Gastroesophageal Reflux in the First Year of Life

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15.1 Introduction

Gastroesophageal reflux (GER) is a frequent phenomenon consisting of the retrograde passage of the gastric juice into the esophagus and, occasionally, its expulsion through the mouth. The main harmful consequences of GER are the loss of nutritional intake and the damage to the esophageal mucosa. The larynx, the tracheobronchial tree, and the lung can also be affected, and other complications may arise. However, although GER is extremely frequent, particularly in young babies, most of them do not suffer from any of these complications. Therefore, to a certain extent, GER is "normal" in them, and only when such harmful effects arise the phenomenon is designated gastroesophageal reflux disease (GERD).

In the present chapter, the causes and mechanisms of GERD during the period of life between birth and the end of the first year are addressed together with the sequence of diagnostic procedures and the rationale of the currently recommended therapeutic measures. A particular analysis of the comorbidities that accompany GERD at this age will be made.

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15.2 Why GER Is So Frequent in Newborns and Young Babies

The stomach is located in the abdomen where positive pressures are permanent and reinforced by gastric peristalsis. In contrast, the esophagus is mostly into the thorax where negative pressures are present during each inspiratory movement. As a consequence of this, a GER-driving pressure gradient from the stomach to the esophagus exists in normal individuals, and only the presence of an efficient anti-reflux barrier fights this phenomenon. The barrier has two main components: The first is the "lower esophageal sphincter" (LES) resulting from the permanent contraction of the distal smooth muscle fibers of the esophagus at the gastroesophageal junction. The second is a sort of "external sphincter" created by the phasic contractions of the striated muscle of the crural sling of the diaphragm formed by the pillars of the hiatus. These contract during inspiration and lengthen the intra-abdominal segment of the esophagus while accentuating the angle of His. The synergic play of these two components closes the distal esophagus, particularly when the GER-driving forces are stronger. Swallowing is possible because the barrier opens at this moment during which inspiration ceases and the LES relaxes allowing the passage of the bolus into the stomach. Esophageal peristalsis is regulated by intrinsic and extrinsic innervations that coordinate propulsive

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contractions with simultaneous relaxations of the sphincter. Peristalsis itself constitutes the second anti-reflux barrier because it is able to clear refluxed material form the esophagus.

However, the barrier function is not 100% effective, and GER occurs rather frequently, specially after meals, even in normal individuals. Some GER is therefore "normally" possible at different times of the day particularly in newborns and young babies who often spit or vomit. They spend long time lying flat and receive large-volume feeds. A certain immaturity of the LES mechanism was proposed as the main mechanism for the failure of the barrier and the frequent occurrence of GER in young babies [1]. However, modern manometric methods demonstrated that the barrier is efficient [2] even in the premature [3]. When sophisticated miniaturized manometric probes became available, it was understood that rather than decreased or abolished LES pressure, which only happens rarely, the main mechanism of these episodes of GER at all ages [4], including young children [5, 6], was the occurrence of non-deglutitory transient lower esophageal sphincter relaxations (TLESR). In some cases the anatomy of the gastroesophageal junction and its relationship with the hiatus are abnormal, mainly by ascent of the junction and part of the stomach into the thorax and then it is appropriate to diagnose hiatal hernia.

If GER is frequent in infants and less frequent in grown-up children, a spontaneous tendency to improvement at this age should be acknowledged. Since "maturation" of the anti-reflux barrier has not been demonstrated, other explanations should be sought. The main one is the acquisition of the standing position, and it is generally admitted that babies who spit or vomit improve progressively during infancy and get rid of these symptoms when they are able to stand up most of the day.

