Esophageal atresia☆
Lessons I have learned in a 40-year experience

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Abstract A brief resume of the highlights in the history of oesophageal atresia is presented. This is followed by research into the etiology, ontogeny and embryology, and microbiological studies. A revised classification of risk factors with consequent survival statistics is presented. Lessons learned in the management of the condition over a 40-year period are reported with particular emphasis on the management of the preterm infant with associated severe respiratory distress, right-side aortic arch, upper pouch fistula, ‘long-gap’ atresia, and the use of gastrostomy and intercostals drains. The incidence and treatment of early and late complications is discussed.

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1. Historical background

The first recorded case of esophageal atresia was in 1670, by Durston [1], who found a blind-ending upper esophagus in one of a pair of female thoracopagus conjoined twins. Credit, however, must be given to Gibson [2], who, in 1697, documented the first classic description of an esophageal atresia with distal fistula. He wrote, “About November 1696, I was sent for to an infant that would not swallow. The child seem’d very desirous of food, and took what was offer’d it in a spoon with greediness; but when it went to swallow it, it was liked to be choked, and what should have gone down returned by the mouth and nose, and it fell into a struggling convulsive sort of fit upon it.” Subsequent postmortem examination confirmed the diagnosis.

The next case report, by Hill [3], appeared almost 150 years later (in 1840). Hill was “called, in the night, to visit Dr Webster’s family... The newborn made no effort to swallow but immediately convulsed... and the drink which had been given returned by mouth and nose, mixed with bloody mucus.” He recommended that “gently stimulating the rectum would remove the difficulty”; however, when an attempt was made to do so, there was “no vestige of an anus!” By the next day, with the “anxious parents, desiring that something might be done,” he attempted to open into the rectum with an “incision about one inch long half way between the scrotum and coccygis.” Hill was the first to document an associated anomaly with esophageal atresia...
and perhaps was the first to attempt to perform posterior sagittal anorectal procedure.

Holmes [4] in 1869 suggested the possibility of an operative treatment, but he added “the attempt ought not, I think, be made.” By 1884 [5] the number of reported cases had increased to 63. In 1888, Steele [6] almost became the first to operate on an infant with esophageal atresia. After consultation one evening, he advised that “by day-light the stomach should be opened and the oesophagus explored.” If “a membrane could be made out across a continuous channel, that it should be perforated in order to give a hope of life.” In the event, through a gastrotomy, the gap was found to be 1.5 in and, therefore, no procedure was performed.

In 1913, Richter [7] proposed an operative plan consisting of ligation of the tracheoesophageal fistula and anastomosis of the 2 ends of the esophagus. Unfortunately, he did not encounter a suitable case in which to attempt the repair.

In 1936, Simpson-Smith [8], in whose honor this Memorial Lecture is delivered, is reported to have been the first to attempt a correction of esophageal atresia at Great Ormond Street Hospital, London, UK.

Lanman [9] was the first to perform an extrapleural repair, in 1936. His patient lived for only 3 hours, and in 1940 he reported his experience with 30 operative cases, all of whom died. He stated that “with greater experience, improved technique and good luck,” success would soon be reported.

Only 3 years later, in 1939, Leven [10] and Ladd [11] independently reported the first survivors, but only after staged reconstruction.

Haight and Towsley [12] performed the first successful primary repair in a 12-day-old female neonate, this after 10 previous unsuccessful attempts.

2. Epidemiology

Esophageal atresia is a relatively common congenital malformation occurring in 1:2500 births. The etiology of the anomaly is largely unknown, but is likely to be multifactorial. The overwhelming majority of cases are sporadic/nonsyndromic with familial/syndromic cases representing less than 1% of the total.

Brown et al [13] carried out a study to determine the incidence of at least one component of the VACTERL (vertebral defects, imperforate anus, tracheoesophageal fistula, and radial and renal dysplasia; see below) association among first-degree relatives of patients with esophageal atresia. Of 1700 families contacted, 579 (34%) responded (from the Tracheoesophageal Fistula Support Group and KEKS—the German equivalent). The incidence of first-degree relatives having 1 or more components of the VACTERL association was 35 (5.5%) in the esophageal atresia group compared with 31 (3.1%) in a control matched population ($P < .01$).

3. Etiology

Three separate studies were carried to elucidate the pathogenesis of esophageal atresia:

1. the ontogeny of peptide innervation of the esophagus;
2. studies on the adriamycin rat model of esophageal atresia;
3. studies on the recently developed mouse model of esophageal atresia.

