FCA Part II
Anaesthetic Refresher Course
2017
Department of Anaesthesia
University of the Witwatersrand
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Local anaesthesia is preferred over general anaesthesia by many ophthalmic surgeons with the main reasons being lower perioperative morbidity with quicker patient recovery and fewer complications.1–3

Anaesthetists have become increasingly involved in eye blocks that were previously performed by surgeons. Good anaesthesia is essential for the performance of safe intraocular surgery and may contribute to the success or failure of the surgery.4,5

Goals of anaesthetic care during elective eye surgery
1. Anaesthesia of the globe, lids and adnexa ensuring pain-free surgery
2. Akinesia of the globe and lids facilitating the surgical procedure, and
3. Rapid recovery with adequate postoperative analgesia4,5

Anaesthetic techniques available:

Type of anaesthesia chosen
This would depend on:
1. The type of surgery
2. The surgeon’s preference
3. Patient’s suitability, and
4. Patient cooperation

Preoperative considerations
A routine preoperative assessment has to be done to ensure that co-morbid conditions are reasonably well controlled.

A focused medical history needs to be taken and should include a history determining if the patient is a suitable candidate for same day surgery.6 A history of anticoagulant or antithrombotic therapies is vital. Patients having cataract surgery that are at a high risk of clotting and embolic complications due to cardiac or vascular pathology should continue therapeutic doses of aspirin and warfarin throughout the perioperative period.7,8 There is,
however, insufficient data available on dual antiplatelet therapy for stents and eye surgery. Eye surgery, if possible, should be postponed until after the minimum period recommended for daily administration of dual antiplatelet therapy.9,10

A full physical examination needs to be done. It is important to determine if the patient will be able to lie supine comfortably under drapes. Conditions that preclude this, e.g. congestive cardiac failure, claustrophobia or back pain need to be excluded.

The patient’s communication and cooperation skills also need to be established. During regional anaesthesia you have to be able to communicate with the patient and the patient has to be able to follow commands such as avoiding all movement.

Monitoring

Standard ASA monitoring, which includes electrocardiogram, pulse oximetry and non-invasive blood pressure monitoring together with capnography is essential. Patients need to be monitored because they can get an occulocardiac reflex or an accidental injection into a blood vessel or the brain.10

Supplemental oxygen should be given to decrease the risk of hypoxaemia during sedation and to have a fresh gas flow to prevent the patient rebreathing clinically significant amounts of carbon dioxide that may occur as a result of completely covering the face.

Vacuum suctioning under the drapes can be used to lower the oxygen concentration and remove expired carbon dioxide.11,12 Before the block is performed one needs to establish good intravenous access.

Sedation and analgesia

Short-acting agents can be given immediately before the block to decrease or eliminate pain of needle insertion and injection of local anaesthetic. Minimal sedation is preferable during the procedure because the surgery requires an awake and cooperative patient. Excess sedation can lead to a restless, confused or unresponsive patient who may have respiratory depression with airway obstruction. This can pose a significant intraoperative challenge. Even minor movement (highly magnified under a microscope) may result in severe eye injury.4

If the patient has pain intraoperatively, a supplemental block with local anaesthesia should be given. Inadequate analgesia should not be substituted with heavy sedation.13

Anatomy of the eye

The orbit is pyramidal in shape with its base at the orbital opening and its apex pointing to the optic foramen. The orbit is occupied by the globe, its muscle cone, loose connective tissue and fat. The globe lies in the anterior part of the orbit and sits high and lateral, therefore it is nearer the roof than the floor and nearer the lateral than medial wall (important for needle insertion points). There are four recti muscles and two oblique muscles that control eye movement. The recti muscles form the muscle ‘cone’ around the globe. The muscle cone encloses the sensory and motor nerves, ciliary ganglion, optic nerve, ophthalmic artery and vein.14

Retrobulbar anaesthesia is injected in the intraconal compartment, whereas peribulbar anaesthesia is injected in the extraconal compartment and hence considered safer since it avoids potential damage to the intraconal structures.

The motor supply to the eye is from the oculomotor nerve (CN III), the trochlear nerve (CN IV) and the abducens nerve (CN VI). CN III supplies all the extraocular muscles except superior oblique and lateral rectus muscles. CN III also supplies levator palpebrae superioris. CN IV supplies the superior oblique muscle and CN VI supplies the lateral rectus muscle. CN IV lies outside the muscle cone and hence is not usually blocked.9

The sensory supply is from the trigeminal nerve (CN V). CN V is divided into the ophthalmic branch which is further divided into nasociliary, lacrimal and frontal branches. The nasociliary branch supplies the cornea, peribulbal conjunctiva and the supranasal quadrant of the bulbar conjunctiva. The rest of the conjunctiva is supplied by the lacrimal, infraorbital and frontal nerves.5

The ciliary ganglion lying within the cone relays sensory fibres from the globe to the ophthalmic division of CN V. It receives a parasympathetic branch from CN III and sympathetic fibres from the carotid plexus.14

Peribulbar (extraconal) block

The peribulbar block (PBB) was first described in 1986 and was developed as a safer alternative to the retrobulbar (intraconal) block (RBB) for providing anaesthesia and akinesia of the eye. Similar clinical efficacy of the PBB and the RBB, as evidenced by similar spreading of local anaesthetic injected, but with a higher risk of complications associated with introducing the needle into the cone, makes the PBB a better alternative to the RBB.15

With PBB the needle is placed less deeply and at a different angle compared to the RBB. The local anaesthetic (larger volume than with RBB) is injected outside the muscle cone and spreads by way of diffusion to block the orbital nerves including the ciliary ganglion, ciliary nerves, CNs II, III, VI and even CN IV. The modifications with needle placement make the PBB less likely to result in perforation of the globe posteriorly, injury to the optic nerve or injection into the brain with resultant brainstem anaesthesia.15,16

Technique

The classic technique involves two injections. An initial inferolateral injection supplemented with a medial injection. A single inferolateral injection is often adequate for anaesthesia but may not be predictable for akinesia.5,17

A needle of ≤ 2.5 cm is recommended to decrease the risk of injury to structures deep in the orbit. Increasing needle insertion depth would be expected to change a PBB to a RBB.18 In addition, a very long needle may reach the apex of the orbit and may result in local anaesthetic being injected through the optic foramen.19,20 The Atkinson needle (blunt tip) is normally used as it may enhance the operator’s ability to identify scleral tissue if it is encountered before perforation of the globe. Indeed in cadavers more pressure is required with short bevel needles to perforate the sclera.21 Some clinicians, however, use sharper needles to minimise the pain of insertion and to theoretically limit the amount of damage to the globe if inadvertent perforation does occur.4
After establishing intravenous access, connecting monitors and giving minimal sedation, the patient is asked to lie supine and look straight ahead.

The first injection is inferior and temporal. The junction of the medial two-thirds and lateral one-third of the inferior orbital rim is palpated, where a groove is felt at the junction of the maxilla and zygoma. Slightly lateral to this point a 2.5 cm needle is introduced through the skin and passed slowly backwards perpendicular to all planes. If the needle tip contacts bone it is redirected slightly superomedially to follow the orbital floor once more. The needle is advanced until its tip is about level with the posterior pole of the globe (until the hub reaches the plane of the iris). The globe should be observed closely for any signs of rotation during insertion, indicating scleral contact. After aspiration 6–10 mls of local anaesthetic is injected slowly. A larger volume is needed to spread into the whole corpus adiposum of the orbit including the intraconal space. The larger volume also allows anterior spread of the local anaesthetic to the lids to provide a block of the orbicularis muscles and to avoid the need for an additional lid block. PBB produces more reliable akinesia of the orbicularis oculi as compared to a RBB.

If the globe becomes tense or propptosed or if the upper eyelid falls during injection then you should stop immediately as this may indicate a RBB which requires a smaller volume of local anaesthesia.

Compression to the eye can be done after injection to lower intraocular pressure, which increases after injection. Applying a pressure of 30 mmHg for 5–10 minutes is usually sufficient.

Assess the block after 5–10 minutes and if a greater degree of akinesia or additional anaesthesia is required a second injection should be performed. In the classic technique the second injection is superior and nasal between the medial one-third and the lateral two-thirds of the orbital roof edge. It is important to remember that at the superior nasal site, the distance between the orbital roof and the globe is reduced, theoretically increasing the risk of globe perforation. Additionally the superior oblique muscle can be injured.

If both medial and lateral injections are planned, the volume of the solution is 4–5 mls for each. It is important to remember that the first injection may increase the risk of complications associated with consecutive injections, as it may distort the anatomy.

Alternate techniques

Numerous alternative techniques and different sites for needle insertion for a PBB have been described. The most common alternative is the medial canthus peribulbar block. Here the needle is introduced at the medial junction of the lids, nasal to the lacrimal caruncle, in a strictly posterior direction to a depth of 15 mm or less. At this site the space between the orbital wall and the globe is similar in size to that of the inferolateral approach and is free from blood vessels. This site can be used as the second injection point when the first inferolateral injection needs to be supplemented.

Complications

The main reason for complications is needle misplacement.

1. Globe perforation
This can occur as a result of direct trauma. More common in patients with myopia (axial length > 26 mm), posterior staphyloma, posterior scleral buckling and severe exophthalmos. The symptoms of globe perforation are variable, ranging from intense ocular pain with abrupt loss of vision and hyptonus, to no signs or symptoms. Globe perforation and rupture is the most devastating complication of eye blocks and has a poor prognosis especially when the diagnosis is delayed.

2. Intravascular injection
Inadvertent intra-arterial injection may reverse the blood flow in the ophthalmic artery up to the anterior cerebral or the internal carotid artery. It can result in convulsions, loss of consciousness or, rarely, cardiopulmonary arrest. Treatment is symptomatic.

Inadvertent intravascular injection can lead to systemic toxicity but is unlikely to because of the small amount of local anaesthetic given. Treatment would be symptomatic and intravenous administration of lipid emulsion.

3. Retrobulbar haemorrhage
This occurs as a result of direct trauma to the artery or vein. It may lead to a compressive haematomata (artery injury) which can threaten retinal perfusion. It is very important that at the time of the haemorrhage an ophthalmologist be present to monitor intraocular pressure and treat appropriately. Surgical decompression may be required, but in most cases surgery has only to be postponed. Venous puncture may occur and leads to a noncompressive haematomata, the consequence of which is less severe and in most cases surgery can be continued.

4. Optic nerve damage
Direct optic nerve trauma by the needle is rare but can cause blindness. Optic nerve damage may also occur as a result of vascular occlusion.

5. Occulocardiac reflex
This occurs as a result of stimulation of the trigeminal nerve (afferent limb) and leads to a response via the vagus nerve (efferent limb). The patient may develop a bradycardia, an arrhythmia or cardiac asystole. It is usually self-limiting but can be treated with atropine.

6. Optic nerve sheath injection
This can result in a subdural or subarachnoid injection. It can cause partial or total brainstem anaesthesia. Depending on the concentration and volume of the local anaesthetic, a bilateral block, cranial nerve palsy with sympathetic activation, confusion, restlessness or total spinal anaesthesia with quadriaparesis, arterial hypotension, bradycardia and eventually respiratory arrest can occur. Treatment is symptomatic until the block resolves.

7. Chemosis (subconjunctival oedema)
This is usually of minimal concern and disappears with pressure.

8. Decreased visual acuity
This resolves with resolution of the block.
9. Myotoxicity
This can occur with a high concentration of local anaesthetic or direct injection into the muscle and can result in muscle palsy.26 Myotoxicity may progress in three steps; firstly the muscle is paralysed, secondly it seems to recover and thirdly a retractile scar develops.5

Agents used
All available local anaesthetics have been used for eye blocks, either alone or as a mixture of two different agents. The choice and concentration of local anaesthetic used depends on:

1. Speed of onset required (lignocaine for quicker onset of action)
2. Duration of block desired or need for postoperative analgesia (ropivacaine or bupivacaine for longer duration)
3. Availability, and
4. Need for akinesia (higher concentration)

Additives

1. Hyaluronidase
This is an enzyme that helps facilitate spread of anaesthetic through tissues by increasing permeability of fibrous septa. It improves the speed of onset and quality of the nerve block. It also reduces the increase in intraocular pressure and the risk of injury to extraocular muscles.4 Concentrations between 1 and 7.5 units per ml are commonly used, but concentrations as low as 0.75 units per ml may be effective.29

2. Clonidine
It enhances intra- and postoperative analgesia when added to the local anaesthetic. At a dose of 1 microgram per kilogram it does not increase the incidence of systemic adverse events such as hypotension or excessive sedation.3

3. Epinephrine
It is sometimes used to increase the duration of action of the local anaesthetic. Its use has decreased with the availability of longer acting agents and also because of fear of vasoaspasm and subsequent retinal ischaemia.2

4. Sodium bicarbonate
Alkalisation of the local anaesthetic solution has been proposed for decreasing pain during injection and accelerating the block onset. The efficacy of this has not been proven.3

References
Molar pregnancies with a focus on the thyroid

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Gestational trophoblastic disease (GTD) represents a spectrum of conditions that arise from abnormal cellular proliferation of trophoblastic tissue of the developing placenta. It encompasses the following main forms:

1. Complete and partial hydatiform mole (non-invasive molar pregnancy)
2. Invasive hydatiform mole
3. Choriocarcinoma
4. Placental site trophoblastic tumour

The latter three forms can invade the myometrium and metastasise, and are collectively termed gestational trophoblastic neoplasia (GTN). Since the introduction of chemotherapy into their management, they are amongst the most curable of all solid tumours, with cure rates of more than 90% even in the presence of metastatic disease. A detailed discussion of GTN is beyond the scope of this review.

