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Congenital and acquired developmental problems of the upper airway in newborns and infants ☆

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ABSTRACT

Aim: To review the current knowledge on congenital and acquired developmental problems of the upper airway in newborns and infants.
Data synthesis: Causes of airway obstruction include problems with the nasal airway (choanal atresia), craniofacial syndromes (Apert syndrome, Crouzon syndrome), problems with facial/tongue anatomy (Pierre-Robin syndrome), the tongue (Down syndrome), or the larynx (laryngomalacia, vocal cord palsy, subglottic stenosis, subglottic hemangioma), along with lower developmental problems (tracheo/bronchomalacia). After establishing a safe airway, a detailed assessment and appropriate management are necessary. Treatment may involve simple observation, conservative management, chest physiotherapy, CPAP ventilation, and surgery, urgently or in a second phase.
Conclusion: Upper airway diseases in neonates and infants may be life threatening, or challenging regarding diagnosis and management. There should be a very low threshold for referring these children, after establishing a safe airway, for a specialist opinion and care in a tertiary unit, if local facilities are limited or unavailable.
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1. Introduction

The upper airway extends from the nasal aperture to the trachea and can be the site of multiple types of congenital or acquired diseases leading to anatomical or functional obstruction [1]. Neonatal airway obstruction may occur in any setting (home, delivery unit, hospital) and in various forms (life threatening, acute, sub-acute, and chronic). Therefore, all physicians involved should be familiar with the clinical presentations and endoscopic findings of the respective diseases, so that appropriate measures can be initiated at an early stage, thus avoiding significant complications.

The aim of the present paper is to review the current knowledge on the development of the airway, give an overview of causes of neonatal airway obstruction, and outline the latest management recommendations.

2. Development and characteristics of the neonatal airway

2.1. Development of the airway

The airway begins to develop as an outgrowth of the ventral part of the foregut at the fourth week of embryonic life. Thus the internal membrane of the respiratory system is of endodermal origin. The muscles and cartilages of the larynx are derived from the branchial arches. Initially the respiratory diverticulum communicates freely with the foregut, but as the diverticulum expands caudally, it becomes separated from the foregut by the oesophago-tracheal ridges, which fuse to form the oesophago-tracheal septum. At that time the internal epithelium also proliferates and occludes the lumen of the airway. This then recanalises so that the definitive airway is usually formed by the seventh week of gestation.

Developmental problems usually arise due to incomplete or non-canalisation (leading to laryngeal webs or atresia, respectively), or difficulties with the separation of the oesophagus and trachea (leading to tracheo-oesophageal fistulas).

The nasal cavity is also important especially in the neonate, and this begins to develop with the development of the nasal placode (a thickening of surface ectoderm) at the end of the fourth week of gestation. During the fifth week the placode is surrounded by the lateral and medial nasal swellings. This leads to the formation of a nasal pit. During the sixth week these pits deepen. The nasal cavity is separated at this point from the oral cavity by the oronasal membrane. This breaks down by the seventh week to form the primitive choanae. Later, once the palate has developed, the definitive choanae are located at the junction of the nasal cavity and the pharynx.

2.2. Characteristics of the neonatal airway

The neonatal airway is both absolutely and relatively smaller than the adult airway. As resistance is inversely proportional to the fourth

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power of the radius, very small decreases in the radius of the airway will lead to a large increase in resistance. The speed of the airflow has to increase to overcome the resistance, leading to turbulent airflow and increased noise, which manifests as stridor-a harsh sound (stridor is derived from the Latin term of "to creak").

The cartilages of the neonatal airway are also softer than that of a child or adult, and therefore more susceptible to extrinsic and intrinsic compressions, thus reducing the radius of the airway.

Finally, the administration of β-agonists tends to make the symptom of the neonatal airway worse, as it annuls the splinting effect of the bronchial muscles.

