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# ANAESTHESIA FOR EXIT PROCEDURE

**AL GQIBA**

Moderator: Dr K Govender



School of Clinical Medicine

Discipline of Anaesthesiology and Critical Care

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# ANAESTHESIA FOR EXIT PROCEDURE

## INTRODUCTION

Ex-utero Intrapartum Treatment (EXIT) procedure, also known as 'operation on placental support' (OOPS) and airway management on placental support (AMPS).<sup>15</sup> The EXIT procedure is a rare surgical procedure performed to ensure foetal airway patency.<sup>1</sup> It consists of partial externalization of the foetus from the uterine cavity during delivery, for managing life-threatening conditions while maintaining placental circulation.<sup>1</sup> Thus eliminating concerns for hypoxia as the placenta continues to provide oxygenation, and preventing potentially catastrophic events during delivery.<sup>1</sup>

Advances in prenatal early diagnosis of foetal congenital airway malformations, are used to identify those that will benefit from this intervention.<sup>1</sup> This, together with the concurrent advancement of surgical techniques, has resulted in improved survival for babies with airway obstruction that would make spontaneous ventilation or placement of an endotracheal tube impossible.<sup>1</sup>

## INDICATIONS FOR EXIT PROCEDURE

### **Indications for an EXIT Procedure<sup>19</sup>**

#### **EXIT-to- Reversal of tracheal occlusion**

- Congenital Diaphragmatic Hernia (CDH) - following tracheal clip or endoluminal balloon

#### **EXIT-to-Airway procedure<sup>19</sup>**

- Foetal neck mass with obstruction (e.g., cervical teratoma, vascular/lymphatic malformation, goitre, neuroblastoma)
- Congenital high airway obstruction syndrome (CHAOS)
- Intraoral masses
- Tracheal atresia
- Laryngeal atresia
- Severe Micrognathia
- Epignathus

#### **EXIT-to-Resection procedure<sup>19</sup>**

- Chest masses with intrathoracic airway obstruction
- Congenital pulmonary airway malformation
- Bronchopulmonary sequestration
- Mediastinal teratoma
- Pericardial teratoma

#### **EXIT-to-ECMO procedure<sup>19</sup>**

- Severe Congenital Diaphragmatic Hernia
- Severe Congenital Heart Disease
  - Hypoplastic left heart syndrome (HLHS) with intact/ restrictive atrial septum
  - Aortic stenosis with intact/restrictive atrial septum

#### **EXIT-to-Separation procedure<sup>19</sup>**

*Cervical teratoma*  
OA, O. (2009). SAJAA, 15(1), 17-21.



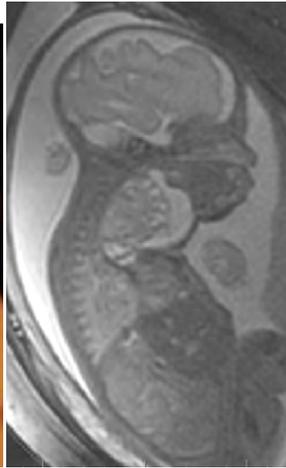
*Cervical hygroma*



OA, O. (2009). SAJAA, 15(1), 17-21.

*3D U/S & MRI: Neck Mass*

*Intraoral Masses*



Kiarash Taghavi, S. B. (2013).  
*J Paediatrics and Child Health*, 49, E420-E427,

Youssef, M. A. (2007).  
*J Indian Assoc Pediatr Surg*, 12(4)

The EXIT procedure allows the airway to be secured by direct laryngoscopy, bronchoscopy, tracheostomy, or surgical intervention, while on placental support.<sup>2</sup>

### **EXIT for reversal of tracheal occlusion**

The EXIT procedure was initially developed to treat fetuses with severe CDH; placental circulation allowed time for removal of clips, foetal bronchoscopy, endotracheal intubation and surfactant administration.

This 'Plug the Lung until it Grows' (PLUG) technique was developed at the Fetal Treatment Centre, San Francisco, as a foetal procedure to induce pulmonary hyperplasia in highly select group of patients with CDH.<sup>12</sup>

Currently, tracheal occlusion is performed with an intratracheal detachable balloon. At EXIT, foetal bronchoscopy is performed; the balloon is pierced and suctioned out through the bronchoscope, and endotracheal intubation is performed after withdrawal of the bronchoscope. This technique avoids neck dissection and associated complications of nerve injury, as well as tracheal injury from the tracheal clips.<sup>12</sup>

### **EXIT-to-Airway procedure**

- Cervical teratomas – composed of tissues from all germ cell layers and can be very extensive.  
Cervical teratomas have varying presentations depending on the size and degree of compression of surrounding structures. Oesophageal compression may result in polyhydramnios that can precipitate pre-term labour. In very rare cases, large cervical teratomas with high vascularity may result in hydrops foetalis, the result of high output cardiac failure in the foetus. Hydrops foetalis is characterised by the presence of excess fluid in two or more body cavities i.e. abdomen, pericardium, thorax or skin and may also be associated with placental thickening. The development of hydrops

increases the urgency of intervention as the danger of foetal demise becomes imminent. Occasionally, it becomes necessary to drain pleural effusions to improve pulmonary function during an EXIT procedure.<sup>1</sup>