There are wide regional variations in the incidence of GTD. The incidence of hydatiform mole ranges from 0.57 to 2.00 per 1 000 pregnancies. One South African study from a single tertiary referral hospital estimates the incidence of molar pregnancy at 1.2 per 1 000 deliveries.

Pathophysiology

The placental trophoblast is composed of a cytotrophoblast, intermediate trophoblast and syncytiotrophoblast, all of which may result in GTD when they proliferate. The syncytiotrophoblast produces human chorionic gonadotropin (hCG).

Hydatiform mole is characterised by varying degrees of trophoblastic hyperplasia and vesicles of swollen hydropic villi, and is associated with absent (complete mole) or abnormal (partial mole) foetal tissue. GTN can develop after 15–20% of complete moles and 1–5% of partial moles, as well as after a non-molar gestation.

Clinical presentation

Molar pregnancies usually present clinically in the second trimester with:

- Vaginal bleeding (most common)
- Anaemia
- Excessive uterine enlargement
- Theca lutein ovarian cysts
- Hyperemesis gravidarum
- Passing vesicles (grape-like tissue)
- Features of pre-eclampsia
- Abdominal pain
- Hyperthyroidism
- Respiratory distress

Diagnosis

- Ultrasonography: A vesicular pattern consisting of multiple echoes (holes) within the placental mass (“snowstorm” or “bunch of grapes” appearance) together with absent foetal tissue is suggestive of a complete mole. A partial mole demonstrates a more focal distribution of placental cystic spaces and the presence of foetal tissue.
- β-hCG: The β-subunit of hCG can be measured quantitatively in urine and blood. Hydatiform moles are associated with markedly elevated levels. A single β-hCG measurement may not differentiate a molar pregnancy from a normal intrauterine pregnancy, a multiple gestation, a pregnancy complicated by erythroblastosis foetalis or intrauterine infections associated with an enlarged placenta. Stable or rising β-hCG levels following evacuation of a molar pregnancy is suggestive of GTN.
- Pathology: Examination of curettage, biopsy, placenta or hysterectomy specimens.

Treatment

Suction curettage is the preferred method of evacuation of a hydatiform mole. Hysterectomy should be considered if
preservation of fertility is not required. Medical induction of labour is not recommended as it increases maternal morbidity, such as blood loss and trophoblastic dissemination. Chemotherapy is the principal therapy for GTN with or without adjuvant surgery or radiation in high risk disease.1

The remainder of this review will focus mainly on hyperthyroidism. Other perioperative considerations in patients presenting for evacuation of a molar pregnancy include the risk of heavy bleeding, pre-eclampsia, trophoblastic embolisation, respiratory insufficiency, cardiac failure, disseminated intravascular coagulopathy and hyperemesis gravidarum with dehydration, ketosis and electrolyte abnormalities.1

FOCUS ON HYPERTHYROIDISM

Hyperthyroidism: Thyroid gland overactivity leading to excessive thyroid hormone production.

Thyrotoxicosis: Clinical syndrome caused by the circulation of excess thyroid hormones.7

HCG biochemistry and physiology

HCG is a placental glycoprotein hormone that consists of two subunits: a β-subunit, which is unique to HCG, and an α-subunit, which is identical to the α-subunit in thyroid stimulating hormone (TSH) and pituitary gonadotropins.1,4

HCG has a plasma half-life of about 24 hours.1 Normal secretion begins in early pregnancy and peaks at 8–12 weeks gestation with levels of 30–100 U/ml.4,6,8 This gradually declines to 5–10 U/ml during the second trimester.1 HCG stimulates TSH-receptors on the thyroid follicular cell.2 Peak hCG secretion results in an increase in total thyroxine (T₄) and triiodothyronine (T₃) levels, and suppression of TSH, which reflects a mirror image to the HCG peak.3 As a result, up to 20% of pregnant women have subnormal TSH levels in the first half of pregnancy, with 1.4% experiencing transient gestational thyrotoxicosis.8,10 The thyroid gland releases more T₄ than the more potent T₃. Most of the circulating T₃ is formed by peripheral partial deiodination of T₄.11

Biological activity is influenced by variations in the structure of the hormone. Normal hCG has weak thyrotropic activity, whereas hCG extracted from molar tissue contains less sialic acid, which confers greater thyrotropic potency.1,12 Furthermore, the addition of desialylated hCG to normal TSH has synergistic effects.12

The main biological function of hCG is the maintenance of corpus luteum function, allowing continued progesterone production. HCG also promotes male sexual differentiation. Hyperemesis gravidarum is associated with increased serum β-hCG levels.1

Causes of hyperthyroidism in pregnancy

Graves’ disease is the most common differential diagnosis of non-transient thyrotoxicosis in pregnancy. Other causes are listed in Table I.

Placental tumours and hyperthyroidism

The association between hyperthyroidism and molar pregnancy was first reported in 1955.6 Hydatiform moles secrete large amounts of hCG, proportional to the mass of the tumour. Measured β-hCG level, the amount of desialylation, and the duration of the molar pregnancy correlate with the severity of hyperthyroidism.4,6,12 The prevalence of hyperthyroidism in patients with hydatiform mole has been reported as 25–64%, with about 5% of patients presenting with thyrotoxicosis.4 Various studies have shown a paucity of clinical features of thyrotoxicosis, despite elevated levels of free T₄ in many molar pregnancies.6 Hyperthyroidism usually becomes clinically evident when β-hCG levels exceed 300 U/ml.13 In a developing country like South Africa, the lack of ultrasound and quantitative β-hCG screening may lead to a higher incidence due to delayed presentation with higher hCG levels. There have also been case reports of hyperthyroidism in patients with choriocarcinoma.6,9

Clinical features

- Sinus tachycardia
- Hypertension
- Cardiac failure
- Hyperactivity
- Insomnia
- Diaphoresis
- Thrombocytopenia
- Palpitations
- Atrial fibrillation
- Weight loss
- Tremors
- Heat intolerance
- Diarrhoea
- Muscle weakness8,11,14

The clinical diagnosis of thyrotoxicosis may present difficulties as many hypermetabolic signs and symptoms are seen during normal pregnancy, i.e. palpitations, heart rate 90 to 100 beats/min, mild heat intolerance, warm skin and decreased effort tolerance.7

Diagnosis

- Elevated serum free T₄ and T₃ concentrations
- Suppressed serum TSH level
- Greatly increased thyroid radiiodine uptake
- Lower T₃/T₄ ratio compared to Graves’ disease and multinodular goitre in which the ratio is > 20.13

Treatment

Evacuation of the mole or effective chemotherapy for choriocarcinoma rapidly achieves clinical and biochemical euthyroidism.6,9

<table>
<thead>
<tr>
<th>Table I. Causes of hyperthyroidism in pregnancyc,9</th>
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<tbody>
<tr>
<td>Category</td>
</tr>
</tbody>
</table>
| PRIMARY THYROID | • Graves’ disease  
• Acute, subacute or chronic thyroiditis  
• Toxic adenoma  
• Toxic multinodular goitre |
| GESTATIONAL | • Transient gestational thyrotoxicosis  
• Multiple gestations  
• Molar pregnancy  
• TSH-receptor mutation  
• Hyperplacotosis  
• Hyperreacto luteinalis |
| OTHER | • Iatrogenic  
• Struma ovarii  
• TSH-producing pituitary adenoma |
**Perioperative anaesthetic management**

Patients present to theatre for suction curettage or, less commonly, hysterectomy. A multidisciplinary team approach involving the anaesthesiologist, gynaecologist, endocrinologist and intensivist is essential.

**History and examination:** Includes identification of thyroid dysfunction and its complications, as well as other sequelae of a molar pregnancy.

**Investigations:** FBC, U&E, thyroid hormone levels, ECG, crossmatch – blood immediately available due to risk of major bleeding.

An ABG, INR/PTT, LFT, CXR and/or echocardiogram may be necessary depending on clinical presentation and baseline investigations.

**Preoperative optimisation – treatment of hyperthyroidism:** Evacuation of the molar pregnancy is the only definitive management of thyrotoxicosis. Antithyroid drugs usually lead to some clinical improvement after one week of therapy, but may need 4–6 weeks for full effect. The combined use of propylthiouracil (PTU), iodide and dexamethasone has been shown to restore serum $T_3$ concentration to normal within 48 hours. Delaying surgery increases the risk of complications such as haemorrhage, pre-eclampsia and pulmonary embolisation. Untreated or poorly controlled hyperthyroidism on the other hand increases the risk of life-threatening perioperative complications, including a thyroid storm. There is no consensus on the optimum time needed for medical stabilisation of the hypermetabolic state. Patients require rapid hormonal improvement and should be clinically euthyroid before surgery. A normal serum TSH is not the primary management target, as it remains suppressed beyond normalisation of free $T_3$.2

- **Antithyroid drugs (thioamides):** PTU; carbimazole; methimazole. Inhibit thyroxine synthesis.2,4 PTU also inhibits peripheral conversion of $T_4$ to $T_3$.5

- **Beta-blockers:** Propranolol. Thyroid hormones sensitise adrenergic receptors to catecholamines. Beta-blockers control the hyperadrenergic effects of thyrotoxicosis ($β_1$) and decrease the peripheral conversion of $T_4$ to $T_3$ ($β_2$). Target maintaining a heart rate < 100 beats/min.13

- **Iodides:** Sodium iodide; potassium iodide; Lugol’s solution. Inhibit thyroid hormone release. Start at least one hour after administration of antithyroid drugs since iodide may cause a reflex release of thyroid hormone.18

The use of plasmapheresis has been reported to decrease thyroid hormone levels more rapidly in preparation for suction curettage. This is however an invasive procedure and patients should be monitored carefully for coagulopathy.3

In a bleeding patient it will not be possible to delay emergency surgery for optimisation of thyroid status. These patients are at a particularly increased risk of developing a thyroid storm. In addition to the above-mentioned drugs, they should receive a glucocorticoid and proceed for surgery with perioperative optimisation. (Beta-blockers are important – however exercise caution in the hypovolaemic hypotensive patient.)

**Anaesthetic technique:** Safe use of general anaesthesia (GA), both volatile- and total intravenous anaesthesia (TIVA) based techniques, and spinal anaesthesia have been reported.5 Evacuation poses a considerable risk of heavy bleeding. GA provides better haemodynamic stability in these patients and is a definitive indication in unstable patients.

Hyperthyroid patients are more sensitive to sympathetic nervous system (SNS) activation, which may lead to tachycardia, hypertension and ventricular arrhythmias. Laryngoscopy and intubation, surgical stimulation and extubation are vulnerable periods. Ensure an adequate depth of anaesthesia and maintain normovolaemia and normothermia.

A short-acting opioid, esmolol, lignocaine, or magnesium sulphate may be used to suppress the response to intubation. Depending on the uterine size, patients will probably require a rapid sequence induction. Incompletely treated hyperthyroid patients can be chronically hypovolaemic, and are prone to an exaggerated hypotensive response during induction of anaesthesia, particularly if bleeding as well.

Successful use of spinal anaesthesia for evacuation of molar pregnancies with thyrotoxicosis has been reported in both bleeding (NOT hypovolaemic) and non-bleeding patients.5,13,16,17 Advantages of spinal anaesthesia include the ease of the technique, providing a sympathetic block, earlier detection of uterine perforation and thyroid storm in an awake patient, and avoiding airway manipulation, the tocolytic effects of volatile agents and the effects of ventilation on the pulmonary system.5,16,17

TIVA using propofol and remifentanil with the concurrent administration of an esmolol infusion has also been used successfully. This technique avoids the tocolytic effects of volatile agents. It decreases the stress hormone release and haemodynamic response to stimulation. It also allows for a dose-dependent decrease in blood pressure and heart rate, which is advantageous in thyrotoxic patients and may decrease blood loss during surgery.18

An oxytocin infusion should be started after dilatation of the cervix and application of suction.2 Oxytocin decreases the risk of bleeding but early administration increases the risk of trophoblastic embolisation and metastases.3

**Anaesthetic drugs:** Hyperthyroidism and its hypermetabolic state can affect the pharmacokinetics of anaesthetic drugs. Propofol or thiopentone may be used for induction of anaesthesia. The latter possesses antithyroid activity.5,18 The volume of distribution and clearance of propofol is increased in hyperthyroid patients, increasing requirements if TIVA/TCI is used.14 Alternatively etomidate can be used in haemodynamically unstable patients. Ketamine, indirect acting adrenergic agonists, and other drugs that activate the SNS or are unpredictable muscarinic antagonists are best avoided in patients with current or recently treated thyrotoxicosis, as they may lead to exaggerated elevations in heart rate and blood pressure.11 Agents causing histamine release (atracurium, morphine) and its associated tachycardia should also be avoided.3,16
Hyperthyroidism does not increase the minimum alveolar concentration of volatile agents and excessive concentrations should be avoided to minimise the associated uterine tocolytic effects, which may increase blood loss. A combination of fentanyl or sufentanil and paracetamol provide suitable analgesia.

Monitoring and vascular access: Standard monitoring; large bore IV access; arterial line (+/- CVP) depending on the severity of hyperthyroidism; close temperature monitoring.

Postoperative care: Hyperthyroid patients should be managed in a high care or ICU. There remains a risk of developing a thyroid storm postoperatively, despite preoperative medical optimisation. Hyperthyroidism resolves rapidly and antithyroid medication can be weaned.

Thyroid storm

A life-threatening hypermetabolic crisis precipitated by infection, trauma, surgery, and labour, with mortality rates as high as 15%. It is a clinical diagnosis with accentuated signs and symptoms of thyrotoxicosis, and dysfunction in one or more organ systems. Table II lists the main clinical features. Free T₄ levels do not correlate with the severity of the symptoms.