15.3 GERD in Newborns and Toddlers Without Concurrent Diseases (Comorbidities)

If GER is "normal" to a certain extent in newborns and young babies, when should we suspect GERD and start diagnostic tests and treatment? It is obvious that a spitting, well-nourished, and happy baby is normal and does not need investigations or treatments. However, when some digestive or respiratory symptoms occur, the suspicion of GERD is reasonable, and some action should be undertaken. GERD induces several symptoms that can manifest themselves simultaneously or not in the same individual:

1. Vomiting: Babies with GERD, in contrast with adults, usually vomit and/or spit. This vomiting is more often post-prandial, but it may occur at any time. Its content is gastric juice with remains of feedings and very rarely with coffee ground staining or bile. In contrast with that of pyloric stenosis, vomiting tends not to be projective and total.
2. Failure to thrive: The loss of nutritional intake due to repeated vomiting may impair weight gain and development. Vomiting and stunting may be the first signs of GERD requiring attention by the pediatrician who should rule out other multiple causes.
3. Irritation, discomfort, and "abdominal pain": Repeated exposure of the esophageal mucosa to refluxed gastric juice leads to esophagitis. A baby with heartburn, dysphagia, or pain can only demonstrate his symptoms indirectly by crying and/or being irritated, unhappy, and unfriendly [7]. Of course, these symptoms can be related to many other conditions, but they should arise the suspicion of reflux esophagitis.
4. Anemia and iron deficiency: Macroscopic bleeding due to esophagitis is rare at this age, but microscopic blood loss may lead to microcytic anemia and low iron levels. Again, other diseases may cause this, but GERD should be actively sought after in these cases.
5. Repeated respiratory tract infection, bronchial reactivity, and pneumonia may be related to micro-aspiration or massive aspiration in children with GER. GERD should be investigated in them in the absence of other reasonable explanations like cystic fibrosis or immune deficiencies.

Most of these symptoms are caused by a variety of pediatric conditions, and pediatricians should rule these out before investigating

GERD [8]. However, given the prevalence of GER in infancy, a high index of suspicion is justified. Fortunately, peptic ulcers, stenosis, or major hemorrhages are not seen anymore, or very seldom, in refluxing infants. Many years ago, Carre pointed out the naturally benign clinical course of what was known at that time as "minor" hiatal hernia during infancy [9]. According to him, two thirds of patients would be asymptomatic (even without specific treatment) after the first 18 months of life, but the remaining third will remain symptomatic or may eventually have serious complications. These are the patients that require active treatment.

15.4 GERD in Newborns and Toddlers with Concurrent Conditions (Comorbidities)

Pediatricians and pediatric gastroenterologists are mainly concerned with children belonging to the above-discussed category of refluxers. Pediatric surgeons, however, have to deal more often with patients in which congenital or acquired concurrent diseases cause or facilitate GERD. Herewith we discuss these conditions and how they impact on the pathogenesis of GERD and its natural course:

1. **Brain damage**: Congenital or acquired diseases of the central nervous system and particularly cerebral palsy are frequently accompanied by GERD. There are many reasons for this: neurologic impairment may trigger the vomiting center and damages the coordination of digestive motility, both at the sphincter and peristalsis levels causing failure of the barrier [10, 11] and defective clearance. TLESRs seems to have less importance in the pathogenesis of GER in these children than in regular refluxers [11, 12] who, on top of this, are often recumbent, scoliotic, spastic, constipated, and affected by frequent respiratory tract infections. GER is facilitated by all these circumstances, and it may be occasionally aggravated by alkaline duodeno-gastric reflux [13] and salivary loss by drooling. These babies are often difficult to feed because of deglutition disorders, choking, or bottle refusal. The irreversibility of these circumstances in brain-damaged children makes spontaneous improvement of GERD over time unrealistic and the benefits of medications limited.
2. **Patients with respiratory tract disease**. There are several circumstances that facilitate GER in patients with respiratory tract disease that is particularly frequent during the first months of life: This may either enhance positive intra-abdominal pressures or accentuate negative thoracic pressures (or both) thus reinforcing GER driving forces. Premature and newborn babies with bronchopulmonary conditions are particularly prone to undergo GERD. Upper airway obstruction, positive airway pressure ventilation [14, 15], medication with xanthines [16], nasogastric tubes [17], and other reasons account for this as well as micro-aspiration or esophago-bronchial reflexes [18]. Weaning off ventilator may be impossible until GER ceases [19]. At this age it is particularly difficult to determine whether respiratory tract disease causes GER or conversely, if GER (aspiration, bronchoconstrictive reflexes, reflux laryngitis or sensitization to allergens after aspiration) accounts for the respiratory disease.