- Cervicofacial lymphovenous malformations – cystic hygromas or cervical lymphangioma  
These cystic masses develop as a result of failure of the jugular lymph sacs to join the lymphatic system early in foetal development. The sacs become filled with lymph-like fluid, gradually distend and compress surrounding structures. They may involve the floor of the mouth, pharynx, larynx and extend into the mediastinum.
- Congenital goitre - A diffuse thyroid gland enlargement may occur in the foetus of mothers with Graves disease. This results from the transplacental passage of thyroid-stimulating immunoglobulin G antibodies. <sup>1</sup>
- Congenital high airway obstruction syndrome (CHAOS)  
This condition encompasses varying degrees of abnormal arrested development of the larynx i.e. laryngeal or tracheal atresia.<sup>1</sup>

### **EXIT-to-Resection procedure**

Foetuses with large intrathoracic masses (mediastinal teratomas or large lung lesions) causing haemodynamic compromise and difficulty with ventilation at the time of delivery may undergo resection during the EXIT procedure. In this scenario, the foetus would undergo a sternotomy or thoracotomy while still on placental support. The mass is will be exteriorised and resected, reducing the compressive effect on the lungs and mediastinum prior to initiating ventilation and delivering the baby.<sup>1</sup>

### **EXIT-to-ECMO procedure**

Exit procedure for conditions that will necessitate emergent extracorporeal membrane oxygenation (ECMO).When difficult transition from foetal to neonatal circulation is anticipated; as in some congenital cardiac lesions or severe congenital diaphragmatic hernia (CDH), the foetus can be placed on ECMO before placental support is discontinued to prevent haemodynamic and cardiorespiratory compromise. This approach has also been used in some foetuses with large intrathoracic masses.<sup>1</sup>

*EXIT-to-ECMO*  
**OA, O. (2009). SAJAA, 15(1), 17-21**



## EXIT-to-Separation procedure

EXIT procedure as a bridge for the separation of thoraco-omphalopagus conjoined twins.



<http://radiographics.rsna.org>

## **PREOPERATIVE PREPARATION**

### **Maternal Preoperative Preparation**

The EXIT procedure is usually scheduled after the 35<sup>th</sup> week of pregnancy, ideally close to term but prior to the onset of labour.<sup>2</sup>

A thorough medical history and physical examination must be performed in all patients, keeping in mind the systemic physiological changes of pregnancy. History of comorbidities is important, because significant cardiac or pulmonary co-existing diseases that increase maternal morbidity can preclude the mother from being a candidate for this procedure. A history of allergies, previous anaesthetic history and any complications should be established.

Thorough airway examination is important as pregnant women are prone to difficult airway, and because the EXIT procedure is done under general anaesthesia.

Laboratory investigations and optimisation:

- Baseline haemoglobin, platelets – keeping in mind physiological changes of pregnancy.
- Crossmatch
- Mother's with Graves's disease, the thyroid function should be assessed to ensure a euthyroid state<sup>1</sup>

Premedication:

- Aspiration prophylaxis – Ranitidine 150mg 2 hours preoperatively per os; Metoclopramide 10mg 30minutes preoperatively intramuscularly and Sodium Citrate 30mls 30minutes preoperatively per os.

Preparation: Informed Consent

Plan for postoperative placement in labour ward high care unit

### **Foetal Preoperative Preparation**

- Rule out chromosomal abnormalities: The presence of a chromosomal anomaly is a relative contraindication to the EXIT procedure and it is usually ruled out by karyotyping performed on a sample obtained during amniocentesis.<sup>1</sup>
- Diagnosis of the airway lesion, identifying other associated congenital anomalies and establishing the indication for EXIT procedure: This is done with 3D ultrasound or ultrafast MRI scan. The following table illustrates the diagnostic information that can be gathered from the ultrasound versus the MRI scan.

Information	US	MR Imaging
Size and location of the lesion	Yes	Yes
Infiltrative characteristics of the mass	Yes	Yes
Tissue characteristics of the lesion*	Yes	Yes
Fetal respiration function	Yes	No
Fetal swallowing function	Yes	Yes
Amniotic fluid volume	Yes	Yes
Fetal airway distortion	No	Yes
Anatomic location of the tongue	No	Yes
Presence of associated anomalies	Yes	Yes
Global anatomy (in conjoined twins)	No	Yes

\*Depends on tissues involved; calcifications are variably seen at US.

Manjiri K. Dighe, S. E. (2011). EXIT Procedure: Technique and Indications with Prenatal Imaging Parameters for Assessment of Airway Patency. *Radiographics*, 31(2), 511-526

- Foetal weight estimation is prudent for the anaesthetic management of the foetus, and is determined preoperatively from ultrasound.<sup>1</sup>
- Associated comorbidities:
  - Hydrops foetalis – a fatal condition characterised by the presence of excess fluid in two or more body cavities i.e. abdomen, pericardium, thorax or skin and may also be associated with placental thickening. It's a complication of large cervical teratomas with high vascularity, that result in high output cardiac failure in the foetus. The development of hydrops increases the urgency of EXIT procedure as the danger of foetal demise becomes imminent.<sup>1</sup>
  - Echocardiography plays a pivotal role in the assessment of the foetus for this procedure as the development of hydrops foetalis can be detected and monitored prior to the EXIT procedure. In addition, to assess ventricular volume status and ventricular function to get an appreciation of baseline foetal cardiac function prior to commencing surgery.<sup>1</sup>
- Plan for post EXIT procedure: Neonatal ICU bed available

