Glossoptosis-Apnea Syndrome in Infancy

F. Cozzi, MD, and A. Pierro, MD

From the Section of Pediatric Surgery, Department of Pediatrics, University of Rome, Rome

ABSTRACT. The clinical and physiologic features of 28 infants with Pierre Robin syndrome and those of 20 infants with various types of nasal obstruction were reviewed to determine whether different causes of upper airway obstructure may lead to a common syndrome. The patients had no significant differences in distribution of main clinical manifestations. Their features included cyanosis with respiratory distress, apneic spells, oropharyngeal dysphagia, vomiting, failure to thrive, cor pulmonale, brain damage, and sudden death during sleep. The common physiologic manifestation appeared to be an oropharyngeal obstruction caused by glossoptosis, which occurred mainly during wakefulness. Upper airway obstruction led to hypoxemia, which, in many instances, was not associated with hypercapnia and was not relieved by oxygen administration. It is concluded that regardless of a specific cause, any airway obstruction that results in a decreased inspiratory pressure overcoming the airway maintaining genioglossus action causes a glossoptosis-apnea syndrome. *Pediatrics* 1985;75:836–843; *Pierre Robin syndrome, choanal atresia, upper airway obstruction, sleep apnea syndrome, sudden infant death syndrome.*

In 1923, Robin introduced the term "glossoptosis" to describe the tongue falling back and causing pharyngeal obstruction.[1] In his view, glossoptosis was responsible for the clinical manifestations constituting the "glossoptotic syndrome" with two different presentations according to the age of the patient. In children aged 6 years or older, the "acquired glossoptosis," most often associated with enlarged adenoids, was responsible for difficulties in breathing leading to physical and mental retardation. In infancy, the "congenital glossoptosis" was more dangerous because it often led to "cachexia and death" due to "respiratory and nutritional insufficiency."

Robin believed that congenital and acquired glossoptosis was always a simple mechanical consequence of a hypotrophy of the mandible. However, glossoptotic obstruction of the pharynx, associated with apneic episodes during feeding or sleeping, has also been observed in infants with choanal atresia or stenosis.[2,3] The present report describes a series of infants with Pierre Robin syndrome or nasal obstruction. The aim of the study was to determine whether glossoptosis occurring in infancy and due to different types of upper airway obstruction can lead to a common syndrome and to determine the relationship of glossoptotic syndrome to sleep-apnea syndromes, which seem to have the same physiologic manifestations.[4–10]

PATIENTS AND METHODS

We reviewed the case notes for all infants with either Pierre Robin syndrome or nasal obstruction who were seen at the Istituto di Clinica Pediatrica between January 1970 and December 1981. Thirty-eight infants were admitted to the surgical ward and ten to the intensive care unit. The minimum diagnostic criterion for suspicion of Pierre Robin syndrome was a receding chin. The minimum diagnostic criterion for suspicion of nasal obstruction was noisy nasal respiration associated with respiratory distress and/or sucking difficulties.

Patient evaluation included a complete history and physical examination, ECG, and radiographs of the upper airways. In 29 patients (25 with receding chin and four with respiratory distress due to rhinitis), radiologic cephalometric assessment[11] was made by one staff radiologist using ordinary lateral film of the skull. Rhinography was performed in patients with suspicion of choanal atresia or stenosis. Endoscopic examination of nose and throat was performed in all patients, and laryngoscopy was performed in those infants with stridor. Evaluation of patients with respiratory distress or failure to thrive included one or more determinations of arterial blood gases and/or chest roentgenogram.

Received for publication Jan 6, 1984; accepted May 15, 1984.
Reprint requests to (F.C.) Istituto di Clinica Pediatrica, Viale Regina Elena, 324, 00161 Roma, Italy.

EEG was used to study patients with suspicion of cerebral damage.

The diagnosis of apneic spells, while infants were awake and asleep, was based on clinical observation of paradoxical inward movements of the anterior chest wall with little or no air entry.[12] The diagnosis of pharyngeal obstruction due to glossoptosis was based on clinical examination of the oral cavity.[2] These observations were made by the parents and/or hospital personnel; in addition, the majority of these glossoptotic-apneic spells were clinically documented (F.C.).

Twenty-eight infants (17 male and 11 female) were referred for further management of symptoms suggestive of Pierre Robin syndrome. In five infants, micrognathia was an isolated defect; in 16 infants, it was associated with cleft palate; and in six infants, it was associated with malformations of first and second arch derivatives. In one of the infants with receding chin, cleft palate, and glossoptosis, the roentgenogram of the skull did not show hypoplasia of the mandible (Fig 1).