3. History and examination of the neonate suggesting airway problems

With the advent of detailed high resolution ultrasound scanning, prenatal diagnosis of potential airway difficulties has become more common. Ultrasound can detect tumours of the head and neck that could cause potential airway compromise, and can also detect congenital high airway obstruction (CHAOS). The features of CHAOS on ultrasound are polyhydramnios, increased echogenicity of the lungs, a dilated trachea (if there is no tracheooesophageal fistula to allow lung fluid to escape) and flattened or inverted diaphragm [2].

More recently ultrafast MRI scanning can be used to assess any masses in more detail, and allow planning of the ex utero intrapartum treatment (EXIT) procedure [3]. The EXIT procedure is a procedure in which the baby's head and shoulders are delivered by caesarean incision. The foeto-maternal circulation is maintained and this allows about 60 min of surgical time for the multidisciplinary team to establish a safe airway by intubation or tracheostomy. This has become more successful as the multidisciplinary team approach has been developed.

Airway obstruction cannot always be diagnosed or predicted prenatally. The main symptom after birth is stridor. This can be inspiratory, expiratory or biphasic. Inspiratory stridor arises from the supraglottic airway (nose to glottis). Airway obstruction more distally may be biphasic or expiratory. Features which should be noted about stridor are its onset after birth, whether it is intermittent, or positional, whether the voice is normal, whether there are any blue spells, and how feeding is affected.

On examination, any dysmorphic features need to be noted, particularly the size of the jaw, any cleft lips or palate, or facial deformities. The rate of respiration and work of breathing also need to be recorded. Severe stridor or a very quiet baby, tracheal tug and subcostal recession are worrying signs, as they imply impending airway disaster. In contrast, cyanosis is a late sign.

Causes of airway obstruction include problems with the nasal airway, craniofacial syndromes, problems with facial or tongue anatomy, problems with the tongue, and problems with the larynx. Although located just below the upper airway, developmental problems of the trachea or bronchi present with similar symptomatology, and will also be discussed in brief.

4. Developmental problems of the neonatal airway

4.1. Nasal problems

4.1.1. Choanal atresia

Choanal atresia is the most common cause of nasal airway obstruction (Fig. 1). It has been attributed to the persistence of the bucco-pharyngeal membrane. It occurs in 1 in 10,000 births, twice as often in girls, and is more often unilateral (unilateral:bilateral 2:1). The problem with choanal atresia stems from the fact that neonates are obligate nasal breathers. When the nose is blocked the child makes an effort to breathe, and when the mouth is closed the tongue is drawn up to the palate. The baby then becomes cyanotic until the mouth is open to cry. The child then pinks up quickly until the mouth is closed and the cycle begins again.

Bilateral choanal atresia is a neonatal emergency. The baby may need to be resuscitated at birth. The aforementioned history will give rise to the suspicion of choanal atresia. Other signs include a failure to pass a fine catheter through the nose, and absence of misting when a cold spatula is placed under the nostrils. The differential diagnosis includes septal deviation, septal dislocation, nasal masses, and encephalocele. Endoscopes may be very useful in the differential diagnosis.

The first priority is to establish an airway, and this can be done by intubation, or the insertion of a McGovern nipple (an oropharyngeal airway fashioned by cutting off the end of a large feeding nipple, placing it in the baby's mouth and attaching it using tapes around the baby's head) with a port for feeding. This will break the mouth seal and prevent airway obstruction. The baby must then be transferred to a specialist centre for definitive management.

If the newborn suffers from bilateral atresia, full examination must be undertaken to ascertain whether there are features of the CHARGE association (coloboma, heart defects, atresia of the choanae, growth retardation, genitourinary abnormalities and ear deformities-about 50% of children with bilateral atresia will have some of the other abnormalities). Further diagnosis of the condition requires imaging with a CT scan. It is vital to decongest and suction the nose prior to scanning in order to delineate the anatomy accurately. Atresia can be bony, membranous, or mixed [4].

Regarding the surgical management, blind puncture of the choanae is no longer used, due to recurrence and the dangers of CSF leaks. The main routes of repair are endo-nasally with the aid of 120° telescope, or trans-palatally. Maintenance of the surgical outcome is a matter of debate as different centres recommend stents to keep the newly formed airway patent or repeated dilations.

