Handbook of Clinical Neurology, Vol. 113 (3rd series)
Pediatric Neurology Part III
O. Dulac, M. Lassonde, and H.B. Sarnat, Editors

Chapter 159

Congenital feeding and swallowing disorders

VÉRONIQUE ABADIE[1]* AND GÉRARD COULY[2]

[1]*Department of Pediatrics, Hôpital Necker-Enfants Malades, Université Paris Descartes and the national reference centre for Pierre Robin syndromes and sucking and swallowing congenital disorders, France*

[2]*Head and Neck Surgery Unit, Hôpital Necker-Enfants Malades and Université Paris Descartes, Paris, France*

INTRODUCTION

Congenital feeding and swallowing disorders represent a field of increasing interest, as analysis of congenital neurological disorders improves. They consist of a large spectrum that was long poorly understood and neglected for two major reasons. The first was the complexity of eating behavior. Secondly, because of the combination of somatic and psychological features, all such disorders that had no clear explanation were classified for many years as "nonorganic failure to thrive" (Rosenn et al., 1980; Ramsay et al., 1993; Reilly et al., 1999). Understanding these disorders is important for the pediatric neurologist since sucking-swallowing disorders may be revealing symptoms of congenital neurological diseases, and since feeding difficulties and swallowing disorders may complicate the course of various neurological diseases, whether progressive or not.

Understanding the causes of congenital feeding and swallowing disorders requires knowledge of developmental physiology that provides clues to etiology and to developmental stages involved (embryo, fetus, perinatal, postnatal). The latter determine how the baby can cope with his disorders by the time he is investigated.

DEVELOPMENT AND PHYSIOLOGY OF FEEDING

Pre- and neonatal period

In the human embryo, the stomodeum is a common bucconasal cavity located at the anterior extremity of the primitive brain and in front of the anterior extremity of the endoderm, the future gastrointestinal tube with which it communicates after the pharyngeal membrane has disappeared (Humphrey, 1974; Couly, 1991). The first embryo movements are reflex flexor and extensor movements of the axis and opening of the mouth (Hooker reflex = mouth opening on lip contact), seen on ultrasound by 10 weeks of gestation (Hooker, 1952). They only require spinal and bulbar metameric innervation. The organizing and regulating centers of sucking-swallowing-ventilation take place very early during the development of the caudal part of the brain (Chatonnet et al., 2002, 2006; Champagnat et al., 2009). They are required for proper orofacial morphogenesis: mandible and temporomandibular articulation growth, horizontalization of the tongue and palate, and closure of the secondary palate.

The sucking-swallowing reflex is triggered by various stimuli: sensitive, tactile, olfactory gustative, and neurohormonal generated in the hypothalamus and limbic system, and gastric tube (pancreas and stomach). In humans, perioral tactile sensitive receptors become active very soon, as shown by prenatal ultrasound, from the end of the first trimester of gestation. By the 14th week of gestation, the fetus can suck the fingers, feet, and umbilical cord, and this constitutes a stimulus for the trigeminal-facial arch reflex. The fetus swallows a growing amount of amniotic fluid that will reach 500 mL/day at term (Ross and Nijland, 1997).

Olfaction is the second sense to appear. By the end of the 4th week of embryonic life, the facial germ originates from the neural crest mesenchyma, namely the first pair of branchial arches. On both sides of the frontal germ, above the stomodeum, a localized ectodermal thickening is induced early by direct contact with the prosencephalic vesicle. These olfactory placodes will turn into the olfactory neuroepithelium. The epithelium of the olfactive placode unfastens itself from the prosencephalic wall as a consequence of the proliferation of the cephalic

*Correspondence to: Véronique Abadie, APHP, Necker, Pédiatrie, 149 rue de Sèvres, Paris, France. E-mail: veronique.abadie@nck.aphp.fr

mesenchyma. During the 5th week, this proliferation generates two crests around the olfactory placode. These internal and external nasal germs define a depression, the olfactory cupule, whose dorsolateral pouch generates the final olfactive neuroepithelium (and the pouch mesial to the Jacobson organ). The axons of the primary olfactory sensorial cells grow and contact the neurons of the anterior wall of the prosencephalon that becomes the telencephalon. By day 50, the olfactory bulb appears from the telencephalon. The subcortical structures required for the olfactive function (behavior, memory) develop during the second trimester. The olfactory brain or rhinencephalon, also called the paleocortex, consists of a very particular system that regresses in the human. Two systems are therefore superimposed: one purely olfactory in the anterior part of the rhinencephalon contributes to discriminate odors and projects on the hypothalamus, the other is part of the limbic formation and determines various motor activities related to visceral sensitivity and endocrine functions, namely reproduction. In the fetus, the detection of aromatic molecules also belongs to the trigeminal system and the vomeronasal organ of Jacobson that is particularly adapted to the detection of molecules in water. Gustative buds develop in men between 7 and 15 weeks of gestation. They are located on the tongue and, following the trigeminal and facial nerves, allow us to distinguish the four elementary tastes: sweet, salty, sour, and bitter (Bossy, 1980).

Olfactory and gustatory abilities cannot be distinguished during fetal life; the rate of fetal swallowing is increased when the taste of amniotic fluid is sweetened and the reverse occurs for bitter taste. Prenatal tasting/olfaction may alter postnatal behavior. Newborn rats have more intense postnatal sucking when they are proposed flavors they have experienced prenatally through the maternal gastric path. Gustatory and olfactory experience begins therefore long before birth and leaves traces in memory that may be definitive (Schaal et al., 1998, 2000, 2004; Delaunay-El Allam et al., 2006).

