Oesophageal atresia (OA) occurs in about 1 in 4500 live births in the UK. Over 50% of infants with this condition will also have other congenital abnormalities. The management of this condition has advanced considerably over the past 30 years, resulting in good outcomes in many of these patients. However, the treatment of OA still presents challenges. This article reviews different aspects of this condition.

Keywords
oesophageal atresia; tracheo-oesophageal fistula; VACTERL; gastro-oesophageal reflux; feeding; anastomotic leak

Key points
1. Diagnosis of oesophageal atresia (OA) and tracheo-oesophageal fistula (TOF) is usually made within the first few hours of life.
2. Over 50% of babies with OA have at least one other significant congenital malformation.
3. Management involves either ‘early’ surgical repair within the first 48 hours of life or ‘delayed’ repair within 6-8 weeks after birth, depending on the anatomical configuration.
4. Most infants without other associated major abnormalities survive.

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Few conditions demonstrate the advances in neonatal surgery more clearly than the management of oesophageal atresia (OA). Although this condition was first described in the literature in 1670, it was not until 1941 that the first successful primary repair was achieved. By the 1960s survival figures of 60-70% were reported, and currently survival rates of >90% are routine. However, the treatment of OA still poses some challenges. This article outlines the anatomy, aetiology, diagnosis and clinical presentation, investigation, initial management, surgical treatment, complications and finally outcome and prognosis of this condition.

Anatomy and classification
An atresia is defined as ‘a congenital absence of a body opening or body passage’. OA occurs in between 1 in 3500 and 1 in 4500 live births in the UK and has a slight male predominance. It can occur in isolation, but is more commonly associated with an abnormal connection between the oesophagus and trachea, a tracheo-oesophageal fistula (TOF). Different anatomical configurations of OA and TOF arise and numerous different numerical and alphabetical classification systems have been described. However, the most helpful classification in practice is a purely descriptive one consisting of 5 main sub-types (see FIGURE 1):

- OA with distal TOF
- OA with proximal fistula
- OA with both proximal and distal TOF
- Isolated OA
- Isolated TOF – also termed the ‘H-type fistula’ due to the anatomical shape of this configuration.

Associated abnormalities
As with many neonatal surgical conditions, OA and TOF are frequently associated with other structural abnormalities. Indeed, between 50-70% of infants with OA have at least one other significant congenital malformation. This highlights an important point that early disturbances of organogenesis frequently affect concurrently developing organs. The most frequently associated abnormalities are cardiac, musculoskeletal, gastrointestinal, and genitourinary. Several patterns of simultaneous abnormalities arise with OA, the most well defined being the so called VATER association (Vertebral defects, Anal atresia, Tracheo-oesophageal fistula, Esophageal, Renal abnormalities). Additional associations include the VACTERL association (Vertebral, Anal, Cardiac, Tracheo-oesophageal, Esophageal, and Radial abnormalities) and the CHARGE association (Colobomata, Heart disease, choanal Atresia, mental Retardation, Genital hypoplasia, and Ear abnormalities).

There is also an association between chromosomal abnormalities such as trisomy 18 and 21. OA/TOF can also be accompanied by other foregut or midgut atresias including duodenal atresia. The clinical outcome of patients with OA and TOF is significantly affected by the presence of other abnormalities (see below).