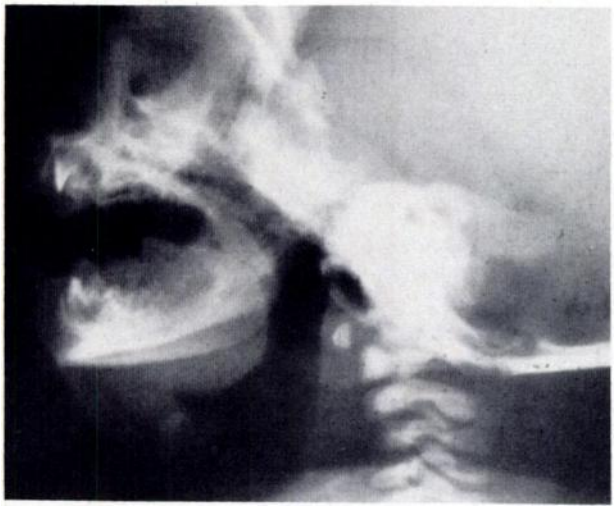

Fig 1. Posterior displacement of tongue without hypoplasia of either mandible or maxilla.

Twenty infants (13 female and seven male) were referred for symptoms suggestive of nasal obstruction (Table 1). The diagnosis of anatomic nasal obstruction was made if we were unable to pass a No. 8 French catheter through the nose into the pharynx. Complete or incomplete obstruction at the level of the posterior edge of the hard palate was demonstrated on lateral skull films of the infant in a supine position after nasal injection of inspissated barium. According to these criteria, infants 1 to 10 had bilateral choanal obstruction; infants 11 to 16 had unilateral choanal obstruction. Bilateral choanal obstruction was complete in infants 1 to 9 and incomplete in infant 10; unilateral choanal obstruction was complete in infants 11 to 13 and incomplete in infants 14 to 16. In addition, infants 17 to 20, who were referred for nasal obstruction associated with apneic blue spells, had no anatomic obstruction at the passage of the nasal catheter and they showed only a swelling of the mucosal lining at rhinoscopy.

In the entire series, 31 infants were referred during the first two weeks of life; eight infants with micrognathia were referred between ages 1 and 8 months; one infant with rhinitis and four infants with unilateral choanal obstruction were referred between ages 1 and 2 months; and four infants with bilateral choanal obstruction were referred between ages 4 and 18 months. Failure to thrive was considered to result from airway obstruction when an infant who had failed to gain weight for a period

TABLE 1. Distribution of Main Clinical Features of 20 Infants with Different Types of Nasal Obstruction

	Choanal Atresia/Stenosis																Rhinitis			
	Bilateral										Unilateral									
	1	2	3	4	5	6	7	8	9	10*	11	12	13	14*	15*	16*	17	18	19	20
Respiratory distress	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+
Cyanosis	+	+	+	+	+	+	+	+	+		+	+	+	+	+		+	+	+	+
Apneic spells	+		+	+	+	+	+	+	+	+		+	+		+		+	+	+	+
Glossoptosis	+		+	+	+	+	+		+		+	+	+	+			+	+	+	+
Opisthotonus			+									+		+	+		+			
Chest deformity			+			+			+	+							+			
Stridor												+			+			+	+	
Hyperphonesis			+						+											
Wheezing													+					+		
Feeding difficulties	+	+	+	+	+	+	+		+		+		+			+	+	+	+	+
Vomiting	+					+			+		+		+				+	+		+
Failure to thrive		+	+	+					+	+				+			+			+
Abdominal distention																			+	+
Brain damage					+		+										+		+	
Cor pulmonale																	+			+
Sudden death														+						

* Choanal stenosis.

longer than four weeks started to gain weight after surgical or spontaneous relief of the obstruction. Cor pulmonale was diagnosed in accordance with the criteria adopted in a recent study of 22 infants and children with obstructive sleep-apnea.[13]

Roentgenograms of the chest were performed in 40 patients and were assessed independently by one staff radiologist. Arterial Po_2 and Pco_2 were measured in blood samples obtained by radial artery puncture in 20 infants and by umbilical catheterization in five infants. Arterial Po_2 and Pco_2 were measured at 37°C with a Radiometer oxygen electrode type 5046 and CO_2 electrode type E 5036, respectively. The pH was measured with the Astrup micro-pH-electrode, model PHM-71MK2. We calculated the alveolar-arterial oxygen difference ($A - aO_2$) using a modified alveolar air equation with an assumed R of .8: alveolar Po_2 = inspired Po_2 − (arterial Pco_2)/R.

Hypoxemia was diagnosed when arterial Po_2 was less than 60 mm Hg, and hypercapnia when arterial Pco_2 was greater than 45 mm Hg. The differences in distribution of clinical and radiologic features were tested by means of χ^2 test.

RESULTS

Clinical Findings

The infants with different types of nasal obstruction had similar clinical features without correlation between the degree of the obstruction and the severity of symptomatology (Table 1). Their symptoms and signs were not different from those of infants with Pierre Robin syndrome (Table 2).

