orphanaesthesia

# Anaesthesia recommendations for patients suffering from

# VACTERL association

**Disease name:** VACTERL association

**ICD 10:** Q87.2

**Synonyms:** VATERS association, VACTERLS association, VACTERL association (ORPHA887), VATER association (ORPHA887), VATER syndrome, ORPHA887**.** Each letter of the mnemonic stands for one or more type of malformation. It is an association rather than a syndrome, as there is no evidence that the malformations are pathogenetically related. However, they occur together more frequently than expected by chance.

VACTERL association is defined by the presence of at least 3 of the following congenital malformations: vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies and limb abnormalities. In addition to these core component features, patients may also have other congenital anomalies.

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Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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**Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net**

## Disease summary

Exact incidence unknown but in the order of 1/10,000 -1/40,000 live born infants.

Originally described in 1973 by Quan and Smith, as VATER association (acronym standing for **V**erterbral anormalies, **A**nal atresia, **T**racheo-oesophageal fistula with O**e**sphageal atresia, **R**adial and **R**enal dysplasia). In 1974, Temtamy and Miller included ventricular septal defect and single umbilical artery to the '**V**'. But in 1975 this was changed to VACTERL by Kaufman and Nora and Nora (where '**C**' stood for **C**ardiac anomalies and '**L**' included limb rather than just radial anomalies)

VACTERL association is a sporadic disease and a positive family history requires careful differential diagnosis with other genetic conditions. Though the exact cause is unknown, it is thought to be multifactorial in etiology, with environmental triggers, including teratogens, interacting with a genetically susceptible genome. Triggers include exposure of the fetus to sex hormones, anti-cholesterol drugs, lead, adriamycin and dibenzepin in the first trimester, as well as babies born to diabetic mothers. It is rarely seen more than once in one family.

Due to the number of organs affected non randomly, it is thought that a "developmental field defect" occurs during blastogenesis (2-4 weeks of gestation), where abnormal structures are derived from the embryonic mesoderm. Males seem more affected than females and rarely multiple individuals are affected in the one family.

VACTERL association is a diagnosis of exclusion. The diagnosis is made clinically when 3 or more congenital defects are present and no clinical or laboratory based evidence exists for the presence of one of the many similar overlapping conditions. There are no validated diagnostic criteria published.

Antenatal diagnosis is challenging, as both skill and experience is needed to interpret scans performed and some features of the association are difficult to detect prior to birth.

Overall prognosis depends on type and severity of anomalies present. Today, the decreased mortality in most children is the result of early detection by ultrasound in the second trimester as well as early surgical intervention and rehabilitation.

Genetic counselling is difficult because of lack of information. Children with VACTERL association have normal development and normal intelligence.

**V – Vertebral and Vascular anomalies** 70% (60-80%)

Small hypoplastic/dysplastic/missing/supernumerary vertebrae; hemivertebrae 'butterfly' vertebrae; wedge vertebrae; vertebral clefts and fusion; caudal regression; tethered cord; branchial arch/cleft abnormalities; rib anomalies; Sacral agenesis; dysplastic sacral vertebrae; Scoliosis or kyphoscoliosis secondary to costovertebral anomalies; C5-6 dislocation and severe stenosis with spinal cord impingement, which is rare, and developmental delay with signs of myelopathy which is even rarer.

Early complications – minimal; Late complications – risk of developing scoliosis/back pain

Single umbilical artery 20% (often included as part of the 'V' in VACTERL). Antenatal diagnosis of the single umbilical artery maybe the first sign of the diagnosis but it is not specific of VACTERL association.

**A – Anal atresia/imperforate anus** 55% (up to 90%)

Noted at birth requiring surgery in the first days of life sometimes several surgeries required to fully reconstruct the intestine and anal canal.

Involvement of rectum/anus relates to major risk of genital abnormalities, especially in females with the risk of recto-vaginal fistulas and urogenital complications.

**C – Cardiovascular anomalies** 75% (40-80%)

Most common defects – Ventricular Septal Defect (VSD) (22-30%) +/- heart failure/ LV dilatation, Atrial Septal Defect (ASD), Tetrology of Fallot (TOF)

Less common defects – truncus arteriosus, transposition of the great arteries, hypoplastic left heart syndrome (sporadic reports), patent ductus arteriosus (PDA), co-arctation of aorta

**T – Tracheo-oesophageal fistula/ E- Esophageal atresia** 32%

15-33% will have associated uncomplicated congenital heart disease eg VSD that do not require surgery.

Esophageal atresia can occur as an isolated defect with an incidence of around 8%.

**R – Renal anomalies** 50-80%

Can be severe with incomplete formation of one or both kidneys or urological problems, e.g. severe reflux or obstruction of outflow of urine from the kidneys; Horseshoe kidneys, cystic, aplastic, dysplastic or ectopic kidneys, hydronephrosis; unilateral +/- bilateral agenesis; pyelonephritis; nephrolithiasis.