The first six months of postnatal life

At birth, two major features take place: ventilation and interruption of constant feeding. Non-nutritive sucking with neither swallowing nor laryngeal closure to prevent aspiration pneumonia consists of sucking bursts that are more rapid than those of feeding sucking (two to three per second). It occurs by 27–28 weeks of gestation. Conversely, feeding sucking requires perfect coordination of swallowing and ventilation. It appears progressively from 33 to 34 weeks, and is not completed before term or even later (Amaizu et al., 2008). It has functional particularities related to the small size of mouth and pharynx due to the size of the tongue and cheeks: the available volume when closing the lips on a teat or pacifier requires that respiration is purely nasal in the newborn. The larynx is high and the velum relatively long, which permits it to be in contact with the epiglottis when swallowing. This provides an additional protection to the upper airways. The feeding sucking reflex is triggered by peribuccal skin receptors (digging reflex) with sensorial, gustatory, and olfactory afferences that are functional before birth. These sensorial afferences come along cranial nerves V, VII, IX and X. They are integrated in programming centers of swallowing rhythm (central pattern generator), which are located in specific parts of the brainstem reticulum, the neurons of which exhibit spontaneous rhythmic properties, and control motor efferences after integration of sensorial and suprabulbar afferences (solitary tract nucleus) (Jean, 1990, 2001). Motor roots of cranial nerves V, VII, IX, X, and XII determine the dynamics of feeding sucking: occlusion of the orbicularis oris around the nipple or pacifier, contractions of cheek muscles causing a pressure then a depression, together with tongue movements. As soon as the milk reaches the reflex zones of swallowing (anterior pillars of the tonsils, posterior pharyngeal wall and posterior pillar of the tonsils), the respiratory tract closes as the palatal velum is in contact with the epiglottis that rises and tilts backward by adduction of the vocal folds. The milk is then pushed laterally towards the glossoepiglottic groove and the piriform sinus (automatic pharyngeal phase). Then the automatic esophageal phase takes place opening the superior sphincter of the esophagus (cricopharyngeal muscle), then reopening the respiratory tract and pushing food backward (primary and secondary peristalsis), and opening the lower sphincter of the esophagus. The swallowing-ventilation coordination only becomes functional around term, explaining the respiratory difficulties that may occur in the premature infant (Lau and Hurst, 1999; Delaney and Arverdson, 2008).

Corticalization of orality: development of the voluntary oral phase

After the second six months of life, major modifications of feeding behavior take place. From the anatomical point of view, elongation of the neck downgrades the larynx (from level C3–C4 in the newborn, C7 in the adult). Growth of the mouth and cavum gives more space to the tongue. The palatal velum no longer touches the larynx when swallowing, but rises and closes the nasopharynx. In addition, cortical structures develop and actively contribute to the oral phase of swallowing. This transition is illustrated by spoon-feeding. By 4 months, when food is offered on a spoon, the baby sucks the content. Then, he will progressively better control the presence of food in his mouth, move it laterally, and decide when to swallow

it (or expel it). Apnea and breathing phases are more prolonged. This takes place before lateral teeth appear. Closing the lips after ingestion also evolves progressively until 1 year of age. Formation of bolus and preparing it to be sent towards the reflex areas of swallowing also begins before teeth erupt. The baby chews with his brain, not with his teeth. The ability to masticate is mature only by 3 years of age, cutting up food with the incisors and moving the jaws laterally when using the molars. The considerable strength of the adult masseter muscles is not reached until about 12 years of age, with the appearance of the last adult molars and growth of the jawbone.

The maturation of voluntary feeding praxis is parallel to the maturation of specific neuromotor structures: the tract originating from the rolandic operculum through the geniculate, and maturation of less specific structures such as pre- and postcentral gyri, premotor, parietal, and temporal cortices, basal ganglia, the pyramidal tract, the tone of neck and trunk muscles, the normal function of which prevents dyskinesia or incorrect posture of the aerodigestive tract. Automatic phases of swallowing, i.e., pharyngeal and esophageal phases, do not change significantly during development (Miller, 1982, 1986, 2008).

Hunger/satiety balance

In the fetus, the concept of hunger/satiety alternation is difficult, since maternal glycemia is constant. Animal models of regulation of swallowing and amniotic fluid flow do not clarify the relationship between this flow and blood levels of maternal neurohormones that regulate the hunger/satiety balance. In addition, links between swallowing and fetal nutrition are mild. Nevertheless, studies in animals estimate that 10% of fetal nutritional intake consists of swallowed amniotic fluid, and that amniotic fluid amino acids and glucose are absorbed by the fetal intestine. This was difficult to prove for the human fetus (Cheng et al., 1996). The fetus is likely able to feel thirst. Thus, increased NaCl concentration of fetal blood or cerebrospinal fluid (CSF) raises osmolality and angiotensin II, and the swallowing rate of the fetal sheep (El-Haddad et al., 2002).

There are many metabolic factors that control neonatal feeding behavior, most of which are unknown. The main factors that stimulate appetite are the decrease of glycemia or of insulinemia, and the increase of glucagon and adrenergic hormones. Regulating factors for hunger/satiety balance are not clearly distinct in newborns, infants, children, and adults. It is fascinating to what extent the healthy child is able to adjust to his needs, just as the majority of adults have a stable body weight until advanced age. In neuropediatrics, this issue is an important one for genetic syndromes causing bulimia and mental retardation, syndromes with feeding difficulties and reduced intake, and children with encephalopathy whose feeding becomes progressively worse.

The hypothalamus is the most important central regulator of food intake. It integrates information from various peripheral organs: gut, fat tissue, and limbic system. Its nuclei project to brainstem areas involved in the modulation of neural gut signals reflecting meal size and composition, as well as detecting circulating signals relaying information regarding nutritional status of the ingested meal and metabolic status of the body, and forebrain limbic areas involved in motivation and reward. The sensory periventricular organs (in hypothalamus and brainstem) lack any blood–brain barrier, as their epithelium is densely vascularized.