Twenty-two infants with micrognathia and 17 with nasal obstruction had cyanosis and dyspnea at rest with inspiratory retractions. A 2-month-old infant (infant 11), and one 18-month-old infant (infant 10) had respiratory distress without cyanosis and only during sleep.

Twenty infants with micrognathia and 16 with nasal obstruction experienced episodes of obstructive apneas. It was nearly always observed that these recurrent blue spells were accompanied by glossoptosis, indrawing of lips and cheeks, and backward displacement of the mandible.

Apneic episodes occurred more often while the infants were sleeping in the supine position or during feeding or crying (Fig 2). Apnea occurred during wakefulness in 21 of the 24 patients with apneic spells who had been referred during the first two weeks of life; but apnea during wakefulness occurred in only five of 12 infants with apneic spells who had been referred after the first month of life ($.05 > P > .01$). Apnea during sleep was recorded in four infants with micrognathia, two with bilateral choanal obstruction, two with unilateral choanal obstruction, and two with rhinitis. The 18-month-old female infant with bilateral choanal stenosis could not go to sleep without sucking her thumb. She was able to breathe through the mouth around the thumb without awakening, but as the thumb was removed the child showed difficult breathing with episodes of obstructive apnea, followed by agitated arousal. Prone position and the use of oropharyngeal or nasopharyngeal cannulae prevented episodes of complete airway obstruction. Most of the infants reestablished a patent airway by crying and moving the tongue forward. Vigorous stimulation or resuscitation was sometimes required to terminate blue spells. Some mothers had learned to pull the tongue down with their fingers.

Six infants with micrognathia and five with nasal obstruction had occasional opisthotonus. Six infants with micrognathia, two with unilateral choanal obstruction, and two with rhinitis had stridor, which later disappeared spontaneously. In two infants with bilateral choanal atresia/stenosis and in nine infants with micrognathia, the chest was hyperresonant. Of the whole series, five infants had wheezing and 11 infants had a deformity of the sternum and/or Harrison's groove. The chest deformities improved or disappeared after relief of obstruction.

Twenty-four infants with receding chin and 15 with nasal obstruction had sucking and swallowing difficulties; this resulted in an unusually long feeding time which was associated with nasal regurgitation, and/or laryngeal penetration, and/or abdominal distention. Three infants with receding chin and one infant with unilateral choanal stenosis

TABLE 2. Distribution of Main Clinical Features in 20 Infants with Nasal Obstruction and 28 Infants with Pierre Robin Syndrome

	Nasal Obstruction	Pierre Robin Syndrome
	No. (%)	No. (%)
Respiratory distress	19 (95.0)	22 (78.6)
Cyanosis	17 (85.0)	22 (78.6)
Apneic spells	16 (80.0)	20 (71.4)
Glossoptosis	15 (75.0)	24 (85.7)
Opisthotonus	5 (25.0)	6 (21.4)
Chest deformity	5 (25.0)	6 (21.4)
Stridor	4 (20.0)	6 (21.4)
Hyperphonesis	2 (10.0)	9 (32.1)
Wheezing	2 (10.0)	3 (10.7)
Feeding difficulties	15 (75.0)	24 (85.7)
Vomiting	8 (40.0)	17 (60.7)
Failure to thrive	8 (40.0)	20 (71.4)
Abdominal distention	2 (10.0)	7 (25.0)
Brain damage	4 (20.0)	4 (14.2)
Cor pulmonale	2 (10.0)	3 (10.7)
Sudden death	1 (5.0)	6 (21.4)