Table II. Burch and Wartofsky scoring system for thyroid storm

<table>
<thead>
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<th>Criteria</th>
<th>Score</th>
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<tbody>
<tr>
<td><strong>THERMOREGULATORY DYSFUNCTION</strong></td>
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<tr>
<td>Temperature (°C)</td>
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<tr>
<td>37.2–37.7</td>
<td>5</td>
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<td>Severe (seizures, coma)</td>
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<td>Severe (jaundice)</td>
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<td>110–119</td>
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<td>130–139</td>
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<td>Moderate (bibasal crackles)</td>
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<tr>
<td>Severe (pulmonary oedema)</td>
<td>15</td>
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<tr>
<td>Atrial fibrillation</td>
<td>10</td>
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</tbody>
</table>

Management

- Supportive measures:
  - Adequate oxygenation and ventilation
  - Intravenous fluids
  - Inotropes/vasopressors
  - Correction of glucose and electrolyte abnormalities
  - Cooling measures (paracetamol; tepid sponging. NOT Aspirin or NSAIDs – may increase free thyroid hormones).
- Management of congestive cardiac failure if present
- Appropriate antibiotics if precipitated by infection
- Drugs: Beta-blockade and antithyroid drugs are used as the first-line treatment.

**Beta-blockers:**
- Esmolol 250–500 µg/kg IV loading dose followed by 50–200 µg/kg/min infusion OR
- Propranolol 1 mg/min IV OR 60–80 mg PO 4–6 hourly, OR
- Labetalol

**Glucocorticoids:** Inhibit peripheral conversion of T₄ to T₃.
- Hydrocortisone 50–100 mg IV 8 hourly OR
- Dexamethasone 2–4 mg IV 6 hourly

**Antithyroid drugs:**
- Carbimazole 40–60 mg PO/NGT daily, OR
- PTU 1g PO/NGT loading dose then 200–300 mg 6 hourly, OR
- Methimazole 30 mg PO/NGT 6 hourly

**Iodides:** Start at least one hour after antithyroid drugs.
- Sodium iodide 500 mg IV 8 hourly, OR
- Lugol’s Solution 10 drops PO/NGT 8 hourly, OR
- Potassium iodide 5 drops PO/NGT 6 hourly

**Magnesium sulphate:** Decreases adrenergic receptor sensitivity to endogenous catecholamines and associated arrhythmias.
- ICU postoperatively with frequent evaluation of cardiac and respiratory status.

Conclusion

All patients with GTD should be assessed for hyperthyroidism. Suction curettage is the preferred method of evacuation of molar pregnancies, and leads to normalisation of thyroid function. Patients with thyrotoxicosis are at increased risk of life-threatening complications such as a thyroid storm, and should be optimised preoperatively by a multidisciplinary team. The challenge to the anaesthetist is further increased in the bleeding patient requiring emergency surgery.
References


Cerebral perfusion monitoring during non-neurosurgical procedures: The practicalities of Near Infrared Spectroscopy (NIRS)/Bispectral Index (BIS)

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Keywords: neuro-monitoring, cerebral perfusion, Near Infrared Spectroscopy (NIRS), Bispectral (BIS), Transcranial Doppler (TCD), monitoring in non-neurosurgical procedures

Introduction

Complex non-neurosurgical procedures such as cardiac surgery, major vascular procedures (including carotid endarterectomy), liver transplantation, orthopaedic procedures in beach chair position, etc. are commonly associated with devastating neurologic complications and poor patient outcome. Neuromonitoring in these procedures assumes a pivotal role in ensuring timely detection and prevention of permanent brain and spinal cord dysfunction.

The most common aetiology of intraoperative neurologic injury that can potentially be detected by neuro-physiologic monitoring is cerebral ischaemia, which may occur as a consequence of hypoperfusion, embolic stroke, or malperfusion.1

Clinically, the major neurologic deficits most commonly observed have been cognitive impairment, seizures, choreoathetosis, bilateral motor deficits and hemiparesis.2

Multimodal integrated techniques are used to monitor cerebral perfusion and thus avoid the above-mentioned complications. There is no one modality that has shown to be superior to the other and in practice monitors are used to complement each other.

Cerebral perfusion monitoring modalities

Cerebral perfusion monitors seek to ensure that adequate perfusion to the brain is maintained at all times. In order to perfuse the brain adequately cerebral perfusion pressure (CPP) has to be maintained, and CPP is defined by the following equation:

\[ CPP = \text{MAP} - \text{ICP (or CVP)} \]

Adequate perfusion of the brain and prevention of ischaemia can be achieved by measuring the following parameters:

- Cerebral oxygenation and cerebral blood flow (CBF)

Cerebral oxygenation monitoring

Near Infrared Spectroscopy (NIRS) monitor

This is a non-invasive, continuous monitor that measures regional cerebral oxygen saturation (rSO2), usually of the frontal area. The values reflect primarily venous saturation as opposed to arterial pulsatile component. Added advantages of NIRS include: that it can identify both hypoperfusion and hyperperfusion; and there is no need for blood flow.5

A number of drawbacks are recognised however, and these include: that it is affected by extracranial blood flow and ambient light; there are no recognised standards or normal values (as variations between individual patients do occur). This means that every patient's baseline is needed, absolute values are not useful, and trends are more important.

Electroencephalogram (EEG) monitor

This is a measure of spontaneous electrical activity generated by the brain, specifically the cortex; therefore the deeper structures are not assessed. It requires a robust machine with multiple electrodes ranging from 8 to 16. Measurements of CBF are implied from changes in the amplitude, frequency and the patterns of the EEG bands (α, β, δ).3

The added limitations are that the raw data produced from the EEG is quite complex, and needs interpretation by experienced personnel and therefore limiting its use. Anaesthetic agents and hypothermia also extensively affect it.

Bispectral Index (BIS) monitor

This is a processed EEG, originally designed to assess the hypnotic level of a patient. But it can now be used to detect cerebral ischaemia in the intraoperative period. The monitor gives a value, called a BIS value ranging from 0 to 100. Reduction in BIS value by more than 10 or by 30–40% may correlate with ischaemia.4

The limitations of this mode of measurement include delay in reporting of about 30–60 seconds due to processing of data from...
raw EEG data. BIS also does not differentiate between localised and global ischaemia.

**Cerebral Blood Flow (CBF) monitoring**

CBF monitoring offers a rational approach to detect and prevent ischaemic insults to the brain and improve outcome in patients undergoing major non-neurologic procedures. Normal value of CBF in young adults is 50 ml/100 g brain tissue/min. The ischaemic threshold is 18 ml/100 g/min and below 10 ml/100 g/min, irreversible brain damage ensues.\(^6\)

The CBF monitors may be classified into two broad categories: direct and indirect measurements.

**Indirect monitoring**

**Transcranial Doppler (TCD)**

This is a non-invasive, bedside technique that measures local blood flow velocity. It presents data graphically as velocity against time. The changes in velocity indicate pathology, e.g. hypoperfusion due to stenosis, thrombosis or hyperperfusion.

The limitations of TCD are that it is operator-dependent, there is signal interference with numerous electromagnetic apparatus in the operating room. In 10–15% of patients, there is a lack of acoustic transtemporal window, and therefore the test cannot be carried out.

**Stump pressure**

During carotid endarterectomy, when the proximal common carotid and external carotid arteries are clamped, the pressure measured in the internal carotid cranial to the clamp site is the stump pressure. It reflects the back pressure on the internal carotid artery, supplied by the collaterals from the circle of Willis. It is considered to be a surrogate marker of perfusion in the ipsilateral cerebral hemisphere from the contralateral side. A pressure below 40–55 mm Hg is often used as a threshold for intervention.\(^4\)

**Direct monitoring**

**Positron Emission Tomography (PET)**

This mode is an invasive, quantitative measure of CBF, cerebral metabolic rate of oxygen (CMRO₂), cerebral blood volume (CBV), and oxygen extraction fraction. It uses a radioactive compound, and requires patients to be transported to a radiology facility, therefore impractical for intraoperative use. Although it is considered a gold standard, it is expensive, not universally available and gives a short single assessment.

**Practical use of NIRS and BIS during non-neurosurgical procedures**

**Near Infrared Spectroscopy (NIRS)**\(^6\)

NIRS is a measure of cerebral perfusion that relies on the difference of absorption spectra between oxyhaemoglobin, deoxyhaemoglobin and the total haemoglobin for calculating estimates of regional cerebral oxygen saturation (rSO₂).\(^2\) (Beer Lambert law).

The technique requires the use of two sensors separated by a fixed distance. The proximal sensor records infrared light reflected from superficial tissue while the distal signal represents the brain tissue saturation. The subtraction between these two signals represents a venous weighted estimate of rSO₂.

**Usefulness of cerebral NIRS**

It is a non-invasive technology that provides continuous monitoring of regional cerebral oxygenation. The machine is portable, sensors are easy to apply, and interpretation of results needs no specialised expertise.\(^9\)

The monitor can identify both hypoperfusion and hyperperfusion. Due to the strategic placement of the electrodes, the watershed area between the anterior and the middle cerebral artery territories are included in the NIRS measurements.

NIRS is relatively resistant to the effects of anaesthetic agents, but can be affected by the indirect changes in the global blood flow due to physiological changes due to drugs. Therefore, to allow meaningful interpretation of neuromonitoring results, steady state anaesthetic depth, physiological variables, such as blood pressure, temperature, and patient position should be kept stable.\(^4\)

In non-neurological procedures NIRS has been found very useful in determining the risk of significant cerebral ischaemia, and therefore implementing appropriate treatment algorithms are the following: procedures in beach chair position, repair of aortic coarctation, aortic aneurism repair, cardiac surgery, carotid endarterectomy, etc.

Spinal NIRS monitoring looks to be an attractive alternative monitoring during procedures such as thoracic and abdominal aorta repair.\(^6,7\) The same advantages as mentioned above apply here. The problematic issues are also as depicted above. For instance, the interference of the surrounding paraspinal space tissues.

**Limitations of NIRS**

NIRS reading is affected by the scalp tissue composition in different individuals, and therefore it is difficult to compare to ‘standards’/‘normals’. Ambient light also affects NIRS reading, necessitating proper padding of the electrodes.

The monitor can only assess regional oxymetry, usually frontal, so clinically relevant focal cerebral ischaemia outside the monitored area may easily go unnoticed. Patients with previous infarcts may produce erroneous measurements.

**Bispectral monitor (BIS)**

Bispectral analysis represents a processed EEG, originally designed to assess the hypnotic level, and therefore avoid awareness. The BIS monitor gives a single numerical reading between 0–100, that denotes the level of hypnosis.\(^4\) It uses...
a set of three disposable electrodes attached to the patient’s frontal and temporal regions. The machine is portable, and in fact some anaesthetic machines are fitted with cartridges for BIS monitoring. The accuracy of the BIS to monitor hypnotic state has been questioned due to inconsistencies associated with it in many studies.4

The recent use of BIS has been to detect cerebral ischaemia during non-neurosurgical procedures. Reduction in BIS value may correlate with ischaemia.4

Limitations of BIS monitor for use in detecting cerebral ischaemia intraoperatively are numerous, and include:

• Delay in reporting owing to the time needed for processing of EEG data.
• Lack of differentiation between global and focal ischaemia.
• Inhalational and intravenous anaesthetic agents decrease BIS value in a dose-dependent manner, ultimately resulting in burst suppression and electrical silence similar to severe hypoperfusion and ischaemia.4,9 Table I gives comparison amongst different types of cerebral perfusion monitors9

Conclusions
Numerous modalities for measurement of cerebral perfusion during high-risk non-neurosurgical procedures are available. The aim of monitoring cerebral perfusion in these procedures is to detect cerebral hypoperfusion, malperfusion, and embolic complications early and therefore avoid cerebral ischaemia. Studies have shown that no single monitor is capable of exclusively and conclusively detecting cerebral malperfusion. A multimodal, complementary approach is recommended.

NIRS promises to be quite a valuable technique to use in non-neurosurgical procedures to avoid neurologic complications associated with these high-risk procedures. On the other hand, BIS has been found to be disappointing in terms of accurately determining depth of anaesthesia as well as detecting cerebral ischaemia.

References

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Detection of Cerebral Ischaemia</th>
<th>Expense</th>
<th>Ease of Use</th>
<th>Comment</th>
</tr>
</thead>
</table>
| EEG | • High false positive rate | ++ | ++ | • Difficult to interpret  
• Does not detect subcortical ischaemia  
• Low sensitivity in previous stroke |
| Somatosensory evoked potentials (SSEPs) | • No more specific or sensitive than EEG | ++ | ++ | |
| Bispectral index (BIS) | • Poor | + | +++ | • No consensus on critical pressure |
| Stump pressure | • High specificity  
• Low sensitivity | + | +++ | |
| Transcranial Doppler (TCD) | • Poor | ++ | + | • Useful for detecting emboli  
• Unusable in 15-20% people  
• No consensus on critical MCAv value  
• Operator dependent results  
• Bulky equipment |
| Near infrared spectroscopy (NIRS) | • High negative predictive value  
• Low specificity  
• Poor positive predictive value | ++ | +++ | • Placement over frontal lobes ot ideal in CEA  
• Signal contamination ++  
• No ‘normal’ range |
| Jugular venous bulb SpO₂ | • Low specificity  
• Poor positive predictive value | ++ | ++ | • Invasive technique |
| Xenon - 133 | • Low specificity  
• Poor positive predictive value | +++ | ++ | • Very expensive  
• Experimental  
• Difficult to interpret results |

Table I. Characteristics of various cerebral perfusion monitors9
Anaesthesia for related living donor liver transplantation

M Hatchett

Wits Donald Gordon Medical Centre Transplant Unit
Dunkeld Anaesthetic Practice

Introduction

The first liver transplant was performed in 1963 in Colorado, USA by Dr Thomas Starzl, a man who is acclaimed world-wide as the father of organ transplantation. His career and list of accomplishments can, and has been, the individual subject of lectures by themselves, but suffice to say that it is difficult to foresee many people surpassing his achievements in medicine. At one stage in his career it was calculated he was producing a scientific paper for publication every seven days. He died in March this year at the age of 90.