Short-term regulation of energy homeostasis is mediated primarily by peripheral signals from the liver and the gastrointestinal tract. In the immediate postprandial period, the presence and energy density of food is determined by gut stretch and chemoreceptors, releasing a variety of peptides, which, in turn, signal the brain via neural and endocrine pathways to regulate short-term appetite and satiety. The long-term control of food intake also involves signals from the adipose tissue, reflecting stored fuels (adipokines). The main peptides involved are CCK (cholecystokinine) that is rapidly released from the small intestine and activates gastric and duodenal vagal afferent neurons sensitive to volume and food composition. Ghrelin is one of the only peripheral orexigenic signals. It is a 28 amino acid peptide produced by gastric mucosa, placenta, and hypothalamus that activates the growth hormone secretagogue receptor. Preprandial increase of ghrelin signals the beginning of the meal. It reduces the activity of vagal afferents to the brain. Amilyn is secreted by pancreatic B cells in response to food intake but its anorectic action is not vagally mediated. Polypeptide Y is produced by the intestinal L cells, causes a delay in gastric emptying, and increases intestinal absorption, resulting in short-term satiety. Its actions on the arcuate nucleus also have long-term anorectic effects. Glucagon-like peptides produced by the distal intestine stimulate insulin secretion and inhibit gastric emptying. Insulin is produced by the pancreas and is positively correlated to adiposity. Insulin receptors present in both hypothalamus and brainstem reduce food intake. Leptin is an adipokin that circulates in proportion to the mass of adipose tissue and downregulates orexigenic peptides such as neuropepide Y and melanin concentrating hormone. Endogenous cannabinoid receptor ligands present in the central nervous system (CNS) (hypothalamus, limbic system, and brainstem) and adipose tissue are detectable in human milk and stimulate suckling in newborns (review in Smith and Ferguson, 2008). Some nutritional components,

such as medium chain fatty acid or amino acids, may affect feeding behavior by modifying appetite modulating neuropeptides. For example, medium chain triglycerols increase plasma levels of CCK. Adding medium chain triglycerides to neonate formula increases energy intake, sleep time and skin temperature (Telliez et al., 2002). Intraventricular injection of leucine and pipecolic acid increase feeding behavior (Tagaki et al., 2003).

Psychoenvironmental aspects

The first mother–child links are mainly based on successful feeding exchanges. From the first hours of life, the mother feels recognized as a mother by her baby, who goes naturally toward her nipple in reaction to physical tension generated by hunger, cold, tactile emptiness. While the mother responds to the needs of her baby, the latter compensates her sensation of maternal emptiness due to parturition. The baby is under the influence of reflex factors, and mother reacts according to her emotions and past history. Harmony of neonatal feeding relates to appropriate integration of various exogenous stimulations: carrying, maternal voice, odors, heat, sight, skin-to-skin contact. This stereotypical scenario and its sequence occurring several times a day structures the development of the child. In addition, endorphins may contribute to the neonatal homeostasis required for the appropriate sequence of feeding and cardiorespiratory regulation.

The development of voluntary feeding praxis depends also on cognitive, affective, and social features. Although it is naturally regulated in the healthy child, it requires learning. Feeding components (grasping, chewing) therefore depend on the cortical and motor abilities of the child, and on the psychological context. The child therefore needs to find the appropriate balance between instinct, which guides him toward the food he requires, and his environment, which will play a major role in new experiences. The mother therefore greatly influences feeding during the first years of life.

SEMIOLOGY AND DIAGNOSTIC STRATEGY FOR SUSPECTED CONGENITAL FEEDING AND SWALLOWING DISORDER

In order to evaluate a congenital feeding and swallowing disorder, the first question is, when to suspect it. This is particularly important for children with neurological or syndromic disorders in which this could occur. It is also useful to the pediatrician in the absence of associated disorders.

Which signs suggest swallowing troubles?

Congenital feeding and swallowing disorders may be clear when the child suffers aspiration pneumonia. In most cases, swallowing disorders are more subtle and should be suspected in case of:

- difficulties in bottle and breast feeding:
  - too long feeding
  - discomfort or unexplained crying during feeding
  - poor intake
  - events during feeding: change of face color, respiratory rhythm, tone, cyanotic access
- drooling: salivary dysphagia results from the inability to swallow the large quality of saliva produced physiologically (several hundred mL per day)
- apparent life-threatening event, mainly when occurring during a meal or on vomiting, or if combined with upper respiratory tract obstruction or followed by abnormal breath recovery
- chronic respiratory disease, recurrent obstruction or pneumonia, chronic cough, asthma-like events, without pulmonary cause
- abnormal upper airway noise
- resistant gastroesophageal reflux impacting weight curve or respiratory tract
- unexplained anorexia, dysphagia, refusal of meal
- excessive nausea reflex, which usually results from poor endobuccal praxis. The baby is bothered by the food or the teat, and allows it to come into contact with the reflex zone. Oral phobia, feeding exclusion, forcing, all increase the nausea reflex, which becomes a means of defense to the infant
- unexplained fever, deterioration of consciousness and general condition of a child with severe neurological disease.

Which symptom is involved?

