth’ of the nose and maxilla, which under normal conditions is responsible for the gradual transition of the baby face into the adult profile. When a child was older at the onset of the abscess followed by destruction of the septum cartilage (5 and 7,5 years respectively), the negative effects on later facial growth appeared to be less prominent. It may be concluded that the younger the child at the time of injury and destruction of the nasal septum, the greater the long-term effects on midfacial growth!

This is significant for clinical outcome studies: results of treatment should be related to the age of the patient at the time of septum cartilage disintegration or surgery. Moreover, follow-up should be extended till after the adolescent growth spurt (Figure 7b, c, Figure 8a-c). Clinical observations related to partial loss of septum cartilage are scarce, and seem to reflect the specific role of various parts of the cartilaginous septum in growth of the face [41].

1.8.1 Nasal surgery in children is ‘special’

The first reason is the essential role of the growing septomaxillary cartilage in midfacial development in combination with the poor wound healing capacity of the cartilaginous nasal skeleton.
Figure 7: (a) 10-year-old boy with a crooked nose due to nasal injury at the age of 5 with multiple fractures and dislocation of septal fragments; the deformity has increased with underdevelopment of nasal dorsum, lacking support of fragmented septum cartilage. (b) 6.5-year-old boy with advancing saddle deformity after septum abscess at the age of 4 years; (c) the same boy after adolescent growth spurt with underdevelopment of the nasal skeleton; nasal tip supported by alar cartilages.

Figure 8: (a) 5-year-old girl with minimal deviation of the nose due to nasal trauma 1 year previously; (b) progressive deformity at the age of 8 years and (c) 15 years.

Secondly, the small dimensions of the anatomical structures which are involved and should be respected when doing nasal surgery in children. Thirdly, the anterior rim of the perpendicular plate should not be considered to be a reliable point of orientation in relation to the anterior skull base as it shifts from an intracranial to extracranial location in growing children. Finally, the gradual ossification of the cartilaginous anlage of the anterior skull base includes a risk for surgical damage to the lamina olfactoria and overlying dura, which might result in liquor leakage.

1.8.1 Nasal surgery in children: questions regarding clinical practice

1. How to restore normal growth of the nasal skeleton (and maxilla) after loss of septal cartilage at a young age and how to minimalize the effects on further development?
2. How to treat acute nasal/septal fractures and prevent later abnormal growth?
3. How to intervene when progressive abnormal development of the nasal skeleton is obvious?
These questions refer to the developmental mechanisms underlying the postnatal growth of the midface and the nasal skeleton in particular, the way they may be influenced by various injuries, and the possibilities or impossibilities of restoring normal growth. Experimental research pertinent to this question is reviewed in the following chapter.

2 Animal studies: exploration of mechanisms of facial growth

First attempts to identify causal factors in the development of the midface date back to the 19th century, particularly in circles of anatomists. For many decennia efforts were mainly focused on the role of the nasal septum. Since the last decades of the 20th century also data were published regarding the role of the growing nasal septum in relation to various types of facial clefts.

2.1 History

Fick, professor of anatomy in Göttingen (Germany), described in 1858 experiments in which he resected parts of the cartilaginous nasal septum, through a trephine opening of the nasal bones, in growing dogs, cats, pigs and goats. At autopsy he found the hard palate – the floor of the nose – to be markedly shortened in antero-posterior direction, and stated that growth of the hard palate was dependent upon the growth of the nasal septum [42]. In 1929 Landsberger resected an anterior portion of the septum in dogs, 2 weeks of age. Six months later he observed that the anterior part of the floor of the nasal cavity was higher than normal. He concluded that the growing nasal septum was an important factor in pushing the floor of the nose – the hard palate – downward [43]. More extensive research was published from the middle of the 20th century. Scott studied the anatomy of the nasal septum cartilage in fetal pigs and human embryos, and demonstrated that at birth the nasal cartilage reaches back to the cranial base. He further hypothesized that the septal cartilage “by its growth will thrust forward the facial skeleton, while separating the facial bones allowing growth to take place at the sutures” [44]. Young Rhesus monkeys were used by Baume for a histological study to prove that septal growth activity at the ethmoid-septal junction is very important in bringing about the downward and forward development of the total middle face complex. Actually he was one of the first to recognize the impact of applying biologic principles of growth to diagnosis and treatment of malocclusion in individual patients [45].

2.1.1 Introduction: Biology-based principles for treatment?

In later years surgical and orthodontic treatment of young patients with clefts became subject of much controversy. Clinical observations on abnormal midfacial development raised questions about the role of the nasal septum. In particular, concepts about the importance of the cartilaginous nasal septum as primary growth center were not ‘of the same tenor’. Moss et al. who were working in the dental field, even strongly denied the growth-regulating ability of septum cartilage [46]. They and also Koski advocated the theory that growth of the septal cartilage is a “compensatory or secondary response to the demands of its functional matrix” being the oral and nasal cavity [47]. Eight years later Moss concluded that growth of the midfacial structures is independent of the nasal septum [48]. Although his hypotheses were well acclaimed at that time, they are nowadays considered as too artificial, and more or less abandoned.

More subtle and discriminating was the theory about midfacial growth from van Limborgh, who hypothesized that intrinsic genetic and epigenetic factors together determine the development of the skull [49]. The growth of the chondrocranium, and thus of the nasal cartilage, would be almost exclusively governed by intrinsic genetic factors. Control of cartilage growth was therefore suggested to be essentially distinct from that of the intramembranous growth of desmocranium which is directed by epigenetic factors. Finally he concluded that the cartilaginous anlage (including the cartilaginous nasal septum) in the facial skull is more important as factor in morphogenesis than the bones.

Melsen studied autopsy material from 123 children aged 0–20 years. She measured in histological and microradiographic sections the increase in size of the vomer which she ascribed to bone apposition on the superior surface whereas increase of the nasal septum dimensions would be mainly due to apposition on the posterior margin [50]. On the basis of her morphological findings she concluded that there was “no reason to believe that the septal cartilage plays a major role in the forward, downward growth of the maxillary complex in man”.

2.1.2 Early experimental studies on midfacial growth in rabbits

Founding a biological basis for the analysis and treatment of the cleft lip, jaw and palate was the objective of animal studies in the field of orthodontics and plastic surgery. Selman and Sarnat reported that extirpation of the frontonasal suture in rabbits, a site of rapid growth, failed to produce a growth arrest of the snout [51]. Sarnat continued this experimental work in rabbits and published a variety of studies of the growth of the face and jaws. As plastic surgeon at a School of Dentistry, he faced many questions in his clinical practice about normal growth and the effects of surgical procedures at the nasosepto-vomeral region. In an attempt to find answers Sarnat and his co-workers designed and performed several experiments in young growing rabbits. They could demonstrate that resection of the “anterior portion” of the nasal septum (including cartilage and mucosa) resulted in a greatly underdeveloped snout, relative mandibular prognathism and malocclusion of the incisors [52], [53], [54].
It was concluded that the cartilaginous nasal septum is important in growth and development of the “upper face” of the rabbit [55]. In his latest paper and referring to previous experiments, he stated that the extent and severity of the deformity varies approximately with the amount of resected cartilage, the age of the animal at the time of surgery and the length of the postoperative survival [56].