As we are all aware, liver transplantation is the only real hope for end-stage liver disease. In kidney disease we have dialysis as a method of prolonging life, albeit very restrictive for the patient and certainly not ideal. For progressive liver disease we have liver transplantation or death. The results and outcomes of liver transplantation have improved exponentially since 1963, particularly as a result of advances in immunosuppression and decreased rejection of transplanted organs. The main problem that still remains is the perennial shortage of donor organs for the huge number of recipients requiring them.

Deceased vs living donors

Traditionally, particularly in South Africa, donor organs have come from brain-dead patients with functional cardiac systems on ventilators. Elsewhere organs have also been procured from controlled non-heart-beating donors (often for religious and cultural reasons), or patients on ECMO support after cardiac death. The huge step forward has been the successful introduction of removal of a portion of a healthy donor’s liver so that both donor and recipient survive thereafter. There is a significant difference in transplant patterns between Western and Eastern countries. The Western countries continue to have higher numbers of liver transplants where the donor organ came from deceased donors, whereas in the Eastern countries, because of religious, cultural and social differences, living donor liver transplants (LDLT) are the commonest means of a patient receiving a transplant.

Critical to the concept of LDLT, specifically for adult-to-adult procedures, is the fact that the liver can regenerate its tissue extremely rapidly. Within two to three months of 40% of a liver having been removed as a donor graft, the liver has regenerated that volume so that it has regained full function. As regards the South African situation with LDLT, most of our cases are those where a parent is donating a portion of their liver to a child. This is usually the left lateral lobe and the volume of liver lost is small relative to the liver’s original volume. The situation is very different where a large proportion of the liver has to be donated because the recipient is an adult. There can then be a problem having sufficient functioning liver tissue for the donor and/or the recipient. This phenomenon is known as ‘small for size’ and can be extremely serious, if not life-threatening.

Advantages of LDLT

1. The LDLT is done as an elective procedure. This means everything is preplanned and controlled. As it is invariably scheduled for a morning start, staff are fresh and all support staff should be readily available. This is in stark contrast to cadaver transplants where there is little, if any, control over when the procedure will go ahead, and often occurs in the middle of the night with on-call staff that may be tired. Ancillary discipline staff may also not be readily available and have to be roused from bed and brought in at short notice.

2. Donors are thoroughly investigated with multiple examinations and investigations over a period of time before being passed fit to donate a liver segment. Any deviations from the norm in the donor’s health usually means they are turned down and other potential related donors are sought. This also translates into a good quality donated organ being recovered. This luxury of extensive preoperative assessment of the donor is not always present with cadaver-derived organs.

3. LDLT procedures allow recipients to ‘jump the queue’. Ordinarily patients placed on the liver transplant list at an institution are prioritised on their MELD score (Model for End Stage Liver Disease). This scoring system is based on the patient’s blood levels for bilirubin, creatinine, sodium, as
well as their INR and their frequency of haemodialysis. The more severe their liver disease, the higher their MELD, and they are then higher on the list and likely to get a transplant sooner than those below them. An alternative score is used for paediatric patients known as the PELD score and is based on measures of bilirubin, albumin, INR, growth failure and patient age. As patients are only placed on the list if it is felt they will demise in the next twelve months without a transplant, and there is a scarcity of donor organs, time and placing can be all important in a patient’s survival. With a LDLT the specific recipient is done as soon as his related donor is considered suitable and the recipient’s position on the list is immaterial.

4. With LDLTs there is a decreased ischaemic time. The time from clamping when the donor segment is removed, to the time when reperfusion occurs in the recipient, is minimal as the two theatres where the donor procedure and recipient procedure occur are usually adjacent theatres and continually liaise with one another. There is thus careful co-ordination to ensure the recipient team is ready to receive and insert the donor organ before it is clamped and removed by the donor team. There is a direct correlation between ischaemic time and graft survival. This contrasts with cadaver organs that may be harvested in Durban, and make a long journey before reperfusion occurs in Johannesburg some hours later. Experienced transplant centres can usually claim a five-year survival rate of above 80% in children receiving a LDLT for biliary atresia.

5. The donor pool is significantly increased by investigating all listed recipients (particularly paediatric ones) as to whether there may be appropriate related living donors.

Disadvantages of LDLT

The main disadvantage of LDLTs is the significant risk posed to the donor. People that agree to selflessly donate a portion of one of their most vital organs to help save a life of a close or extended family member, or occasionally even a friend, must be lauded for their courage and sense of humanity, and every effort made to minimise any danger to them. Figures differ dramatically from centre to centre but morbidity figures of 25%, and mortality rates of 2%, are relatively commonplace.

The horrific occurrence of a healthy donor losing their life because of a medical problem, whilst trying to aid another, has far-reaching effects on many people. Besides the patients themselves, the effect on the donor’s nuclear and extended families is devastating. As well, the publicity occurring from a death of a donor in a LDLT can be severe enough to close a well-established transplant programme in a respected institution. This has occurred in the United States previously and, as usually happens, the one bad event is always remembered long after the hundreds of good ones have been long forgotten. There have been cases where the donor has survived and has left hospital with a new lease on life, but the recipient has demised. There have also been incidents where the recipient has done well, but post LDLT the donor has had a huge insult to his own hepatic function and has had to receive a liver transplant himself.

Potential donors must be made acutely aware of all possible adverse outcomes and dangers. Repeated visits and discussions with the physicians involved must be held and subjects discussed until the potential donor clearly understands the possible dangers. An impartial physician, who is not part of the transplant team, is appointed as an advocate to any potential donor. This person must make sure the donor is completely informed about the procedure and is under no external family pressure to donate. On occasion when it is detected that the family is attempting to coerce someone into donating, the physician can actually say to the family that the person is ‘unsuitable’ for some vague health reason so that he is not ostracised at home for refusing to donate.

The guiding principle for LDLTs is that doctors need to maximise benefits to the recipients, while minimising risks to donors.

Donor assessment

1. A potential donor must be a relative (with special permission a friend is sometimes allowed to donate).
2. Donor must be a healthy adult over 18 years of age and usually less than 60.
3. Donor and recipient must be of the same blood group.
4. Physicians consult.
5. Surgical consult.
6. Cardiological consult including Echo. If any cause for concern an angiogram may be done.
7. Psychologist consult.
8. Ultrasound abdomen.
9. CAT scan triple phase abdomen.
10. MRCp if adult to adult being considered.
11. In females a PAP smear is done, and if over 50 years of age a mammogram is done.
12. If all investigations are acceptable, an assessment of liver size and shape has to be made. The graft to recipient body weight ratio has to be determined, as well as the graft weight relative to the weight of the whole donor liver.
13. 3D CT angiography will reveal if the vasculature is such that the graft can be separated from the donor liver and still contain an adequate artery and vein to enable successful anastomosis in the recipient.
14. 3D MR cholangiography gives the necessary information about the bile duct anatomy of the donor organ.
15. An idea of the shape of the donor organ must be obtained. A thin flatter section of tissue is preferable in adult to child transplants and is more commonly obtained in females.

Points of interest:

1. Positive testing for HIV, Hep B and Hep C exclude patients from being donors. An exception is made in Eastern countries where a person is Hep B antibody core positive. Hepatitis B infection in Asia is rampant and if past infection/immunity is detected in the donor, the recipient is given immunisation and lamivudine is administered and the LDLT can go ahead. Naturally this is if a more acceptable donor cannot be found.
2. ABO incompatible LDLTs have been done in dire emergencies where time is running out for the recipient and no alternative donors are available. Extra immunosuppression is required.
3. and a stormy course can ensue.
4. Well-controlled hypertension and well-controlled diabetes mellitus are not necessarily exclusion criteria in most centres.
5. Pregnancy is naturally an exclusion criterion for liver transplantation. There is a case recorded, however, of a second semester parturient in Taiwan donating a liver lobe to her child when no other donor could be found. Both donor and recipient did well and mom delivered a healthy term baby. Obviously this would be a very last resort and would only be considered with full education on the risks and danger being imparted the potential donor. In the case done it was recorded that it was done at the mother’s insistence.

Donor anaesthesia

As regards the actual anaesthesia, this is relatively standard as for all hepatectomies. All the above-mentioned extensive investigations are done prior to the anaesthetist performing his preoperative assessment. Unless the patient’s cardiorespiratory and general health is excellent, he will not be presenting for a donor hepatectomy procedure, but naturally all aspects must be rechecked and all investigation results studied.

An epidural should always be discussed with the patient as regards analgesia. The incision is a horizontal “bucket-handle” one and is particularly painful postoperatively. I find the rectus sheath catheters for local anaesthetic infusion superb for midline incisions, but less so for the horizontal incisions. The usual epidural contraindications for back pathology apply, but other contraindications will probably have been eliminated during the extensive investigative phase. Naturally the patient must agree to the epidural insertion. If an epidural is not used, other standard regimens of analgesia using opiates must be employed. Check the coagulation status prior to the removal of an epidural catheter as post-hepatectomy derangement can occur.

A standard general anaesthetic technique is used with intubation, ventilation and muscle relaxation. Some articles in the literature recommend using atracurium or cisatracurium in case liver metabolism is diminished by the procedure but I think that is highly unlikely. With the advent of sugammadex I feel this is unnecessary.

A large bore peripheral line should be inserted so fluids can be given rapidly if required. Some articles advocate having a rapid fluid administration mechanism in theatre such as a Level One pump.

An arterial line must be inserted for beat-to-beat blood pressure monitoring and repeat blood gas sampling, and a CVP must be inserted for venous pressure monitoring and good access. The patient should be kept ‘dry’ as regards fluid replacement. The literature is virtually unanimous in the conclusion that decreased venous pressure decreases bleeding from the liver during surgery. Many articles give a definitive number for the CVP (usually 4 to 5 mmHg) over which bleeding increases. Other authors feel an absolute CVP number is inaccurate and not particularly meaningful. The consensus is, however, that fluids must be severely restricted until after the hepatectomy is done, and thereafter fluids status restored with rapid administration. Hypotension intraoperatively should be rectified with vasopressors. Low venous pressure is aided by the epidural which redistributes fluid in dilated vessels. If necessary, venodilators like nitroglycerine can be added but I have never felt a need to employ this method. There are also reports in the literature of air embolism occurring as the liver is divided if the venous pressure is too low. Besides the CVP being used as an indicator of venous fluid status, there are also many references advocating Stroke Volume Variance as a useful indicator.

In good hands the blood loss during the surgery is relatively small. The newer technology available to the surgeons as regards cutting and coagulating simultaneously has changed the volume of blood lost over the last 20 years exponentially. We always routinely have a perfusionist in theatre available to do cell-saving if required.

Serial blood gases done intraoperatively give information regarding metabolism, blood loss, ventilation and fluid status.

At the end of the procedure the patient is usually extubated, unless there are specific reasons not to do so. Transfer to ICU follows and meticulous attention must be paid to monitoring of the patient’s liver function and coagulation profile. Small for size scenarios can occur if a large graft has been taken. The liver hypertrophies quickly and regains full size within three months. If there is a marginal deficit in liver tissue and function, ICU support for a few weeks may be enough to allow the donor to regenerate enough tissue to survive and regain normal function. In rare extreme cases donors have ended up requiring transplant themselves as liver function has been so greatly impaired.

Conclusion

The introduction and successful mastering of LDLT has been a huge step forward in the 54 year history of liver transplantation. It has provided a potential source of organs for patients with fulminant liver disease that have days to find one. Countless infants have been saved that would previously have perished, via the donation from a parent of a small liver segment. The work involved can be very taxing, arduous and stressful, but proficient experienced units have very high levels of success and provide an invaluable service.

Bibliography

Deaths due to obstetric haemorrhage increased by 24.7% between 2002 and 2011. The majority of these deaths were deemed preventable. Uterine blood flow at term approximates 700 ml/min making bleeding from the uterus a potentially life-threatening complication that requires a rapid response.

Keywords: maternal mortality, massive obstetric haemorrhage, antepartum haemorrhage, postpartum haemorrhage, blood transfusion, cell salvage, antifibrinolytics

Introduction

For centuries the peripartum period was a dangerous period in the lives of new mothers. The mortality rates were largely inaccurate till the introduction of national registries. In Britain, the Registration of Deaths Act was passed in 1837. At this point the definition of maternal death was not well defined leading to further inaccuracies in the data. With time and better definitions, however, they were able to get more accurate data. The quest was then on to improve maternal mortality rates. Mothers were dying from puerperial sepsis, bleeding, seizures and illegal abortions. These causes of death remain amongst the most common factors involved in maternal morbidity and mortality.

Death due to bleeding remains a big problem, especially in low-income developing countries where 99% of all maternal mortality occurs. While death is the worst outcome related to obstetric haemorrhage, the majority of patients with life-threatening obstetric haemorrhage survive the ordeal. It may thus be useful to also look at these “near-misses”. Data on near-misses are less readily available. A recent systematic review of near-misses due to postpartum haemorrhage (PPH) puts the global mortality index for PPH at 6.6%. Morbidity index is the number of deaths as a percentage of the total number of severe maternal outcomes. Severe maternal outcomes are deaths plus near-misses. There was again a very big difference between low-income countries and high-income countries with low-income countries having an iMMR (institutional Maternal Mortality Rate) for PPH of 95/100 000 live births vs 5/100 000 live births in high-income countries.