Once a symptom has raised the possibility of sucking/swallowing trouble, one needs to determine precisely which symptom is involved, in order to chose proper investigations and determine the cause. History and observation of the child when eating allow the physician to distinguish:

- sucking troubles properly speaking: abnormal closure of lips on the nipple or pacifier, insufficient anteroposterior movements of the tongue, efficacy of the intrabuccal depression. The tongue, its anatomy, the tone of its base, its position, eventual fasciculations should be searched for. Analysis of the nausea reflex is also important. The baby does not suck or does not swallow, so his saliva stagnates.
- swallowing disorders: sucking seems fine but the child either fails to swallow or coughs on swallowing. Pharyngeal clearance is poor and the glossoepiglottic folds remain obstructed during feeding. Aspiration pneumonia may be direct (on swallowing) or indirect (during reflux)

- velar insufficiency: milk goes to the nose during feeding or reflux
- ventilation disorders: nasal obstruction, glossoptosis, pharyngeal collapse, and stridor all produce more or less noisy inspiratory dyspnea, between feeds or during feeding
- swallowing-ventilation coordination defect: inspiration defect following a burst of sucking, causing cyanosis or abrupt rejection of the teat with sensation of asphyxia
- hunger/satiety equilibrium troubles. The baby sucks correctly but not long enough, as he had reached satiety following insufficient volume intake
- feeding behavior troubles. The baby starts sucking normally then stops, arches, then pushes back the teat and refuses to resume sucking
- feeding refusal. The baby cries or pushes back the teat, tightens the lips or turns the head as soon as he sees the bottle or the spoon, with no anomaly out of the meals.

Mechanism and context

Once the symptom is identified, the mechanism of the trouble needs to be determined. Is the symptom caused by a brain lesion?, a muscular lesion?, an anatomical anomaly of the pharynx or the larynx? a digestive pain? : is it an anomaly of the extrapyramidal control of movement, of the central command of aerodigestive crossing within the brainstem; is it due to ear nose and throat anatomy or functional anomaly of the digestive tube, to pain or discomfort?

It is then necessary to determine the context in which the disorder occurs in order to identify the global cause. Is the disorder isolated? Does it result from a cardiorespiratory or neurological disorder? Is the latter part of some malformation complex? Is it genetic, metabolic, clastic, or toxic?

INVESTIGATIONS

None is systematic since each has its advantages and its limits, and they are complementary. Most are functional investigations based on experience:

- Fiberoptic endoscopic upper airways evaluation is required in most instances since it confirms aspiration pneumonia by the presence of saliva under the vocal cords. It tests pharyngolaryngeal sensitivity, the glossopharyngolaryngeal tone, and laryngeal dynamics. When performed on swallowing some colored substance, it is possible to determine the mechanism of the disorder. Anteroposterior laryngomalacia with curling of the epiglottis into an omega shape suggests brainstem involvement. Collapse of the base of the tongue is seen in Pierre Robin syndrome, whereas global hypomotility is observed in neuromuscular disorders. General anesthesia is required to investigate malformations: angioma, tumor, cyst, diastema, or fistula (Cummings et al., 2005).
- Radiocinema or videofluoroscopic evaluation of swallowing may confirm aspiration pneumonia if needed. It shows barite dynamics, anatomical and functional aspects of tongue movements, pharyngolaryngeal movements, esophageal opening, and closure of upper airways. It causes considerable radiation exposure.
- Facial electromyography (EMG) and dynamic electromyography of sucking-swallowing investigates the various cranial nerves: V, VII, trigeminofacial reflex, IX, X, and XII. During feeding it should record muscle innervated by cranial nerve IX and muscle innervated by cranial nerve X; it also investigates the brainstem reticular formation. It is mainly useful to investigate conditions with cranial nerve involvement, such as Möbius syndrome, when the distinction between agenesis and clastic lesion proves difficult (Baudon et al., 2009).
- Peripheral EMG is mainly useful when either muscular dystrophy or myasthenia is suspected.
- Esophageal manometry is useful when esophageal motility control seems to be involved, as in the Pierre Robin sequence. The lower sphincter tone is increased, and fails to release on swallowing, waves are giant and do not propagate normally (Baujat et al., 2001).

The other investigations aim at determining the cause of the disorder.

- Brain magnetic resonance imaging (MRI) is often not helpful because of the size of the anomalies (Smith and Ferguson, 2008). However, it allows exclusion of rare tumors, posterior fossa malformations, and clastic lesions when they are large.
- Other investigations are directed toward neurological, genetic, or metabolic causes.
- Finally, investigations that evaluate the impact of the disorder comprise: lung computed tomography (CT) to disclose respiration pneumonia, polysomnography, hematosis, and cardiac ultrasonography.

MAIN CAUSES OF CONGENITAL FEEDING AND SWALLOWING DISORDERS

There are many causes and they are diverse (Table 159.1). Their relative frequency is unknown since it depends on the recruitment of the team. Any classification is arbitrary. In the following section, causes will be classified based on anatomy. Cardiac and/or respiratory disorders that disturb sucking/swallowing will not be addressed. Among congenital neurological diseases, only those for which feeding and swallowing disorders are the main symptom are addressed. For many genetic syndromes the mechanism of the disorder remains poorly

Table 159.1

Classification of the main primary causes of feeding and swallowing difficulties in children, classified according to anatomical plan with an example for each localization (nonexhaustive list)

Suprabulbar lesions	Brainstem lesions	Neuromuscular causes	ENT causes	Oro-digestive causes
Cortical anomalies: anoxia Central hypotonia: Down syndrome Extrapyramidal dystonia: lysosomal disease Appetite dysregulation: Prader–Willi Post-stress anorexia: postmalformation surgery, postneonatal ICU, postparenteral nutrition	Posterior fossa malformation: PCH, CDG syndrome Tumor of the brainstem Agenesis cranial nerves: Möbius syndrome Clastic lesion of the brainstem Craniovertebral junction anomalies Syndrome involving development of rhomencephalon: Pierre Robin, CHARGE, Del 22q 11	Congenital Steinert myotonia Neuromuscular blocks Congenital muscular diseases	Pharyngolaryngeal malformations Faciocraniostenosis Laryngomalacia Laryngeal sensitivity deficiency	Complicated GOR Achalasia of the upper esophageal sphincter Digestive motricity anomaly: Noonan syndrome, Costello syndrome Excessive pain: Williams syndrome

ICU, intensive care unit; PCH, Pontocerebellar hypoplasia; CDG, congenital disorder of glycosylation; GOR, gastroesophageal reflux.

understood and their place in the classification may therefore seem arbitrary.