Hitchcock et al [14,15] carried out detailed investigations of the ontogeny and distribution of neuropeptides in the human fetal and infant esophagus. At 8 weeks, protein gene product (PGP) and synaptophysin were present in immature neurons throughout the cytoplasm, but from 10 weeks, synaptophysin was localized solely at nerve synapses. S100 immunoreactivity was also detected from 8-week gestation onward and was confined to glial tissue. Nerve cell size increased with maturation from 6 μm at 8 weeks to 20 μm at term. The numbers of cells, nerve density, and myenteric fraction all peaked at 16 to 20 weeks of gestation, which is around the time when fetal swallowing first occurs in utero.

Cheng et al [16] investigated abnormalities of neuropeptides on the esophagus of fetal rats with adriamycin-induced esophageal atresia. Immunoreactivity for S100 and galanin were significantly elevated in the atresia group, whereas Calcitonin gene-related product (CGRP) and substance P were also elevated. PGP-stained nerve tissue formed a complete ring around the plane of the myenteric plexus in the control rat, whereas in the atresia group, nerve tissue appeared in clusters. He postulated that the abnormal distribution of nerve tissue in the atretic esophagus may contribute to the dysmotility seen in esophageal atresia [17].

An adriamycin model of esophageal atresia in the mouse was established in view of the greater availability of molecular probes and genetic strains in the mouse compared with the rat model. Ioannides et al [18] in his first series of experiments showed that in the absence of tracheoesophageal separation, the dorsal fistula retains its nonrespiratory commitment, that is, is of foregut origin and stains negative for Nkx2.1, a marker for respiratory elements. In a further series of experiments, Ioannides et al [19] showed that sonic hedgehog expression undergoes a reversal in the doroventral patterning during tracheoesophageal separation. This doroventral patterning is disturbed in the adriamycin mouse model of esophageal atresia.

4. Microbiology

A study of organisms from the upper esophageal pouch before anastomosis showed that of 29 infants where the primary repair took place within the first 24 hours of life, no organisms were isolated in 16, whereas the remaining 13 grew normal oropharyngeal organisms only, whether or not
they received prophylactic antibiotics. All 11 infants in whom the primary repair was delayed grew similar oropharyngeal organisms. *Pseudomonas* and *Serratia* were isolated only in those receiving antibiotics [20].

A bacteriologic study of 24 neonates with esophageal atresia showed that compared with healthy neonates, the rate of intestinal colonization was prolonged, with *Staphylococcus albus* predominating in the first week, whereas bifidobacteria were almost completely absent. The onset of colonization seemed to be temporally related to the establishment of enteral feeding [21].

### 4.1. Prenatal diagnosis

Stringer et al [22] working in Harrison’s unit in San Francisco showed that in 87 mothers, whose fetus was found to have a small or absent stomach, only 15 (17%) had esophageal atresia at birth. However, when the small or absent stomach was accompanied by hydramnios, the positive predictive value for esophageal atresia was 56%.

### 4.2. Associated anomalies

There is a well-known incidence of additional congenital anomalies in infants with esophageal atresia. In a cohort of 253 infants, 122 (48%) had 213 associated anomalies as shown in Table 1 [23]. At least 3 components of the VACTERL association were present in 10% of our patients. Of the cardiac anomalies, ventricular septal defect was the most common, followed by clinically significant patent ductus arteriosus and tetralogy of Fallot. The VACTERL association [24] was attended by an increased mortality rate of 24%, chiefly because of major cardiac anomalies or multiple associated malformations.

The CHARGE association [25] (coloboma of the eye, heart anomaly, choanal atresia, retardation, and genital and ear anomalies), present in 2% of our cases, carried a high mortality rate (70%), mainly related to the presence of major cardiac anomalies.

In the presence of duodenal atresia associated with esophageal atresia and tracheoesophageal fistula, ligation of the distal tracheoesophageal fistula takes precedence and in favorable circumstances may be combined with primary esophageal anastomosis followed by duodenoenterostomy [26].

Cleft lip and palate were present in 2.6% of our cases and were associated with a mortality of 54%, again because of severe cardiac anomalies or the presence of multiple associated anomalies [27].

### 4.3. Preoperative investigations

Preoperatively, confirmation of the diagnosis was established with a large-caliber (F.G. 10) nasogastric tube (Replogle type) in the upper esophagus combined with an x-ray of the chest and abdomen, the latter to determine the presence of intestinal gas indicative of a distal tracheoesophageal fistula. A fine nasogastric tube is liable to curl up in the upper pouch or occasionally to pass through the trachea and down the distal fistula giving a false impression of an intact esophagus.

Preoperative echocardiography is essential to define the anatomy of the heart and to determine the position of the arch and descending aorta. A right-sided aortic arch was found in 2.5% of 476 infants with esophageal atresia. There was a high incidence of associated anomalies, of which 42% was cardiac. If a positive diagnosis of a right aortic arch is made preoperatively, the operative repair should be carried out through a left thoracotomy. If the right aortic arch is only discovered at thoracotomy, the repair should be attempted from the right, but if difficulty is encountered, an approach from the left should be undertaken but the presence of a double aortic arch should be considered [28].