   A particular case is that of babies with apparent life-threatening events (ALTE), (pauses of apnea or cardiorespiratory arrests) that might be related to GER. Whether these episodes are caused by GER or not is an open issue. pH tracings, polysomnographic recordings [20, 21], and pH-MII recordings [22, 23] clarified only in part this issue. ALTE could be related to both acidic and non-acidic reflux episodes [24], but a clear link between both phenomena is not convincingly demonstrated [25, 26].
3. **Patients previously treated for esophageal atresia (EA) with or without tracheoesophageal fistula (TEF)**: This is a rare malformation (1:3500 newborns) consisting in the majority of cases of the interruption of the upper esophagus behind the trachea and the presence of a fistula connecting the

trachea with the lower end of the esophagus. This is the more common type, but about 10% of the patients have no fistula, and the two ends of the interrupted organ are quite far apart (long-gap cases). Smaller proportions have other uncommon varieties of the malformation. Current overall survival of about 90% [27, 28] makes lifelong follow-up and quality of life important issues for these patients and GERD a problem since 25–60% of survivors suffer it [29, 30] with increasing prevalence with time [31]. Swallowing difficulties may be related to the structural anomaly of the esophagus itself, but reflux esophagitis is found upon endoscopic and biopsy assessments in high proportions ranging between 20% [32] and 53% [33], and postoperative anastomotic stenoses refractory to dilation are in part related to the repeated exposure to gastric juices [34]. Barrett esophagus is diagnosed in a growing number of these patients during adolescence and adulthood [35], and the risk of esophageal cancer in the long run is considered manyfolds higher than in the regular population [36]. Vomiting, heartburn, apneic spells, and respiratory tract disease may be related to GER in these children and deserve attention and treatment during the first year.

There are several explanations for the high incidence of GER in survivors of EA/TEF repair: the muscle and mucosal layers of the reconstructed esophagus are definitely abnormal. The esophagus is shortened because anastomosis always involves some tension [37] and the extrinsic and intrinsic innervations that regulate motility are defective [38–40]. The LES is often ascended and functionally poor [41, 42], and, in addition, gastric motility may be abnormal as well, and duodenal emptying may be slow in cases with associated malformations or malrotation. All these dysfunctions are more relevant in long-gap cases and particularly in those without fistula in which the anastomosis is always under important tension and GER is practically constant [35, 43–45].

4. **Patients previously treated for congenital diaphragmatic hernia (CDH)**: This is another rare condition (1:3500 newborns) consisting of a posterolateral defect of either side of the diaphragm allowing the passage of intra-abdominal viscera into the thorax. The lungs are more or less hypoplastic, and persistent pulmonary hypertension threatens survival even with the best prenatal and neonatal care. In addition, these babies may bear other malformations or malrotation due to the distorted anatomy of the fetal abdominal organs. Ultrasonography allows prenatal diagnosis and in some cases treatment. The more sophisticated support measures (vasoactive drugs, nitric oxide, oscillatory ventilation, ECMO, etc.) are necessary after birth in order to keep these babies alive. Survivals close to 70–80% can be expected in high volume centers if hidden mortality (prenatal deaths, terminations, etc.) is excluded. Long-term follow-up and quality of life became also a priority in this condition [46]. That GERD was associated with CDH was pointed out long ago [47] after a dilated esophagus was found in babies with CDH [48]. GERD is more frequent in those with large hernias [49] and in those who require ECMO [50, 51]. It causes problems in up to 54% of cases [31, 52] and produces esophagitis in about 50% and Barrett's esophagus in some of them [53].

In these babies, the play of pressures between the abdomen and the thorax is abnormal due to lung hypoplasia and tight abdominal closure [54, 55]. The hiatus is under tension due to surgical repair or to replacement of one of its rims by a synthetic patch. The esophagus has poor motility as a result of abnormal innervation [56], and gastric emptying may be slowed due to seemingly abnormal innervation and to malrotation or adhesions [49].