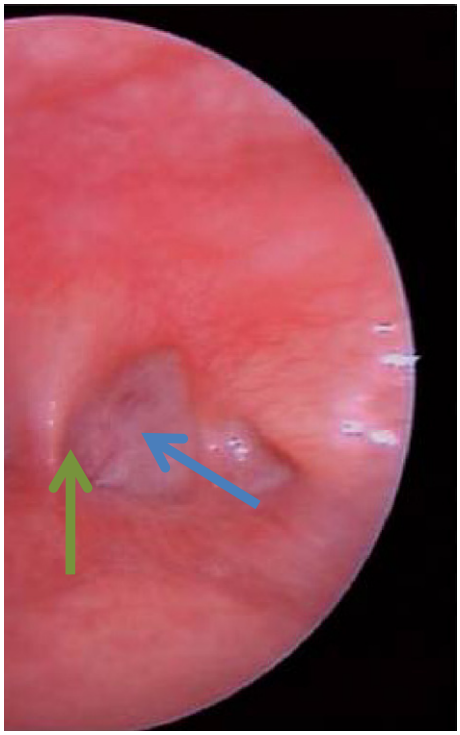

Fig. 1. Right choanal atresia (endoscopic view through the mouth. Green arrow vomer, blue arrow membranous atresia).

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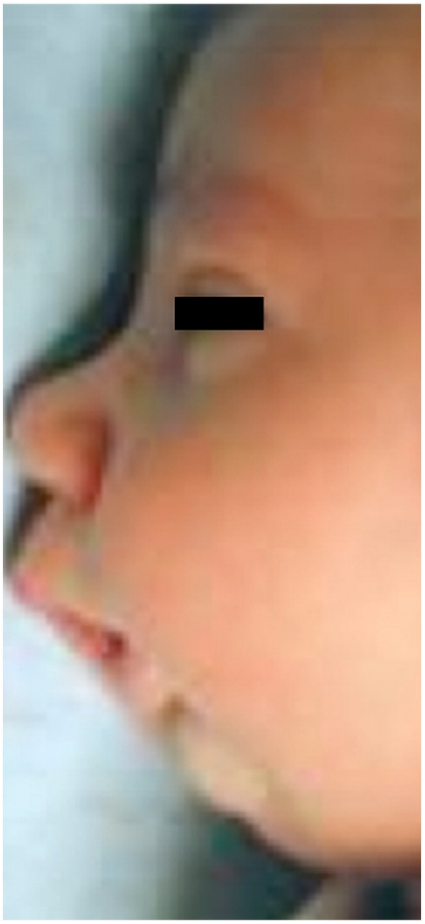

Fig. 2. Retrognathia in Pierre-Robin syndrome.

4.2. Craniofacial syndromes with the potential for airway obstruction

Any syndrome which is associated with enlarged tongue (e.g. Down), small jaw (e.g. Pierre Robin), or mid-face hypoplasia (e.g. Apert or Crouzon — Fig. 2) could lead to airway difficulties. Treatment involves stabilising the airway, and either wait for normal growth to resolve the problem, or initiate continuous positive airway pressure (CPAP — e.g. in Down syndrome children), or perform mid-face advancement.

4.3. Laryngeal causes of airway obstruction

4.3.1. Laryngomalacia

Laryngomalacia is the most common cause of infant stridor and is responsible for 60–70% of the cases [5]. The cause is a deformity of the laryngeal cartilages with an omega shaped epiglottis, short arytenoepiglottic folds and possible excess mucosa over the arytenoids (Fig. 3). It is a congenital condition, but symptoms do not typically occur until the first few weeks of life, as it is only then that sufficient airflow is achieved to cause the stridor.