Today one would argue that at least the following aspects in the pioneering studies of the Sarnat-group have been disregarded:

1. as a result of their surgical approach via the anterior nasal nares, visual control of the resection is not possible due to the anatomical conditions of the rabbit’s nose, in particular the small diameter of the nasal lumen (certainly in young animals) and the voluminous dimensions of the os turbinatum;
2. the resections seem to encompass for at least the anterior half of the septum including septal cartilage as well as overlying mucosa, and thus creating large anterior perforations;
3. observations concerning the upper jaw are restricted to the anterior part, i.e. the premaxilla; consequently, effects on growth of the maxilla have not been investigated!
4. standardisation is failing in a) the age at surgery (between 2 and 7 weeks, which is a period of rapid growth of nose and upper jaw), b) the postoperative survival time (between 1 and 21 weeks), c) the number of animals per series (between 6 and 12);
5. measurements had not been performed.

The relevance of these pioneering experiments for current surgery of the nose in children appears to be restricted because resection of large parts of the septal cartilage including overlying mucosa is a non-used clinical procedure. Today great emphasis is laid on reconstruction of the nasal skeleton and creation of anatomical conditions which may offer the best chances for optimal growth of nose and upper jaw.

2.1.3 Facial clefts and growth of the midface: cleft syndrome?

In the mid-sixties van Limborgh described a collection of dried human skulls with facial clefts present at the Laboratory of Anatomy of the University of Amsterdam, the Netherlands, and dating back from a period before surgical interventions were done [57]. These skulls showed patterns of deformities characteristic for the type of cleft. Three years later Atherton presented another group of human skulls with non-repaired clefts of the jaw and palate with similar specific anomalies [58]. Skulls with unilateral cleft alveolus and palate, for instance, demonstrated a displacement of the premaxilla to the non-cleft side, whereas the maxilla on the cleft side showed a medial collapse and retroposition of the posterior part compared to the non-cleft side (Figure 9).

Figure 9: Palatal view of a human skull with an untreated unilateral cleft of alveolus and palate (Dept. of Anatomy and Embryology, Amsterdam MC). The maxillary segment on the cleft side demonstrates a medial collapse and a retroposition (different position of tuber maxillae on both sides); deviation in lateral direction of premaxilla/maxilla on non-cleft side; septo-vomeral deviation.

The question was raised whether these anomalies in facial development were primary in nature as part of a ‘cleft syndrome’, or secondary as reaction to the presence of a cleft cq. the absence of a suture [59].

2.2 Experiments on the growing midface

The open ends of Sarnat’s studies as well as the questions mentioned above stimulated us, the authors, to start our first research in this field. Also for us the experimental animal of choice was the young growing rabbit as it seemed an excellent model. It has a convenient size for facial surgery at a young age, can easily be obtained in larger numbers, shows only minor variations within one thoroughbred type of the species (New Zealand White) and is not too expensive. On the other hand, an objection would be that the rabbit’s facial anatomy differs too much from the human. The constituting elements of the human and rabbit facial skeleton, however, show sufficient significant similarities to allow conclusions which may be relevant for understanding developmental pathology of the human face.

Accurate description of the rabbit’s facial skeleton by Craigie and later by Frick was found in the literature but was missing for the nasal skeleton [60], [61]. Some anatomical aspects relevant for the present study are summarized here.

2.2.1 Anatomy of the bony facial skeleton of the rabbit

The upper jaw of the rabbit has on both sides 2 anatomical components: the premaxilla (or os intermaxillare) and the maxilla. The left and right premaxillary bone, anteriorly interconnected, support each one large anterior and one smaller posterior incisor (Figure 10, Figure 11). The an-
terior nasal spine is connected to the nasal septum by the septospinal ligament. The premaxilla is connected to the maxilla via the premaxillo-maxillary suture. The maxillae on both sides support a complex of 6 molars and are connected in the midline by their palatal processus. Each premaxilla has 2 additional extensions. The processus mediales from either side of the midline form a sulcus enclosing the paraseptal cartilages. The processus frontales extend in frontal direction lateral to the nasal bones and superior to the spongious part of the external wall of the maxillary sinus. Both nasal bones relate to the frontal bones via the sutura nasofrontalis. This intertwined configuration of the various facial bones makes it a very strong construction for lengthening of the snout.

2.2.2 Measurements of facial skull growth (geometrical study)

A geometrical method of measuring the skulls was developed [62], [63]. On standardized photographs of the lateral sides of the skulls 10–19 points were defined and measured in a rectangular coordinate system with reference to the length of the line between the most cranial point of the lambdoid suture (SL) and the most caudal point of the spheno-occipital synchondrosis (SSO) (Figure 12a). The occipital part of the skull is of desmocranial origin and not participating in the development of the face. The diagrams were compiled and statistically evaluated by a multivariate analysis according to Hotelling $T^2$ and Student-T test. In later studies the 95% elliptiform confidence areas of the variety of the X- and Y-coordinate of the measuring points were added to the diagram. Per series a minimal number of 10 animals were included.

2.2.3 Postnatal growth, experimental period

The growth of the skull was studied in 12 series of rabbits varying in age from 0 to 24 weeks after birth (Figure 3b). After the 8th week a gradual decline of the growth rate was observed. Only minimal growth was observed between the 20th and 24th week of age, which was chosen as the end of the experimental period. Surgery was performed after weaning at the age of 4 weeks. The facial skeleton appeared to grow faster and over a longer period [63]. The different proportions of facial skull and brain skull in 4 and 24-week-old rabbits are the result of extra growth of the nose and upper jaw during this period in comparison to the brain skull (Figure 10). The molar complexes in the maxilla are equally involved in this extra forward growth of the upper jaw!

2.2.4 Facial clefts in rabbits: cleft syndrome!

A series of experiments was designed to test the effects of facial clefts – surgically made at the age of 4 weeks – upon later growth of the facial skeleton. In a first experiment a solitary cleft lip (on one side) appeared not to interfere with skeletal growth. In a second series also the premaxillo-maxillary suture was resected, the cut edges were covered with mucosa, and the midpalatal suture resected, thus creating a unilateral cleft lip, alveolus and palate [63].

In the adult stage skulls of animals with an unilateral cleft lip, jaw and palate, the maxillary complex posterior to the cleft demonstrated a retroposition compared to the unaffected side (Figure 13a, b). The cleft apparently did interfere with the forward movement of the maxilla as occurring during undisturbed growth. The maxilla, premaxilla and bony nasal pyramid on the non-operated side demonstrated a deviation to that side. The total length of the upper jaw on the non-cleft side did not seem to be affected. Sutures provide a structural continuity and are a site of growth. The importance of this combination was demon-
strated by replacing the premaxillo-maxillary suture and midpalatal suture by implants of non-sutural bone (crista iliaca) in 4-week-old rabbits [63]. This resulted in marked anomalies during further growth: an extreme underdevelopment of the maxilla on the operated side, whereas the growing upper jaw on the non-operated side deviated to the other (operated) side (Figure 14a, b). The molar complex at the repaired cleft side is positioned more anteriorly. Slightly better results were achieved by Griffioen et al. after implantation of rib cartilage that included the osteocartilaginous junction, the periosteum and perichondrium [64].

The severe maldevelopment observed after a primary osteoplasty of alveolar-palatal clefts illustrates the significance of experimental research prior to the introduction of new surgical techniques, in particular in growing children [65].