### 4.4. Risk classification

The Waterston et al [29] classification proposed in 1962 and still widely used was reevaluated in 1994. Although original survival in his 3 categories were 95%, 65%, and 6%, because of improvements in surgical technique, anesthesia, and pre- and postoperative management, current survival rates in the 3 groups were 99%, 93%, and 71%. An alternative categorization was proposed as follows [30]:

<table>
<thead>
<tr>
<th>Group</th>
<th>Birth weight</th>
<th>Survival</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>&gt;1500 g, without major cardiac anomaly</td>
<td>97%</td>
</tr>
<tr>
<td>2</td>
<td>&lt;1500 g or major cardiac anomaly</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>&lt;1500 g and major cardiac anomaly</td>
<td>22%</td>
</tr>
</tbody>
</table>

These survival rates have again improved recently and presently stand at 98% for group 1, 82% for group 2, and 50% for group 3 [31].

### 5. Management

The operative repair of esophageal atresia is urgent, but is not an emergency except in a preterm infant with respiratory distress requiring ventilatory support. In these extreme
cases, we advocate emergency transpleural in continuity ligation of the fistula. If the condition of the infant improves dramatically after the ligation, primary anastomosis may be performed. In most cases, however, the operation is terminated and priority is given to resuscitation, which is continued pending improvement in the respiratory status. A delayed primary anastomosis should be attempted within 7 to 10 days as failure to do so will result in refistulization of the tracheoesophageal atresia [32,33].

There is considerable debate of the value of preoperative endoscopy in esophageal atresia. There are proponents of routine esophagoscopy, whereas others advocate preoperative bronchoscopy to determine the site of the distal tracheoesophageal fistula, to exclude an upper pouch fistula and to document the presence of tracheomalacia. As the overall incidence of an upper pouch fistula is less than 2%, whereas in isolated esophageal atresia it is at least 13%, my own choice is to reserve preoperative endoscopy to the isolated atresia group only (K Patil, L Spitz, EM Kiely, personal communication, 2000).

6. Operative approach

The operative approach of choice is via a posterolateral right extrapleural thoracotomy with minimal handling of the esophageal ends. The fistula is divided close to its entry into the trachea and the tracheal defect is sutured with interrupted fine nonabsorbable sutures. The proximal blind end of the esophagus is mobilized only sufficiently to provide a technically acceptable anastomosis. It is important to ensure that the distal esophagus is patent down into the stomach as cartilaginous “rests” can occur in the wall of the distal esophagus and cause mechanical obstruction [34,35]. Recently, the thoracoscopic approach for the correction of esophageal atresia has been adopted with excellent results reported.

7. Long-gap atresia

This group comprises a blind distal esophagus without a fistula. The importance of excluding a proximal fistula is again emphasized. At initial gastrostomy, the gap between the proximal and distal esophagus is measured radiologically (with metal sounds or contrast). A long distal segment with a “beak” may indicate an occluded fistula [36]. My policy is that a gap measuring less than 2 vertebral body widths would be amenable to primary anastomosis. With a gap of 2 to 6 vertebral bodies, delayed primary anastomosis should be possible at 8 to 12 weeks of age, whereas with a gap greater than 6 vertebral bodies, the chances of saving the esophagus are remote and it may be in the patient’s best interests to abandon attempts at anastomosis, to perform a cervical esophagostomy, and to replace the esophagus at a later stage (3-4 months) [37]. A recently adapted strategy in these cases is to perform a primary gastric transposition at 4 to 8 weeks of age without a prior cervical esophagostomy.

8. Esophageal replacement

Our procedure of choice is the gastric transposition. In a series of 192 gastric transpositions carried out for a variety of indications, there was a 4.6% mortality rate (mostly because of multiple previous failed attempts to retain the original esophagus), a 12% leak rate, and a 20% stricture rate, most of which responded to dilatations [38]. Overall, more than 90% of patients had a highly successful long-term outcome [39].

9. Gastrostomy

As recently as the 1980s, fashioning of a gastrostomy was routine practice in the treatment of esophageal atresia. A randomized control trial of trans-anastomotic tube vs gastrostomy showed that there was no difference in anastomotic leak or stricture rate among the 2 groups, whereas there was a 3-fold increase in the incidence of gastroesophageal reflux and the subsequent need for antireflux surgery in the gastrostomy group [40]. As a result, routine gastrostomy was dispensed with and only used for specific indications.