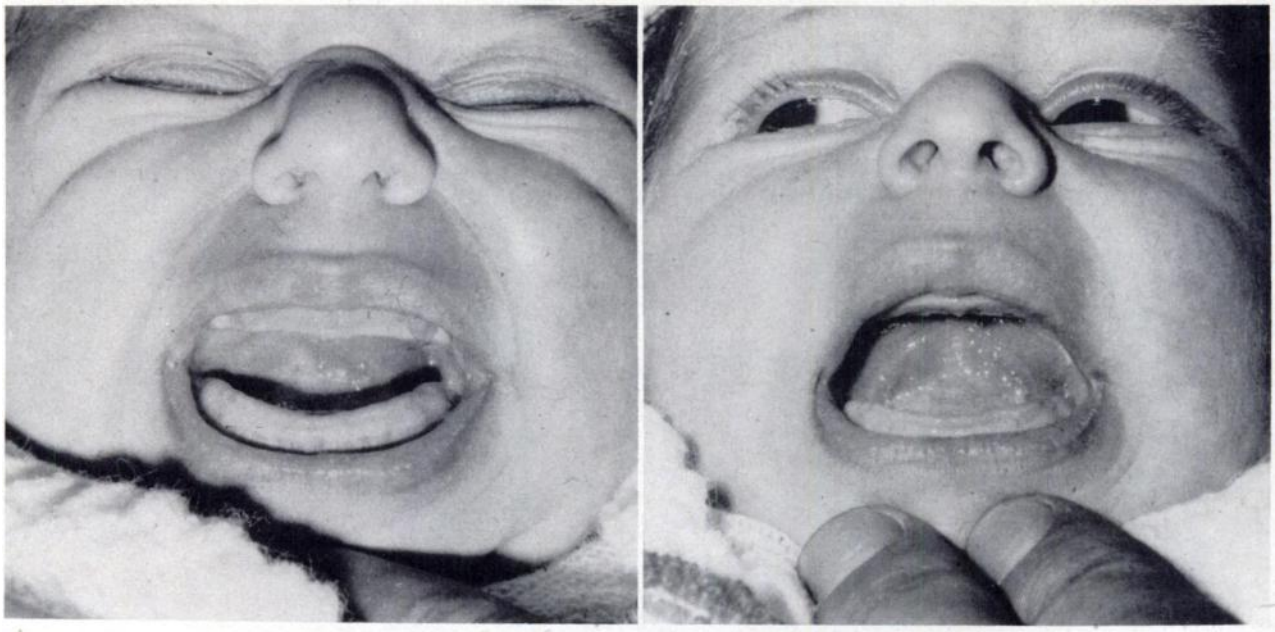

Fig. 2. Glossoptosis-apnea in infant with congenital stenosis of left choana. During crying (left) tongue is sucked backward and seals palate (right).

(infant 16) had only feeding problems. This group of infants without respiratory problems included the infant with glossoptosis without underdevelopment of the mandible, as well as one infant with a severe degree of micrognathia. Vomiting occurred in 25 of 39 infants of the whole series with feeding difficulties. Nineteen infants with micrognathia, one with glossoptosis without micrognathia, five with bilateral choanal obstruction, one with unilateral choanal obstruction, and two with rhinitis failed to gain weight. Failure to thrive was always found in infants with persistent airway obstruction. Surgical relief of choanal obstruction was soon followed by weight gain.

Two newborn infants with bilateral choanal atresia were moribund on admission and developed signs of cerebral damage and eventually died. One of these (infant 5) had a prolapsed cord, fetal distress during delivery, and neonatal asphyxia. In the other infant (infant 7), the brain injury was secondary to blue spells starting ten minutes after a normal delivery. Two other infants (infants 17 and 19), born after normal gestation and delivery, were admitted during the first few hours of life because of abundant yellow secretion from the nose associated with respiratory distress and blue spells. They subsequently developed brain damage, which was judged to be secondary to the airway obstruction. Two neonates with micrognathia who were born after normal gestation and delivery had apneic blue spells soon after birth and subsequently developed signs of physical and mental retardation, probably due to asphyxic brain damage. Two other micrognathic infants had brain damage; we were unable to determine with certainty whether the cerebral lesion occurred in utero.

Three patients with micrognathia and two with rhinitis had cor pulmonale, which subsequently resolved. Five infants with micrognathia and one with unilateral choanal stenosis were found dead in their cribs; autopsy revealed no plausible cause of death. In addition, the 5-month-old infant with glossoptosis without micrognathia was found dead in her crib at home not long after she had had an upper respiratory tract infection; autopsy was refused. In the present series, four additional infants with micrognathia died of respiratory failure.

Chest Film Findings

Both infants with micrognathia and those with nasal obstruction showed a discrepancy between severity of respiratory distress and radiologic findings. Chest film changes were similar in infants with different causes of upper airway obstruction (Table 3). All infants with rhinitis, ten infants with choanal obstruction (eight with bilateral choanal obstruction and two with unilateral choanal obstruction), and 17 infants with micrognathia had pulmonary congestion. Three infants with rhinitis, six infants with choanal obstruction, and 12 infants with micrognathia had hyperinflated lungs and/or peribronchial thickening; these changes were more common in those infants with long-standing airway obstruction. Segmental or subsegmental area of opacity rapidly cleared in subsequent films. In ten infants, gaseous bowel distention was evident on roentgenograms.

TABLE 3. Distribution of Chest Film Changes in 18 Infants with Nasal Obstruction and 22 Infants with Congenital Micrognathia

	Nasal Obstruction	Micrognathia
	No. (%)	No. (%)
Increased vascularity	14 (77.7)	17 (77.2)
Hyperinflated lungs	9 (50.0)	12 (54.5)
Aerophagia	7 (38.8)	3 (13.6)
Small areas of collapse/consolidation	6 (33.3)	13 (59.1)
Peribronchial thickening	5 (27.7)	10 (45.4)