The multidisciplinary facets of this procedure mandates that all physicians involved in the management of the mother and the foetus have an understanding of the prenatal history, maternal and foetal concerns, and the necessary steps to ensure a smooth execution of the procedure.<sup>1</sup>

Preoperative multidisciplinary meetings, that include the parents, are vital in preparation for the EXIT procedure and are extremely important as the indication for each procedure is different. The disciplines involved in these meetings should include the obstetricians, or maternal–foetal medicine specialist, paediatric surgeons, anaesthesiologists, paediatric cardiologists, neonatologists, otorhinolaryngologist, theatre and labour ward delivery nurses, an echocardiographer, as well as representatives from the blood bank.<sup>1</sup>

Each of these disciplines is introduced and their role in the procedure is explained in detail for the understanding of the family as well as the other practitioners present. The obstetrician and/or paediatric surgeon explaining the nature, pathophysiology of the lesion and the indication for the EXIT procedure so that the whole team is on board.<sup>1</sup>

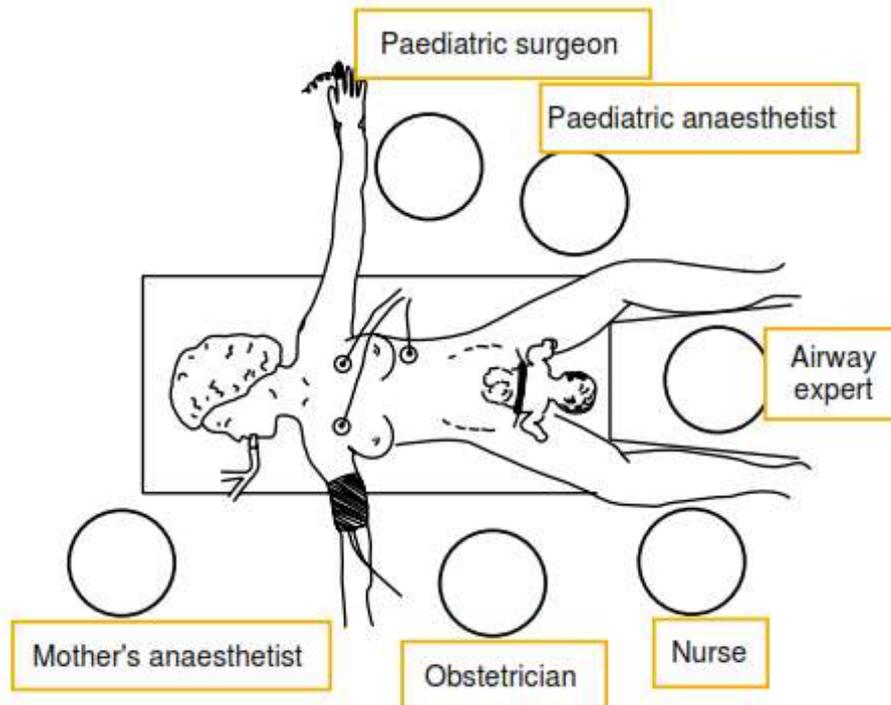
## INTRAOPERATIVE CONSIDERATIONS

The EXIT procedure requires two anaesthesiologists for the management of the mother and her foetus.<sup>4</sup>

Anaesthesia for this procedure differs from a conventional caesarean-section and general anaesthesia is the preferred technique.<sup>4</sup>

### The EXIT procedure is not a Caesarean Section

EXIT procedure	Caesarean Section (C/S)
<b>Goals:</b> <ul style="list-style-type: none"> <li>- Controlled uterine hypotonia to preserve uteroplacental circulation.</li> <li>- Reach a deep plane of maternal anaesthesia, but maintain normal maternal blood pressure.</li> <li>- Preserve uterine volume so as to prevent placental abruption</li> <li>- Achieve a surgical level of foetal anaesthesia without cardiac depression.</li> </ul>	<b>Goals:</b> <ul style="list-style-type: none"> <li>- Maximise uterine tone to prevent postpartum haemorrhage</li> <li>- Minimize the transplacental diffusion of inhalational anaesthetic agents to avoid neonatal depression (if performed under GA)</li> </ul>



The EXIT procedure with the fetus partially delivered and the suggested positions of the multidisciplinary team.

*Nicola Zadra, F. G. (2004). Best Practice & Research Clinical Anaesthesiology, 18(2), 259-271.*

### **Maternal intraoperative anaesthetic requirements for the EXIT procedure**

- Multidisciplinary team with all team members present: obstetricians, or maternal-foetal medicine specialist, anaesthetists, midwives, neonatologists, paediatric surgeons, paediatric cardiologists, otorhinolaryngologist, and theatre nurses.
- Use of World Health Organization surgical safety checklist.
- Understanding the anatomical and physiological changes of pregnancy
  - Thorough preoperative assessment particular attention to airway assessment and co-morbidities – preparation of appropriate airway equipment
  - Aspiration prophylaxis
  - Preoxygenation 100% oxygen via a close-fitting mask to fractional end tidal oxygen concentration > 0.9
  - General anaesthesia - Rapid sequence induction
- Avoiding aorto-caval compression : positioning 15 degrees left lateral tilt or with leftwards manual displacement of the uterus
- Invasive continuous blood pressure monitoring
- High concentration of volatile agents and tocolytics to provide uterine relaxation
  - Uterine relaxation is critical to prevent uterine contractions and placental separation.
- Avoiding and treating hypotension - phenylephrine to maintain maternal blood pressure (consider continuous infusions depending on patient requirements)

*OA, O. (2009). Anaesthesia for EXIT procedure: A review. SAJAA, 15(1), 17-21.*

As outlined above, there are a number maternal considerations that must be managed during the EXIT procedure.