The stridor is typically positional, worse on feeding or activity, but the voice is normal and there are usually no cyanotic spells, unless the condition is severe. The diagnosis is often presumed, but in the authors' opinion all children with stridor should be referred for airway assessment, which should include endoscopic assessment of the airway. This is because secondary airway abnormalities may be associated with laryngomalacia [6]. In fact, the more severe the laryngomalacia, the higher the likelihood of a secondary lesion. Gastro-oesophageal reflux disease (GERD) is associated with severe laryngomalacia, but it is unclear whether it is the increased negative pressure due to the obstruction which causes acid to be "sucked up" from the stomach, or whether it is the reflux which makes the laryngomalacia worse.

If the child is not severely affected, initial management involves close observation. Usually the stridor will resolve by the age of 2 years. The child's weight must be monitored closely over time.

Children with failure to thrive, cyanosis, severe hypoxaemia, or severe obstructive sleep apnoea need surgical intervention. This usually involves arytenoepiglottopexy and possible removal of excess tissue for the arytenoids. Supraglottoplasty (trimming of the redundant floppy tissue from the area above the vocal cords) represents another option. Initially cold steel techniques were used to perform these procedures, then the laser became more popular. Cold steel has again become popular, however, the literature suggests that the technique makes little difference to the outcomes [7]. Complications include postoperative aspiration, and supraglottic stenosis. It should be noted that only a very small percentage of neonates with laryngomalacia will require surgical management.

4.3.2. Vocal cord palsy

Vocal cord palsy is the second most common cause of stridor, accounting for 15–20% of cases. Bilateral vocal cord palsy can be idiopathic, or caused by central nervous system immaturity, various lesions, the Arnold Chiari malformation, or by birth trauma. Unilateral palsy can be caused by birth trauma, or secondary to previous intervention (i.e. due to cardiac or neck surgery).

Bilateral vocal cord palsy is presented as stridor, especially on activity, often with a normal voice, which deteriorates, thus leading to respiratory distress, and may need airway intervention. Aspiration may also occur.

Management of the child involves assessment using flexible nasendoscopy (Fig. 4). Direct rigid laryngoscopy is useful to distinguish between fixation of the arytenoids and vocal cord palsy. Once the diagnosis has been made, further assessment is required to determine the cause of the vocal cord palsy. Imaging of the head, neck, and mediastinum by means of a CT/MRI scan may be necessary.

Bilateral vocal cord palsy may require tracheostomy, or treatment of the underlying cause (if determined). Follow-up may show improvement over time, and endoscopic cordectomy (with laser) may facilitate de-cannulation. Other considerations include proper nutritional support, always bearing in mind the risk of aspiration.

4.3.3. Subglottic stenosis

Subglottic stenosis can be either congenital or acquired (Fig. 5). Congenital stenosis accounts for 15% of laryngeal malformations. It is thought to be caused by incomplete recanalisation of the airway in the third month of gestation. The most extreme form, laryngeal atresia, can be diagnosed prenatally, with the EXIT procedure (as

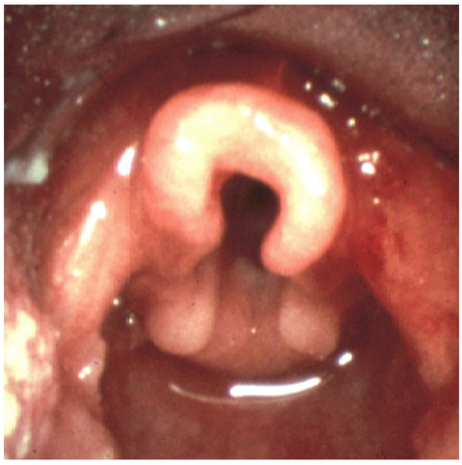

Fig. 3. Laryngomalacia (Source: Wikipedia™ "The Free Encyclopedia").