In South Africa there has been a worrying trend where the number of deaths due to bleeding has been steadily increasing since 2002. This trend, however, has also been observed in high-income countries. In South Africa, the iMMR for obstetric haemorrhage was 19.51/100 000 live births in the 2002–2004 triennium compared to 24.32/100 000 in the 2008–2011 triennium. This is an increase of 24.7%. The majority (89%) of deaths due to bleeding could have been prevented. One-third of deaths due to bleeding were at or after Caesarean delivery.

Studies on near-misses in South Africa are scanty. Soma-Pillay reported a mortality index for bleeding of 2% in the Pretoria Academic Complex, while Maswime reported a near-miss rate of 2.1/1 000 Caesarean deliveries for bleeding at or after Caesarean section in a cross-sectional prospective study in 13 urban public hospitals in South Africa. Significant morbidity associated with obstetric bleeding includes acute kidney injury, coagulopathy, acute respiratory distress syndrome, shock, loss of fertility and pituitary necrosis.

Definitions

- Massive obstetric haemorrhage
  - Blood loss of more than 1 500 ml
  - A decrease in the haemoglobin of more than 4 g/dl
  - The need for transfusion of more than 4 units of packed red cells
- Antepartum haemorrhage
  - Bleeding from or into the genital tract that occurs after the 24th week of gestation but before delivery

Definitions

- Massive obstetric haemorrhage
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  - The need for transfusion of more than 4 units of packed red cells
- Antepartum haemorrhage
  - Bleeding from or into the genital tract that occurs after the 24th week of gestation but before delivery

You have known me for 9 months
But I have never met you
You had fed me for a lifetime
But I never got as much as a spoonful from your hand
You had loved me so much
Yet I never got a hug from you
For you had given your life so I can live
The same blood that was my breath
  Took yours away...
  Mom, I love you so much
  I wish you were here.
  “Dorinka~”

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  Took yours away...
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  I wish you were here.
  “Dorinka~”
Postpartum haemorrhage

- Primary
  - Obstetric bleeding that occurs from the time of delivery up to 24 hours postpartum
- Secondary
  - Obstetric bleeding that occurs from 24 hours up to six weeks postpartum

Antepartum haemorrhage

Placenta abruption

*Abruptio placentae* complicates about 1% of pregnancies and up to 20% of premature deliveries occurs because of abruption.14–16

Placenta abruption occurs when placental separation occurs before the birth of the fetus.17 It can be complete or partial. The rupture of the spiral arteries with subsequent formation of a retro-placental clot causes the separation.18–20 Surrounding tissue and myometrium is also damaged in the process. Foetal demise can occur especially with a more than 50% abruption.17

Clinical signs associated with severe abruption include vaginal bleeding (usually dark blood), severe abdominal pain and severe uterine contractions.15 Mild cases may be asymptomatic and a retroplacental clot only detected after delivery of the placenta. Blood loss can also be concealed within the uterus in up to 20–30% of cases.19

There are multiple risk factors for placenta abruption.14,15,21–29

### Risk factors for abruptio placentae

- Abruption in previous pregnancies
- Pre-eclampsia
- Advanced maternal age
- Intrauterine growth retardation
- Presentations other than vertex
- Polyhydramnios
- Multiparity
- Low BMI
- Intrauterine infection
- Premature rupture of membranes
- Abdominal trauma
- Pregnancy after assisted reproductive therapy
- Smoking and illicit drug use
- Short umbilical cord

Complications associated with abruptio placentae.17

Maternal:

- Coagulopathy
- Hypovolaemic shock
- Adult respiratory distress syndrome
- Renal failure
- Need for blood transfusion
- Hysterectomy if uncontrolled bleeding

Foetal:

- Intrauterine growth retardation
- Foetal distress
- Foetal death

Neonatal:

- Preterm delivery
- Small for gestational age infant
- Neonatal death

Coagulopathy complicates about 10% of cases with abruption placenta. When there is intrauterine foetal demise, the incidence goes up to 30%.30 The biochemical picture is that of low fibrinogen, low platelets and increased fibrinogen degradation products (FDP).

The placenta, myometrium, amniotic fluid and the decidua have very high levels of tissue factor (TF) and tissue factor pathway inhibitor (TFPI).50,51 Tissue factor in placenta is up to 7 800 times higher than the plasma concentration. Tissue factor is even more abundant in the placenta of patients with pre-eclampsia.32

With placental abruption, TF and TFPI are released from the damaged placenta and myometrium and concentrate in the retroplacental clot. From there, they enter the maternal circulation where they cause activation of the tissue-factor pathway. The resultant widespread coagulation leads to a consumptive coagulopathy. Fibrinolysis of the intravascular clots results in the formation of fibrinogen degradation products. High levels of FDP have an anti-coagulant effect.33 FDP also interferes with uterine contractility further aggravating the bleeding.34

Couvelaire described a complication of utero-placental apoplexy as early as 1911.35,36 Utero-placental apoplexy was later called Couvelaire uterus. Couvelaire uterus occurs in approximately 5% of abruption cases.35,37 Blood from the damaged placental vessels extravasates into the decidua and laterally into the myometrium and can extend to the serosa. It gives the uterus a characteristc blue colour. The uterus becomes thin and weak and there is a risk of uterine rupture especially in the presence of intense uterine contractions.38 The presence of Couvelaire uterus is not necessarily associated with uterine atony and the mere presence thereof is not per se an indication for hysterectomy.39

**Placenta praevia**

A placenta covering the internal os, or implanting close to the internal os, is known as a placenta praevia. It is a complete placenta praevia when the internal os is covered, or a marginal placenta praevia when the leading edge of the placenta is within 2 cm from the os, but not covering it. The quoted incidence of this complication ranges between 0.15%40 to 2.5%.41

Although the exact pathophysiology is unknown, it seems that a scarred uterus is a major contributing factor.42

Placenta praevia presents as painless vaginal bleeding in the third trimester. The lower segment starts to form in the third trimester. As the myometrium thins out, the placental attachment in this area is disrupted. The lower segment has an abundance of type 2 PGE, receptors that cause relaxation. With decreased contractility in the lower segment, the bleeding vessels cannot be occluded by contraction and bleeding continues.
An abnormally invasive placenta poses a major bleeding risk to the mother. Blood loss may be between 3 000–5 000 ml.53,56 Mortality from this condition has been reported to be as high as 7%.57 Other complications include the risk for DIC, emergency hysterectomy, ARDS, acute renal failure and injury to surrounding structures.53

Women with risk factors should be identified antenatally and delivery of confirmed cases should be carefully planned. The timing of delivery should be individualised and the optimum timing seems to be around 34 weeks gestation and after foetal lung maturation has been achieved.53,58 The management should be multi-disciplinary. Various modalities are employed to decrease the blood loss and to try and save the uterus in women who desire future fertility. Successful pregnancy afterwards is, however, rare. These strategies include internal iliac balloon catheters, uterine artery embolisation, internal iliac artery ligation and postoperative methotrexate. If placenta percreta is suspected, other surgical disciplines also need to be involved in the surgical delivery. Urological injuries are a concern. The bladder is often involved. The ureters need to be identified and protected and the placement of ureteric stents should be considered.53

The majority of cases are delivered by Caesarean section.59 Due to the potential risk for torrential blood loss, general anaesthesia is the safer choice. Blood bank should be alerted to the possible need for massive blood transfusion. Preoperative haemoglobin levels should be optimised. From a surgical prospective, it is best to avoid manual removal of the placenta.53

**Uterine rupture**

This rare complication can result in significant maternal and foetal morbidity and mortality. Uterine rupture occurs when there is full thickness rupture of the myometrium and the peritoneum covering the uterus. This is in contrast to scar dehiscence where the peritoneum remains intact and the foetus is not expelled into the abdominal cavity. The scar edges in dehiscence typically do not bleed. Uterine rupture can occur in both scarred and unscarred uteri. It is, however, more common in cases with previous uterine surgery especially classical uterine incision. Other causes of uterine rupture include induction or augmentation of labour, over-distention of the uterus, abnormal placentation, dystocia, advanced maternal age and post-dates.

The clinical signs are significant vaginal bleeding, severe abdominal pain, foetal distress or foetal demise and palpation of foetal parts.

**Other causes of antepartum haemorrhage**

- Cervicitis
- Trauma to genital tract
- Vasa praevia
- Foetal blood vessels running close to or across the internal os

**Advanced abdominal (extrauterine) pregnancy**

This rare complication happens when an ectopic pregnancy progresses past 20 weeks gestation within the abdominal cavity.60 The placenta implants into abdominal or pelvic organs, blood vessels or the abdominal wall. About 1% of ectopic pregnancies progress to advanced abdominal pregnancies.61–63 The diagnosis is not always straightforward and the physician needs to maintain a high index of suspicion. There are some clues that should alert the physician to a possible extrauterine pregnancy. These include a history of vaginal bleeding and abdominal pain in the first trimester or persistent abdominal pain, history of previous pelvic surgery, history of infertility or fertility treatment, abnormal foetal lie, painful foetal movements, oligohydramnios, abnormal appearance of the placenta on ultrasound with absence of myometrial tissue between the uterus and the bladder,64 features of foetal demise or failed induction of labour.65 The pregnancy may also be complicated by pre-eclampsia as the placentation is abnormal.

Foetal complications are even more common than maternal complications. Foetal demise is the most common outcome
with reported incidence of between 40–95%. In cases where placental blood flow is sufficient, the foetus can survive to term. Foetal abnormalities can occur due to vascular disruptions or due to the compression from surrounding abdominal structures. Craniofacial abnormalities, joint problems, limb and central nervous system disruptions are the most common associated morbidities.

If the diagnosis is made preoperatively, it allows the physicians to plan the delivery and to have blood products readily available. There is controversy around whether the placenta should be removed or left in situ. Removal of the placenta may be associated with torrential bleeding that may be difficult to control especially if the liver or spleen was the site of placental implantation. Bleeding is associated with high maternal mortality. Leaving the placenta in situ may also lead to complications of sepsis, necrosis or postoperative ascites.

Choice of anaesthesia should take into consideration that there is the potential for massive blood loss.

Postpartum haemorrhage

Postpartum haemorrhage complicates around 5% of pregnancies. Postpartum haemorrhage is defined as acute blood loss of more than 500 ml in vaginal deliveries and more than 1 000 ml in Caesarean deliveries. The problem with using this definition is that blood loss is often under-estimated. Another way of estimating blood loss would be to observe the haematocrit. Unfortunately this is also not particularly useful as torrential bleeding may become life-threatening before a drop in haematocrit is observed, while intravenous clear fluids and antenatal haemoconcentration may also make the value unreliable.

Risk factors associated with postpartum haemorrhage

- Previous PPH
- Assisted conception
- Increased BMI
- Advanced maternal age
-Previous C/S
- Abnormal placentation
- Placenta praevia especially anterior location
- Placenta abruption
- Invasive placenta
- Overdistended uterus
- Multiple gestation
- Polyhydramnios
- Abnormal lie
- Post dates
- Macrosomia
- Uterine fibroids
- Known uterine abnormality
- Chorio-amnionitis
- Instrumental and Caesarean deliveries
- Physiological 3rd stage (vs active management)
- Retained placenta
- Emergency C/S
- Labour induction/augmentation

Tocolysis

- Longer duration of labour
- Pre-eclampsia and HELLP syndrome
- Coagulation abnormalities
- Predelivery anaemia

Causes of postpartum haemorrhage

One or more of the so-called 4 Ts may be the cause of PPH

- Tone
  - Responsible for about 70–90% of cases of PPH
  - May be episodic and unpredictable
  - Included in this category is uterine inversion and abruption placenta
  - Volatile anaesthetic agents decrease uterine tone

- Tissue
  - Retained placenta or products of conception
  - Abnormal placentation

- Trauma
  - Uterine rupture
  - Genital tract lacerations/episiotomy
  - Broad ligament haematoma/surgical trauma

- Thrombin
  - Coagulopathy genetic/acquired

Prophylaxis and treatment of postpartum haemorrhage

Oxytocics

Oxytocin is the first-line drug in the prevention and treatment of uterine atony. It is also the cornerstone of ‘active management of the third stage of labour’ which in itself is one of the recommendations to decrease the incidence of postpartum haemorrhage.

Oxytocin has a short half-life and thus needs to be given as an infusion to prevent uterine atony. The infusion dose needs to be individualised to every patient and situation. A patient with risk factors for PPH will need a higher dose than a patient with no risk factors presenting for an elective delivery. Internationally the infusion dose range from 5 IU/h to 10 IU/h. The infusion needs to be continued for at least four hours after Caesarean delivery. The South African ESMOE guidelines suggest an infusion of 20 IU/1 000 ml crystalloids at 125 ml/hour. This can be increased to 80 IU/1 000 ml over eight hours. Big bolus doses should be avoided as it is associated with haemodynamic compromise. Dose-finding studies in patients presenting for elective Caesarean section found that doses between 0.35–3 IU were associated with acceptable uterine tone without the side-effects seen with bigger doses. Patients with risk factors such as obstructive labour will need the higher doses in this range.

Patients who are in labour for more than six hours or those who receive exogenous oxytocin for induction or augmentation
of labour, have down-regulation of oxytocin receptors and may need bigger doses of oxytocin or even a different class of uterotonic. Prostaglandins

Prostaglandin E₂ (PGE₂) is formed via the arachidonic pathway. Its receptor has four subtypes (EP₁, EP₂, EP₃, EP₄). Activation of EP₁ and EP₃ leads to uterine contraction whilst EP₂ and EP₄ binding is associated with relaxation of the uterus. Prostaglandin F₂α is no longer available in South Africa. It was used in resistant uterine atony and was given directly into the myometrium. Side-effects included nausea, vomiting, diarrhoea and bronchospasm.