Aetiology and pathoembryology
The aetiology of OA/TOF remains unclear. The condition does not appear to occur spontaneously in other mammals. The associated structural abnormalities, such as those found with the VACTERL and CHARGE associations, tend to suggest a generalised insult during early embryology. Infective agents have been suggested, as has a deficiency of Vitamin A. Prolonged use of contraceptive pills and exposure to high levels of progesterone during pregnancy
have also been implicated\textsuperscript{12-13}. In rodent models, Adriamycin exposure can give rise to OA with TOF\textsuperscript{15}, but it is unclear how closely this model of OA mimics the human situation. The pathoembryology of OA and TOF also has not been fully determined. The oesophagus and trachea are integrally related during normal development, with both sharing a common origin (FIGURE 2). During organogenesis, these organs go through the stages of separation and elongation, and tracheo-oesophageal malformations can occur if abnormalities occur during either of these steps\textsuperscript{16}. Whether the TOF is of respiratory or oesophageal origin has been the source of much debate\textsuperscript{17}. At a molecular level, the patterning gene sonic hedgehog seems to have an important role in the overall dorsoventral patterning of tracheo-oesophageal development\textsuperscript{18}. When the TOF is of respiratory origin has been the source of much debate\textsuperscript{19}. At a molecular level, the patterning gene sonic hedgehog seems to have an important role in the overall dorsoventral patterning of tracheo-oesophageal development\textsuperscript{20}. Some groups have reported an improved detection rate within about 8 hours of ventilation\textsuperscript{21}. The baby with OA and distal TOF often develops abdominal distension as air passes through the TOF into the stomach and then into the gastrointestinal tract. This becomes clinically significant if an associated gastrointestinal atresia (particularly duodenal atresia) is present, prompting the need for urgent surgical intervention. The ‘H-type’ TOF frequently does not present in the immediate postnatal period, but instead presents with recurrent episodes of cyanosis or choking in the neonatal period or recurrent chest infections or right upper lobe pneumonia in the older infant or child.

\textbf{Diagnosis and clinical presentation}

The suspicion of oesophageal atresia is raised by the antenatal ultrasound findings of polyhydramnios and a small or absent stomach bubble. However, these findings are positively predictive in only 40-50% of cases\textsuperscript{22}, a figure that is increased to 56% if the stomach is absent completely\textsuperscript{23}. The sonographic finding of a blind upper oesophageal pouch (‘upper neck pouch sign’) is more predictive when seen, but is less consistently identified\textsuperscript{24}. Some groups have reported an improved detection rate with magnetic resonance imaging\textsuperscript{25}. The clinical diagnosis of OA and TOF is usually made within the first few hours of life. In the newborn period, the baby with OA and TOF appears to be ‘mucousy’ and presents with drooling of saliva and often mild respiratory distress. In those babies that are fed before these features are observed, the first feed is followed by regurgitation, choking, coughing, and even cyanosis. The clinical diagnosis is confirmed by failure of passage of a nasogastric tube, which coils in the upper oesophageal pouch. The baby with OA and distal TOF often develops abdominal distension as air passes through the TOF into the stomach and then into the gastrointestinal tract. This becomes clinically significant if an associated gastrointestinal atresia (particularly duodenal atresia) is present, prompting the need for urgent surgical intervention. The ‘H-type’ TOF frequently does not present in the immediate postnatal period, but instead presents with recurrent episodes of cyanosis or choking in the neonatal period or recurrent chest infections or right upper lobe pneumonia in the older infant or child.

\textbf{Investigation}

\textbf{Investigations for OA/TOF}

Chest X-ray confirms the diagnosis of OA demonstrating the nasogastric tube coiled in the gas filled upper oesophageal pouch. A distal TOF fills the distal oesophagus with air and this feature can be used to estimate the ‘gap length’ of the atresia using the adjacent vertebral bodies for comparative measurement. Pure oesophageal atresia and oesophageal atresia with proximal fistula on the other hand, give the findings of ‘gaslessness’ on plain abdominal X-ray (FIGURE 3). Contrast studies are rarely indicated for the investigation of the more common configurations of OA/TOF. The exceptions to this are for investigating the gap length in pure oesophageal atresia, in which the gap length is usually long and the definitive surgical correction often delayed (see below), and for the diagnosis of ‘H’ type TOF in which the prone oesophagogram (a contrast oesophageal study performed in the prone position) is the investigation of choice.