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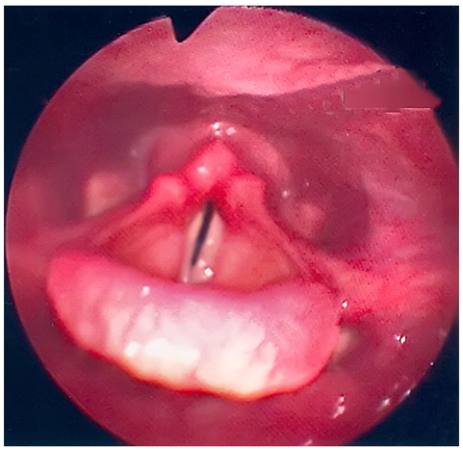

Fig. 4. Bilateral vocal cord palsy. The true vocal cords are seen in a median to paramedian position (adductive paralysis).

discussed above) allowing management of the obstructed foetal airway. Less extreme forms include membranous hypertrophy, and oval shaped cricoid ring.

Symptoms usually occur in the first few months of life, especially with the onset of a respiratory inflammatory episode. The child has biphasic stridor, the voice is usually normal, but there may be a barking couch. The symptoms may be indistinguishable from croup, but should be suspected when "croup"-like episodes are recurrent or prolonged.

Any child who cannot be easily intubated with an age appropriate tube, or is difficult to extubate should have their airway "sized". The best way is to use an endotracheal tube; the size which is most appropriate to the airway is the one which has a leak between 10 and 25 cm H_2O pressure.

The most commonly used classification for subglottic stenosis is the Cotton Myers classification, which compares the diameter of the area of the largest endotracheal tube which fits in the airway to the expected from the age of the child. The classification has 4 grades; a) I, 0–50% stenosis, b) II, 50–75% stenosis, c) III, 75–99% stenosis, and d) IV no detectable lumen [8]. Grades I and II may be managed conservatively, as long as the child is growing and thriving, and does not need frequent treatment for exacerbations. Grade III to IV (following the EXIT procedure) stenosis can be treated by endoscopic or open procedures, which may involve laser, endoscopic cricoid split, laryngotracheal reconstruction, or cricotracheal resection.

Acquired stenosis should be suspected where there has been traumatic or prolonged intubation. The incidence increased in the 1970's and 1980's, as more very low birth weight and premature babies survived. However, this led to better understanding and management of intubated neonates (e.g. shorter time periods of intubation and earlier tracheostomy). Thus, the related incidence has been dramatically reduced. Initial treatment may include a period of "laryngeal rest" and appropriate antireflux treatment. If further treatment is deemed necessary, the related methods of management are similar to the ones employed in congenital stenosis (previously described).

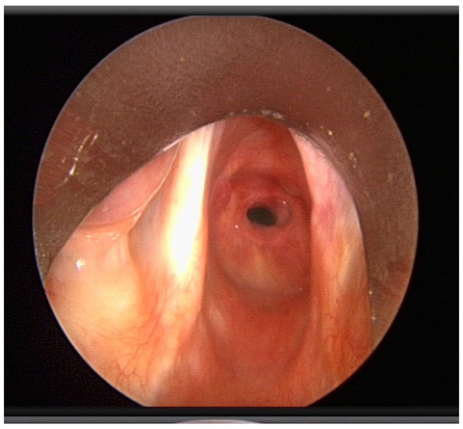

Fig. 5. Subglottic stenosis (Source: Wikimedia™ Commons).

4.3.4. Subglottic hemangioma

Subglottic hemangiomas are vascular malformations located below the level of the true vocal cords. They account for 1.5% of laryngeal abnormalities, and females are affected twice as often as males. While 50% of children with a laryngeal hemangiomas have a cutaneous hemangioma as well, only 4% of those with cutaneous hemangiomas have laryngeal hemangiomas. However, there seems to be an increased risk of laryngeal hemangioma, if there is a "beard" distribution of a cutaneous hemangioma [9].

Subglottic hemangiomas are associated with an alarming mortality rate that can reach 50%, if the lesions are left untreated. Indeed, approximately two thirds of these hemangiomas present with a 70% or worse airway narrowing.

Subglottic hemangiomas may lead to feeding difficulties, barking cough, stridor, respiratory distress, and even acute airway obstruction. They do, however, demonstrate a unique course characterized by proliferation during the first year of life, and involution thereafter.

Diagnosis is made during microlaryngoscopy, with the lesion appearing red or bluish and compressible. Normal appearance of the glottis and the supraglottis should not stop the examiner to assess the subglottic area in a neonate with airway problems.