Surgical measures

Measures that the surgeons can take include B-lynch suture, uterine tourniquet, intrauterine balloon catheter, selective arterial devascularisation and hysterectomy. Interventional radiological strategies include balloon occlusion and arterial embolisation. These may not be readily available in the acute setting when bleeding is already occurring.

Anaesthesia for the parturient with obstetric bleeding

It is important to note that the pregnant patient can appear stable despite significant blood loss up to 1 500 ml. This is due to the physiological changes of pregnancy. By the time the arterial blood pressure starts to decrease, the patient may already have lost 25% of her blood volume. In addition, the pregnant uterus has an average blood flow of about 700 ml/min near term, thus there is a potential for rapid blood loss. These factors have important implications for the choice of anaesthesia. Regional anaesthesia should only be considered in cases with mild bleeding where there is no maternal or foetal compromise and where the risk for torrential bleeding is low. In most cases, however, general anaesthesia may be the preferred option.

The anaesthetic considerations are those related to obstetric anaesthesia such as need for rapid sequence induction, prevention of aspiration, prevention of aortocaval compression as well as considerations for potential massive blood loss.

Large bore intravenous access should be established and fluid resuscitation started in haemodynamically unstable patients. Invasive monitoring should be considered. Plans should be made for postoperative care as a large proportion of patients with massive bleeding will require ongoing intensive care after surgery.

Blood transfusion in obstetrics

An additional risk associated with blood transfusion in obstetric patients, is the risk of haemolytic disease of the foetus and newborn (HDFN) in subsequent pregnancies. Historically, this complication was mostly associated with rhesus D negative mothers expecting a rhesus D positive baby after a previous pregnancy with a rhesus D positive foetus. With the introduction of anti-D immunoglobulin immunisation of Rh negative mothers, the syndrome is now mostly due to ABO incompatibility and other alloantibodies. Transfusion of blood products in women of childbearing age, should thus take this into consideration and unnecessary transfusion should be avoided.

Transfusion of blood products should ideally be individualised based on point-of-care tests. A patient blood management strategy (PBM) should be followed rather than a “one-size-fits-all” dogma. A rough guideline would be to aim for a haemoglobin > 8 g/dl, prothrombin time < 1.5 x mean control, aPTT < 1.5 x mean control and fibrinogen level of more than 2 g/L. In addition, pH should be maintained above 7.2, temperature above 35 °C and ionised calcium above 1 mmol/L. There is evidence that fibrinogen plays an important part in coagulation in the obstetric patient. Fibrinogen level less than 2 g/L has a 100% positive predictive value for severe PPH. The best blood product to increase the fibrinogen level is cryoprecipitate. Cryoprecipitate contains 10 times more fibrinogen than fresh frozen plasma. To raise the plasma fibrinogen level by 1 g/L requires only 3 ml/kg of cryoprecipitate instead of the 30 ml/kg FFP that would be needed to achieve the same result.

The use of recombinant factor VII remains controversial. It should only be considered when other measures have failed and in an attempt to prevent hysterectomy. It should, however, not delay the decision to do a life-saving hysterectomy. It also should not be given unless the haematocrit is adequate, platelet count > 50 x 10⁹/L, fibrinogen > 1 g/L, pH > 7.2 and temperature > 34 °C. The dose is 90 μg/kg over 3–5 minutes.

Cell salvage in Caesarean delivery

Cell salvage involves the collection of blood from the surgical field, processing and washing those cells and re-infusing them to the patient. In obstetric patients, the blood from the surgical field will be contaminated with amniotic fluid and foetal debris including foetal blood and foetal squamous cells. The concern is thus that amniotic fluid in this cell-saved blood can cause iatrogenic amniotic fluid embolism with resultant DIC and that the foetal components can lead to maternal allo-immunisation.

The amniotic fluid contains tissue factor and it is this factor that is thought to cause the coagulopathy seen in amniotic fluid embolism. Modern cell salvage technology is able to reduce the total amount of tissue factor in the salvaged blood by 89% and eliminate the active proportion of tissue factor completely.

Foetal squamous cells and foetal haemoglobin are still detectable in the salvaged blood but their levels are comparable with maternal venous blood at the time of placental separation. Multiple studies examined parturients who had received cell-salvaged blood. There were no serious complications reported in more than 299 patients and the risk of using cell-saved blood in obstetrics seems to be the same as for the general population. Precautions to be taken are to discard blood and amniotic fluid collected before the delivery of the foetus and to use leukocyte depletion filters. Leukocyte depletion filters have been
associated with a precipitous decrease in arterial blood pressure. This is thought to be due to cytokine release from the trapped leukocytes. If this complication occurs, it is advised to stop the transfusion.127

Rho(D) immune globulin should be considered in Rh-mothers after the use of cell-salvaged blood.

The role of antifibrinolytics in obstetric bleeding – WOMAN Trial

Antifibrinolytics have shown promising results in reducing blood loss and mortality due to bleeding in a variety of surgical situations, trauma and other indications.128–132 The CRASH-2 trial129 showed a significant decrease in death due to bleeding when tranexamic acid was given (4.9%) vs control (5.7%). The MATERRs studies130,131 have also shown decreased mortality in the military trauma setting.

There have also been studies done in elective Caesarean deliveries where tranexamic acid was given prophylactically before skin incision and this was associated with a significant reduction in perioperative blood loss as well as a lesser reduction in haematorcit and haemoglobin levels when compared to the controls.133,134

There is, however, a theoretical concern about the use of antifibrinolytics in pregnant patients due to their physiological hypercoagulable state.135,136

The WOMAN trial137 (Worldwide Maternal Antifibrinolytic trial) is currently underway and results are expected soon. The aim of the study is to evaluate the use of tranexamic acid in the treatment of postpartum haemorrhage. It is an international multi-centre randomised double-blind placebo-controlled trial. Women with a clinical diagnosis of postpartum haemorrhage after normal vaginal delivery or Caesarean delivery who are eligible to enter the trial are randomised to receive either 1 g of tranexamic acid or saline. The sample size will be 15 000 patients.

A previous Cochrane review identified three trials where tranexamic acid was used as prophylaxis,138–140 However, the study designs in these trials were of poor quality. The latest WHO recommendations on the management of postpartum haemorrhage and retained placenta state that tranexamic acid can be considered but that the evidence for its use, is weak.139

References


Carcinoid syndrome

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Keywords: carcinoid syndrome

Introduction

Carcinoid tumours are derived from enterochromaffin cells (also known as Kulchitsky cells) and arise from the different embryonic divisions of the gut. Under electron microscopy, they typically contain numerous membrane-bound neurosecretory granules containing hormones and biogenic amines. Carcinoid tumours are the most common endocrine tumours found in the gastrointestinal tract. They account for 13 to 34% of all tumours of the small bowel and 17 to 46% of all malignant tumours of the small bowel.1

Carcinoid tumours may be increasing in frequency with the highest incidence in some racial groups (4.5 per 100 000 in African males), suggesting a genetic role associated with their development. The sites of highest incidence are the gastrointestinal tract (67.5%) and the broncho-pulmonary system (25.3%). Within the gastrointestinal tract, approximately 40% of tumours occur in the small intestine, with a further 27% in the rectum and 10% in the stomach.2 It should be noted that the carcinoid syndrome occurs in less than 10% of patients with carcinoid tumours. Carcinoid syndrome is the clinical spectrum produced by release of amine and neuropeptide substances into the systemic circulation by carcinoid cells. 71% of patients with midgut carcinoids have metastatic disease at presentation.3 Vasoactive substances released by carcinoid tumours in the gastrointestinal tract pass via the portal system to the liver where they are metabolised. In order to manifest clinically with the carcinoid syndrome, these vasogenic substances need to spill over into the systemic circulation. This situation typically occurs when carcinoid tumours metastasise to the liver and substances secreted bypass this metabolism and thereby exert more widespread systemic effects. Carcinoid syndrome is especially common in tumours of the ileum and jejunum but also occurs with bronchial, ovarian, and other carcinoids.4

Classification

One of the more clinically useful classifications of carcinoid tumours is according to the division of the primitive gut from which the tumour cells arise and the vascular supply of the digestive tract: the foregut, midgut, and hindgut (Table I). Foregut carcinoids can occur in the thymus and bronchi and may secrete adrenocorticotropic hormone producing Cushing's syndrome. Carcinoid tumours on rare occasions develop in the ovary.

Clinical presentation

Carcinoid tumours are slow growing and may be asymptomatic for years. Initial presentation is typically with vague abdominal discomfort that is often misdiagnosed as irritable bowel syndrome.5 The average time from onset of symptoms to

Table I

<table>
<thead>
<tr>
<th>Location</th>
<th>Clinical</th>
<th>Biochemical</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOREGUT</td>
<td>Atypical carcinoid, ZE, acromegaly, Cushing’s syndrome</td>
<td>$\text{SHTP}$, histamine, peptide</td>
</tr>
<tr>
<td>Lungs, stomach, liver, biliary tract, pancreas, and first portion of the duodenum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIDGUT</td>
<td>Classic carcinoid</td>
<td>$\text{SHT}$, $\text{SP}$, $\text{CGRP}$, kinins and peptides</td>
</tr>
<tr>
<td>Distal duodenum, the small intestines, the appendix, the right colon, and the proximal transverse colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HINDGUT</td>
<td>Silent</td>
<td>Non-secretory</td>
</tr>
<tr>
<td>Distal transverse colon, the left colon, and the rectum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\text{SHTP} = 5$-hydroxytryptophan
$\text{S-HT} = 5$-hydroxytryptamine (serotonin)
$\text{SP} =$ Substance P
$\text{CGRP} =$ Calcitonin gene related peptide
$\text{ZE} =$ Zollinger-Ellison
correct diagnosis is nine years. Appendiceal carcinoids may be found incidentally at appendectomy. Jejunoeileal carcinoids are more likely to present with abdominal pain, obstruction, or signs of carcinoid syndrome. The classic carcinoid syndrome is characterised by episodic cutaneous flushing, diarrhoea, bronchoconstriction, hypo- or hypertension and carcinoid heart disease (Hedinger syndrome). Carcinoid heart disease, which eventually occurs in over 50 percent of patients with carcinoid syndrome, may be the initial presentation of carcinoid disease in as many as 20% of patients. Carcinoid heart disease typically affects the right side of the heart causing fibrous thickening of the endocardium. This results in retraction and fixation of the tricuspid and pulmonary valve leaflets. Tricuspid regurgitation is found in almost all cases, but tricuspid stenosis and both pulmonary regurgitation and stenosis may occur. The pathogenesis of the plaque is not completely understood. The plaque is composed of smooth muscle cells, myofibroblasts and an overlying endothelial cell layer. The diet drugs, fenfluramine and dexfenfluramine, which interfere with serotonin metabolism produce cardiac valve lesions very similar to carcinoid lesions.

Diagnosis

A combination of biomarkers and imaging studies are used to diagnose and locate carcinoid tumours. Ideally tissue specimen is required for confirmation of diagnosis. The most common markers for midgut carcinoid are plasma chromogranin A and urinary 5-hydroxindoleacetic acid (5-HIAA) excretion. A positive result for 5-HIAA has a 73% sensitivity and a 98% specificity for carcinoid tumour. Serum chromogranin A is a glycoprotein secreted with other hormones by neuroendocrine tumours and is 68% sensitive and 86% specific for carcinoid tumours. New markers, such as pancreaticastatin, neurokinin A, and plasma 5-HIAA may improve the diagnostics and prognostification.

Various imaging techniques, including endoscopy, endoscopic ultrasound, and video capsule endoscopy, may be used to locate the tumour. Computed tomography (CT), magnetic resonance imaging (MRI), and diagnostic imaging using radiolabeled somatostatin analogs (Indium-111 pentetreotide [111-In pentetreotide, OctreoScan], and positron emission tomography (PET scan) using Gallium Ga-68 DOTATATE [68-Ga DOTATATE]) are the primary imaging modalities used to identify carcinoid tumours.

### Table II. Clinical manifestations carcinoid syndrome

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>Frequency</th>
<th>Description</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>85–90%</td>
<td>Long-lasting violaceous face and neck (foregut carcinoid)</td>
<td>Kallikrein, 5-HTP, Histamine, Substance P, PG</td>
</tr>
<tr>
<td>Gastrointestinal hyper-motility</td>
<td>70–80%</td>
<td>Watery, profuse. Associated nausea, vomiting</td>
<td>Gastrin, 5-HTP histamine, PG, VIP</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>15%</td>
<td>Wheezing</td>
<td>Histamine, 5-HT</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>35%</td>
<td>Progressive</td>
<td>Small bowel obstruction, ischaemia</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>30%</td>
<td>Carcinoid heart disease</td>
<td>5-HTP</td>
</tr>
<tr>
<td>Pellagra</td>
<td>5%</td>
<td>Diarrhoea, dermatitis, dementia</td>
<td>Niacin deficiency</td>
</tr>
</tbody>
</table>

S-5-HTP = 5-hydroxytryptophan
PG = prostaglandins
VIP = Vasoactive intestinal peptides

### Treatment options

Surgery is the treatment of choice for resection of primary localised tumour or for any obstructive pathology. Even in the presence of distant metastases, resection of the primary tumour and mesenteric mass is being advocated. The aim of surgical treatment for small intestinal carcinoid tumours should be the complete curative en block resection of the primary tumour and its mesenteric lymph node metastases.