GER is frequent during the first year after CDH repair [57, 58], and it tends to taper off in the ensuing years [31]. Apparently, only a small proportion of patients maintain sphincteric and peristaltic dysfunctions over the

years [59]. Feeding difficulties, prolonged respiratory difficulties, and vomiting may require active treatment of GERD.

5. **Patients previously treated for anterior abdominal wall defects (AAWD)**. These are congenital malformations consisting of anterior body wall defects that may be of two varieties: Omphalocele or exomphalos (1:4000 newborns) is an embryonic condition in which a part of the periumbilical wall is replaced by a gelatinous sac containing the bowel and the liver. Gastroschisis or laparoschisis (1:8000 newborns) is a fetal, acquired defect in which there is right-sided paraumbilical abdominal wall orifice that allows for the bowel and other organs to eviscerate into de amniotic fluid. In both cases, surgical repair involves reintegration of viscera into a reduced abdominal space and closure of the wall that to a variable extent causes increased abdominal pressure [60]. In addition, there is always non-rotation or malrotation due to the extra-abdominal position of the bowel during fetal life, and these, together with deficient innervation and interstitial Cajal's cell density [61, 62], delay intestinal transit postoperatively facilitating GER and hiatal hernia. GER often accompanied by esophagitis has been demonstrated in 43% of patients with omphalocele and in 16% of those with gastroschisis [63].

15.5 How and When to Use Diagnostic Tests for GERD in Newborns and Toddlers

Since GER is to some extent a "normal" phenomenon, diagnosis of too frequent or excessively prolonged episodes becomes a quantitative issue, and this explains the variety of the diagnostic procedures applied. Most of them are relatively invasive and costly, and therefore, their use is withheld until well-grounded suspicion of GERD is established. This is particularly true for young babies who do not collaborate, require miniaturized equipment, and, above all, might benefit from the spontaneous tendency to improvement.

ASPGHAN and ESPGHAN recommendations extensively review the diagnostic methods used in children [8]. In short, contrast meal is widely available, but it is irradiating, scarcely sensitive, and definitely unspecific. However, it may show stenosis, hiatal hernia, or malrotation and give some information about gastric emptying. Ultrasonography is too operator-dependent and is of no common use for this purpose. Extended pH monitoring is probably the accepted "gold standard," but it only informs about acid reflux and has "normal" values that vary too much with age. Extended multiple intraluminal impedance measurements coupled with pH monitoring (MII-pH) is currently the more informative tool since it is able to detect non-acidic or alkaline refluxes as well as acidic ones. However, the equipment is expensive, the tracings are difficult to analyze, and computerized measurements may be misleading. Isotopic studies are more specific and less irradiating than contrast meal, but they do not provide the same morphologic information. Manometry in all its varieties, pull-through sphincteric measurements, micro-catheter-perfused and sleeve sensor-prolonged sphincteric and esophageal body measurements, and high-resolution manometry, is too complicated and expensive (in terms of equipment and time consumption) to be routinely used for diagnosis at this age. Endoscopy and biopsy require sedation or anesthesia at this age, and although they inform about some morphologic features of the esophagus and the stomach, their main focus is the mucosal consequences of GER that may be absent in refluxers with apneic spells or respiratory symptoms. Finally, laryngoscopy and studies of lipid-laden macrophages or pepsin in bronchial aspirate are only used in cases of respiratory tract disease of highly suspected GER origin.

A recent review shows clearly the limitations of diagnostic tests for GER in children [64].