2.2.5 Studies in other animals

Chierici et al. made complete unilateral surgical clefts of premaxilla and hard palate in Rhesus monkeys of unknown age, and followed them for 1–1.5 year. In this period an asymmetry of the upper jaw became obvious as well as a medial collapse of the posterior maxillary segment on the cleft side. A retroposition is not mentioned, but (non-specified) deviations of the nasal septum with an altered position of the ala of the nose on the cleft-affected side are described. The lateral wall of the nasal cavity was found to be relatively independent of shape and position of the tooth-carrying part of the maxilla [66]. Chierici and his co-workers concluded that deformities associated with cleft palate are “due to appositional responses of normal structures to an abnormal environment”.

They disregarded completely, however, the significance of the growing nasal septum in the development of the anomalies they had observed.
All animals showed a straight snout of normal length. In a minority of the skulls a small bone defect remained at the junction of the osteotomy line and the internasal suture. Even subtotal resection of one nasal bone could not disturb the normal outgrowth of the nose in young animals, as long as the underlying cartilage of the corresponding upper lateral was not injured.

2.2.7 Midfacial growth after partial resection of the lateral nasal wall

In the last 15 years pediatric functional endoscopic sinus surgery (FESS) has been advised for ostiomeatal problems in children. Contradictory reports on the effects of this procedure for the development of the midface have been published. The results of various studies in animal models (rabbits and piglets) suggested that midfacial growth was seriously affected by sinus surgery implicating that pediatric FESS might not be as innocent as it was sometimes advocated [68], [69], [70]. In our experiment a visually controlled microscopic approach through the nasal dorsum, as described for the septoplasty procedure, and entering the nasal cavity lateral to the upper lateral cartilage was chosen. Using this approach enlargement of the ostium appeared not to lead to facial growth disturbances [67]. The previously mentioned anomalies in piglets and rabbits might be attributed to unintended surgical traumatisation of the cartilage underlying the bony nasal skeleton.

2.2.8 Conclusions

The combination of anomalies of the facial skull like deviation of the maxilla to the non-cleft side and retroposition of the molar complex on the cleft side, which develop in growing rabbits after surgically-made facial clefts, are similar to the anomalies earlier described for human skulls with untreated clefts by van Limborgh [59] and Atherton [58]. The answer to their question whether the cleft-associated anomalies are secondary to the interruption of the upper jaw c.q. the absence of the premaxillo-maxillary suture, should be answered positively! A second conclusion is that in case of a unilateral cleft of alveolus and palate a forward shift on that side fails to occur resulting in a retroposition of the maxilla and the molar complex on the cleft side. Due to the lost connection with the maxilla on the cleft side, the growing septum will only “pull forward” the premaxillary complex on the non-cleft side. Under these asymmetrical conditions the growing septum, the anterior parts of the nasal bones and the upper jaw will gradually move to the non-cleft side. The apparent negative effects of replacement of a suture by non-sutural bone were reason to re-investigate the role of the nasal septum in midfacial development. Osteotomy, subtotal resection of the nasal bone and partial resection of the lateral nasal wall did not disturb normal outgrowth of the rabbit snout.

2.2.6 Osteotomy and resection of nasal bones

Unilateral or bilateral transverse osteotomy anterior to the frontonasal suture in young rabbits were tested for their possible effects on growth of the nasal dorsum [67].
2.3 The cartilaginous nasal skeleton of the rabbit

2.3.1 Anatomy

The cartilaginous septum reaches in posterior direction as far as the sphenoid and is firmly connected anteriorly to the premaxilla via the septospinal ligament. The perpendicular plate is small; the vomer is represented by 2 thin plates of bone on both sides of cartilage. Poublon found that in neonatal rabbits the upper lateral cartilages run from the tip of the nose under the entire length of the nasal bones to the anterior cranial base [71]. Septum and upper lateral cartilages are one T-bar-shaped structure (Figure 15). In the adult rabbit the upper lateral cartilages have lost the connection with the anterior cranial base and extend only halfway under the nasal bony dorsum. A decrease in width in the more cranial parts result in a triangular shape. The dome-like alar cartilages look like bulging extensions not separated from the upper laterals, and medially connected with a prolongation of the cartilaginous septum (Figure 18). In several other mammals (dog, guinea pig, horse) it was shown that the cartilaginous nasal skeleton consists of a septum with bilateral extensions (T-bar) of various size and shape [72], [73], [74].

2.3.2 Resection of upper lateral cartilages and nasal growth

Subtotal resection of the upper lateral cartilage on one side has marked consequences for further growth of the bony nasal skeleton: a shortening and flattening of the overlying nasal bone (Figure 16a). Moreover the most anterior part of the nasal bones is deviated to the non-operated side [71], [75].

Figure 15: Microscopic transverse section of the septum and lateral cartilages, composing the septodorsal (T-bar shaped) cartilage supporting the nasal dorsum.

2.3.3 Resection of parts of the septal cartilage including mucoperichondrium

The effects of resection of various parts of the septal cartilage in young rabbits were studied with an approach to the nasal cavity different from the method described by Sarnat [52]. After a median incision of the skin and a transverse osteotomy, the left nasal bone was elevated and rotated aside. This approach to the septodorsal cartilage, was tested in a separate experiment which did not result in any asymmetry, deviation or shortening of the snout during further growth. Interruption of the antero-posterior axis of the cartilaginous nasal septum in young rabbits, whether by resection of the anterior, central or posterior part appeared to inter-
vene with midfacial growth and result in abnormal short noses and upper jaws into adulthood [76] (Figure 17a, b, c). The extra growth of the premaxilla-maxilla and nasal bones did not occur; consequently the proportion between brain skull and facial skull remain largely unchanged after surgery at the age of 4 weeks (Figure 10). Resections not including the basal part of the septum (sphenospinal zone) did not interfere with lengthening of the upper jaw; they resulted in a saddling of the nasal dorsum with one exception, later discussed (viz. 2.4). In addition resection of upper middle part caused a significant shortening of the nose with a deflection of the upper jaw. Apparently the mere presence of an intact basal zone of septal cartilage between sphenoid and anterior nasal spine guarantees a normal increase in length of premaxilla and maxilla.

2.3.4 Conclusions

All defects of the septum (to be discussed in 2.5) and upper laterals, described above, resulted in a form of underdevelopment of the midfacial skeleton. Apparently the cartilaginous nasal septum is a “growth center” within the developing midfacial bony skeleton [63]. It was demonstrated that in particular the extra growth of the nasal bones and the premaxilla-maxillary complex, changing the rabbit’s baby face to its adult physiognomy, is dependent on an intact growing septo-dorsal cartilage. The growing T-bar-shaped septodorsal cartilage may be considered to “pull forward” the nasal bones and premaxilla. The traction is transferred to the maxillary part of the upper jaw via the premaxillo-maxillary suture, at the same time stimulating sutural bone formation. Lengthening and relative forward displacement of the upper jaw are enhanced by the growing nasal septum.

2.4 Microscopic anatomy of the nasal septum

The septum in rabbits varying from 4 to 24 weeks of age all demonstrated the same specific pattern of areas with thinner or thicker cartilage [77], [78]. Two zones of thicker cartilage based on the sphenoid extend forward to the nasal dorsum and the anterior nasal spine, respectively (Figure 18). Referring to the resection experiments, previously discussed, it is evident that resection of the dorso-posterior part lies outside the sphenodorsal zone of thick cartilage (Figure 17c). Growth of cartilage in the sphenodorsal zone is considered to contribute to the growth of the nasal dorsum, in particular the nasal bony pyramid. Cartilage growth will also result in lengthening of the sphenospinal zone and thus “pushing forward” the anterior nasal spine of the premaxilla and the connected maxillary parts of the upper jaw.