#### Maternal induction of anaesthesia

General anaesthesia with rapid sequence induction is performed to secure the airway after adequate pre-oxygenation. Left uterine displacement in order to avoid aorto-caval compression is mandatory.

#### Monitoring

Standard ASA monitoring, together invasive continuous blood pressure monitoring with an arterial line.

Monitoring of the blood pressure with the use of an arterial line allows prompt management of maternal hypotension caused by the increased concentration of inhalational agents and /or nitroglycerine required for uterine relaxation. Large bore intravenous access is mandatory.

Following induction of anaesthesia, a repeat ultrasound is performed to assess foetal well-being as well as placental location and foetal lie. This is important to dictate the location of the uterine incision.<sup>1</sup>

#### Maternal maintenance of anaesthesia

##### Uterine relaxation

Uterine relaxation is the single most important factor that determines the success of this procedure. Following skin incision, the anaesthetic agent is maintained at 1.5–2 times minimal alveolar concentration (MAC) to achieve profound relaxation of the uterus at the

time of hysterotomy. No particular halogenated agent has any benefit over the other in terms of inducing uterine relaxation.

The resulting vasodilatation causes hypotension, which should be promptly managed with fluids and sympathomimetic agents.

Intravenous agents such as nitroglycerin (boluses of 50–100 mcg) are also be used to augment uterine relaxation in order to prevent uterine contractions and placental abruption while the baby is partially delivered and being operated upon. Pharmacokinetic studies have demonstrated placental transfer of nitroglycerin with no significant haemodynamic effects in the foetus. This is most likely related to the rapid placental metabolism, short half-life, and high maternal-foetal gradient of nitroglycerin.<sup>11</sup>

In addition to nitroglycerin, magnesium sulphate and nifedipine also provide uterine relaxation but their effects are not easily reversible and they may complicate the anaesthetic with adverse effects such as prolonged muscle relaxation. Therefore, they are not routinely utilised for the provision of uterine relaxation during this procedure.

Hysterotomy is only performed when an acceptable level of uterine relaxation is appreciated by manual palpation of the uterus by the surgeons. Incision of a relaxed uterus can result in massive blood loss, therefore a special hysterotomy stapling device is used to minimise blood loss. This device clips the myometrium and amniotic membrane together establishing a bloodless field as it cuts.

Administration of 100% oxygen to the mother is recommended till the baby is delivered in order to maximise foetal oxygenation although oxygen/air combinations have been used. Nitrous oxide does not cause uterine relaxation and may worsen maternal hypotension so it adds no benefit to the procedure prior to complete delivery of the baby.<sup>11</sup>

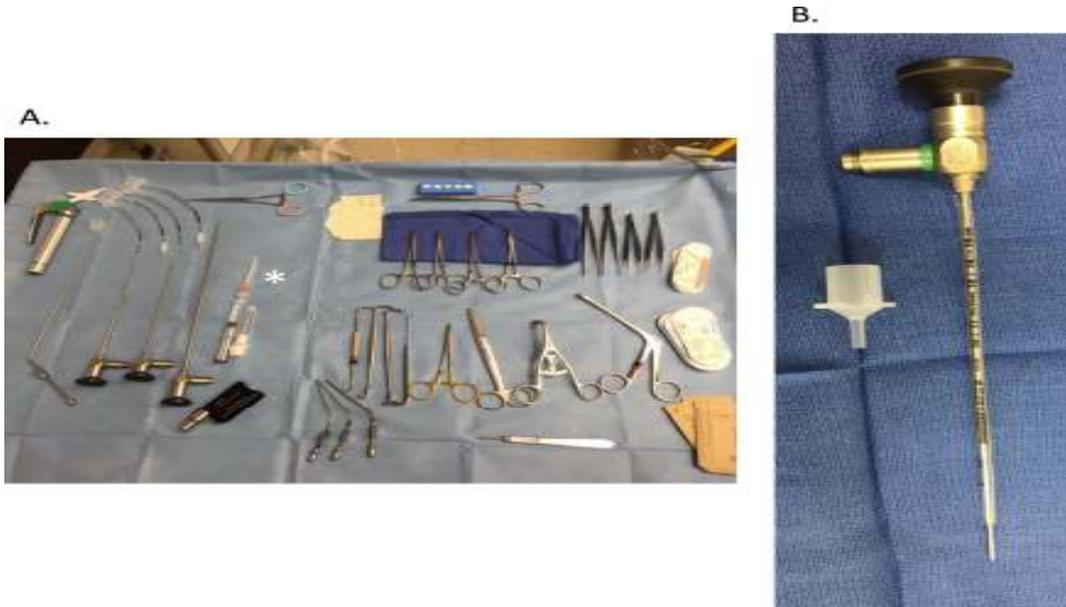
### **Fetal intraoperative anaesthetic requirements for the EXIT procedure**

Attention to the following issues is paramount in decreasing foetal morbidity related to the EXIT procedure.