15.5.1 How to Test Children Below 1 Year Without Comorbidities

Most infants with suspected GER or GERD do not need any diagnostic procedure and can be managed expectantly under the more usual dietary, postural, and eventually antacid measures (see below). Only those who do not respond to these simple measures, who keep vomiting, fail to gain weight, emit blood in their vomit, or have alarming respiratory symptoms, require diagnostic tests. Contrast meal is widely available, but it is doubtful that it should be used at all in these cases because its "normality" does not exclude GERD and the presence of GER upon it is not diagnostic of GERD. pH monitoring is probably the first line of diagnosis. It is scarcely invasive, does not require collaboration, and informs reliably about excessive acid exposure. However, it has some limitations since babies fed five or six times per day have the gastric juice buffered to pH >4 for 2 h after each meal and this "blinds" the esophageal electrode for almost half the duration of 24 h. Normal values of acid exposure (reflux indexes) are set at higher values than at other ages, but this does not totally compensate for the insufficiencies of the method. It is true that the number of episodes and the timing of acid refluxes are well displayed and can confirm that GERD is present. Most probably impedance studies will replace standard pH metering in the future because the nature of the information provided by this procedure is much richer. However, there are still limitations that have been mentioned already. Endoscopy and biopsy are probably indicated in babies without comorbidities that are extremely irritated and in those with either blood in the gastric content or with microcytic anemia. Manometric studies are not routinely used in the clinical setting at this age. Of course, they may show insufficient LES pressures, excessive number of TLESR, or disturbed motility, but all these will not impact on the therapeutic attitudes, and therefore it can be concluded that it should be reserved for the investigation of the phenomenon rather than for its diagnosis. Isotopic GER and gastric emptying studies are probably not necessary in most of these patients.

15.5.2 How to Test Children Below 1 Year with Comorbidities

Newborns and small babies with concurrent conditions require a different approach. In many of them, GER may seriously threaten their health and even their life. The expectancy of a spontaneously favorable outcome is unrealistic in them due to the persistence of the mechanisms of GER (posture, spasticity, scoliosis, structural anomalies of the esophagus and/or the hiatus, innervation defects, malrotation, delayed gastric emptying or jejunoileal transit difficulties, etc.). It is therefore reasonable to perform GER diagnostic procedures once the suspicion is reasonable.

Contrast meal is probably the first and more accessible one in this group. In spite of its scarce sensitivity and specificity, it depicts the anatomic distortions caused by the concurrent condition (hiatal hernia, flattening of the angle of His, malrotation, gastric emptying, etc.) that should be known in case of surgery. pH monitoring should probably be performed next, and the use of two electrodes (one esophageal and other one gastric) helps to detect alkaline reflux and delayed gastric emptying [13]. It is generally available and scarcely invasive. The interpretation should take into account not only the reflux index but also the number of episodes of GER and the tracings of both the esophageal probe and the gastric one (if available). MII-pH will probably replace pH metering in the near future, but it is not yet available everywhere.

Endoscopy-biopsy is the best procedure to detect esophagitis. It is probably indicated in cases with blood in the vomit or iron deficiency.

In summary, our approach to diagnosis in children with comorbidities should be proactive but limited to contrast meal, pH monitoring (or MII-pH), and endoscopy-biopsy in selected cases.

15.6 Tools for the Treatment of GERD in the First Year of Life

If GER is a consequence of the failure or transient relaxation of the anti-reflux barrier allowing acid and/or alkaline exposure of the esophageal

mucosa, the treatment of GERD should be directed to one or several of these factors:

Non-operative treatment: This cannot reestablish a failing anti-reflux barrier, and it rather aims at decreasing the pressure gradients, at limiting the harmful effect of the refluxed juice on the esophagus, and at facilitating esophageal clearance. However, all these aims are hard to reach in young infants.

Lifestyle changes are limited at this age. Postural treatment pursues reducing GER by gravity and thus minimizing direct contact of the esophagus with gastric juices. Maintaining the baby in an upright position with a chair or crib is of little help. The prone position that was recommended years ago was abandoned because of the increased risk of sudden death, and therefore, the preferred position is supine with the head elevated [8].

Thickening of the feeds with vegetal products like rice cereal, corn or potato starch, or various bean gums decreases regurgitation but does not impact either on the episodes of GER or acid exposure [8, 65]. AR formulas are based on these additions, and they are designed to avoid excessive caloric intake. These formulas should be routinely used as first treatment, together with some postural help, in babies who regurgitate or vomit but maintain weight gain.

Helping the esophagus to get rid of the gastric juice whenever this is refluxed seems a good idea, and prokinetic drugs were introduced to enhance clearance and hasten gastric emptying. However, there is no convincing evidence of the efficacy of these drugs, and, on top of this, the more popular of them, Cisapride, had to be withdrawn from the market because of cardiac risks. Other drugs like metoclopramide, domperidone, erythromycin, or bethanechol cannot be recommended at this age because there is no evidence of their benefits and also because they may have serious secondary effects [8].