Figure 17: (a) Lateral view of an adult rabbit skull 20 weeks after resection of the middle one-third of the septum cartilage. Shortened nasal dorsum with “saddle”. Malocclusion with cross bite of incisors. (b) Graphic representation of the mean coordinates of 19 measuring points on the lateral side of the skulls: N (nasion), N1-6 (points on the internasal suture at 5 mm from nasion and 5 mm between consecutive points), SM (anterior of zygomatic process) and PT (posterior point of zygomatic process; control group (thin line) compared with experimental (thick line) group (resection of 10mm) with 95% elliptiform confidence areas of the variety of the X and Y coordinate of the measuring points). (c) Overprojection of diagrams of the skulls in 4- and 24 week-old unoperated animals and after resection of middle one-third of the septum. SSO-SL has been used as reference. Interruption of the anteroposterior axis of the septum by partial resection (central one-third) prevents further ‘extra growth’ of the nose and premaxilla/maxilla.
The specific three-dimensional organization of the nasal septum with thinner and thicker zones is a feature common to young rabbits and children [79]. After submucous resection of the middle one-third, normal lengthening of the nose is seriously impaired. As a consequence all noses are too short in the adult stage despite the partial formation of new cartilage in the defect.

2.5 Submucosal septal resection: effects on midfacial growth in rabbits

A next step was to study the effects of current submucous septal interventions. Mucosal elevation (“tunneling”) on one or both sides did not affect septal growth and nasal development [80]. The effects on midfacial growth after submucous resection of the middle one-third of the septum, partial middle one-third (leaving in situ a dorsal strut) and a vertical strip of 1–2 mm were studied, respectively.

2.5.1 Submucosal resection of the middle one-third (10 mm) of the septum

The effects on nasal development appeared to be similar to those found after corresponding resections including the mucoperichondrium (see 2.3.3). The antero-posterior dimensions between the borders of the surgical defect had decreased in almost all cases, likely due to growth of the remaining parts of the septal cartilage. Histological examination demonstrated that new cartilage was frequently formed by chondroblasts migrating from the perichondrium into the submucoperichondrial “space” between the cut ends which were rapidly overgrown by fibrous cells originating from the perichondrium [81]. Elsewhere the two perichondrium layers immediately converged thereby closing off the defect: no new cartilage could be formed (Figure 19a).

2.5.2 Submucosal resection of middle one-third saving a dorsal strut

Resection of two-third of the total height of the septum leaving a dorsal strut in situ caused in all cases a lower and shorter nasal dorsum compared to control skulls [82]. Although occlusion was maintained, the upper jaw was shorter than normal.
Also Rhys Evans and Brain reported adverse effects on midfacial growth in young rabbits after subjection to partial septum resection with saving of a narrow dorsal strut. Foreshortening of the nose and maxilla with gross malocclusion were observed. Despite the marked formation of neocartilage the subsequent development of the nose, and frequently the maxilla, was greatly retarded [83], [84]. After resection of just a partial basal strip (of the middle one-third) the skulls displayed no or slight deviations of the remaining septum. The external nose had a normal appearance, and the measurements showed no significant differences in comparison with the control series [82]. As these defects are positioned within the area of the vomer where the perichondrium is attached to the bony gutter, there remains open space easily to be filled by newly formed cartilage. The defect will be bridged and growth disturbance is prevented.

2.5.3 Submucosal septum resection of 1–2 mm

 Interruption of the antero-posterior continuity of the septum cartilage by 1–2 mm at a young age did not result in a diminished length of the upper jaw, twenty weeks later [80]. The nasal bones, however, were shortened. In all animals the separated parts of the septum were reconnected by their perichondrium: end-to-end or side-to-side due to release of interlocked stresses (viz. 2.7) Obvious differences were observed between the superior region under the nasal dorsum, and the inferior part – the thick basal rim – of the septum between sphenoid and anterior nasal spine. Under the nasal dorsum the septum demonstrated apparent overlapping ends, deviations or angulations at the meeting point of the previously separated fragments of the septum (Figure 19b). These malformations may prevent that actual growth of the septum cartilage does contribute to lengthening of the nasal septum and, thus, to lengthening of the nasal bones. At the basal side, where the septal cartilage is thicker and supported sidways by the vomeral wings, the edges closed mostly end-to-end [81]. As a consequence only inferiorly cartilage growth results in lengthening of the basal rim of the septum cartilage and contributes to a normal length of the developing upper jaw.

2.5.4 Studies in other animals

One of the larger longitudinal and cephalometric studies of the growing midface in animals had been started in 1974 by Siegel. The first experiments were evaluating the effectiveness of resection of varying amounts of the nasal septum in baboons [85]. Although the exact age of the monkeys was unknown an important conclusion was that the amount of growth retardation of the facial skull can be varied by delaying the moment of surgery or by varying the amount of cartilage resected. Based on our later observations we could agree with these conclusions.

In the nineties Siegel and Mooney demonstrated in chimpanzees significant changes in the normal nasal capsule shape and size as a direct consequence of resection of the septo-premaxillary (septospinal) ligament [86]. As they wrote “It should be an important issue in the primary repair of cleft lip and nose”. Freng and Haye interrupted the antero-posterior axis of the cartilaginous septum in 4 months old cats and followed further development up to the age of 14 months. The experimental period was considered to be the equivalent of a human lifespan between 6 years and the adult age. Final assessment was made on cephalometric measurements, based on lateral radiographs [87]. Their surgical intervention included a submucous resection of a strip of 4x2 mm of septal cartilage interferring with the antero-posterior axis of the septum, followed by immediate reimplantation. This procedure did not show any facial growth disturbing effect. Based on lateral cephalograms, however, their observations could not exclude possible deviations. Moreover, frontal sections through the nose of the operated animals show overlap of cut edges, dislocations and occasional perforations [88]. Considering the results presented it seems difficult to maintain the statement that “surgery might be advisable at a very young age”.

Stenström and Thilander found no signs of regeneration after removing a small portion of the septal cartilage just in front of the perpendicular plate in 3–6 days old guinea pigs [89] from which they concluded that the nasal septum cartilage only plays a subordinate role in midfacial development.

One of the very few more recent studies by Cupero et al. demonstrated at cephalometric analysis in growing ferrets (only 3 animals per group!) no statistically significant differences between the submucoperichondrial removal of a 5x3 mm piece of septal cartilage (with preservation of the dorsal and caudal struts) and the excision of a 4 mm piece of vomer bone (with preservation of all septum cartilage) [90]. They concluded that functional septoplasty does not result in facial growth disturbances although a larger sample will need to be studied to confirm this preliminary conclusion only based on lateral cephalograms. The presence or absence of deviations was not mentioned nor which part of the vomer (alae or the median part) was resected.

2.5.5 Conclusions

The effects of resection of nasal septum parts on midfacial growth depend on the dimensions of the created defect. A larger interruption of the antero-posterior continuity leads to shortening of upper jaw and nasal bones; a minor defect mostly does not interfere with lengthening of the snout. Deviations and angulations are frequently found.
2.6 Septoplasty, wound healing and growth

Septoplasty may include the repositioning of parts of the septum cartilage. In clinical and experimental studies the fate of this cartilage, in particular the viability of the tissue, has been discussed. Mostly it was concluded that autologous cartilage grafts do survive in vivo [91], [92]. The efficacy of the presence of the perichondrium for cartilage survival was stressed in some publications but denied in others [93]. All investigators observed angulations, spurs, fibrous union of cartilage fragments and lamellar bone remodeling which could occur after re-implantation of an autograft. Recurrence of deformation as well as dislocation at the site of implantaion and even loss of grafts have been reported for children [94], [95]. Data on wound healing of nasal cartilage have only been fragmentarily reported and were mostly limited to studies ex vivo or at later stages in life.