Kidney failure can occur early in life and may require kidney transplant.

Other renal abnormalities that can occur but are typically considered non-VACTERL include hypospadias, UTI; urethral atresia/ stricture, ureteral malformation; genital abnormalities, fistula connecting genitor-urinary (GU) and anorectal tracts (up to 25%).

**L – Limb defects incl. radial anormalies** up to 70% (40-50%),

Includes displaced, absent or hypoplastic thumb/s, polydactyly, syndactyly and radial aplasia/ dyplasia/hypoplasia; radial ray deformities; radioulnar synostosis; club foot; hypoplasia of great toe/tibia; lower limb tibial deformities

Bilateral limb defects tend to have kidney/urological problems on both sides. Unilateral limb defects tend to have kidney/urological problems on the same side.

**Other-** Growth deficiencies; failure to thrive

## Typical surgery

VACTERL association defects are treated post birth with issues being approached one at a time.

Management is divided into 2 stages: 1) centers around surgical correction of the specific congenital anomalies, incompatible with life, e.g. tracheo-oesophageal fistula, certain types of severe cardiac malformations and Imperforate anus/anal atresia in the immediate post-natal/neonatal period, followed by 2) long term medical management of sequelae of the congenital malformations eg renal and vertebral anomalies.

Even though optimal surgical correction is carried out in early life, some patients will continue to be affected by their congenital malformations throughout life.

**V** – Spinal surgery for vertebral anomalies and scoliosis (underlying costovertebral anomalies are common). Vertical expandable prosthetic Titaniuim rib (VEPTR) for treatment of thoracic insufficiency syndrome (TIS). Prophylactic detethering of spinal cord to prevent irreversible deficits (in filum terminale lipoma +/- low lying spinal cord) or at least halt progression of deformities (though not routinely offered if patient has anal atresia with tethered spinal cord). Laminectomy for back pain/ scoliosis. Spinal Cord stimulator. Occipital stabilization. Cervical laminectomy and resection of posterior elements followed by stabilisation/fusion/traction (for congenital C5-6 dislocation).

**A** – Anal atresia or imperforate anus – surgery in first few days of life. Sometimes several surgeries for full reconstruction of intestine and anal canal. Imperforate anus – either complete correction immediately post birth or colostomy formation followed by reanastomosis and 'pull-through' surgery. Atresia – repair without colostomy in infancy.

**C** – Ventricular septal defect, atrial septal defect, tetrology of fallot, transposition of great arteries, truncus arteriosus correction. Ranges from anatomical abnormalities that do not require surgery to necessitating several stages of challenging surgery.

**TE** – Tracheo-oesophageal fistula repair/ Oesphageal atresia usually repaired in first few days of life with primary anastomosis (extrapleural approach/ thorascopic/ thoracotomy) unless other factors (long gap, low general condition, other major abnormalities) make this impossible, where a staged procedure is carried out (cervical oesphagostomy, abdominal oesphagostomy, ligation of distal oesophagus with gastrostomy and feeding jejunostomy). TEF repair almost always precedes repair of congenital heart disease if both are present.

Oesphageal stenosis - dilatation of oesphagus via balloon

Tracheal stenosis – slide tracheoplasty

Laryngo-tracheo-oephageal Cleft – conservative management for type 0 and 1; primary closure using either endoscopy or external surgery for types 2-4 (and if conservative management fails in type 0 and 1)

GOR – Nissen Fundoplication

Diaphragmatic hernia repair

Tracheomalacia – thoracoscopic aortopexy

**R** – Surgery is done mainly to prevent damage from kidney and urological problems including persistent cloaca abnormalities ie dilatation of stenotic bulbar urethra

Genitourinary abnormalities - reconstructive surgery, treated in a staged manner; primary repair (rectovaginal fistula, hypospadias)

**L** – Plastic surgery for polydactyly, syndactyly, wrist radialization, but above all pollicization for the severe degrees of thumb hypoplasia. Bilateral trochanteric surgery – hip dysplasia secondary to scoliosis.

## Type of anaesthesia

General anaesthesia is needed for VACTERL association children due to the complexity of surgery undertaken. No reports of contraindications to either TIVA or volatile anaesthesia including nitrous oxide.

No reports of regional blocks being contraindicated in VACTERL patients.

Care must be taken or even avoided when doing caudals or neuraxial blocks in VACTERL patients especially if they have an imperforate anus, genitourinary abnormalities or sacral dimple, as they frequently have occult spinal dysraphisms eg tethered spinal cord, meningocele or lipomyelomeningocele. When planning a neuraxial technique, a spine ultrasound should be performed. Difficult neuraxial block placement and failure has a higher incidence in patients with vertebral column abnormalities versus patients without spinal abnormalities. The utilization of ultrasound has aided in accurate needle placement for neuraxial techniques when spinal pathology is present.