Decreasing the number and duration of TLESRs was the reason for the introduction of a new drug, baclofen, that has some success in adults, but it is not approved for young patients [8].

Finally, neutralizing or decreasing the acid contained in gastric juice would reduce its harmful action on the esophageal mucosa. Buffering antacids like magnesium or aluminum hydroxide may be absorbed and increase aluminum serum levels. Surface protective medications like alginate or sucralfate are effective for on-demand decreasing acid exposure, but their prolonged use may also increase serum aluminum, and there are no studies on their long-term effects in babies. Inhibitors of histamine-2 receptors (H2RAS) like cimetidine, ranitidine, or famotidine are effective in reducing acid exposure and help to heal esophagitis, but after some time, their effect decreases (tachyphylaxis). They also have some side effects, and they are being progressively replaced for proton pump inhibitors (PPI) like omeprazole, lansoprazole, and esomeprazole. These are definitely more effective for acid suppression, decrease of acid exposure, and healing of esophagitis. However, they have some side effects at this age like gastroenteritis, respiratory tract infections, parietal cell hyperplasia with gastric polyps, enterochromaffin cell hyperplasia, and others [66]. In addition, they are not approved for use at this age in which the evidence of their benefits is not fully convincing [8, 67, 68].

Surgical treatment: In turn, surgery that has no effect on motility, acid secretion, alkaline exposure, or gastric emptying (except in a few selected cases) can rebuild the failing anti-reflux barrier in a quite efficient and permanent way. The aims of anti-reflux surgery are to relocate the gastroesophageal junction below the diaphragm if it is elevated, to lengthen the intra-abdominal segment of the esophagus to allow the positive abdominal pressures to play on it, to accentuate the angle of His, and to create a full or a partial (anterior or posterior) wrap with the gastric fundus able to compress the distal esophagus and act as a valve when the stomach is full. In some cases in which feeding problems are predominant, the procedure may be accompanied by a gastrostomy. In rare instances when there are demonstrated gastric emptying problems, a pyloromyotomy or pyloroplasty may be a useful adjunct. All these operations are currently performed by laparoscopy except when local factors make this approach more difficult.

The gold standard of anti-reflux operations is the complete fundal wrap-around first described by Nissen [69]. It decreases acid (and alkaline)

exposure, reestablishes a pressure barrier, and reduces the frequency and duration of TLESRs [70–73]. However, this operation reduces gastric compliance leading to early fullness and sometimes to "dumping" syndrome; it may cause transient dysphagia and can have other surgical complications. Anterior hemi-fundoplications, as described by Ashcraft [74] or Boix Ochoa [75], may work well [2, 76, 77] but are less effective in patients with comorbidities [2, 78]. Posterior fundoplication, according to Toupet [79], is quite similar to an incomplete Nissen wrap-around, and its results should be more or less similar [80, 81]. It is interesting to notice that the institutions where Ashcraft's or Boix-Ochoa's operations were developed finally embraced Nissen's operation since laparoscopic approach was introduced. This demonstrated that finally complete wrap-around was not as bad as pretended by the introducers of these alternative techniques.

In a few desperate cases (particularly in neurologically impaired children), esophagogastric disconnection may be an alternative to repeated failures of fundoplication [82–84]. However, this operation is rarely indicated in the first year of life.

15.7 Treatment of GERD in the First Year of Life

In children without comorbidities, the recommendations of the NASPGHAN-ESPGHAN [8] are more than well founded and should be followed. Happy spitters do not need any treatment (except perhaps AR formula if they are bottle fed). Infants with persisting vomiting and other symptoms, like insufficient weight gain, bleeding, or recurrent respiratory tract disease, in which investigation demonstrated GER require thickening agents and acid suppression with either H2RAS or PPIs. However, it should be pointed out that the limitations and scarce solid evidence of the beneficial effects of both changes in lifestyles and medications at this age throw the suspicion that the unquestionable success of these recommendations might be based in most cases on the spontaneous favorable course of events during this period of life.