- Maintaining feto-placental circulation to prevent placental separation following partial delivery of the foetus.
- Providing foetal anaesthesia for foetal airway manipulations.
- Neonatal airway equipment prepared, sterile and ready:
  - Laryngoscope (blades 0, 00 & 1)
  - Rigid bronchoscope (2.5–3 mm)
  - Array of different size, styletted paediatric endotracheal tubes
  - Facemask, Guedels airway and Laryngeal mask airway (LMA)
  - Flexible intubating bronchoscope (2.5 mm)
  - Tracheostomy tray
  - Ambu bag with manometer attached to oxygen source
  - End-tidal carbon-dioxide detector to confirm endotracheal intubation
- Providing adequate foetal monitoring or surveillance until delivery - pulse oximeter dedicated for baby monitoring with foil placed over the pulse oximeter probe to decrease ambient light interference.

- Thermoregulation: warm ambient theatre temperature to 30degrees Celsius; plastic bag to cover baby's head upon partial delivery if feasible
- Amnioinfusion: warm Ringers lactate infusion to maintain amniotic fluid volume
- Pre-calculated anaesthetic and resuscitation drugs prepared: Fentanyl, Vecuronium, Atropine, Adrenaline and Calcium.
- Type O negative packed red cells, pre-calculated and subdivided.

OA, O. (2009). *Anaesthesia for EXIT procedure: A review. SAJAA, 15(1), 17-21.*



Fibreoptic intubation and surgical airway set-up for EXIT.<sup>17</sup>





Foetal head delivered during EXIT procedure Foil placed over the pulse oximeter probe to decrease ambient light interference.

*Shinjiro Hirose, M. R. (2003). The EXIT procedure. Seminars in Neonatology, 8, 207-214.*





Laryngoscopy and Bronchoscopy during an EXIT procedure to secure the foetal airway.  
*Shinjiro Hirose, M. R. (2003). The EXIT procedure. Seminars in Neonatology, 8, 207-214.*



Cervical teratoma resection during an EXIT procedure. There is gross anatomic distortion. The black arrow shows tracheal deviation to the right and anteriorly.  
*Shinjiro Hirose, D. L. (2004). Journal of Pediatric Surgery, 39(3), 375-380.*

### Fetal anaesthesia considerations

#### Maintenance of feto-placental circulation

Support of the foetus during the EXIT procedure depends entirely on the preservation of uteroplacental gas exchange. Both uterine and umbilical artery blood flow influence foetal oxygenation. Uterine artery blood flow is affected by maternal systemic blood pressure and myometrial tone.<sup>5</sup> Maintenance of maternal blood pressure within 10% of baseline is therefore critical for adequate foetal oxygenation during the EXIT procedure.<sup>5</sup>

Uteroplacental gas exchange is also dependent on umbilical artery blood flow, which is influenced by foetal cardiac output and placental vascular resistance. Therefore preservation of foetal cardiac output is important in maintaining foetal oxygenation.

The foetal cardiac output is more dependent on heart rate. In addition, the high vagal tone and low baroreceptor sensitivity cause the foetus to respond to stress with a decrease in heart rate. The foetus primarily relies on increased heart rate to increase cardiac output in

response to stress. This preserves oxygenation for the brain at the expense of the rest of the body.<sup>6</sup>

Circulating blood volume in the foetus is quite low; the average mid gestation foetus has an estimated foetal-placental blood volume of 50 to 70 mL (110 mL/kg). So a minimal amount of surgical blood loss can precipitate hypovolemia. Additionally, altered coagulation factors predispose to bleeding and cause difficulty in surgical haemostasis. Inhalation anaesthetics also destabilize the foetal cardiovascular system by causing direct foetal myocardial depression, vasodilation, and changes in arterio-venous shunting.<sup>6</sup>

Therefore, assessing foetal cardiovascular stability requires intraoperative monitoring of foetal heart function by echocardiography, foetal pulse oximetry, and even foetal blood gases to maximize foetal safety.<sup>6</sup>

### Monitoring

Fetal oxygenation is monitored via a dedicated pulse oximeter for the baby. A sterile sheath should be made available for placement of the pulse oximeter cable onto the surgical field.<sup>1</sup> The challenges to adequately placing a saturation probe monitor on the foetus include; vernix and ambient light interference. To overcome this, the hand and monitor are covered with small foil wrap and an overlying sterile towel. Foetal saturations of 70% are normal; bradycardia or saturations below 50% indicate significant hypoxia. The ultrasound or Doppler are alternatives for foetal heart rate monitoring.<sup>1</sup>

### Prevent hypothermia

Warm ambient theatre temperatures are required during foetal exposure to prevent hypothermia in the foetus. Limiting foetal surgical time, placing a plastic bag to cover baby's head upon partial delivery and using warm irrigation fluids also helps prevent hypothermia.<sup>1</sup>

### Amnioinfusion

Loss of amniotic fluid during the procedure, results in decreased uterine volume that may result in contractions and inadvertent foetal expulsion or placental separation during the procedure.