### Somatostatin analogue therapy

Somatostatin is a 14-amino acid peptide that binds to somatostatin receptors expressed on the majority of carcinoid tumours. Octreotide and the long-acting analogue lanreotide bind to the somatostatin receptors inhibiting the release of vasoactive amines. A depot form of octreotide (Sandostatin LAR) is administered on a monthly basis eliminating the need for self-administered daily subcutaneous octreotide. A depot preparation of lanreotide is also available (Somatuline Depot). Overall, octreotide and lanreotide have similar efficacy in symptom control and reducing tumour markers and serotonin levels.

### Liver therapies

Complete hepatic resection of metastases is considered where feasible. Cytoreductive hepatic surgery is somewhat more controversial and may be of benefit in carefully selected patients. Here liver metastases are debulked by resection in combination with ablative therapy which may help palliate symptoms and hormonal overproduction. Liver directed ablative therapy may include bland embolisation, chemo-embolisation, or radio-embolisation. Experience with radio-embolisation using yttrium-90 (90Y)-labeled resin or glass microspheres is limited but growing. Studies suggest that this technique reduces symptoms in a significant number of patients with functioning neuroendocrine tumours.

### Other treatment modalities

- Telotristat is a new agent recently approved in the United States for use in carcinoid tumours in combination with somatostatin analogues. The mechanism of action is through inhibition of the enzyme tryptophan hydroxylase (Trp hydroxylase), the rate limiting enzyme for the conversion of tryptophan to 5-hydroxy-tryptophan (Figure 1).
Two pivotal trials, TELESTAR and TELECAST, explored the role of telotristat ethyl in the management of patients with carcinoid syndrome refractory to somatostatin analogue monotherapy. These studies found that patients with carcinoid syndrome not adequately controlled by somatostatin analogues, treatment with telotristat significantly reduced the number of bowel movements and urinary 5-hydroxyindoleacetic acid.18

- Interferon therapy has been used in refractory cases of carcinoid syndrome. In one study, 17 of 36 patients (47%) with metastatic carcinoid tumour who were treated with human leukocyte interferon had objective hormonal responses for a median duration of 34 months.19 Unfortunately interferon usage is often associated with debilitating toxicities, which can include fatigue, depression, and flu-like symptoms.

- Everolimus is a derivative of sirolimus and works similarly to sirolimus as an inhibitor of mammalian target of rapamycin (mTOR). Based on evidence from the RADIANT-4 trial, the US Food and Drug Administration approved everolimus for the treatment of adult patients with progressive, well-differentiated non-functional, neuroendocrine tumours of gastrointestinal or lung origin with unresectable, locally advanced or metastatic disease. The trial showed treatment with everolimus was associated with significant improvement in progression-free survival in patients with progressive lung or gastrointestinal neuroendocrine tumours.20

- Peptide receptor radioligand therapy — Radiolabelled somatostatin analogues (e.g. 90-Y-DOTA tyr3-octreotide, 90Y-edotreotide, or 177Lu-DOTA0,Tyr3-octreotate) can be used to deliver targeted radiation to somatostatin receptor-expressing tumours. Studies suggest response to radioligand therapy is associated with improved survival.21

### Perioperative management of patients with carcinoid syndrome

Patients with carcinoid syndrome may be presenting for surgery related to the carcinoid tumour (resection of primary or secondary mass), or for unrelated surgery. On occasion, patients may present for surgery with previously undiagnosed carcinoid disease (e.g. bowel obstruction). The primary goal is to prevent release of vasoactive mediators by avoiding factors that trigger release of these vasoactive amines. The height of catastrophe is the so-called ‘carcinoid crisis’ with resulting haemodynamic instability, hyperthermia, shock, arrhythmia, flushing, or bronchial obstruction. The introduction of octreotide and other somatostatin analogues has changed the perioperative management of carcinoid syndrome dramatically and they form the cornerstone of pharmacotherapy.

### Preoperative

Careful communication between the surgeon, endocrinologist and anaesthesiologist is required for optimal outcome. Fluid and electrolyte abnormalities, malnutrition and anaemia may need to be corrected before proceeding with surgery. Careful preoperative evaluation of the cardiovascular system is essential to delineate cardiac reserve in the face of carcinoid heart disease. Echocardiography is the most readily available technique to assess the extent of cardiac involvement. Cardiac magnetic resonance imaging has been shown to provide clear anatomic and functional information on both tricuspid and pulmonary valves in situations where adequate windows are unobtainable using echocardiography.22 High right-sided pressures secondary to pulmonary stenosis, or severe tricuspid regurgitation may lead to hepatic congestion and pulsatility predisposing to significant intraoperative blood loss during hepatic resection.

Preoperative optimisation includes pharmacotherapy which either blocks the effect of vasoactive substances, prevents the release of these substances, or a combination of both. A lack of symptoms before surgery does not preclude a potential carcinoid crisis with surgical manipulation of the carcinoid tumour during the operative procedure.

Octreotide remains the mainstay for prevention and treatment of the carcinoid crisis. There is some variation between institutions regarding dose and timing of octreotide administration. What is commonly accepted, however, is that octreotide therapy needs to be commenced prior to surgery and continued throughout the procedure with supplemental dosing based on clinical response. The half-life of octreotide is 60–90 min and can be administered subcutaneously or intravenously.23 Some authors have recommended the preoperative subcutaneous administration of 100 µg of octreotide and another 100 µg administered intravenously just before induction of anaesthesia. An intravenous octreotide infusion at the rate of 50–100 µg.h⁻¹ can be administered during surgery.24 Another regimen suggests a continuous infusion of 50 µg.h⁻¹ for 12 hours prior to surgery to reduce hormonal activity with supplemental doses on an ad hoc basis.25 It should be noted that octreotide has widespread effects, important among these are QT prolongation, bradycardia, conduction defects, abdominal cramps, nausea, and vomiting.
Other pharmacological agents that have been used in the perioperative period include corticosteroids, ketanserin, which blocks effects at 5-HT2 receptors, methysergide, and cyproheptadine, which has antiserotonin and antihistamine effects. However, strong evidence for use of these agents is somewhat lacking. Aprotonin, a serine protease inhibitor, has been used in the past to control bradykinin production and the associated flushing, with limited success. Histamine release is most likely to occur with gastric carcinoids and prophylactic administration of antihistamines may be of benefit in selected cases. Anxiolytic premedication is recommended as there are case reports of emotional stress triggering serotonin release.

**Intraoperative management**

Regional anaesthesia for intra- and postoperative analgesia in the form of a thoracic epidural for patients undergoing laparotomy is acceptable and effective for decreasing the surgical stress response which may precipitate a carcinoid crisis. This benefit should, however, be weighed against the potential exacerbation of intraoperative hypotension associated with release of vasoactive mediators during surgery.

**Monitors**

Dramatic changes in blood pressure are commonplace during surgery for carcinoid syndrome. Thus, in addition to standard monitoring, invasive monitoring is considered mandatory. In some institutions, invasive monitoring in the form of central venous access and invasive arterial blood pressure monitoring is established prior to anaesthesia with the potential of a carcinoid crisis ensuing during the induction process. Brisk bleeding may be encountered as abdominal carcinoids have a rich blood supply. Reliable large bore vascular access is appropriate. Transoesophageal echocardiography can be extremely useful especially in the presence of proven carcinoid heart disease. Non-invasive cardiac output monitors may be useful to guide fluid responsiveness through measurement of stroke volume variation as well as the ability to calculate indices such as systemic vascular resistance. Central venous pressure monitoring (CVP) is essential in cases of resection of hepatic metastases as maintenance of a low CVP has been shown to reduce intraoperative blood loss during liver resection. A carcinoid crisis may manifest initially with severe bronchospasm during the procedure and thus careful note should be taken of any unexpected changes in airway pressures.

**Induction**

The aim is for a stable, smooth induction with minimal catecholamine release and adequate depth of anaesthesia before intubation. The pharmacological agents used to obtain anaesthesia are debatable with no absolute contraindication to any particular drug; however, it would seem intuitive to avoid agents that cause histamine release such as atracurium and large boluses of morphine. Remifentanil has the advantage of titratability, ultra-short context sensitive half time and lack of histamine release and as a result has been used to good effect for patients with carcinoid syndrome. These advantages are offset by the potential for hypotension as a common side-effect.

**Vasoconstrictors**

Response to vasoconstrictors can be unpredictable as administration of catecholamines such as epinephrine and norepinephrine may trigger a carcinoid crisis thus paradoxically further lowering the blood pressure. Cautious administration of small doses of phenylephrine has, in some reports, been found to be useful. Other agents that have been used with variable success include vasopressin and angiotensin. Unfortunately these agents are not readily available in all centres.

**Carcinoid crisis**

Cutaneous flushing may be the harbinger of an impending carcinoid crisis. Hypotension tends to occur when large bulky hepatic metastases are manipulated during the surgical procedure. Surgery should cease until haemodynamic stability is attained as further manipulation of the tumour mass can exacerbate the hypotension. Boluses of octreotide form the cornerstone of management of a carcinoid crisis. Hypotension from other aetiologies such as blood loss and hypovolaemia need to be excluded and treated appropriately. In the event of bronchoconstriction, traditional agents such as beta-2 agonists may exacerbate the bronchoconstriction by triggering further release of vasoactive amines from the carcinoid tumour. Octreotide is especially useful for bronchospasm that is resistant to other treatments. Hyperglycaemia may result from serotonin release and should be managed appropriately.

**Postoperative**

Management in an intensive care environment is appropriate as further recrudescence of carcinoid syndrome may occur in cases of incomplete excision or undetected metastases. The octreotide infusion should be continued into the postoperative period. Delayed emergence, presumably as a result of high circulating levels of serotonin, has been described. 5-HT, antagonists such as ondansetron are first-line agents in the prophylaxis and treatment of perioperative nausea and vomiting. Effective postoperative analgesia is essential to ameliorate emotional and physical stress that could potentially trigger release of vasoactive amines from residual carcinoid tumour.

**Conclusion**

Patients presenting for surgery with carcinoid syndrome pose unique challenges for the anaesthetist involved. A thorough understanding of the pathophysiology of the disease process is essential for a successful outcome. Introduction of octreotide and other somatostatin analogues has revolutionised the perioperative management of this disease. Careful cardiac evaluation is critical to detect the presence and extent of carcinoid heart disease. Drugs that are traditionally used to treat intraoperative hypotension and bronchoconstriction may actually provoke further release of vasoactive substances from the tumour thus aggravating the situation. Potential for a carcinoid crisis should not be underestimated even if symptoms appear to be adequately controlled in the preoperative period.


Analgesia for thoracic surgery

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Thoracic surgery has come full circle in terms of incisions employed, returning to the small incisions with which it began in its infancy.¹ With major advances in surgical and anaesthesia techniques, medicine and technology, more complex surgery can be performed with minimally invasive incisions.¹

Thoracic incisions are indicated for a wide variety of cardiothoracic and non-cardiothoracic procedures. All anaesthetists should be able to manage anaesthesia and analgesia involving thoracic incisions.

Failure to control pain in the immediate postoperative period, along with pre-existing thoracic pain, are strong predictors of chronic post-thoracotomy pain.² Postoperative pulmonary complications can be avoided or reduced considerably by administering good analgesia.

Thoracic incisions

Thoracic incisions can be used both therapeutically (e.g. excision of pulmonary, oesophageal or mediastinal malignancies, chest trauma, spinal surgery) and diagnostically (e.g. open lung biopsy and mediastinoscopy).¹³

The choice of incision among the many that exist depends on the surgeon, balancing adequate exposure for a successful outcome with preserving chest wall function and appearance.¹ Median sternotomy and partial sternotomy allow access to midline structures. In general, nomenclature for thoracotomy incisions is determined by their relationship to the latissimus dorsi muscle which is itself considered to be lateral.¹ A standard posterolateral thoracotomy transects the latissimus dorsi muscle. An anterolateral thoracotomy transects the serratus anterior muscle.¹ The thoracotomy incision gives good exposure to the entire hemithorax including lung, oesophagus, mediastinum and cardiac structures and aorta on the left.¹

The anterolateral thoracotomy has regained popularity for use in minimally invasive cardiac and thoracic surgery, trauma front room thoracotomy for rapid access to the aorta, pericardium and other structures.¹

Muscle-sparing thoracotomy causes reduced postoperative pain with less analgesia requirements and improved shoulder girdle strength although surgical exposure may be compromised.¹

Video-assisted thoracoscopic surgery (VATS) can be performed on lungs, pleura, oesophagus and posterior and middle mediastinum.¹ Advantages of VATS include reduced pain postoperatively, better cosmesis and improved shoulder girdle function.¹ Long-term benefit in terms of pulmonary function is yet to be proven.¹ Generally, three small incisions are required: one for the camera in the seventh or eighth intercostal space and two for the operating ports in the fifth intercostal space.¹ Intercostal neuralgia usually results from pressure on the nerve adjacent to a trocar.¹

Other incisions used to access the thorax include the anterior mediastinoscopy (staging and diagnosing advanced upper-lobe lung cancers), transverse thoracosternotomy (resection of large mediastinal masses, double-lung transplantation, bilateral lung metastases, trauma resuscitation) and thoracoabdominal (thoracoabdominal aneurysms, gastro-oesophageal junction malignancies, lower thoracic and upper lumbar spine pathology) incision.¹

The rest of this article will focus on analgesia for what is the most popular thoracic incision: the thoracotomy.