In cases with comorbidities, proactive treatment should be undertaken once GERD has been demonstrated. Long-term administration of PPIs, although with scarce evidence, remains the first tool. It is recommended in neurologically impaired patients [85] and in those previously operated for EA/TEF [86] although their effects on the latter were not fully conclusive. With the same lack of evidence, they are used in children operated upon for CDH [87]. It is certainly more questionable to rely on acid suppression in cases with respiratory tract disease although the contribution to this of esophago-bronchial reflexes could be minimized. There is no room for prokinetic treatment in these cases with comorbidities given the structural origin of dysmotility.

The role of surgery is certainly limited in the first year of life. In fact, the proportion of patients operated upon for GER below 2 years is small at least in Europe. American series show that a more aggressive surgical approach is often accepted on the other side of the ocean [88–92].

In babies without comorbidities, anti-reflux surgery is indicated when non-operative treatment fails in symptomatic patients (growth failure, persistent esophagitis, or stenosis) and in some cases with respiratory manifestations of GER and particularly in those with recurrent pneumonia due to aspiration [8]. In exchange, surgery is frequently used for the treatment of children with GERD and concurrent conditions.

The most questionable indication for surgery is the presence of repeated episodes of ALTE that can be put in relationship with episodes of GER after profound study with polysomnographic and pH monitoring or MII-pH monitoring [20–23]. Non-acidic reflux episodes are frequent in young infants [93], and ALTE could be related to both acidic and non-acidic ones [24]. However, there is no agreement on this interpretation [25, 26, 94]. Nevertheless, since the association of GER and ALTE may be deadly, anti-reflux surgery might be indicated in a few cases.

Neurologically impaired patients that are undernourished due to obvious feeding difficulties may certainly benefit from anti-reflux operations often accompanied by a gastrostomy. In fact, close to 50% of indications in the USA correspond to this group of patients [95]. The issue

of whether a Nissen should be added if gastrostomy is indicated has not been resolved, but it is reasonable to accept that gastrostomy alone may improve the status of the patient if GERD has not been demonstrated [96–100]. On the contrary, if a Nissen is necessary to treat GERD in a neurologic patient, addition of a gastrostomy may be a useful adjunct.

Babies previously treated for EA/TEF benefit from anti-reflux surgery when their GERD remains symptomatic for several months. Anastomotic stenosis refractory to repeated dilations, recurrent pneumonias, or insufficient weight gain may improve after surgical creation of an anti-reflux valve. However, the particular anatomy of the esophagogastric junction in these cases (high junction, small stomach, no angle of His) makes surgery more difficult and less effective [30, 101].

Up to 15% or 20% of babies operated upon for CDH may require anti-reflux surgery during the first year [57, 58, 102, 103] and definitely less in the ensuing years [31, 59]. Sometimes they can only be extubated after a fundoplication, and more often surgery is offered on the basis of unmanageable respiratory situations accompanied by difficulties for oral feeding. Also in this case, the local anatomy (distorted hiatus, patch, etc.) may make surgery difficult. Preventive fundoplication during CDH repair has been proposed [104, 105], but its benefits are not fully proven [106].

The contribution of GERD to the problems of babies operated at birth for AAWD corresponds rather to later months of the first year. Difficulties in transit due to malrotation, adhesions, or malposition of the hiatus cause GERD that becomes bothersome later. Fundoplication in both omphalocele and gastroschisis may be indivated in up to 50% of cases, and its performance during abdominal wall closure has been proposed [107].

15.8 Results of the Treatment of GERD

The main problem with the assessment of the results of non-operative treatment of GERD in children is the lack of consistent evidence on the effects of these measures at an age in which ethical concerns, lack of collaboration, and age and size diversity preclude (or make very difficult) the performance of randomized controlled trials (RCTs). Not many have been published on the efficacy of PPIs to treat esophagitis [108] or on the benefits of prokinetics [109–111]. In fact, the lack of really "normal" controls at this age is a barrier difficult to overcome. And thus, as stated by the ASPGAHN/ESPGAHN recommendations, no much solid evidence is available about the benefits of most of the non-operative treatments proposed for individuals this young [8]. Moreover, the evidence is even less solid when considering the long-term effects of medications like PPIs or others in infants. The risks of changes in the microbiota, neoplasia, and others are sometimes discussed but have not been studied. Nevertheless, the issue is not whether or not these treatments should be administered or not (probably they should) but whether or not they add substantially to the spontaneous improvement of GERD at that particular age.