For thoracoscopic procedures, ventilation will need to be adjusted to normalize or allow for permissive hypercapnoea secondary to CO2 insufflation. Also regular desufflation of thoracic cavity needs to be undertaken to restore sufficient oxygenation. Some patients with congenital heart disease may not tolerate the physiologic changes that accompany insufflation with thoracoscopic or laparoscopic procedures.

## Necessary additional diagnostic procedures (preoperative)

Because of multiple systems affected by this association, baseline investigations are necessary to rule out or determine the severity of the condition in addition to the usual physical observations including height and weight.

**Vertebral anomalies –** X-ray, Ultrasound (USS) and/or CT/MRI of the spine

**Anal Atresia –** Physical examination/observation, abdominal ultrasound +/- additional testing for genitourinary anomalies (Urethrocystography, Urethroscopy, Intestinal Barium Examination, Abdominal/ Perineal USS, AXR)

**Cardiac malformations –** ECG (arrhythmias), Echocardiogram +/- Cardiac CT/ MRI/ Angiogram (exclude cardiac or vascular abnormalities; evaluate structure and function of heart). Paediatric cardiology consultation. CXR (cardiomegaly)

**Tracheo-esophageal fistula –** Physical examination/observation (contrast studies are rarely required); CXR – PA/lateral; CT/MRI (tracheoesphageal cleft) + CXR (aspiration evidence) and Endoscopy; AXR (diaphragmatic hernia)

**Renal anomalies –** Renal Ultrasound +/- voiding cystourethrogram; CT urogram multislice; abdominal CT; Urine M/C/S

**Limb anomalies –** Physical examination, X-rays (skeletal survey – limbs, hips, rib); angiography (radial artery hypoplasia)

**Blood Work** – Full blood count- Hemoglobin, Hemocrit, Electrolytes, Renal function, Liver and Bone profiles, Vitamin D, Glucose, Group and Save, Cross Match; Coagulation/ Bleeding time; Chromosome analysis;

**Post dialysis** – blood urea, electrolytes, weight,
(Pt with abnormalities of the heart and kidney may be more at risk for Hemolytic Uremic Syndrome)

**Pulmonary workup –** CXR +/- Respiratory function tests

## Particular preparation for airway management

Airways can be anatomically challenging in VACTERL patients secondary to their craniofacial-vertebral deformities. A difficult airway trolley should be available in the operating room when anaesthetizing these patients.

VACTERL children may have other associated abnormalities eg cleft lip and palate, hemifacial microsomia (hypoplastic mandible +/- webbed neck), and present for various types of surgery. A difficult airway and hence intubation should be anticipated.

Additionally extra equipment maybe needed for patients with cervical instability.

Extubating patients with difficult airways need to be taken with considerable caution. Depending on the surgery undertaken, some of these children will need postoperative intensive care ventilation for a few days, whilst others may be deemed safe to extubate on the operating table. History of an increased risk of aspiration eg cleft lip/palate, trachea-oesphageal fistula, may preclude early extubation.

There are reports of difficult intubation and tracheal damage in patients with oesophageal atresia. In patients with a TEF, endotracheal tube placement and mechanical ventilation can be especially challenging. This can be secondary to the proximity of the fistula to the carina, causing gastric insufflation, aspiration of gastric contents from the fistula, and prematurity, with an incidence of 30% in patients with a TEF. To properly position the ETT, an intentional mainstem intubation can be performed with subsequent withdrawal of the ETT just above the carina. Therefore, the ETT is positioned just above the carina and below the fistula, avoiding gastric insufflation and inadequate ventilation. This may not be possible with very large or pericarinal fistulas. Often, prior to intubation, rigid bronchoscopy is performed to define the anatomy, size and location of the fistula.

Isolated tracheal stenosis/atresia may exist which will cause impossible ETT intubation. Urgent tracheostomy will be needed. If laryngeal stenosis only is present then smaller ETT should be used rather than the correct size. Be careful in recently repaired laryngeal cleft when inserting ETT as it could damage the repair/reconstruction.

## Particular preparation for transfusion or administration of blood products

Since there are major operations that will be undertaken in VACTERL infants eg Cardiac, TOF/OA, spinal operations, gastrointestional and diaphragmatic hernia etc – blood products need to be ordered and issued before the procedure is underway.

## Particular preparation for anticoagulation

Patients may have coagulation issues secondary to chronic renal failure and being on dialysis. They may also be at a higher risk of developing uraemic haemolytic anaemia.

Otherwise no reports on coagulation issues in VACTERL patients.

No particular reports for any anticoagulant regimen.

## Particular precautions for positioning, transport or mobilisation

Not reported.