10. Postoperative chest drains

Chest drains were routinely placed after extra- or transpleural anastomosis in the belief that air or salivary leaks would evacuate through the drains. In practice, major leaks resulted in tension pneumothorax, which required the placement of a new thoracostomy tube. Minor leaks were generally contained and did not require tube drainage. As a consequence, routine chest drains are no longer used.

11. Anastomotic leaks

Overall, approximately 10% of primary anastomoses leak, most are minor, which seal spontaneously [41]. Major leaks develop early (days 1-3) and present with a tension pneumothorax. We advocate early reexploration for these major leaks as most are because of technical problems at the anastomosis, which require an additional 1 to 2 sutures, following which there is an uninterrupted postoperative recovery.

12. Anastomotic strictures

Strictures at the anastomotic site were recognized in 37% of our cases. Most were minor and responded to 1 or 2 dilatations. There is a strong direct relationship between gastroesophageal reflux and stricture formation (relative risk, 2.29). Other risk factors include anastomotic tension and leakage [42]. With meticulous handling of the esophageal ends, preservation of the blood supply, and care to include the mucosa in each and every suture of the anastomosis, strictures can be kept to a minimum.
13. Recurrent tracheoesophageal fistula

Of 242 infants, 20 (8%) developed recurrent fistula [43]. All presented with respiratory symptoms ranging from coughing and choking during feeds, apneic or cyanotic attacks, to recurrent respiratory tract infections. The mean age at onset of symptoms was 20 weeks. The investigations of choice for recurrent fistula are tube cine-esophagogram and bronchoscopic cannulation of the fistula. The latter is an essential preliminary in the operative repair of recurrent fistula.

14. Tracheomalacia

Wailoo and Emery [44] demonstrated a structural abnormality in the trachea of infants who died with esophageal atresia. The cartilaginous component was incomplete and softened and there was an increase in the length of the transverse muscle. They postulated that this was the cause of the tracheomalacia present to a significant degree in 10% of patients, half of who require surgical correction. The tracheal collapse occurs during expiration and causes the typical hoarse cough, but in severe cases results in acute life-threatening episodes of cyanosis or apnea. The area of collapse is sharply restricted to the trachea at or just above the site of entry of the distal tracheoesophageal fistula. An infant presenting with life-threatening episodes because of tracheomalacia requires an urgent aortopexy [45,46].

15. Gastroesophageal reflux

Significant reflux occurs in 40% of infants after repair of esophageal atresia, half of who will require antireflux surgery. Reflux is more common after anastomosis under tension, after gastrostomy, and after delayed primary repair. It has been implicated in the pathogenesis of anastomotic stricture. Symptoms consist of acute or chronic respiratory problems, recurrent vomiting, and failure to thrive. Some infants cannot be weaned off ventilatory support until an antireflux procedure is performed.

The diagnosis is established on contrast swallow, pH monitoring, and endoscopy.

Surgical treatment is problematic owing to the inherent dysmotility of the distal esophagus. A short, floppy Nissen fundoplication is the procedure of choice, but in early infancy, carries a high recurrence rate (>40%) and should be undertaken only after failure of intensive antireflux therapy [47].

Cheng et al [48] performed electrogastrography in 18 infants with esophageal atresia. The dominant frequencies in the esophageal atresia group did not differ significantly from those of the controls, but the range of frequency distribution was significantly wider in the esophageal atresia group. This suggested disturbed electrical activity of the stomach, which could result in poor electromechanical coupling and abnormal gastric contraction and may contribute to the increased incidence of gastroesophageal reflux.

16. Respiratory function

There is a demonstrable increase in the frequency and duration of respiratory tract infections during the first 3 years of life. This tendency has been attributed to the esophageal dysmotility and/or gastroesophageal reflux with recurrent aspiration or to a primary respiratory abnormality. Respiratory function tests performed in infants soon after the repair of esophageal atresia show abnormal patterns of airflow and increased airway resistance [49].

17. Dysmotility

Most patients with esophageal atresia have disordered esophageal motility. This results in long-term swallowing problems, and children are advised to take fluids liberally with meals and to avoid doughy white bread and cakes. In the long term the patients learn to cope with this disability and most lead “normal” adult lives.

18. Parent support groups

As a consequence of the many short- and long-term sequelae of esophageal atresia, parent support groups have become established in many countries. The Tracheoesophageal Fistula Support Group in the United Kingdom was one of the first of such groups and they provide support, advice, and comfort to new members; produce regular newsletters; run group meetings; and raise funds for research.

I conclude with the words of Willis Potts, which are as relevant today as they were in the 1950s [50].

To anastomose the ends of an infant’s oesophagus, the surgeon must be as delicate and precise as a skilled watchmaker. No other operation offers a greater opportunity for pure technical artistry.

References