A widely accepted aim in the management of subglottic hemangiomas is to maintain airway patency, promote lesion regression, avoid tracheostomy, and minimize the therapeutic side effects, until the lesions enter the natural phase of involution. Unfortunately, a watchful-waiting policy can only be applied in the minority of patients who do not demonstrate respiratory or feeding difficulties.

Systemic steroids have been the gold standard in the treatment of symptomatic subglottic hemangiomas until recently. Interferon-α, vincristine, cyclophosphamide, and other drugs have also been used in refractory hemangiomas, but some of them are associated with significant side-effects. The incidental discovery that propranolol induced early regression of infantile hemangiomas during their proliferative phase by Leaute-Labreze et al. [10], along with its low side-effect profile, attracted significant attention, and propranolol-based regimens emerged as a new and effective method of treatment in a growing volume of literature. However, the use of propranolol for proliferative infantile hemangiomas in the first year of life is still officially considered "off label" [11].

A number of surgical interventions have also been attempted, especially in cases not responding to medical therapy. Tracheostomy can no longer be considered as first-line treatment, mainly due to the associated morbidity (including the serious impact on child's and family's quality of life), and the need for close care postoperatively. However, in life threatening acute conditions, tracheostomy may be the only way of securing the airway. With regard to steroid administration, intra-lesional steroids may reduce the related systematic morbidity, however, the outcome is variable. Moreover, they often involve prolonged intubation and stay in a paediatric ICU, and the associated risks are also not considered acceptable by many authors. Laser ablation is considered a reasonable option for localized hemangiomas not causing extreme airway narrowing. Extensive circumferential narrowing is not suitable for laser debulking, due to the risk of postoperative scarring, and the ensuing subglottic stenosis. Hence, open resection and laryngo-tracheal augmentation may be ultimately required. However, these are relatively major surgical procedures with serious potential complications. Moreover, they demand inpatient management, intensive care units, and vast related experience on behalf of the operating surgeon.

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4.4. Tracheo/bronchomalacia

Tracheomalacia is caused by an abnormality of the tracheal wall cartilage allowing the trachea to collapse during respiration. Type 1 is characterised as primary tracheomalacia, type 2 is associated with extrinsic compression, and type 3 is associated with intra-tracheal inflammation. The incidence is reported to be 1 case per 2100 newborns [12].

Affected infants are presented with wheezing at 4–8 weeks of life. Investigations include CT scanning to look for vascular rings. The definitive diagnosis is made at bronchoscopy. Differential diagnosis includes cystic fibrosis, asthma, and other diseases.

The treatment of tracheomalacia, if needed, is surgical, and may involve tracheostomy always having in mind the location of the problem, airway stenting, and aortopexy (in case of acute life-threatening conditions, and provided that the tracheomalacic portion is segmental and does not significantly involve the main bronchi).

5. Conclusion

Causes of airway obstruction include problems with the nasal airway, craniofacial syndromes, disorders of the facial or tongue anatomy, and laryngeal diseases, along with developmental problems in the trachea or bronchi.

The neonatal airway is different to that of an adult and the neonate is prone to desaturation and to becoming acidotic very quickly. For this reason any abnormalities in breathing must be taken very seriously, and rapid assessment, diagnosis, and effective treatment should be initiated, which will allow the child to thrive.

There should be a very low threshold for referring these children for a specialist opinion in a tertiary unit, if the facilities (diagnostic, anaesthetic, or surgical) are unavailable. Endoscopy and bronchoscopy remain the gold standard for diagnosing most airway lesions.

Treatment may involve simple observation, if the condition is self-limiting and the child is thriving, without significant respiratory or feeding difficulties. Management includes medical treatment, chest physiotherapy, CPAP ventilation, or surgery that may be required in serious cases. Beta-agonists tend to make the symptoms of the neonatal airway worse, as they remove the splinting effect of the bronchial muscles.

Conflict of interest statement

The authors have no financial interests, and have not received any financial support for this article.

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