\textbf{Investigations for associated abnormalities}

Plain radiographs are also useful for detecting associated abnormalities such as duodenal atresia, vertebral anomalies, sacral agenesis, and additional or absent ribs. A preoperative echocardiogram is performed to exclude cardiac abnormalities and to confirm whether a right sided aortic arch is present. If the latter is confirmed, many surgeons would then opt to perform the OA/TOF surgical correction through the left chest. Abdominal ultrasound is performed to exclude renal abnormalities. An ultrasound of the lower spinal cord is useful, especially if vertebral anomalies have been identified.

\textbf{Initial management}

The baby with OA/TOF may require initial resuscitation. If respiratory distress is present, the baby may also require ventilation. However, if a baby with distal TOF is ventilated, the urgency for surgical ligation of the TOF is increased due to the risks of worsening respiratory distress and gastric perforation. Surgery in these patients should therefore be performed within about 8 hours of ventilation\textsuperscript{26}. The most important elements of the pre-operative management of the non-ventilated baby with OA/TOF are prevention of aspiration of pharyngeal secretions and reflux of gastric contents through the TOF. The former is treated either by regular intermittent suctioning or continuous aspiration of the upper pouch using a double-lumen lower pressure catheter, the Replogle tube\textsuperscript{27}. The baby should be positioned in a head-up/slightly upright position to minimise gastric reflux. Intravenous fluids and broad spectrum antibiotics are commenced. Routine pre-operative blood tests are performed including full blood count, urea and electrolytes, blood glucose, clotting screen, and cross-match. Many centres also routinely perform chromosomal analysis in these patients. If associated abnormalities have been identified, the severity of these should be assessed before definitive surgery for the OA/TOF is performed.

\textbf{Surgical treatment}

The three main priorities of oesophageal atresia/TOF surgery were helpfully outlined
by Myers as:
- First, save the baby's life (division of TOF and treatment of associated life-threatening conditions)
- Second, restore gastrointestinal continuity
- Third, if possible do this by preserving the native oesophagus.

These criteria apply to all configurations of TOF but the order of priority is particularly applicable when dealing with the very premature baby and the baby presenting with a long-gap OA. The broad principles of the surgical approaches for the three configurations of narrow gap OA are as follows:

**Narrow gap with TOF**

The term ‘narrow gap’ is subjective but is used to define the majority of babies with OA with TOF in which the gap length of the OA is short enough to enable primary repair. As outlined above, the gap length is usually expressed as the number of vertebral bodies distance between the proximal and distal oesophageal ends as estimated on chest X-ray. However, this can often misrepresent the actual situation at surgery. Indeed, the term ‘narrow gap’ often underestimates considerable surgical difficulty and endeavour on the part of the neonatal surgeon.

In the non-ventilated baby without other severe abnormalities, surgery is normally performed within the first 48 hours of life. At the start of the surgical procedure, the upper pouch is usually assessed using a rigid oesophagoscope and the position of the TOF identified by rigid bronchoscopy. Using a right-sided thoracotomy incision (usually through the 4th intercostal space) and a retropleural approach, the TOF and both oesophageal ends are identified. A left sided incision is used if a right aortic arch has been diagnosed preoperatively.

The TOF is divided from the trachea and oversewn with interrupted sutures. The oesophageal ends are then mobilised, the blind end of the proximal oesophageal pouch excised, and the two oesophageal ends joined with interrupted full thickness sutures. Many surgeons place a nasogastric feeding tube across the anastomosis to protect it (transanastomotic tube) and also to enable initial postoperative feeding to be delivered distal to the anastomosis. Some surgeons insert a retropleural chest drain at the end of the procedure to enable an anastomotic leak to be detected.

**Long-gap OA with or without proximal TOF**

This configuration of OA presents the greatest surgical challenge. The definition of long-gap is again subjective, but the suggestion by the Melbourne group that the term ‘long gap’ be reserved for pure OA or OA with proximal fistula alone is helpful at a practical level as it distinguishes it from ‘wide gap’ OA with distal TOF that can usually be repaired using the conventional methods described above. In broad principles, long gap OA is treated either by delayed primary repair or oesophageal replacement.