Brainstem lesions

Brainstem lesions are the most frequent since sucking/swallowing mechanisms are generated and regulated at this level.

Malformations of the posterior fossa

Diagnosis is suspected or confirmed by MRI before the molecular cause can be sought. They are rare but often severe, and this justifies systematic brain MRI investigation of congenital feeding and swallowing disorders. Their nature determines prognosis and genetic counseling (Walsh, 2003). The following list is not exhaustive

- Joubert syndrome has a remarkable clinical and MRI presentation (see Ch. 193).
- Congenital disorders of glycosylation (CDG) are more variable with an expanding phenotype (see Ch. 179).
- Pontocerebellar atrophy or hypoplasia, mainly type I hypoplasia, may reveal itself with total neonatal lack of sucking, arthrogryposis, trismus, nystagmus, and massive hypotonia (see Ch. 192).
- Dandy–Walker syndrome combines hydrocephalus with posterior fossa cyst and agenesis of cerebellar vermis.

Neonatal brainstem tumors

Neonatal brainstem tumors are rare, often severe but and may paradoxically have better prognosis than later in life (Thompson and Kosnik, 2005).

Agenesis of cranial nerves

Pure Möbius syndrome combines bilateral paralysis of the sixth and seventh cranial nerves, but additional nerve palsies are frequent. It may result from clastic lesions in some instances but familial cases exhibit autosomal recessive or dominant transmission. MRI is most often normal and it is facial and sucking/swallowing EMG that permit diagnosis (Gorlin et al., 2001).

Clastic lesions of the posterior brain

Early embryopathic viral (cytomegalovirus (CMV), chickenpox), clastic lesions, embryopathic toxic (valproic acid, alcohol, misoprostol), or perinatal brainstem ischemia, generate severe troubles combining signs of early damage (retrognathism, glossoptosis, arched palate) and sucking/swallowing/ventilation troubles that have a poor prognosis.

Craniovertebral junction involvement

Craniovertebral junction involvement may be the consequence of Chiari malformation or compression due to achondroplasia. It is often difficult in these instances to determine whether brainstem disorders result from compression or an associated malformation, which is important when considering surgery to the occipital bone.

Brainstem developmental and rhombencephalic syndromic involvement: neonatal brainstem dysfunction

Neonatal brainstem dysfunction exhibits four clinical signs (sucking/swallowing anomalies, gastroesophageal reflux, pharyngolaryngomalacia, vagal hyperreactivity) combined with particular anomalies of laryngeal dynamics and esophageal motricity. It is likely to express brainstem reticular dysfunction that coordinates cranial nerve function.

Pierre Robin syndrome

In this condition orofacial motricity is deficient early in the context of a malformative association comprising retrognathia, glossoptosis, and posterior cleft palate. Retrognathia and glossoptosis worsen ventilation obstruction. There are sucking/swallowing coordination disorders (Abadie et al., 2002). When retrognathia and glossoptosis are mild or lacking, the diagnosis of Pierre Robin cannot be suspected. In practice, there is a double challenge: on the one hand dealing with sucking/swallowing disorders and on the other reaching the proper diagnosis. Indeed, in half the cases the Pierre Robin sequence is part of a larger malformation syndrome (Holder-Espinasse et al., 2001). In the absence of cleft palate, the Pierre Robin sequence is no longer considered but rather neonatal brainstem dysfunction (NBD):

- NBD may be isolated (variously called neonatal oroesophageal dyskinesia or delayed maturation of the sucking-swallowing reflex) and usually resolves itself within a year or two (Leroy-Malherbe et al., 1994; Abadie et al., 2001). Spoon-feeding progressively replaces the defective suckling, and pharyngolaryngomalacia clears. History, the clinic, manometric and laryngoscopic findings permit suspicion of the diagnosis.
- NBD with suprabulbar involvement. This is combined with more diffuse brain dysfunction, namely cortical functions.
- NBD with polymalformation. This is encountered in genetically determined malformations. In CHARGE syndrome, cranial nerves are often involved. Facial involvement is asymmetrical, peripheral, and nonprogressive. It usually does not improve. Cranial nerves IX and X are usually symmetrically involved centrally since the course is favorable within a few months. Hyposmia partly explains the persistence of feeding difficulties (Chalouhi et al., 2005; Blake et al., 2008).

In the microdeletion chromosome 22 syndrome, the aerodigestive tract involvement is also frequent, although milder than in the Pierre Robin or CHARGE syndromes. Although sucking and swallowing difficulties, including reflux and velar defect, are a nuisance, it is mainly rhinolalia that disturbs children, some of whom are unintelligible (Shprintzen, 2008).

In malformative syndromes involving embryogenesis of branchial arches, namely the first (Goldenhar, Franceschetti, Nager), sucking/swallowing disorders are quite frequent (Gorlin et al., 2001).

In several other syndromes, congenital feeding and swallowing disorders exist but the mechanism remains unexplained, whether NBD (Kabuki syndrome), or massive hypotonia (Down syndrome), or other factors of feeding behavior (see later).

In many chromosomal anomalies, sucking is poor and feeding insufficient.

In various rare genetically determined malformative syndromes involving the face, oral function is affected, most often centrally in the brainstem. In those cases, malformation features predominate (Cooper-Brown et al., 2008). Macrosomic children from diabetic mothers also belong to this group.