## Probable interaction between anaesthetic agents and patient's long-term medication

Not reported.

## Anaesthesiologic procedure

Avoid suxamethonium in patients with chronic renal failure, due to hyperkalemic arrhythmias and arrest. Dialysis should be used to lower the potassium level prior to surgery.

No reports of either intravenous or inhalation anaesthetic agents being contraindicated.

Intravenous access can be challenging in patients with limb abnormalities.

For patients with TEF coming for repair, a rigid bronchoscopy is helpful to aid in ETT positioning. Anaesthesia with spontaneous ventilation versus positive pressure ventilation can avoid gastric insufflation through the fistula and subsequent pneumoperitoneum.

Patients with oesophageal atresia having had oesophageal reconstruction repair with a piece of colon, are at risk of aspiration including silent aspiration (up to 50%), as there is no lower oesphageal sphincter (LOS) present and motility is slow. Consider antacids +/- prokinetic agents and nil orally for 12 hours preoperatively. Rapid sequence induction (RSI) with adequate preoxygenation with elevation of head of the bed at induction of anaesthesia. Use clear mask so visualization of aspiration is possible and have a large bore suction available.

## Particular or additional monitoring

Forced air warming device should be used to prevent drop in the infant/ neonate's (especially with low birth weight) core temperature.

Arterial and Central Venous Line (CVL) are usually inserted in patients having prolonged operations, operations involving hemodynamic instability or major fluid shifts eg. cardiac and TOF/OA operations. Radial arterial line placement may be difficult or impossible if radial or upper limb anomalies are present.

NIRS (Near InfraRed Spectroscopy) can be used for Cardiac and Thoracoscopic repair of TOF/OA to ensure adequate oxygenation of cerebral tissues (though there are no consistent reports regarding this).

## Possible complications

Patients with TOF/OA have susceptibility to respiratory infections (atelectasis and pneumonia) due to weakness in tracheal muscles & hyper reactive airways. These patients need active respiratory care with physiotherapy and antibiotics pre & postoperatively.

Acute life threatening events (10-20%) may occur postoperatively in OA patients which include gastro-oesphageal reflux and tracheomalacia. In one study GOR occurred in 52% of patients.

Patients that are premature (<1500g) or have associated major cardiac conditions have an increased mortality rate post TOF/OA repair.

Patients with laryngeal clefts may present with chronic cough, aspirations, recurrent pneumonias and respiratory distress.

## Postoperative care

Postoperative monitoring depends on type of surgery undertaken and preoperative medical condition.

Major operations, i.e. TOF/OA repair, laryngeal cleft, cardiac surgery, will require intensive care admission postoperatively for continued ventilation +/- paralysis, haemodynamic monitoring and appropriate fluid management, close observation for the development of potential complications as a result of surgery, feeding including total parental nutrition, antibiotics and analgesia.

## Information about emergency-like situations / Differential diagnostics

*caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease*

Tracheal agenesis/stenosis with tracheooesphageal fistula can be associated with VACTERL Association. Respiratory insufficiency in the newborn infant may be overcome by intubating the oesophagus or performing emergency tracheotomy and applying positive pressure ventilation. Success is not always possible.

## Ambulatory anaesthesia

Not reported.

## Obstetrical anaesthesia

Physiology during pregnancy can affect and even worsen the pre-existing conditions of VACTERL parturients mainly cardiac, spinal and respiratory/ airway.

General, neuraxial (epidural +/- spinal) or a combined anaesthetic technique is possible after evaluating the issues pertinent to the individual patient. A full assessment needs to be undertaken in order to choose the optimal anaesthetic technique.

Beware that parturients may have a difficult airway and/or respiratory insufficiency (restrictive lung disease) due to major thoracocervical spinal abnormalities. The severity of the restrictive lung disease can negatively impact on ventilation +/- oxygenation during neuraxial or general anaesthesia. Airway assessment is important including Mallampati score. CXR and respiratory function tests will help to further define the extent of spinal abnormalities and any lung abnormalities, e.g. collapse, degree of lung expansion, respiratory reserve etc. Respiratory follow-up throughout pregnancy is important. Awake fiberoptic intubation should be considered as a backup if direct laryngoscopy is felt to be dangerous.

Before a regional technique is undertaken, one needs to elicit with MRI where the spinal cord medulla ends and also define what spinal malformations if any, exist e.g. segmentation in the lumbar region. Due to fixed lumbar scoliosis, it may be difficult to find lumbar landmarks for needle placement. Ultrasound can be used as an adjunct in this case (and it may reduce the incidence of dural puncture). Neuraxial anaesthesia can be used for both peri- and post operative analgesia, though inadequate dermatomal block is a known complication.

ECHO is needed to rule out any abnormal cardiac morphology present. Cardiology follow-up for optimization is important.

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