Both approaches have their merits and the decision regarding which one to perform is based partly on features of the gap-length and partly on the expertise/preference of the individual neonatal surgeon.

In all cases, the initial approach for long-gap OA involves excluding a proximal TOF using a combination of rigid bronchoscopy and rigid oesophagoscopy. These are present in up to 25% of cases of long-gap OA and must be ligated if found. In addition, an evaluation of the gap length, and also the length of the distal oesophagus that is above the diaphragm, is important.

In general, if the distal oesophagus protrudes above the diaphragm, delayed primary repair is an option. If, however, the distal oesophagus is purely intra-abdominal, oesophageal replacement is required.

Delayed repair is classically performed 6-8 weeks after birth. The rationale for delayed repair is that there is some evidence that the gap-length reduces with growth, but probably more importantly the tissue strength increases from the newborn period making suture repair of a tight anastomosis feasible. Ongoing suctioning of the proximal oesophageal pouch is vital in these patients in order to prevent aspiration. This can either be done using continuous Replogle tube suctioning or frequent intermittent suctioning is used in some centres. Either approach requires fairly intensive nursing input. A gastrostomy is performed in these babies to allow gastrostomy feeding during the pre-repair period, but also to enable serial evaluation of the distal oesophageal pouch by either introducing radiolucent ‘sounds’ or by instilling radiographic contrast media. Combined with the Replogle tube in the upper pouch, the gap length can be assessed. The definitive repair follows the same approach of the ‘narrow’ gap, but extensive dissection and mobilisation of the distal oesophagus is often required.

If it is clear that delayed primary repair is not possible from the outset, oesophageal replacement can either be performed early (within the first few weeks of life) or as a delayed procedure. If the latter is chosen, a cervical oesophagostomy is usually performed (bringing the proximal oesophagus as a stoma in the neck in order to temporarily defunction it) and a gastrostomy is created for feeding. A detailed discussion of oesophageal replacement is...
beyond the scope of this article, but the possible substitutes include the stomach (either as a created tube graft or as a gastric transposition)\(^9\), the small bowel\(^9\), or the colon\(^9\). A number of different approaches exist for each substitute and there are many factors influencing the indications/ preferences for each.

TOF alone

This configuration occurs in about 4% of cases of reported congenital oesophageal abnormalities. Before commencing the surgical ligation of the TOF, it is helpful to identify it using bronchoscopy and oesophagoscopy and once identified, many surgeons cannulate it, in order to enable clear identification during surgery. Most ‘H-type’ TOFs can be successfully divided and ligated through a right sided cervical approach, but occasionally a thoracotomy is required for the low TOF.

Postoperative care

After repair of OA/TOF, the baby may require ventilatory support. This is particularly useful if the oesophageal anastomosis has been under excessive tension and paralysis of the baby for a few days may be advantageous to prevent anastoamotic disruption\(^9\). Postoperative feeding regimes demonstrate considerable inter-surgeon variation. A few surgeons feed the baby by mouth on the first postoperative day, while others will only feed via the transanastamotic nasogastric tube until a routine contrast study is excluded an anastamotic leak.

Complications

The complications of surgery for OA and TOF alone can either occur in the early post-operative phase or arise later. Early complications include anastomotic leak, oesophageal stricture, and recurrent TOF. Delayed complications include gastrointestinal reflux (GOR), disordered peristalsis, and tracheomalacia.

Anastomotic leak

Anastomotic leaks have been reported in up to 15% of OA repairs, but clinically significant major leaks or disruptions only occur in <5%\(^9\). Excessive tension of the anastomosis, poor surgical technique, and ischaemia of the oesophageal ends are all factors contributing to anastomotic leak. Most minor leaks are self-resolving, especially if a retropleural operative approach has been used and a mediastinal drain is present or introduced. A major leak can be life-threatening as a result of the sequelae of major sepsis and therefore prompt treatment is required. This consists of conservative treatment with broad spectrum antibiotics, nil by mouth, and adequate tube drainage, or re-anastamosis if complete disruption has occurred.