2.6.1 Septoplasty in children and nasal growth

Disappointing and even negative effects of septum surgery (septoplasty) in children were already known to be described by Hayton [96] and later by Ombrédanne [97]. The findings after this intervention on the growing nose led to extreme caution in dealing with nasal anomalies in young children. During the fifties and sixties, however, prudence decreased and preliminary reports of successful septoplasties were published [98], [99], [100], [101], [102]. It has to be stipulated that in these publications the age of the children at the moment of surgery, and thus the exact moment in the growing phase, were varying considerably and the follow-up period was always much too short in relation to the adolescent growth spurt. Huizing actually described for the first time in 1979 a boy who had developed characteristic midfacial disturbances more than 12 years after his septum correction at a young age [103]. Also Pirsig reported some years later that although less radical techniques had been developed, the long-term results using this conservative approach had shown to be good as well as poor [104].

In corrective septum surgery the original structure of the nasal skeleton is respected as much as possible. Sometimes, however, larger parts of the cartilage have to be removed, trimmed to size, crushed or rotated before re-implantation.

2.6.2 Re-implantation of septum cartilage in experimental animals (‘septoplasty’)

Due to release of interlocked stresses within septal cartilage, incision of the antero-posterior axis will be immediately followed by overlap of the cut edges (viz. 2.7 Interlocked stresses). If a part of the septal cartilage is resected, the distance between the cut ends will diminish. End-to-end reimplantation is only possible after adapting the dimensions of the implant (trimming) to the smaller dimensions of the gap in the septum. Nevertheless increasing dislocations of the implant during further growth resulted in serious deviation of the septum, preventing the growing septum to contribute to lengthening of the nose (Figure 20a). Reimplantation did not prevent shortening and sometimes saddling of the nose though the viability of the re-implanted cartilage was high, with an increase in length of around 50% during the experimental period [33]. This coincides with clinical observations as described by Huizing [103] and Pirsig [104]. Realization of a proper end-to-end connection between various parts of the septum appeared to be a most critical point in preventing surgery-induced growth anomalies in the long run [105]. Re-implantation of resected parts in rabbits reduced septal perforations to a minimum.

2.6.3 The use of crushed cartilage

Implants of autogenous crushed cartilage did partially survive and later showed signs of vigorous growth and deviations without any positive effect on development of the nose [106], [107]. In the early phase areas of necrotic chondrocytes are found next to clusters of viable cartilage cells which tend to enlarge by vast redifferentiation (Figure 19b).

Although the use of crushed cartilage has proved its value in reconstructing the nasal septum of adult patients, experimental data have clearly demonstrated the limitations for application in the growing nose [106]. It appears appropriate as filling tissue between perichondrial layers to prevent perforation or scar retraction. It lacks however the mechanical strength to transform growth into lengthening of the septum (Figure 20). It is, therefore, not suitable for septoplasty in the growing period.

2.6.4 Polarity of autogenous implants

The cartilaginous nasal septum, as was discussed previously, shows an obvious antero-posterior polarity in its distribution of thinner and thicker areas. Data on the embryological development of this specific 3-dimensional organization of the septum appeared not to be available. It has been reported by Copray that even in vitro, in organ culture, the septal cartilage of rats maintains a predominantly anteroposterior growth [108]. Nolst Trenité observed that the polarity in morphology and growth of the nasal septum seems to a high degree independent of external conditions. This might imply that in a clinical situation resected parts of the septum should be re-implanted without changing the antero-posterior axis! The loss of a 3-dimensional organization in crushed grafts intervenes with the potentiality to develop into a specific morphological entity [106].

2.6.5 Conclusions

Submucosal implants of non-crushed or crushed cartilage to fill septum defects did not restore normal growth of the cartilaginous septum, nor contributie to midfacial...
development. Promising data on new ways to avert growth anomalies have been published using intraseptal implants of PDS foil (see 2.9).

2.7 Interlocked stresses

Fry [109] described the phenomenon of interlocked stresses for ex-vivo isolated cartilage of the human nasal septum of varying ages (0–79 years), a concept earlier introduced by Gibson and Davis for human rib cartilage [110]. They supposed forces locked within the matrix of cartilage existing in a state of balance between tension (in the 3-dimensional network of collagen fibres) and pressure (generated by water bounded to hydrophilic proteins). By scoring or incision of cartilage – interrupting the fibrous network – these stresses could be released, resulting in a changing form of the cartilage. Interlocked stresses have also been demonstrated in the septum cartilage of young rabbits – in vivo and in situ – by an immediate overlap in antero-posterior direction after cranio-caudal of the nasal septum submucoperichondrially [111]. A second incision after an interval of 3 weeks, ±6 mm anterior and parallel to the previous one resulted again in an immediate overlap of approximately 1.5 mm. The stresses are apparently rebuilt in three weeks when the mechanical continuity of the septum is restored (Figure 21a, b).

2.7.1 Scoring of septum cartilage: controlled deformation

Fry [112] suggested a scoring technique to be used in septoplasty. Multiple superficial incisions are made to let the cartilage bend or unbend. After superficial scoring the cartilage always warped in the direction away from the scored side. It was suggested that next to the number of incisions the depth of the scores might relate to the degree of bending. Because of the unreliable and often disappointing results many investigators preferred full thickness incisions or implantation of crushed cartilage. Both these procedures, however, weaken the cartilage structure dramatically which may have an adverse effect on the structural support of the nasal dorsum [113], [114].

The relation between the depth of the incision and the immediate bending was studied in more detail [115]. To exclude the effects of gravity nasal septa of rabbits were submerged in a saline bath. On these conditions scoring less than 15% of the total cartilage thickness did not result in effective warping. A linear relation was found between depth of incision and degree of bending for incisions up to 50% of the thickness. No differences were found between the septa taken from young and adult rabbits. There are no data pertinent to effects of scoring on the mechanical strength – weakening – of the septal cartilage, nor the effects on later midfacial development. The application of a laser technique to reshape deformed cartilage has been advocated but bears the risk of chondrocyte degeneration and tissue necrosis [116].

2.8 Hyaline cartilage: histology and some immunohistochemical aspects

In normal septal cartilage a network of collagen fibers could be demonstrated, aligned perpendicular to the surface and forming a mantle at the periphery of the cartilage in the transitional zone between perichondrium and cartilage, the most proliferative, so-called cambium layer. Here cells (chondroblasts-chondrocytes) with their surrounding proteoglycans-containing matrix are held captive between these collagen fibers. Izumi et al. reported that in particular TGF-β1 is important in initiating and promoting the expression of collagen type II which is specific for hyaline cartilage [117]. Silver and
Glasgold stated that any cartilage wound healing response which does not lead to replacement of collagen type II will result in tissue with abnormal morphologic and mechanical properties [118].

Later Verwoerd-Verhoef et al could demonstrate by immunohistochemical staining for collagen type II that injury to the cartilage surface resulted in loss of the growth factors TGF-β1 and TGF-β2 in the superficial layer [34].

With ageing wound healing and regenerative capacities appeared to decrease considerably. Still the question is not answered decisively whether the various TGF-β types play a significant role at a site of cartilage repair.