Decreased amniotic fluid volume may also result in umbilical cord compression by the foetus or surgical instruments. In order to prevent this, continuous replacement of amniotic volume with infusion of warmed lactated Ringer's solution is mandatory to maintain uterine volume. This also has the added benefit of keeping the foetus in a warm moist environment.<sup>1</sup>

### Providing foetal anaesthesia

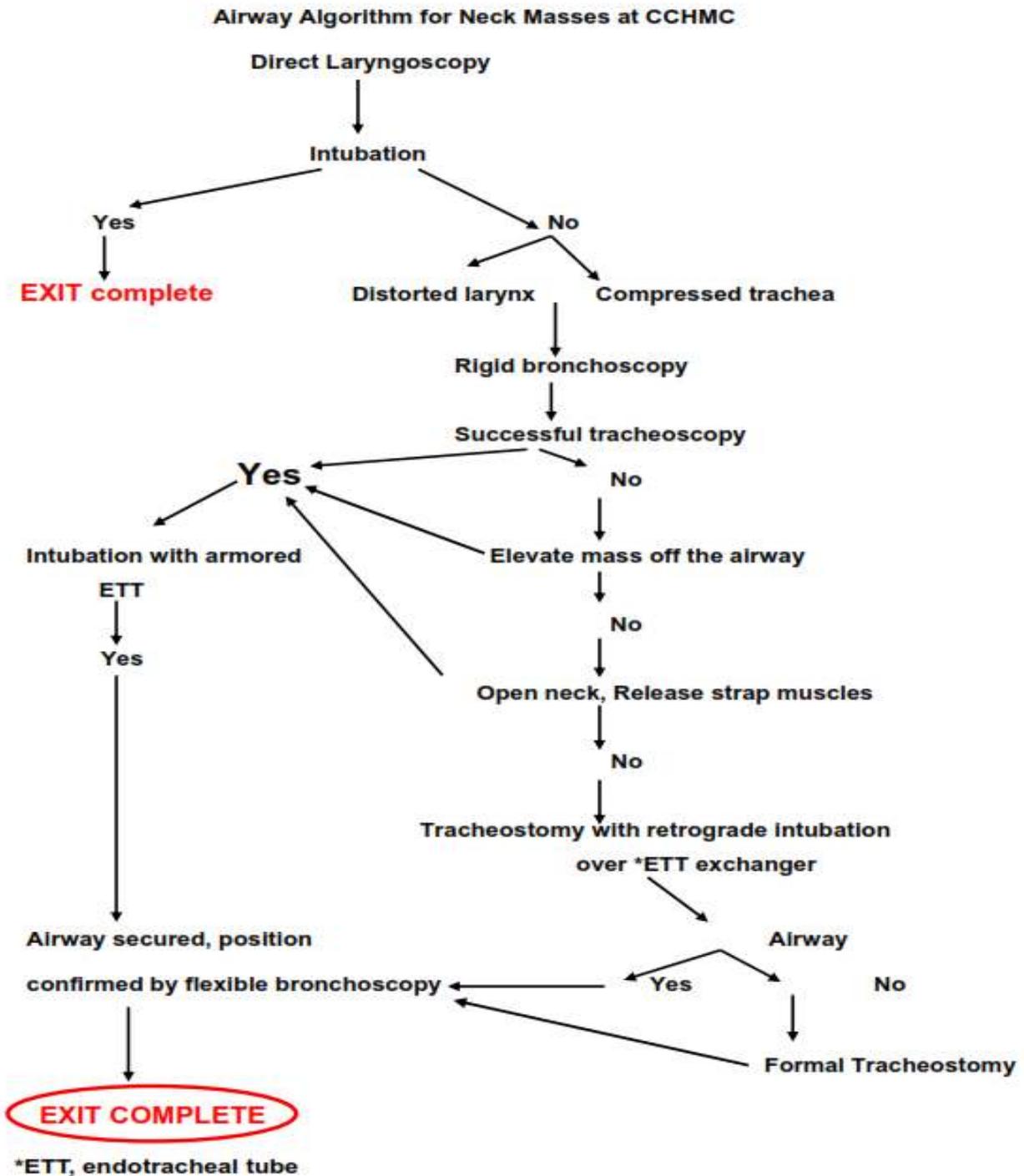
Despite the baby being anesthetised by halogenated agents received through uteroplacental blood flow, occasional movement may occur. Precalculated opioids and muscle relaxants may be administered to provide additional analgesia and muscle relaxation prior to any instrumentation or incision. Atropine administration helps prevent a vagal response.

### Foetal airway manipulations

Endotracheal intubation is attempted by direct laryngoscopy, bronchoscopy or tracheostomy. A carbon dioxide colorimetric device should be available for confirmation of

once the airway has been secured. Once placement is confirmed, the tube is typically secured to the gums with sutures by the surgeon.

Algorithm to secure the foetal airway for neck masses during EXIT procedure; developed at the Cincinnati Children’s Hospital.



Shinjiro Hirose, M. R. (2003). The EXIT procedure. *Seminars in Neonatology*, 8, 207-214.

## POST EXIT MANAGEMENT



Preop Oropharyngeal teratoma

Post EXIT procedure – postoperatively

Youssef, M. A. (2007). EXIT procedure for CHAOS: First case in Alexandria. *J Indian Assoc Pediatr Surg*, 12(4).