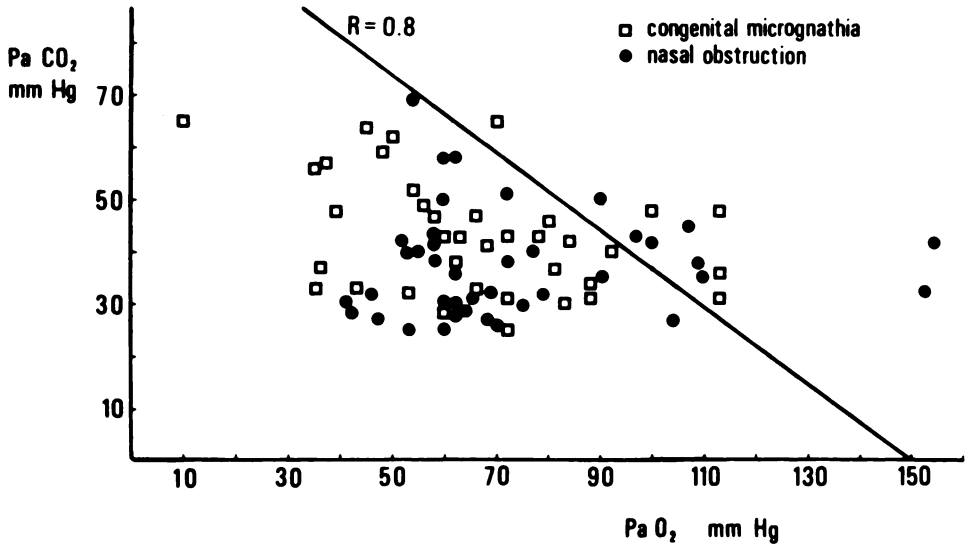

Fig 3. Values of one or more determinations of arterial oxygen (Pa_{O_2}) and carbon dioxide (Pa_{CO_2}) tensions. Hypoxemia is not always associated with hypercapnia in patients with different causes of airway obstruction (congenital micrognathia *v* nasal obstruction).

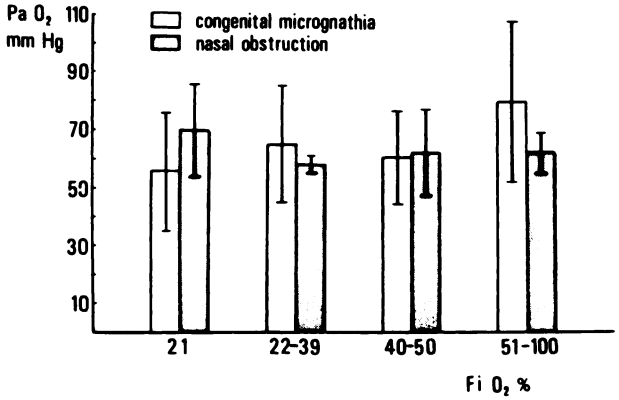

Fig 4. Breathing at higher pressure of inspired oxygen (Fi_{O_2}) produces no definite differences of arterial oxygen tension (Pa_{O_2}) in infants with different causes of airway obstruction (congenital micrognathia *v* nasal obstruction). Values are means ± SD.

Blood Gases

Monitoring of arterial blood gases during more severe phases of respiratory distress (Fig 3) showed hypoxemia and hypercapnia associated with respiratory acidosis at one or more determinations in five of the 14 infants with micrognathia (35%), and in three (two with rhinitis and one with bilateral choanal obstruction) of 11 infants with nasal obstruction (27%). During phases of moderate respiratory distress, five of the 14 infants with micrognathia (35%), and six (four with bilateral choanal obstruction and two with unilateral choanal obstruction) of 11 infants with nasal obstruction (54%) showed hypoxemia with normocapnia or hypocapnia at one or more determinations.

Increasing oxygen concentration in the inspired air did not modify arterial P_{O_2} (Fig 4), but resulted in a considerable increase of $A\text{-}a_{O_2}$ (alveolar-arterial oxygen difference) (Fig 5) in both infants with congenital micrognathia and infants with nasal obstruction.

DISCUSSION

Pierre Robin Syndrome

In the present series, infants with micrognathia had feeding and respiratory problems not much different from those first described by Robin.[1] Sudden crib death,[14,15] cor pulmonale,[16-18] and sleep-related apnea[12,13] have more recently been described as possible clinical features of the syndrome. Robin's concept of glossoptotic pharyngeal obstruc-

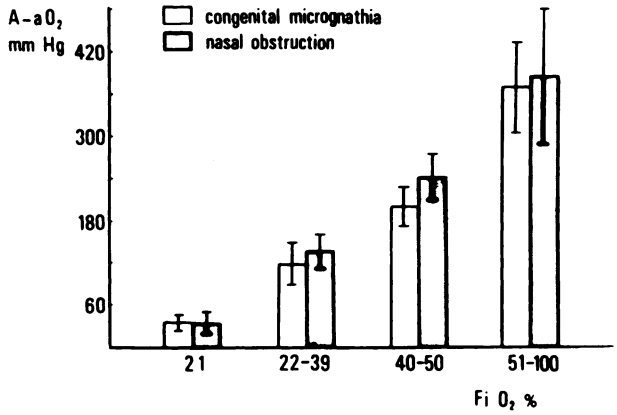

Fig 5. Greater pressure of inspired oxygen (FiO_2) results in greater alveolar-arterial oxygen differences (A-aO_2) in infants with different causes of airway obstruction (congenital micrognathia *v* nasal obstruction). Values are means ± SD.

tion as a simple mechanical consequence of the underdevelopment of the mandible has changed with better knowledge of the mechanism involved in maintaining the patency of the pharyngeal airway.