2.8.1 Wound reaction and healing of hyaline cartilage of the septum

In young rabbits, the wound reaction of septum cartilage – fractured after trauma or cut during surgery – involves a zone of regressive changes and necrosis of the chondrocytes developing within three days over a distance of 1–3 mm. In the neighbouring zone the cartilage cells are highly activated, as shown by many mitoses. One week after the injury the collagen fibers present in hyaline cartilage have closed ranks and demarcate the border between the viable cartilage and the superficial necrotic area. This necrotic tissue is invaded by polymorphonuclear cells and macrophages which take care of resorption of the dead material [34]. Three to five weeks later a firm fibrous layer covers the former wound edges (Figure 19a, b).

When the middle one-third of the nasal septum is resected, the defect is filled with exudate that after three days becomes invaded by cells from the perichondrium. The bilateral perichondrial layers just dorsal of the vomerine alae and under the nasal dorsum tend to fuse whereas in the middle part (the thickest zone of the septum) there remains an intermediate space completely occupied by proliferating cells from perichondrial origin. These cells start to differentiate into chondroblasts; the newly formed cartilage with smaller cells and less intercellular substance is separated from the pre-existent tissue by a sometimes substantial fibrous cover. The regenerated cartilage forms a thin bridge between the anterior and posterior fragments of the original septum. This thinner layer of new cartilage is progressively bending and deviations develop during further growth.

Similar observations were already done by Kvinnland and Breistein, who found extensive cartilage regeneration after resecting approximately 50% of the cartilage anterior to the perpendicular plate in newborn and 1-day-old rats [119]. Jeffries and Rhys Evans carried out a histological study in order to investigate the regeneration of septal cartilage in rabbits. They showed that submucosal resection resulted in some regenerated cartilage which could not prevent midfacial retardation and malocclusion [84].

When the defect is filled with an autologous implant (re-implantation of the resected middle one-third) the wound healing of the margins takes place in a similar way on both sides. Despite careful positioning of the graft initially, side-to-end or side-to side dislocation occurred from the second week on. Three to five weeks later a firm fibrous layer is covering the former wound surface (Figure 19b, Figure 20a). End-to-end connections at the interface which are nearly always intervened by a fibrous layer were only found at the most thick locations, dorsally and ventrally in the septum [120].

2.8.2 Wound reaction of elevated mucoperichondrium

Although elevation of the mucoperichondrium seemed not to affect nasal growth, at tissue level it appeared to result in short-term effects with swelling of the lamina propria and exudate, and a more prolonged proliferative effect of cell production [81]. The outer layer of the perichondrium consists predominantly of fibrous tissue [121], [122]. Cells of the inner (cambium) layer, lying most closely to the cartilage, were suggested to be the source of chondroneogenesis [123], [124]. Mucoperichon-
drial elevation might occasionally cause lesions of the cambium layer, resulting in local cartilage formation. Part of the septum cartilage in the rabbit is protected on both sides by the vomeral wings. Here, septum perichondrium and vomer periosteum are interconnected. After resection of septal cartilage the perichondrium was found to remain adherent to the vomer blades which keep the defect open. Then, the space appeared to be filled with large quantities of new chondrogenic cells produced by the perichondrium and redifferentiating into cartilage (Figure 22). This chondrogenic potential of perichondrium was earlier demonstrated both in vitro and in vivo by Skoog and Ohlsen [125] and Engkvist [126].

After resection of septal cartilage the perichondrium was observed. These in vitro experiments clearly demonstrated growth of the wound surface could be observed! However, in the third series explants were completely denuded from perichondrium. Wound healing was studied at the cut edges of the implants. In series I from 3 days onwards fibrous cells are growing over the wound surface of the explants. In explants only covered by the inner perichondrial layer (cambium, series II) no fibrous overgrowth of the wound surface could be observed! However, in this series the majority of the explants showed new cartilage formation, defined by positive staining for collagen type II. The cut edges of the cartilage in series III, denuded from both perichondrial layers, remained free of any overgrowing cells and no new formation of cartilage was observed. These in vitro experiments clearly demonstrate specific functions for the two layers of perichondrium. New cartilage is only formed by the cambium and not by the underlying cartilage and also not by the outer layer of perichondrium.

Where the outer layer of perichondrium is connected to the vomeral wings, and “prevented” from expanding over the cut edge of the cartilage, the outgrowth of cells from the cambium layer seems abundant, resulting in the formation of substantial quantities of cartilage, some times even bridging the gap.

2.8.3 Conclusions

It is evident that understanding the distinguishing role of outer perichondrium, cambium and septum cartilage during wound healing of the septum may be essential for the development of new surgical techniques to create a cartilaginous septum which is straight and shows normal growth. It seems sensible to explore methods to delay the overgrowth by the outer perichondrium and/or stimulate cartilage formation by the cambium.

It should be appreciated that this newly formed cartilage might differ from the original septum cartilage in morphology and growth potential, and may not respond equally to the physiologic stimuli in nasal growth. Consequently, this neocartilage formed after septal trauma or surgery at a young age might contribute to a disharmonious development of the growing nose [128]. Future studies are needed to tackle this problem.

2.9 Current developments

When speaking about the use of grafts there might always be the need for more cartilage than is available. Implants of artificial material, like proplast and later gore-tex, have been proposed, used in humans and tested in growing animals by Nolst Trenité [129]. In the young growing rabbit these materials appeared to have disastrous effects with the most serious growth inhibition. Reactions of inflammation and expulsion have been observed. In the last decade a polydioxanone (PDS) foil has been used by Boenisch and Nolst Trenité in the reconstruction of traumatic anomalies of nasal septum and ear cartilage in adult patients [130]. PDS is a resorbable material which appeared to prevent postoperative sequelae like recurrent deviations and re-dislocation of grafts. In a preliminary study the use of PDS foil in the reconstruction of septal defects in growing rabbits was investigated. The 40 specimens represented the condition of the nasal septum at 5 intervals (between 2 and 25 weeks) and after 8 different interventions. PDS foil seemed to stimulate cartilage regeneration. After resection of the middle one-third of the septum the defect was covered by PDS underlying the mucoperichondrium. Twenty-five weeks later the material was resorbed, and the space between the perichondrial layers which were in the early phase separated by the PDS, was completely filled with newly formed cartilage. This young tissue had a hyaline appearance and was nicely integrated with the original cartilage fragments [131]. After re-implantation of a resected piece of septum cartilage, crushed or non-crushed and sutured on the PDS, deviations and duplications which could be expected, did occur significantly less. The foil is suggested to support the implant and enhance cartilage regeneration.

It is not noted if growth of the snout was undisturbed.
In the nineties our group had developed a method to investigate the feasibility of a composite graft of demineralised bone matrix (DBM) enfolded in ear perichondrium to produce new hyaline cartilage in vivo (Figure 23). Bean et al showed that the bone matrix is resorbed within 3–4 weeks and ingrowth of chondroblasts derived from the overlying ear perichondrium has occurred [132]. This neocartilage could be successfully harvested and transplanted into a defect of the nasal septum or cricoid. Growth of the cartilage graft was obtained but there were also disadvantages [133]. In a minority of the experimental animals we found some local enchondral ossification. Another negative point is that two operations are needed, first to execute the procedure of enfolding the carrier (DBM) in ear perichondrium behind the pinna, secondly the harvesting of the newly formed cartilage and transplantation into the septum defect. Later we could determine that collagen type I was absent in the newly generated cartilage whereas it contained collagen type II and proteoglycans with hyaluronic acid binding regions [134]. This indicated the presence of hyaline cartilage. In a second study the conditions which enhance chondrogenesis in a composite graft of of perichondrium and DBM were investigated by in vitro culture [135]. The results suggested that DBM itself has few chondrogenic qualities but functions merely as a spacer for cell ingrowth. In a third, more fundamental study the chondrogenic potential of the DBM was investigated by van Osch et al. [136]. Implantation without an envelope of perichondrium never resulted in cartilage formation. Immunohistochemical tests only showed a faint staining for growth factors. The fast resorption of the scaffold material seemed a positive factor in the chondrogenesis. The fear for contamination with prions, which are responsible for the mad cow disease, has since then considerably reduced the use of DBM in otorhinolaryngology.