Suprabulbar lesions

- Feeding disorders in cerebral palsy appears later, with spoon-feeding and voluntary chewing. Swallowing disorders are not at the forefront. It is mainly the secondary orality (voluntary feeding skills) that is delayed and troublesome. Similarly, children with major cortical lesions such as holoprosencephaly or anencephaly, the primary sucking and swallowing reflex is present but the secondary phase of feeding cannot settle.
- Various early extrapyramidal dystonias may begin with digestive symptoms: crying, difficulties holding a pacifier in the mouth or beginning sucking, squirming, bursts of opisthotonos. The clinical and imaging context allows diagnosis of Krabbe disease or neurotransmitter disorders, Aicardi–Goutières syndrome or anoxic lesions of basal ganglia: kernicterus, inborn errors of metabolism.
- Phobia, stress, posttraumatic opposition of babies operated on at birth for various digestive (e.g., esophageal atresia, omphalocele) or cardiac disorders, or following prolonged resuscitation. Suprabulbar, including cortical and limbic functions may be permanently affected from the very first months of life. However, these are feeding behavior disorders, not true swallowing disorders.
- Mastication immaturity, intolerance to new textures, hypernausea of the immature or mildly defective child also express dysfunction of voluntary feeding skills.
- The regulation of the appetite can also be affected by inborn or acquired disorders affecting the hunger/satiety balance in various conditions. The most

typical is Prader–Willi syndrome in which sucking is initially very poor and gastric feeding is usually required. After the age of 2 years, this pseudo-anorexia changes into compulsive bulimia. Growth hormone treatment, initiated for anthropometric reasons, may reduce uncontrollable hunger. This proves that the neurohormonal cascade GH-Ghrelin-IgF is involved (Benarroch et al., 2007). Similarly, the RAVINE syndrome (Réunion – Anorexie – Vomissements – Incoercibles – NEurologie), first described on Réunion island, was initially considered to be a severe psychogenic neonatal anorexia, whereas a mitochondrial dysfunction is the cause of anorexia, uncontrolled vomiting, and neurological deterioration (Renouil et al., 1999). Inborn errors of metabolism often cause anorexia for various reasons: appetite is altered by continuous enteral glucose feeding, poor flavor of diet milks, psychological consequences on the alimentary mother-child link, and also probable interference with poorly understood aspects of neurohormonal or metabolic regulation of appetite and behavior.

- In Down syndrome, central hypotonia, hyperlaxity, dyspnea in case of heart disease, macroglossia, hypotonia of orbicularis oris, laryngomalacia, and obstructive rhinitis cause sucking/swallowing disorders in the first months of life, although after 3 years of age these clear and are replaced by greediness that may cause obesity. Nevertheless, chewing difficulties and obstructive sleep apnea is frequent (Shott, 2006).
- In syndromes with excessive irritability and sensitivity to pain or noise, such as Williams–Beuren syndrome, sucking is particularly difficult because of frequent reflux and labial hypotonia. Furthermore, these children have a very poor tolerance of pain and because of hypersensitivity gastroesophageal reflux is intolerable. These syndromes show that not all children perceive pain with the same intensity, and that reaction to similar pain may vary greatly.

Neuromuscular disorders

- In the congenital form of Steinert's myotonic dystrophy, sucking/swallowing disorders may cause pharyngeal obstruction with severe respiratory distress.
- Congenital neuromuscular block may severely affect facial and pharyngeal muscles, with insufficient sucking, respiratory obstruction, and poor coughing reflex. It is the variability during the day and normal contact that provide the clue to this diagnosis.
- Congenital myopathies or dystrophies are rarely revealed by pharyngeal troubles although this is not exceptional. Arthrogryposis may be an additional feature generating a syndrome of fetal immobility, both oral and global.
- Disorders of laryngeal sensitivity may result from chemical burns. When laryngeal sensitivity disorder is congenital, it may be part of a more diffuse congenital syndrome of insensitivity to pain, the most frequent being Riley–Day syndrome in which repeated and overlooked episodes of aspiration pneumonia can cause unexplained recurrent or chronic pneumonia.

Peripheral esophageal and ENT disorders

Various congenital malformations of the upper airways may produce early sucking/swallowing disorders. Signs of obstructive ventilation usually suggest a local disorder such as angioma, cyst of the base of the tongue, diastema laryngeal fold. These malformations require endoscopy. In malformative syndromes with faciostenoses and involvement of the cavum and glossoptosis (Crouzon, Pfeiffer, and Apert syndromes), sucking/swallowing disorders often result from both upper airways obstruction and glossal hypotonia. Some functional anomalies of the aerodigestive tract and laryngeal paresis have no central explanation. This is particularly the case with laryngomalacia and severe esophageal atresia. Disorders of laryngeal sensitivity are encountered in early mucosal lesions and epidermolysis bullosa that can cause aspiration pneumonia. Although mainly seen in adults, cricopharyngeal achalasia or hypertonia of the upper sphincter of the esophagus may be congenital and occur in the neonate as dysphagia.

Syndromes with probable or confirmed disorders or digestive motricity

In some genetic malformation syndromes, feeding and swallowing disorders are frequent (Sullivan, 2008). The mechanisms are often difficult to determine, and they may be varied. In the Noonan, cardiofaciocutaneous and Costello syndrome spectrum, sucking troubles, laryngomalacia, and severe reflux are frequent before the age of 3 years. In Costello syndrome, some children have diffuse troubles of intestinal motricity of the small intestine. In Silver–Russell syndrome, children exhibit early satiety, intractable gastroesophageal reflux, and troubles of intestinal motricity. In Cornelia de Lange syndrome, massive reflux is observed; it causes variable feeding troubles that may require surgery.