During normal breathing, the intrathoracic inspiratory depression does not result in a collapse of musculomembranous pharyngeal walls because a neuromuscular mechanism acts, prior to inspiration, to stiffen the floppy structures of the pharynx.[19] The action of the genioglossus muscle plays a crucial role in maintaining the patency of the pharyngeal airway because the velolingual sphincter (anterior wall of the pharynx) is a dynamic flap valve and it may easily obstruct the pharynx when negative inspiratory pressure overcomes the genioglossus force.[7]

Our clinical observations suggest a spectrum of neuromuscular activity of the genioglossus in infants with micrognathia because in some infants, there was no correlation between the severity of symptoms and the degree of micrognathia. Infants at the lower end of the spectrum may have glossoptosis even without hypoplasia of the mandible (Fig 1).

In 1923, New[20] first described as "congenital flaccid tongue" a condition causing, mainly during sleep, episodes of pharyngeal obstruction in an underweight infant with a simple rhinitis. The same clinical picture has been subsequently reported in a few patients with glossoptosis without micrognathia. Possible causes of glossoptosis include a primary disorder of CNS control of muscular tone[21] or an anatomic abnormality of the tongue.[22] Investigations using electromyography have shown a diminished genioglossus activity in a family cluster of the adult sleep-apnea syndrome.[8] In this family, an adult and an infant died suddenly, as did our patient with glossoptosis without micrognathia. Even in patients with abnormal genioglossus function, however, the final pathway leading to glossoptosis apnea may be the increase in airflow resistance caused by the functional pharyngeal airway narrowing due to posterior displacement of the tongue.[23] Episodes of upper airway infection may exacerbate an underlying neuromuscular abnormality.

Nasal Obstruction

Most investigators have reported[3,24,25] that bilateral choanal obstruction is a neonatal surgical emergency, whereas unilateral choanal obstruction is a condition usually recognized later in childhood, unless associated with temporary obstruction of the normal nostril. In the present series, infants with either unilateral or bilateral choanal obstruction, as well as the four infants with inflammatory blockage of the nose, showed no differences in symptomatology or in referral age. In addition, we found no differences in clinical features between infants with nasal obstruction and those with Pierre Robin syndrome.

The common pathogenic mechanism of respiratory and feeding problems in infants with different types of nasal obstruction appeared to be a backward and upward displacement of the tongue causing episodes of complete or incomplete obstruction of the pharynx. Our previous studies of intraesophageal pressure in infants with choanal atresia pointed to negative intrathoracic pressure as the main cause of glossoptotic airway obstruction.[2] Clinical observations of a larger series of patients indicate that at times there was no correlation between the degree of nasal obstruction and the severity of symptoms. We believe that a neuromuscular abnormality of the genioglossus may play an important role in the pathogenic mechanism of glossoptosis-apnea in patients with nasal obstruction.

The abnormal response to a minor degree of nasal obstruction in the four infants with rhinitis in our present series suggests a diminished genioglossus airway maintaining action. The same problems found in the four infants we studied have sometimes been reported in association with a simple rhinitis, and this has been explained by the known inability of some infants to breathe through the mouth.[12,26] In the infants we studied, the apnea associated with inflammatory nasal obstruction appeared to be related to glossoptosis.

Respiratory Status

It is generally accepted that patients with upper

airway obstruction have greater difficulty in breathing-in than in breathing-out; the consequent alveolar hypoventilation leads to hypoxemia and hypercapnia. Surprisingly, several infants in the present series with micrognathia or with nasal obstruction had clinical and/or radiologic evidence of overdistention of the lungs, which was occasionally associated with wheezing, mainly of expiratory nature, and with a degree of hypoxemia which was greater than the degree of hypercapnia. Upper airway obstruction, therefore, may be associated with pulmonary disease similar to that found in lower airway obstruction.

In many cases (Fig 3), the points where arterial P_{O_2} and P_{CO_2} meet are situated to the left of the line representing the respiratory quotient of .8 and are often below the value of 45 mm Hg for arterial P_{O_2}. Primary hypoventilation cannot explain these findings, which are due to failure of gas exchange within the lung. A number of factors can contribute to an alveolar-arterial oxygen difference, including ventilation-perfusion inequalities and/or right-to-left shunting. However, the most likely cause for such a large alveolar-arterial oxygen difference at high O_2 concentration as we observed is an intrapulmonary right-to-left shunt. During the first few months of life, another possible cause of alveolar-arterial oxygen difference may be a persistent fetal circulation.