Figure 23: Complete integration after implantation of young cartilage in septum defect; new cartilage was constructed through implantation of composite graft of DBM and perichondrium in the ear of the rabbit.

To evaluate the feasibility of newly developed cartilage grafts an animal model was designed by ten Koppel et al. in a so-called ‘pinna punch’ model [137]. Multiple holes (punches) in the rabbit ear were filled with grafts of different types of generated cartilage and after 3 weeks assessed for quality, quantity and integration in a semi-quantitative grading system. It appeared to be a reliable and efficient method for a first evaluation of newly formed grafts.

### 2.9.1 Tissue engineering

The technique of culturing cells in vitro and composing these cells into tissue (tissue-engineering) is passing through a period of fast and promising development, although the results are not yet good enough for clinical application at a large scale in otorhinolaryngology. In orthopedics autogenous chondrocyte implantation is being used more extensively, and it is estimated that over 30,000 patients have been treated with this “cartilage tissue engineering method”. In the head and neck area a recent publication by Macchiarini et al. has attracted much attention [138]. The authors have implanted a tissue-engineered trachea, containing patients’ own epithelial cells and mesenchymal stem-cell-derived chondrocytes in a 30-year-old woman with end-stage bronchomalacia. To generate cartilage from isolated cells, chondrocytes seem the better option to guarantee cartilage production. Human nasal septal chondrocytes were cultured for different periods of time in monolayer or suspended in alginate and cultured as construct (Alginate Recovered Chondrocyte method) by Chia et al. They concluded that tissue-engineered cartilage with the ARC method, and without the use of a scaffold, has the histologic and gross appearance of native cartilage [139]. Auricular cartilage also forms an excellent source for cells to produce cartilage [140].

A comparison of different chondrocytes for use in tissue engineering of cartilage constructs by Isogai et al. on bovine cells revealed that each chondrocyte type maintains its particular developmental characteristics, which is a critical observation in the design and elaboration of any tissue-engineered cartilage model [141]. This conclusion is confirmed by recent data of Hellingman et al. who used a micro-array study to compare human nasal septum and auricular chondrocytes of the same donors [142]. Although chondrocytes are the best cells to form extra cartilage, it is not always possible to harvest sufficient autogenous cartilage to obtain the number of cells required. Therefore, researchers are investigating more and more the application of stem cells. Adult stem cells can be obtained from bone marrow or adipose tissue in fairly large quantities. These cells may be differentiated into various lineages amongst which are chondrocyte-like cells, by the addition of growth factors [143], [144]. One of the current problems of the use of adult stem cells for cartilage repair is the instability of this tissue. Upon implantation it mineralizes and transforms into bone via the enchondral ossification pathway [145], [146].

### 2.10 Final remarks

1. The septodorsal cartilage should be appreciated as playing an essential role in the development of the midfacial bony and cartilaginous skeleton; growing...
cartilage and growing bone are interacting; defects, fractures or incisions of the septum cartilage may interfere with normal development of the premaxilla-maxilla; interventions including the premaxillary-maxillary sutures will seriously affect the development of all nasal supporting structures.

2. The organisation of the cartilaginous septum is obviously complex; special zones have special functions in postnatal growth of the midface. The growing dorsolateral cartilage is interacting with sutural growth of the midfacial skeleton.

3. Understanding the mechanism of midfacial development is the basis for timing and technique of surgical treatment of congenital or acquired nasal pathology.

4. The restricted wound healing capacity of septum cartilage is currently the essential factor in limiting the effectiveness of surgical interventions and should be recognized during planning and surgical intervention.

5. Extrapolation of animal data to humans should be done with caution but the lessons learned from animal studies contribute to understanding congenital or postraumatic developmental growth anomalies of the nose and midface in children. Secondly they contribute to guidelines for surgery of the supporting skeleton of the growing nose, as summarized in the following chapter.

3 Discussion and recommendations

3.1 Summary of part 1 and 2

The growing nose in children presents (as discussed in part 1):

• an age-specific anatomy of the nasal skeleton in children and adolescents
• the growth spurt of the nose at different ages in girls and boys
• a complex organisation of the septum cartilage with growth zones and fracture prone areas
• poor wound healing capacity of nasal cartilage after accidental or surgical injury which might have immediate and late consequences for further growth of the midface.

Animal research has further elucidated (as discussed in part 2):

• the essential contribution of the septal and dorsolateral parts of the nasal cartilage for the development of bony nasal skeleton, maxilla and premaxilla;
• the importance of specific growth zones in the cartilaginous septum to growth of the nasal dorsum and lengthening of the upper jaw;
• the mechanisms underlying normal or abnormal growth after injuries of the cartilaginous or bony nasal skeleton.

Current research should provide methods to overcome the poor wound healing capacity of nasal cartilage, which still is a limiting factor in the restoration of normal growth of the midface.

3.2 Clinical aspects

Surgical intervention to the nose in children may be an elective procedure or indicated after a recent trauma. Treatment modalities are generally evaluated by follow-up studies. Criteria for successful treatment include not only an improved nasal form and function at short notice but also the quality of the later development of nose and midface.

Clinical evidence of the effects of rhinosurgery at a young age is still fragmentary. In general, publications refer to a small number of patients. Information is frequently incomplete regarding the age of the individual patient at the time of trauma and surgery, the observed deformities or lesions, and the surgical procedure(s) [147]. Moreover, an adequate follow-up of nasal form and function as well as facial development – at least continued till after the adolescent growth spurt – is not presented in the majority of the reports. Objective data are scarce but indispensable when the conclusions imply normal growth after surgery [148], [149], [150]. Metrical data may be of less importance in case of apparent defective development of the nose in children after closed reduction of nasal fractures [151], [152].

3.2.1 Literature

An anthropometrical method was used by Béjar et al. to study the nose in 28 patients about 3.4 years after an external septoplasty [153]. The age at the time of surgery ranged from 6–15 years. Surgery included excision, refashioning and reinsertion of the quadrilateral cartilage. The authors conclude that only growth of the nasal dorsum could have been negatively influenced by external rhinoplasty.