The baby is delivered and carried to the adjacent operating room, warmly swaddled and hand ventilated during transfer with an ambu bag. The surgical procedure is completed in the adjacent operating room at this time if necessary, or the baby is prepared for transfer to the Neonatal Intensive Care Unit for ventilator management as necessary. <sup>1</sup>

### Maternal anaesthesia after delivery of baby

Once delivery of the baby occurs, uterine tone needs to be rapidly restored in order to prevent massive maternal haemorrhage from uterine atony. This is achieved by quickly reducing the concentration of inhalational agents, just as the cord is being clamped. <sup>1</sup>

Oxytocin bolus, then subsequently infusion in crystalloid solution is started immediately. Additional uterotonic agents may be required depending on the duration of uterine relaxation during the procedure. When adequate uterine contraction is achieved, the placenta will be spontaneously expelled. Blood products should be available in the operating room and administered if necessary.

Additional analgesics should be administered as per the discretion of the anaesthetist: simple analgesics, opioids, ketamine, transversus abdominal plexus (TAP) block and post-operative PCA morphine.

Extubate when fully awake and haemodynamically stable, then transfer to labour ward high care unit for further monitoring for postpartum haemorrhage and management.

## COMPLICATIONS OF THE EXIT PROCEDURE

### Foetal complications<sup>11</sup>

- Foetal bradycardia, acidosis –due to deterioration of foetal blood flow during the EXIT procedure
- Foetal hypoxia
- Death
- Pneumothorax
- Abruptio placenta and bleeding
- Respiratory distress syndrome is common after EXIT and surfactant can be given prophylactically to premature infants.

### Maternal complications<sup>11</sup>

- Intraoperative hypotension
- Post-EXIT uterine atony – Postpartum Haemorrhage

## OUTCOMES POST EXIT PROCEDURE

### **Foetal outcomes post EXIT procedure**

Hirose et al did a retrospective review of all patients who underwent an EXIT procedure from 1993 to 2003, at the Paediatric Surgery & Fetal Treatment Centre, University of California.

The variables evaluated include indication for EXIT, gestational age at EXIT, birth weight, maternal blood loss, operative complications, operative time, and survival rate. Technique, personnel, and anaesthetic management were also reviewed.

Long-term follow-up was available for all the 52 patients.

Findings:

- Indication for EXIT procedure:
  - 45 patients underwent EXIT for reversal of tracheal occlusion for CDH
  - 5 patients underwent EXIT procedure for neck masses
  - 2 patients underwent EXIT procedure and tracheostomy for CHAOS
- Average gestational age at EXIT: 32 +/- 2.5 weeks
- Average birth weight: 1895 +/- 653grams
- Average maternal blood loss: 970 +/- 510mls
- Operative complications: 6 patients tracheostomy dependent
- Operative time: 20 – 120 minutes
- Survival rate: all patients were delivered alive post EXIT; but currently 27 of the patients (52%) are alive. All deaths have been in patients with congenital diaphragmatic hernia.
- They did not elaborate on the cause of death in these patients.

They concluded that the EXIT procedures is an excellent strategy for establishing an airway in a controlled manner, avoiding “crash” intubation or tracheostomy. It can be performed with minimal maternal morbidity and with good outcomes. The EXIT procedures have evolved from an adjunct to foetal surgery to a potentially life-saving procedure in foetuses with airway compromise at birth.<sup>13</sup>

Another study in which the authors reviewed 31 cases reported in the literature, which the EXIT procedures were performed for neck masses. Of these cases 29 of the infants were alive and there have been only two reported deaths. One death was due to parental wishes to avoid tracheostomy, and the other occurred on the first day of life secondary to pharyngeal haemorrhage and endotracheal tube dislodgement.<sup>12</sup>

### **Maternal outcomes post EXIT procedure**

Recently, Noah et al. reported short-term maternal outcomes after EXIT procedures and compared them with patients who underwent routine caesarean section. The EXIT procedures last on average twice as long, with significantly higher rates of superficial wound infections (15% vs. 2%,  $P = 0.03$ ) and a trend towards higher rates of endometritis (15% vs. 10%,  $P = 0.50$ ).<sup>15</sup> The estimated blood loss was significantly higher in the EXIT group when compared with caesarean section (1104 mL vs. 883 mL,  $P < 0.001$ ) with a consequent higher transfusion requirement.<sup>15</sup> However the postoperative hospital length of stay post EXIT procedure was not significantly different from routine caesarean delivery.<sup>13</sup> There have been no reported emergency hysterectomies, thromboembolic events or maternal deaths following an EXIT procedure.<sup>15</sup>

Long-term maternal outcome following the EXIT procedure was reported by Farrell et al. There have been no maternal deaths from EXIT procedures. Of 45 respondents after foetal surgery, 35 attempted repeat pregnancy and 32 were successful with 31 live births. Notably, two women had a previous history of infertility. From this, it appears that foetal intervention does not adversely affect long-term maternal fertility.<sup>12</sup>

## CONTROVERSIES

### **General Anaesthesia (GA) versus Regional Anaesthesia (RA) for EXIT procedure**

There are no studies in the literature comparing GA vs. RA for this procedure.

Regional anaesthesia offers the advantage of avoiding airway manipulation and lowers the risk of aspiration.

There is one case report under spinal anaesthesia and two case reports of EXIT under epidural analgesia plus GA, where the epidural was only utilised post EXIT for maternal analgesia.