For the same reasons, surgical treatment of GERD should be applied cautiously during the first year of life. The objective evidence of its benefits is weak, and the few published RCTs about this matter are restricted to compare two modalities of operation [92, 112, 113] or details of the same operation [90] but not to clarify the key issue of whether operation itself is better than no operation at this age. Of course, it is beyond doubt that some patients benefit from anti-reflux surgery, but they cannot be compared with similar, non-operated patients, and this casts doubts about the appropriateness of such operations.

And surgery has an additional problem that is easily linked to the operation itself: complications [91]. If a child treated chronically with PPIs acquires an infection or a tumor, many explanations can be found for these. However, if a child having a fundoplication has dumping syndrome, ascent of the wrap into the thorax, failure of the new valve or even dysphagia, wound infection, or adhesive obstruction, the operation itself will be blamed at once, and this is why pediatricians and pediatric gastroenterologists are so reluctant to propose indications for surgery [114, 115].

Even if the surgeon is convinced after many years of practice and critical observation of

his/her own results of the benefits of surgery for treating GERD in children below 1 year with comorbidities (and a few without them), it is fair to inform objectively their families about the potential complications and the expectations of success than can be summarized as follows.

In children without comorbidities, a good Nissen holds well in the vast majority of cases, and a normal life without dysphagia or early satiety after the first weeks following the operation can be foreseen.

Neurologically impaired children reunite the conditions for long-term failure of the wrap (not to talk about the outcome of the primary disease). A proportion of 25% after the first 12 months [116] is a reasonable figure. In many cases, the benefits of the wrap are obvious as demonstrated by parent satisfaction [117] and reduced readmissions [118]. On these bases, reoperation is acceptable when necessary. However, more than two or three failures may indicate other strategies like chronic PPIs or esophagogastric disconnection.

Children with respiratory symptoms of GERD respond well after operation when the problem is repeated aspiration (recurrent pneumonias and atelectasis) but less well when the respiratory disease is bronchoconstrictive like asthma or asthma-like bronchitis. In these cases, the patterns of nocturnal episodes of GER can orient the prediction of success of the operation [119]. In general, in the presence of "asthma" and GER, the surgical indications should be limited to cases refractory to all medical treatments with long nocturnal episodes of reflux [8].

The majority of children requiring surgery for GERD after repair of EA/TEF are improved by the creation of a new valve. However, in one third or more of them, the wrap fails after a few months due to the previously addressed unfavorable local conditions [116]. The proportion of wrap failures is particularly high, and this should be discussed prior to the operation. In this particular group of patients, however, there is increasing evidence of chronic esophagitis evolving into Barrett's esophagus, including some cases of intestinal dysplasia and even cancer. This has been observed even in cases with successful anti-reflux operations. Endoscopic surveillance for life is probably warranted in all them.

Babies operated upon for CDH and surgically treated for GERD have also a considerable proportion of wrap failures but certainly smaller than the neurologically impaired or EA/TEF ones. Babies who require fundoplication are usually the more severe cases in which respiratory, neurocognitive, or nutritional issues are predominant.

The experience with babies operated upon for AAWD and GER is limited, but it does not seem for the proportion of failures to be higher than in regular refluxers.

15.9 Conclusion

GERD is a serious problem during the first year of life in some patients without concurrent conditions and in many of those who suffer them. It would be naïf to believe that this complex phenomenon can be approached only by suppressing acid secretion. But it would be as naïf to believe that surgical creation of a new anti-reflux mechanism will suffice in all cases. A balanced approach is mandatory, and it should be taken into account that patients without comorbidities tend to improve during the first year of life. The use of medication at this particular age lacks evidence and so does anti-reflux surgery. Every effort should be made to design RCT to answer these uncertainties.

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