Relationship to Sleep-Apnea Syndromes

Some patients with anatomic causes of upper airway obstruction (micrognathia, nasal obstruction, enlarged adenoids and tonsils, laryngeal stenosis) as well as some patients without anatomic obstruction, may have similar cardiorespiratory problems caused by frequent episodes of central and/or obstructive apnea during sleep.[5,27,28] The pathogenic mechanism of these obstructive sleep apneas may be an oropharyngeal collapse.[4–10]

About 50 years ago, a similar pathogenic mechanism of pharyngeal obstruction was called glossoptosis by Robin, who also first noticed the correlation between "acquired glossoptosis" and the clinical picture caused by enlarged adenoids, the abnormality most frequently found in children with obstructive sleep-apnea.[13,29] However, in 26 of 36 infants of the present series (72%), the glossoptotic pharyngeal obstruction occurred while the infants were awake, therefore, without the decreased genioglossus activity caused by rapid eye movement (REM) sleep. This easier occurrence of glossoptosis-apnea during wakefulness may be explained by the fact that in early infancy the nasopharyngeal airway is particularly prone to closure by backward displacement of the tongue as the larynx and other cervical structures occupy a higher position in infancy.[30]

Still the infant is at a disadvantage because he or she must breathe through the nose. The reason for this inability to breathe through the mouth has been found to be an incapacity of some infants to break the adherence of the tongue to the palate; this normally occurs in infancy during sleep.[31] Consequently, during rapid eye movement sleep, many normal infants have an inadequate response to nasal occlusion, and this may lead to apnea, poor arousal, and inability to induce breathing through the mouth by crying.[32] Variable levels of impaired arousal may be responsible for either sudden crib death or acute hypoxemic brain damage, complications found in about one fourth of the infants in the present series.

If one accepts these explanations, it follows that the glossoptosis-apnea syndrome should include all sleep-apnea syndromes. Apnea during wakefulness, sudden death, and hypoxic brain damage may be features related to the infant's own anatomy and physiology.

Relationship to Sudden Infant Death Syndrome (SIDS)

Both retrospective[33,34] and prospective[35,36] studies of a large series of victims of SIDS indicate that when compared with a control group of normal infants, victims of SIDS have a significantly higher incidence of many abnormalities. Features found resemble those of the infants of the present series, substantiating the hypothesis that the apnea due to aspiration of the tongue may be a possible mechanism of SIDS.[37]

This concept differs from that of passive pharyngeal obstruction favored by pressure of the baby's face against the mattress in the prone position.[38] This theory does not explain the relationship between SIDS and upper respiratory tract infections.[39] Conversely, the concept of glossoptosis-apnea due to aspiration of the tongue is in agreement with the finding that about 50% of victims of SIDS have only inflammatory changes of the respiratory tract. The airway obstruction caused by inflammatory edema produces an increase in the negative inspiratory pressure, and this may be sufficient to displace the tongue backward in subjects such as the infants of the present series with genioglossus dysfunction. The consequent functional pharyngeal narrowing promotes episodes of oropharyngeal collapse during sleep. In infancy, this glossoptosis-apnea may be life-threatening.

In infants with genioglossus dysfunction, the use of an oropharyngeal cannula or a glossopexy should be considered to prevent sudden death and hypoxic brain damage.