MANAGEMENT

Managing congenital feeding and swallowing disorders comprises several steps. For each component, whether a reflex or a praxis is involved has to be determined since

only praxis can be rehabilitated; the course of the disease needs to be identified, as well as which neurological and cognitive tools will enable the child to compensate, and the nature of personal and familial psychic context:

1. Specific treatment of the cause is only possible in metabolic diseases accessible to treatment and in case of neuromuscular blockade.
2. Facilitating suckling skills requires taking several small steps to improve babies' abilities: soft and slit bottle teats/pacifiers, thickened milk, position the head in the body axis, place the child in a vertical position for feeding, ensure the neck is not in extension, ensure taste is agreeable, enrich calories, maintain meal fragmentation throughout the day.
3. Prevention of deleterious effects of aspiration pneumonia. Aspiration is the only contraindication to oral feeding. It is then recommended not to insist but insert a nasogastric tube then a gastrostomy if this lasts over 6 months. This enteral feeding should be exclusive if the child suffers from aspiration pneumonia, partial if the child can suck a little. For saliva aspiration pneumonia, atropinic patches (Scopoderm, scopolamine) may help, but thickening of lung secretions may be harmful. The risk of aspiration may require antireflux surgery together with gastrostomy.
4. Prevention of malnutrition. In infancy, weight gain is very rapid; enteral complement nutrition with a gastric tube which is well tolerated should be provided early whenever needed. Bolus feeding is more physiological and less appetite suppressing than nocturnal feeding. If intake is insufficient, the means for caloric enrichment should be set up early, and texture improved. Carob starches are the most efficient thickeners for these babies. For children with congenital degenerative diseases whose feeding disorders will definitely occur or worsen (such as Rett syndrome, adrenoleukodystrophy, storage diseases), undernutrition should be anticipated with taste of food and hypercaloric diets, taking into account the taste and abilities of the child. It is very difficult for families to determine when feeding complement is required since this looks like a further stage in the worsening of the child and the acceptance of reality. Complementing must be advised early and described as an improvement of comfort for the child, and as enabling the end of the conflicts over feeding that are so devastating for both the child and the parents. Percutaneous gastrostomy is usually advised as first line therapy.
5. Rehabilitation. Sucking cannot be rehabilitated; it needs to be facilitated. The pharyngeal and esophageal phases of swallowing cannot be rehabilitated either. Conversely, the oral phase, orofacial praxia intrabuccal chewing, preparation of the food bolus in the mouth, and its posterior propulsion can all be efficiently rehabilitated, facilitated, and corticalized, and progressively become voluntary. This praxis-oriented orthophonic task is useful for children with neonatal brainstem dysfunction who will recover or compensate by the early development of cortical feeding functions. Rehabilitation requires games, massages, mimicry, and blowing. Its efficacy depends therefore on the child's psychomotor development and self-confidence.
6. Posture. The larynx closes better when the neck is not in extension. Muscular symmetry is also important during swallowing. Therefore, the baby needs to drink the bottle in an upright sitting position; the hypotonic child needs to be made vertical, with the head in the axis, in order to prevent aspiration pneumonia. This is particularly important for polyhandicapped children, for whom proper positioning for meals and adapted tools are essential.
7. Preventing posttraumatic anorexia. In order to prevent the loss of baby's sucking reflex, and to help him be the actor of his rehabilitation, his body comfort, his founding experience of orality needs to be preserved. Care therefore needs to take into account pain, reflux, and vomiting, to improve the taste of food, and to avoid conflicts when food or medication is administered. With the contribution of a physiotherapist, the baby's body needs to be respected and global motricity stimulated (NIDCAP). Finally, parents need help in order to understand feeding troubles, and accept techniques of nutrition, so that anxiety and a sense of guilt do not worsen the child's difficulties. A psychologist plays a major role listening to the parents, restoring to mothers their maternal function, explaining the reasons for the difficulties that may prevent the proper development of the mother–baby link, and laying the foundations of a harmonious psychic life.

References

Abadie V, André A, Zaouche A et al. (2001). Early feeding resistance: a possible consequence of neonatal oro-oesophageal dyskinesia. Acta Paediatr 90: 738–774.

Abadie V, Morisseau-Durand MP, Beyler C et al. (2002). Brainstem dysfunction: a possible neuroembryological pathogenesis of isolated Pierre Robin sequence. Eur J Pediatr 161: 275–280.

Amaizu N, Shulman R, Schanler R et al. (2008). Maturation of oral feeding skills in preterm infants. Acta Paediatr 97: 61–67.

Baudon JJ, Renault F, Goutet JM et al. (2009). Assessment of dysphagia in infants with facial malformations. Eur J Pediatr 168: 187–189.

Baujat G, Faure C, Zaouche A et al. (2001). Oroesophageal motor disorders in Pierre Robin syndrome. J Pediatr Gastroenterol Nutr 32: 297–302.

Benarroch F, Hirsch HJ, Genstil L et al. (2007). Prader–Willi syndrome: medical prevention and behavioral challenges. Child Adolesc Psychiatr Clin N Am 16: 695–708.

Blake KD, Hartshorne TS, Lawand C et al. (2008). Cranial nerve manifestations in CHARGE syndrome. Am J Med Genet 146A: 585–592.

Bossy J (1980). Development of olfactory and related structures in staged human embryos. Anat Embryol 161: 225–236.

Chalouhi C, Faulcon P, Le Bihan C et al. (2005). Olfaction evaluation in children: aplication to CHARGE syndrome. Pediatrics 116: 81–88.

Champagnat J, Morin-Surun MP, Fortin G et al. (2009). Developmental basis of the rostro-caudal organization of the brainstem respiratory rhythm generator. Philos Trans R Soc Lond B Biol Sci 364: 2469–2476.

Chatonnet F, Thoby-Brisson M, Abadie V et al. (2002). Early development of respiratory rhythm generation in mouse and chick. Respir Physiol Neurobiol 131: 5–13.