Lateral skull radiographs have also been used to document and quantify late effects of nasal trauma during childhood [154]. Measurements on these radiographs in 29 adults demonstrated a reduced angle of nasal projection and a reduced downward and forward growth of the maxilla were observed. Presently it is recognized that follow-up of nasal growth by periodic radiographs may bear the risk of damaging the eye lenses. Many publications concerning the treatment nasal injuries or progressive maldevelopment of the nose in children only present instructions concerning the surgical technique without referring to the effects on later development of the nose [155],[156],[157],[158]. A review of surgical and developmental aspects of rhinosurgery in children and a summarizing state of the art ‘anno 2000’ have been presented by Pirsig [159], [160]. He promoted the dialogue between clinicians and researchers by identifying clinical problems and emphasizing the surgical relevance of developmental mechanisms in children.
It may further be emphasized that "a child's nose" is a generalization. Taking into account the postnatal anatomical development, the progressive maturation of skeletal tissues and evolution of morphogenetic processes underlying nasal growth, the effects of surgery (or injury) should be specified for subgroups of children with different ages, like 3–6, 7–10 years etc. Patient (child) and parents should be informed of the potential benefits of the surgery, and of the rationale to continue a follow-up of the facial growth till after the adolescent growth spurt. Secondly, in communicating results of surgery representative photographic documentation is paramount to define qualifications as normal or abnormal, which are in essence subjective.

### 3.3 Treatment management

#### 3.3.1 Recent nasal trauma: examination

A correct diagnosis of fractures and dislocations of the bony and cartilaginous nasal pyramid in children is often hampered by the small dimensions of the nose or abundant swelling of the soft tissues during the first days after trauma. The maxilla, orbital rim and palate should be examined to exclude additional fractures; radiological examination may be advisable. When in doubt the examination – inspection, palpation and anterior rhinoscopy – should be repeated after a few days when the soft tissue swelling has diminished. Re-examination under general anaesthesia may be combined with surgical treatment. Decongestion of the mucosa prior to rhinoscopy may be helpful for a correct assessment of the septum. The sensitivity, however, of children under the age of 6 years for sympatomimetic (in nasal drops) should be recognized!

Fractures of the bony nasal pyramid do not occur as frequently in children as in adults because in children the nasal bones are less prominent and the majority of the nasal skeleton is cartilaginous. Moreover a dehiscence of the sutures bordering the nasal bones may occasionally be observed, which should be treated by prolonged gentle compression on both sides. In general the same techniques as for elective surgery are used for the treatment of recent traumatic deformations of the nasal skeleton.

#### 3.3.2 Haematoma or abscess of the nasal septum

Diagnosis and treatment of a haematoma or abscess of the nasal septum and dorsum is urgent to prevent cartilage destruction [161]. Next to drainage, repositioning of the mucosal membranes and antibiotic protection, implants of homologous cartilage have been used to preclude later saddling of the nasal dorsum. Also, the implantation of multiple small pieces of cartilage, fixed together by fibrin glue, have been used [162]. Normal growth of nose and midface after such procedures has not been substantiated by an adequate follow-up. To achieve a successful long-term result the implant material should provide support and be able to grow between the mucoperichondrial layers. Recently it was suggested to store the septum with a single large cartilaginous implant. Autologous grafts of ear cartilage were affixed to a polydioxanone (PDS) foil, to ensure good tissue-to-tissue approximation of the individual grafts [163].

#### 3.3.3 Haematoma of the nasal dorsum with rupture of the upper lateral cartilage

The external branch of the anterior ethmoidal artery is reaching the subcutis of the nasal dorsum via a ‘foramen’ in the upper lateral cartilage at the caudal rim of the nasal bones. In case of rupturing of an upper lateral cartilage following external trauma, the anterior ethmoidal artery becomes involved. The resulting haematoma can often be diagnosed at anterior rhinoscopy as a bulging of the lateral nasal wall between the caudal edge of the upper lateral cartilage and the cephalic margin of the alar cartilage: the recommended place for evacuation of the haematoma.

*Note:* Externally the haematoma is often initially concealed by facial edema!

It is advisable to approximate a dislocated upper lateral cartilage to the nasal bone by nasal packing. A dorsum haematoma bears the risk of infection, resulting in an abscess with cartilage necrosis and scar formation.

#### 3.3.4 Closed reduction in young children

The prevailing method of managing acute nasal fractures in young children is closed reduction under general anaesthesia. A combination of elevation of the nasal dorsum – thereby straightening the nasal septum – and prolonged external digital compression of the nasal bones is usually successful in restoring nasal morphology. The elasticity of the septodorsal cartilage and its capacity of regaining its original form are essential for the success of the manipulation. Nasal packing is contra-indicated in young children as they are still "programmed" for nose breathing. Repositioning of dislocated nasal bones is mostly possible. In exceptional cases a 2 mm osteotome may be used to mobilize dislocated parts and produce a satisfactory alignment of the nasal bones, externally controlled by palpation.

#### 3.3.5 Rhinosurgery in children as an elective procedure; recommendations

Severe breathing problems due to septum pathology and external distortion of the nose are generally accepted to be indications for surgery, in particular when the malformations appear to be progressing. For most children with less evident pathology it may be a good advice to document first the progression of the pathology for a certain period before making a definite decision on the indication for surgery [164]. In some...
cases postponing surgery till after the adolescent growth spurt may be preferred to diminish the risk. Based on experimental evidence and clinical observations, the following guidelines are relevant:

1. Uni- or bilateral elevation of the mucoperichondrium has no negative effects on further growth. Unilateral mucosal elevation may have the advantage of stabilizing the position of separated parts of the septum. The mucosa of the nasal floor should not be elevated to prevent damage to the incisive nerves. Mind the risk of injuring the cranial base in young children because of the highly variable grade of ossification of septum and cranial base.

2. Identify defects and (older or recent) fractures of the septum, and their relation to the specific growth and support zones.

3. Mobilize deviated or overlapping cartilaginous fragments by separating adherent fibrous tissue; adapt form and size of the fragments to reconstruct a straight septum in the midline.

4. Avoid incisions through the growing and supporting zones, in particular of the (sphenoid-ethmoido-dorsal zone.

5. Posterior chondotomy or separation of the septal cartilage from the perpendicular plate (in particular the dorsal part) should be avoided as this area is of paramount importance for support and further growth (length and height) of the nasal septum and nasal dorsum;

6. Resection of a deviating basal rim of the cartilaginous septum is not expected to have consequences for the outgrowth of the nasal dorsum, on the condition that the most anterior part and thus the septospinal ligament remain intact;

7. Reconstruct defects in the cartilaginous nasal septum, preferably with autologous septum cartilage to minimize the risk of septum perforation or scar formation between the bilateral mucosal membranes; recurrent deviations or dislocation, however, may complicate further development;

8. Resection of a crista septi or a spina vomeri will not harm nasal development, as the cartilaginous septum (being the dominant growth center of the nose) is based on the caudal thickened rim of the perpendicular plate;

9. Do not transect the septospinal ligament (connecting the cartilaginous septum to the premaxilla) as it anchors the septum in the midline and thus plays a role in the forward growth of the upper jaw;

10. Reposition a luxated caudal rim of septum cartilage into a columella pocket and suture it between the medial crura of the alar cartilages;

11. When both upper laterals have been separated from the septum, they should be carefully reconnected to prevent later deviations of the cartilaginous nasal dorsum.

12. Mobilization of nasal bones in combination with reconstruction of a malformed septum bears the risk of postoperative instability of the (corrected) supporting structures, resulting in new anomalies during further growth.

13. Intraseptal blood collection should be avoided in order to minimize the chance of infection and subsequent cartilage necrosis.

14. Alloplastic or biomaterials are not capable of growth and implanted in a growing septum may disturb septal growth.

15. To date there is no evidence in experimental studies of an advice against the open approach.

The age-specific anatomy, the effects of wound healing and the risk of interfering with processes of facial growth, should always be regarded when doing nasal surgery in children. Rhinosurgical procedures, which may be considered effective and safe in adult patients are not necessarily safe or effective in children.

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