Oesophageal stricture

This is a common complication of surgical repair for OA. Although a symptomatic stricture is less common than the clinically insignificant ‘narrowing’ that is commonly seen on routine post-repair oesophagogram or oesophagoscopy\(^9\), the incidence of oesophageal stricture requiring dilatation was as high as 40% in some series\(^9\). Stricture occurs more frequently if gastrooesophageal reflux is also present and if an oesophageal leak has occurred. Symptoms include dysphagia, food bolus or foreign body obstruction, and respiratory problems from aspiration\(^9\). Treatment involves oesophageal dilatation (often repeated) and resection if the stricture is unduly tight or non-responsive to dilatation.

Recurrent TOF

This complication occurs in 5-10% of cases after initial division and ligation. The cause of this is thought to be secondary to a minor oesophageal anastomotic leak initiating an inflammatory process in the area of the TOF repair. The diagnosis of recurrent TOF is sometimes difficult and often requires a combination of radiography, bronchoscopy, and rigid oesophagoscopry. Surgical repair is usually required, although injection of fibrin glue into the TOF has been reported\(^9\).

Gastro-oesophageal reflux (GOR)

GOR occurs in up to 70% of infants following OA/TOF repair. However, this figure must be considered in the light of the high incidence of GOR in normal infants. GOR is most common in the delayed primary repair of OA alone group. This is because the extensive mobilisation of the distal oesophagus and the greater tension of the anastomosis results in the intra-abdominal oesophagus being pulled into the chest, thereby removing one of the main components that normally prevents GOR. Symptomatic GOR presents as recurrent non-bilious vomiting, dysphagia, recurrent anastomotic stricture, and respiratory symptoms if overflow into the trachea occurs. Diagnosis is confirmed by upper gastrointestinal contrast study and a 24 hour pH study. Non-operative treatment consists of reducing stomach acid with the use of histamine-2 blockers (ranitidine or omeprazole), reducing reflux with feed thickeners and positioning the infant in an upright position. However, up to 50% of
the atretic oesophagus. Often this only presents with mild clinical symptoms, but can cause dysphagia, food-bolus obstruction, and respiratory symptoms. The problem is greatest in the long-gap group.

Tracheomalacia

Tracheomalacia affects up to 20% of patients after OA and TOF repair and arises from movement of a weakened tracheal wall. It is thought to arise as part of the development of abnormality of TOF, although some studies suggest that the two conditions arise separately. Symptoms include a characteristic ‘seal bark’ cough, but severe respiratory symptoms may arise including acute apnoea. Although many of these resolve spontaneously or remain clinically insignificant, surgical intervention is required in up to 10% of cases.

Surgery involves suspending the aorta from the underlying sternum in order to stabilise the underlying anterior tracheal wall.

Outcome and prognosis

Although oesophageal atresia may present with difficult surgical challenges and a wide range of postoperative complications can develop, the survival of these patients is largely dictated by the associated abnormalities rather than the OA/TOF itself. The worst prognosis is in those patients with associated cardiac, chromosomal, or major pulmonary anomalies. Birthweight is also a prognostic indicator. The original Waterston classification of risk groups, distinguished between three groups of babies:

- infants >2500g with no abnormalities (Group A)
- those 2000-2500g with no other abnormalities or >2500g with moderate associated abnormalities (Group B)
- infants with birthweight <2000g with no other abnormalities or higher birthweight with severe cardiac anomalies (Group C).

With more recent developments in neonatal management, the Spitz classification has now identified a birthweight of <1500g and major congenital heart disease as being the worst prognostic group with a survival rate of 22% compared with a survival rate of 97-100% in those babies >1500g without major heart disease.

Conclusions

The overall management of oesophageal atresia remains one of the challenging areas of neonatal surgery. The outcome for these patients has improved dramatically over recent years and most infants without other associated major abnormalities survive. A multidisciplinary approach is essential to enable the best outcome in these patients.

References