REFERENCES

1. Robin P: Glossoptosis due to atresia and hypotrophy of the mandible. *Am J Dis Child* 1934;48:541–547
2. Cozzi F: Glossoptosis as a cause of apneic spells in infants with choanal atresia. *Lancet* 1977;2:830–831
3. Winther LK: Congenital choanal atreisa: Anatomic, physiological, and therapeutic aspects, especially the endonasal approach under endoscopic vision. *Arch Otolaryngol* 1978;104:72–78
4. Bohlman ME, Haponik EF, Smith PL, et al: CT demonstration of pharyngeal narrowing in adult obstructive sleep apnea. *AJR* 1983;140:543–548
5. Gastaut H, Tassinari CA, Duron B: Etude polygraphique des manifestations episodiques (hypniques et respiratoires) diurnes et nocturnes du syndrome de Pickwick. *Rev Neurol* 1965;112:568–578
6. Felman AH, Loughlin GM, Leftridge CA, et al: Upper airway obstruction during sleep in children. *AJR* 1979;133:213–216
7. Remmers JE, de Groot WJ, Sawerland EK, et al: Pathogenesis of upper airway occlusion during sleep. *J Appl Physiol* 1978;44:931–938
8. Strohl KP, Saunders NA, Feldman NT, et al: Obstructive sleep apnea in family members. *N Engl J Med* 1978;299:969–973
9. Suratt PM, Dee P, Atkinson RL, et al: Fluoroscopic and computed tomographic features of the pharyngeal airway in obstructive sleep apnea. *Am Rev Respir Dis* 1983;127:487–492
10. Walsh RE, Michealson ED, Harkeload LE, et al: Upper airway obstruction in obese patients with sleep disturbance and somnolence. *Ann Intern Med* 1972;76:185–192
11. Pruzanksy S, Richmond JB: Growth of mandible in infants with micrognathia. *Am J Dis Child* 154;88:29–42
12. Rowe LD, Hansen TN, Nielsen D, et al: Continuous measurements of skin surface oxygen and carbon dioxide tensions in obstructive sleep apnea. *Laryngoscope* 1980; 90:1797–1803
13. Brouillette RT, Fernbach SK, Hunt CE: Obstructive sleep apnea in infants and children. *J Pediatr* 1982;100:31–40
14. Dennison WM: The Pierre Robin syndrome. *Pediatrics* 1965;36:336–341
15. Nicolaj P: L'ipoplasia della mandibola con glossoptosi (sindrome di Robin) quale causa di cornage nel lattante. *Clin Pediatr* 1955;37:378–392
16. Jeresaty RM, Huszar RJ, Basu S: Pierre Robin syndrome. *Am J Dis Child* 169;117:710–716
17. Cogswell JJ, Easton DM: Cor pulmonale in the Pierre Robin syndrome. *Arch Dis Child* 1974;49:905–908
18. Mallory SB, Paradise JL: Glossoptosis revisited: On the development and resolution of airway obstruction in the Pierre Robin syndrome. *Pediatrics* 1979;64:946–948
19. Brouillette RT, Thach BT: A neuromuscular mechanism maintaining airway patency. *J Appl Physiol* 1979;46:772–779
20. New GB: Congenital obstruction of the larynx and pharynx. *JAMA* 1923;81:363–366
21. Nicolaj P: Considerazioni patogenetiche sulla sintomatologia presentata dai lattanti affetti da micrognazia e glossoptosi. *Clin Pediatr* 1955;38:669–681
22. Bigotti A, D'Agostino G: Un raro caso di glossoptosi senza ipoplasia mandibolare: sindrome di Pierre Robin incompleta. *Minerva Med* 1959;50:3255–3257
23. Cozzi F: Familial obstructive sleep apnea, letter. *N Engl J Med* 1979;300:506–507
24. Mc Govern FH, Fitz-Hugh GS: Surgical management of congenital choanal atresia. *Arch Otolaryngol* 1961;73:627–634
25. Weseman CM: Management of choanal atresia in the newborn. *Laryngoscope* 1973;83:1160–1166
26. Sjovall K: The use of an oral airway in the treatment of respiratory distress of infants. *Acta Paediatr* 1963;52:153–158
27. Guilleminault C, Tilkian A, Dement WC: The sleep apnea syndromes. *Annu Rev Med* 1976;27:465–484
28. Lugaresi E, Coccagna G, Berti Ceroni G, et al: La "maledizione di Ondine" il disturbo del respiro e del sonno nell'ipoventilazione alveolare primaria. *Sist Nerv* 1968;20:27–37
29. Guilleminault C, Eldrige FL, Simmons FB, et al: Sleep apnea in eight children. *Pediatrics* 1976;58:23–30
30. Moss ML: The veloepiglottic sphincter and obligate nose breathing in the neonate. *J Pediatr* 165;67:330–331
31. Ardran GM, Kemp FA: The nasal and cervical airway in sleep in the neonatal period. *AJR* 1970;108:537–542
32. Swift PGF, Emery JL: Clinical observation on response to nasal occlusion in infancy. *Arch Dis Child* 1973;48:947–951
33. Carpenter RG, Gardener A, Pursall E, et al: Identification of some infants at immediate risk of dying unexpectedly and justifying intensive study. *Lancet* 1979;2:343–346
34. Naeye RL, Messner J, Specht T, et al: Sudden infant death syndrome temperament before death. *J Pediatr* 1976;88:511–515
35. Working party for early childhood deaths in Newcastle: Newcastle survey of deaths in early childhood 1974/'76 with special reference to sudden unexpected deaths. *Arch Dis Child* 1977;52:828–835
36. Naeye RL, Ladis B, Drage JS: Sudden infant death syndrome: A prospective study. *Am J Dis Child* 1976;130:1207–1210
37. Cozzi F, Albani R, Cardi E: A common pathophysiology for sudden cot death and sleep apnea: The "vacuum-glossoptosis syndrome." *Med Hypotheses* 1979;5:329–338
38. Tonkin S: Sudden infant death syndrome: Hypothesis of causation. *Pediatrics* 1975;55:650–661
39. Beckwith JB: The sudden infant death syndrome: A new theory. *Pediatrics* 1975;55:583–584