Chatonnet F, Borday C, Wrobel L et al. (2006). Ontogeny of central rhythm generation in chicks and rodents. Respir Physiol Neurobiol 154: 37–46.

Cheng W, Mya GH, Saing H (1996). Does the amniotic fluid protein absorption contribute significantly to the fetal weight? J Paediatr Child Health 32: 39–41.

Cooper-Brown L, Copeland S, Dailey S et al. (2008). Feeding and swallowing dysfunction in genetic syndromes. Dev Disabil Res Rev 14: 147–157.

Couly G (1991). Développement Céphalique. Embryologie, Croissance Pathologie. CdP, Paris, pp. 58–61.

Cummings CW, Haughey BH, Thomas JR et al. (2005). Otolaryngology. Head and neck surgery. 4th edn. Elsevier Mosby, Philadelphia.

Delaney AL, Arverdson JC (2008). Development of swallowing and feeding: prenatal through first year of life. Dev Disabil Res Rev 14: 105–117.

Delaunay-El Allam M, Marlier L, Schaal B (2006). Learning at the breast: preference formation for an artificial scent and its attraction against the odor of maternal milk. Infant Behav Dev 29: 308–321.

El-Haddad MA, Chao CR, Sheng-Xing MA et al. (2002). Neuronal NO modulates spontaneous and ANG II-stimulated fetal swallowing behavior in the near-term ovine fetus. Am J Physiol Regul Integr Comp Physiol 282: R1521–R1527.

Gorlin RJ, Cohen MM, Hennekam RCM (2001). Syndromes of the Head and Neck. 4th edn. Oxford University Press, Oxford.

Holder-Espinasse M, Abadie V, Cormier-Daire V et al. (2001). Pierre Robin sequence: a series of 117 consecutive cases. J Pediatr 139: 588–590.

Hooker D (1952). The Prenatal Origin of Behavior. Hafner, New-York, London.

Humphrey T (1974). Central representation of the oral and facial areas of human fetus. In: J Bosma (Ed.), Oral Sensation and Perception. 3rd edn.. Symposium. Ch. C. Thomas, Springfield, pp. 98–136.

Jean A (1990). Brainstem control of swallowing: localization and organization of the central pattern generator for swallowing. In: A Taylor (Ed.), Neurophysiology of the Jaws and Teeth. MacMillan, London, pp. 294–321.

Jean A (2001). Brainstem control of swallowing: neuronal network and cellular mechanisms. Physiol Rev 81: 929–969.

Lau C, Hurst N (1999). Oral feeding in infants. Curr Probl Pediatr 29: 105–124.

Leroy-Malherbe V, Husson B, Landrieu P et al. (1994). Syndrome of delayed maturation of the sucking-swallowing reflex. Arch Pediatr 1: 20–25.

Miller AJ (1982). Deglutition. Physiol Rev 62: 129–184.

Miller AJ (1986). Neurophysiological basis of swallowing. Dysphagia 1: 91–100.

Miller A (2008). The neurobiology of swallowing and dysphagia. Dev Disabil Res Rev 14: 77–86.

Ramsay M, Gisel EG, Boutry M (1993). Non-organic failure to thrive: growth failure secondary to feeding-skills disorder. Dev Med Child Neurol 35: 285–297.

Reilly SM, Skuse DH, Wolke D et al. (1999). Oral-motor dysfunction in children who fail to thrive: organic or non-organic? Dev Med Child Neurol 41: 115–122.

Renouil M, Fourmaintraux A, Cartault F et al. (1999). Severe anorexia in infants in Réunion: a new autosomal recessive disease? Arch Pediatr 6: 725–734.

Rosenn DW, Loeb LS, Jura MB (1980). Differentiation of organic from nonorganic failure to thrive syndrome in infancy. Pediatrics 66: 698–704.

Ross MG, Nijland MJ (1997). Fetal swallowing: relation to amniotic fluid regulation. Clin Obstet Gynecol 40: 352–365.

Schaal B, Marlier L, Soussignan R (1998). Olfactory function in the human fetus: evidence from selective neonatal responsiveness to the odor of amniotic fluid. Behav Neurosci 112: 1438–1449.

Schaal B, Marlier L, Soussignan R (2000). Human foetuses learn odours from their pregnant mother's diet. Chem Senses 25: 729–737.

Schaal B, Hummel T, Soussignan R (2004). Olfaction in the fetal and premature infant: functional status and clinical implications. Clin Perinatol 31: 261–285, vi–vii.

Shott SR (2006). Down syndrome: common otolaryngologic manifestations. Am J Med Genet C Semin Med Genet 142C: 131–140.

Shprintzen RJ (2008). Velo-cardio-facial syndrome: 30 years of study. Dev Disabil Res Rev 14: 3–10.

Smith PM, Ferguson AV (2008). Neurophysiology of hunger and satiety. Dev Disabil Res Rev 14: 96–104.

Sullivan PB (2008). Gastrointestinal disorders in children with neurodevelopmental disabilities. Dev Disabil Res Rev 14: 128–136.

Tagaki T, Bungo T, Tachibana T et al. (2003). Intracerebroventricular administration of GABA-A and GABA-B receptor antagonists attenuate feeding and sleeping-like behavior induced by L-pipecolic acid in neonatal chicks. J Neurosci Res 73: 270–275.

Telliez F, Bach V, Leke A et al. (2002). Feeding behavior in neonates whose diet contained medium-chain triacylglycerols: short-term effects on thermoregulation and sleep. Am J Clin Nutr 76: 1091–1095.

Thompson WD, Kosnik EJ (2005). Spontaneous regression of a diffuse brainstem lesion in the neonate. J Neurosurg 102: 65–71.

Walsh L (2003). Congenital malformations of the human brainstem. Semin Pediatr Neurol 10: 241–251.