The disadvantages of RA for this procedure are as follows;

- The foetus is not anaesthetized during the procedure and will require additional anaesthetic and analgesic agents to be given directly to it.
- Additional tocolytic agents need to be administered with the regional anaesthesia. This worsens maternal hypotension and increases the risk of postoperative uterine atony.
- EXIT procedures are usually long and may outlast the effect of a single-shot spinal.
- The risk of maternal haemodynamic instability may be greater if bleeding problems should arise intraoperatively.<sup>11</sup>

Majority of the case reported in the literature for the EXIT procedure were done under GA. General Anaesthesia offers the advantage of simultaneous induction of both mother and foetus through placental penetration of anaesthetic agents and adequate uterine relaxation.<sup>4</sup>

The disadvantages of GA are that obstetric patients have difficult airway, prone early desaturation and are high risk for aspiration.

Although associated with higher rates of morbidity and mortality among global obstetric population, general anaesthesia is the preferred technique for the EXIT procedure.<sup>4</sup>

### **Maintenance of Anaesthesia: Inhalational agents vs. TIVA vs. Other techniques**

Maternal haemodynamic stability during anaesthesia for this procedure is essential to maintain placental perfusion. Similarly, adequate uterine relaxation with the option for fast reversal to avoid postpartum haemorrhage is required.<sup>14</sup> Most author use a high dose (2 X MAC) of the potent inhalation agents, isoflurane or sevoflurane, to maintain anaesthesia, while providing uterine relaxation.

The potential disadvantages of the above-mentioned "standard" anaesthetic plan for EXIT procedure are maternal hemodynamic instability and excessive uterine bleeding.<sup>14</sup>

However, there are no case reports on the use of Total Intravenous Anaesthesia (TIVA) as maintenance for the EXIT procedure.

Alexander Ioscovisch et al used Remifentanil-Nitroglycerin combination as an anaesthetic support for the EXIT procedure. Anaesthesia was maintained with a combination of nitrous oxide 60%, oxygen 40% and remifentanil infusion titrated up to 0.8 mcg/kg/min. Nitroglycerin (NTG) infusion, as a continuous low dose was used for uterine relaxation. The patient remained haemodynamically stable, throughout the 40 minute EXIT procedure. Remifentanil resulted in no adverse effects to the mother or new born. They concluded that a combination of remifentanil and NTG ensures stable intraoperative haemodynamics, good surgical conditions, and fast anaesthetic recovery after the EXIT procedure.<sup>14</sup>

### **Foetal Anaesthesia & Analgesia: issue of foetal pain**

The definition of pain consists of two parts; objective and subjective components. Firstly a reaction to actual or impending tissue damage is generated from the peripheral sensory nervous system. This is described as nociception and is the objective part of the definition. Parallel to this is the subjective emotional experience of pain that requires presence of consciousness.<sup>18</sup>

#### Foetal pain perception

The hormonal stress response can be detected in the foetus as early as 20 weeks gestation. Even though stress hormones may not necessarily reflect pain perception, many studies demonstrate simultaneous hormonal and hemodynamic responses to invasive stimuli in the foetus. These responses can be abolished by administering an analgesic leading to the belief that the foetus perceives pain and thus requires anaesthesia for surgical procedures.<sup>16</sup>

The nociceptive pathway exists anatomically along with the cortical activity by mid-gestation. Peripheral nociceptors are present throughout the foetal body by 20 weeks gestation. The spino-thalamic connections are formed at 14 weeks and completed at 20 weeks. The thalamo-cortical fibres are formed at 17 weeks and completed by 26 weeks gestation. Since the serotonin-inhibitory pathway develops after birth, it might be possible that the foetus perceives more pain than the infant.<sup>16</sup>

There has been significant concern for anaesthesia induced neurotoxicity raised for foetal surgery.

Although exposure to anaesthetic agents during foetal surgery may trigger neuron cell degeneration, exposure to pain during this period alters the development of brain too.<sup>16</sup>

Therefore, analgesics should be administered to the foetus during the third trimester when the EXIT procedure is performed.<sup>16</sup>

Apart from the capability of the foetus to feel pain; the other motivation to justify administration of anaesthesia is foetal immobilisation.<sup>18</sup> This reduces the chances of accidentally traumatising the foetus, and facilitates the work of the surgeon, such that the procedure takes less time.<sup>18</sup>

## **CONCLUSION**

The EXIT is an exceptional obstetric procedure bound for life saving foetal airway interventions. Prenatal diagnosis of foetal malformation in the cervical or oral region with obstruction of the upper airway is essential to reduce perinatal morbidity and mortality.<sup>2</sup> Preparation for an EXIT procedure involves detailed multidisciplinary planning, because of multiple anaesthetic and surgical issues critical for its safety and success.<sup>4</sup>

Anaesthesia for EXIT procedure is a rare, but evolving field, with only one case report in Africa (Egypt), and most of the available evidence based on clinical experience. We need more studies in this field.

**Level of Evidence of articles used in this booklet**



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LEVEL		NO.	REFERENCES
1a	Systematic Reviews	11	1;3;5;6;11;12;13;15;16;18;19
1b	Randomized controlled trials	-	-
2	Cohort studies	-	-
3	Case Reports	8	2;4,7;8;9;10;14;17
4	Editorials & Opinions	-	-

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