Anatomy and pathophysiology of pain in thoracic surgery

The sensory afferents transmitting nociceptive stimuli after thoracotomy include⁴⁻⁵:

- skin incision and intercostal muscles (intercostal nerves T₄⁻T₆)
- chest drains (intercostal nerves T₇⁻T₈)
- mediastinal pleura, lung and mediastinal structures (vagus nerve, CN X)
- central diaphragmatic pleura (phrenic nerve, C₃⁻C₅)
- ipsilateral shoulder (brachial plexus)
- parietal pleura is innervated (intercostals and the phrenic nerves) and is pain-sensitive while the visceral pleura is sensitive mainly to stretch
• latissimus dorsi and serratus anterior muscles (thoracodorsal and long thoracic nerves from the C5 to C7 roots of the brachial plexus)

The intense pain of thoracotomy is due to muscle division, rib retraction or resection and destruction of the intercostal nerves. The posterolateral thoracotomy incision usually spans approximately six dermatomes commencing at the third dermatome posteriorly to the seventh or eighth dermatome anteriorly. Varying degrees of transection of the latissimus dorsi, serratus anterior, pectoralis major and the intercostal muscles occur. Pressure on the intercostal nerves is caused by aggressive retraction to improve exposure and may result in acute intercostal neuritis. Up to three chest drains may be required after thoracotomy and are often inserted in the eighth or ninth intercostal space which falls outside of the analgesia provided by the epidural or paravertebral block.

Other factors which contribute to pain post-thoracotomy are prolonged lateral decubitus position, non-specific shoulder pain and extreme anxiety associated with this major procedure. No single analgesic technique can inhibit ALL these pain afferents. Analgesia should thus aim to be multimodal.

Why is analgesia post-thoracotomy important?

An audit by Niraj et al confirmed that 25% of patients experience persistent moderate to severe pain at six months that severely affects quality of life in 40% of patients post-thoracotomy. Risk factors for chronic post-thoracotomy pain identified in this audit included male sex, age > 60 years, preoperative pain and acute pain postoperatively. The noxious effects of surgery interact with preexisting and concurrent pain, psychological and emotional factors as well as social environment to determine the nature, severity, frequency, and duration of chronic postsurgical pain.

Poor analgesia post-thoracotomy results in poor ventilatory mechanics with shallow breathing and impaired coughing which result in atelectasis, retention of secretions both of which result in hypoxaemia, hypercapnia and respiratory failure which are accentuated in patients with existing lung disease. The rate of these complications has decreased to around 10% with improved postoperative pain management.

Cardiovascular dysfunction can result from poor pain control as increased sympathetic tone results in increased myocardial oxygen demand, increased afterload, myocardial dysfunction and arrhythmias. The incidence of deep venous thrombosis and pulmonary embolism is higher with poor analgesia as mobilisation is delayed. Longer hospital stay with particular increase in ICU admissions has been demonstrated as a result of poor analgesia.

Post-thoracotomy chronic pain (PTCP) syndrome is a very common (incidence 30%–60%) and debilitating condition and studies suggest that aggressive treatment of acute post-thoracotomy pain may reduce the incidence.

Choice of analgesic technique

Surgical strategies for reducing post-thoracotomy pain include: non-spreading VATS procedures, muscle-sparing techniques, less rib retraction and rib preservation. Strict layered closure is essential and approximating each individual layer of muscle correctly. In addition, care should be taken to avoid over-approximation of the ribs as this adds to postoperative pain.

Factors that determine the choice of analgesia are: the anaesthetist’s preference (skill and experience), patient factors (contraindications, preferences), surgical factors (type of incision), and system factors (available equipment, monitoring, nursing support). The patient should be counselled adequately to allay anxiety and encourage compliance.

‘The ideal post-thoracotomy analgesic technique will include three classes of drugs: opioids (patient-controlled analgesia (PCA)), anti-inflammatory agents, and local anesthetics (epidural, intrathecal, paravertebral blocks, intercostal nerve blocks, cryoprobe neurolysis).

Systemic agents

Systemic opioids

These may effectively control background pain but fail to address the acute pain associated with cough or movement. The dose of opioids required to address acute pain results in sedation and hypventilation in the majority of patients with generally inadequate pain control associated with sleep disruption when opioid levels drop below the therapeutic range.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

These anti-inflammatory agents are analgesic and can ‘reduce opioid consumption more than 30% after thoracotomy and are particularly useful treating the ipsilateral shoulder pain that is often present postoperatively and is poorly controlled with epidural analgesia. NSAIDs act by reversibly inhibiting cyclooxygenase with decreased platelet function, gastric erosions, increased bronchial reactivity, and decreased renal function as side-effects.

Paracetamol

This is ‘an antipyretic/analgesic with weak cyclooxygenase inhibition and can be administered orally or rectally in doses up to 4 g/day. It is effective against shoulder pain and has a low toxicity compared with more potent cyclooxygenase-inhibiting NSAIDs.

Ketamine

‘Low-dose intramuscular ketamine (1 mg/kg) is equivalent to the same dose of meperidine and causes less respiratory depression. Low-dose intravenous infusions may be effective in patients with refractory pain or those with contraindications to more common techniques. The psychomimetic effects of ketamine are seldom seen with analgesic doses.
**Dexmedetomidine**

This is a selective adrenergic $\alpha$-receptor agonist, which has been shown to be a good adjunct for post-thoracotomy analgesia because it can significantly reduce opioid requirements when used in combination with epidural local anaesthetics. \(^4\)

*Maintenance infusion doses for analgesia in children and adults are in the range of 0.3 to 0.4 $\mu$g/kg/hr;* \(^4\) *It is associated with some hypotension, but it seems to preserve renal function.* \(^4\)

**Local anaesthetics**

**Intercostal nerve blocks**

These can be an effective adjunct to methods of post-thoracotomy analgesia. \(^4\) They can be performed percutaneously or under direct vision during thoracotomy. \(^4\) Unfortunately, the duration of analgesia is limited by the type of local anaesthetic used and repetition of the block would be needed to maintain analgesia. \(^4\) Continuous infusions through indwelling intercostal catheters are difficult to position reliably percutaneously. \(^4\) Nerve blocks are useful supplements for the pain associated with the multiple small port incisions and chest drains following VATS. \(^4\)

There is a risk of intravascular injection, which one should be meticulous to avoid. The block should be placed near the posterior axillary line to ensure cover of the lateral cutaneous branch of the intercostal nerve. \(^4\) Total bupivacaine dose for a single session of blocks should not exceed 1 mg/kg (e.g. for a 75-kg patient: 3 mL bupivacaine 0.5% with epinephrine 1:200,000 at each of five levels). \(^4\)

**Interpleural analgesia**

Local anaesthetics placed in the interpleural space produce a multilevel intercostal block. \(^4\) The analgesia is extremely dependent on patient position, infusion volume, chest drains, and the type of surgery. \(^4\) This technique is unreliable in the analgesia it offers. \(^4\)

**Cryoprobe neurolysis**

*Application of a $-60 \, ^\circ\text{C}$ probe to the exposed intercostal nerves intraoperatively produces an intercostal block that can persist for up to six months. This can be moderately efficient to decrease postoperative pain but is associated with an incidence of chronic neuralgia that has led many centres to abandon the technique. Transcutaneous electrical nerve stimulation (TENS) may be useful in mild to moderate pain but is ineffective when pain is severe.* \(^4\)

**Thoracic epidural analgesia (TEA)**

TEA is considered by many to be the gold standard for analgesia following post-thoracic and upper abdominal surgery. \(^5,9\) The catheter is usually sited at the midpoint of the dermatomal distribution of the skin incision. \(^5\) Although lumbar epidural catheters have been utilised, TEA is superior due to synergy achieved by using local anaesthetics and opioids for neuraxial analgesia. \(^5\)

Post-thoracotomy, TEA reduces splinting, dynamic pain scores and results in improved mucociliary clearance which all add to improved postoperative respiratory mechanics. \(^4,8\) Thus, the likelihood of postoperative pulmonary complications occurring, especially in patients with poor respiratory reserve, is reduced. \(^8\) Better compliance to physiotherapy and reduced ICU and hospital are additional benefits. \(^8\)

The majority of thoracotomies in the USA receive TEA at between T3 and T8 with infusions of bupivacaine and fentanyl or hydromorphone. \(^4\) Combinations of local anesthetic and opioids provide better epidural analgesia at lower doses than either drug alone. \(^4\) Synergy exists between opioids and local anaesthetics to produce segmental epidural analgesia: local anaesthetic seems to facilitate entry of the opioid from the epidural space into the cerebrospinal fluid. \(^4\) Bolus techniques are more likely to result in haemodynamic and respiratory instability than infusions which have been used safely in postoperative wards in some institutions. \(^4\) Epidural catheters allow for a wide spread of local anaesthetic with a single injection point, thus eliminating the need for multiple punctures as with PVBs. \(^4\) A smaller volume of local anaesthetic is required to produce a good block compared with PVBs. \(^8\) The placement and use of TEA prior to the start of surgery has the added benefit of allowing pre-emptive analgesia which is lost by placing the PVB after the surgical incision. \(^8\)

The doses of bupivacaine used for TEA do not seem to cause significant reduction in lung mechanics or increase in airway resistance in patients with severe emphysema. \(^4\) Increased FRC has been demonstrated in healthy volunteers administered a thoracic level epidural, presumably due to an increase in thoracic gas volume caused by a fall in the resting level of the diaphragm without a fall in tidal volume. \(^4\)

The highly lipid-soluble agents (e.g. fentanyl, sufentanil) are associated with narrow dermatomal spread, rapid onset, and low incidence of pruritus/nausea and can be potentiated by epinephrine. However, these lipid-soluble agents have significant absorption and systemic effects when used as epidural infusions. For incisions that cover many dermatomes (e.g. sternotomy) or for procedures that have combined abdominal and thoracic incisions (e.g. oesophagectomy) the hydrophilic opioids (e.g. morphine, hydromorphone) are preferable. \(^4\)

The use of TEA reduces post-thoracotomy cardiovascular (supraventricular tachy-arrhythmias) complications by blunting the stress response to surgery, thus reducing sympathetic outflow which results in coronary vasodilation. \(^8\)

In inexperienced hands, the risk of neurological injury and dural puncture when placing TEA is significant because the anatomy is different and difficult. \(^8\) The difficulty in placing thoracic epidurals has been decreased by the use of the paramedian approach in the midthoracic levels. \(^4\) Indeed, TEA may be easier to teach as the loss of resistance that identifies the space is easier to perceive and reproduce as is placement of the catheter compared to paravertebral blocks. \(^8\)

The rate of failure of the block ranges between 1 and 30% compared to 6.8 to 10% for PVBs and is largely dependent on the technique used and the experience of the individual placing the block. \(^8\)
Paravertebral blocks

Paravertebral blocks (PVB) have increased in popularity in recent years. The paravertebral space lies deep to the endothoracic fascia that the intercostal nerve traverses as it passes from the intervertebral foramen en route to the intercostal space. It is bordered anteriorly and laterally by the parietal pleura, posteriorly by the superior costotransverse ligament and medially by the intervertebral foramen as the spinal nerves emerge from the spinal column.

The thoracic PVB produces sensory and sympathetic block of multiple thoracic dermatomes unilaterally or bilaterally (with low likelihood of epidural spread) allowing for more specific analgesia and fewer side-effects. They can be performed using landmark, nerve stimulator, ultrasound-guided techniques or under direct vision intraoperatively.

Performed correctly, continuous PVBs can provide good analgesia for thoracotomy which is as effective as continuous TEA. Continuous paravertebral block has been found to be as effective as thoracic epidural infusion for post-thoracotomy pain.

Thoracic PVBs have been purported to have fewer side-effects when compared to TEA. The unilateral nature may explain better pulmonary function with greater peak expiratory flow rates, higher oxygen saturations, reduced infections and less hypoventilation. Studies have shown reduced stress response, nausea and vomiting and reduced hypotension with PVB. There is a risk of pneumothorax which is largely circumvented by the placement of an ipsilateral chest drain at the end of surgery. The risk of serious neurological injury is reduced presumably because of distance from the epidural space and spinal cord.

‘Studies comparing paravertebral versus thoracic epidural analgesia for thoracotomies have suggested the following advantages for paravertebral blockade: comparable analgesia, fewer failed blocks (perhaps due to placement under direct vision), decreased risk of neuraxial hematoma, and less hypotension, nausea, or urinary retention.’

A significant disadvantage of PVB is that ‘a single-level PVB may have unreliable and limited analgesic coverage that only spans 2 to 4 dermatomes, thereby requiring multiple injections.’

‘The American Society of Regional Anesthesia and Pain Medicine advises against the use of deep and plexus blocks including PVB in patients on antithrombotic or thrombolytic therapy.’

New frontiers?

Although TEA and thoracic PVB are considered the gold standard in managing post-thoracotomy pain, they are not without complications, not least of which is a significant failure rate of 15% for TEA and poor coverage of the chest-tube inserting sites. The serratus anterior plane block is a possible addition to traditional regional analgesia, while the continuous erector spinae plane block is a possible alternative.

The serratus anterior plane (SAP) block

This interfascial plane block is a novel technique and may be considered to be the transversus abdominis plane (TAP) block of the chest wall. To perform the SAP block, local anaesthetic solution is injected, under ultrasound guidance, into either the facial plane superficial or deep to the serratus anterior muscle. Thus the lateral cutaneous branches of the intercostal nerves are blocked as they course through, prior to dividing into the anterior and posterior branches supplying sensation to most of the chest wall. Effective blockade of the lateral branches of intercostal nerves T2 to T9 has been demonstrated in healthy volunteers.

The posterior primary rami, the anterior cutaneous branches or the intercostal nerves (near the sternum) and the supraclavicular nerves (immediately below the clavicle) may not be covered by this block.

Haemodynamic stability is maintained because no autonomic block occurs with the SAPB as compared to TEA and PVB. The SAP block has been used successfully to provide analgesia post-thoracotomy, rib fracture, thoracoscopy, shoulder surgery, and breast surgery. Chu et al described a series of three patients in whom SAP block was used together with multilevel continuous ultrasound-guided thoracic PVB for analgesia for chest tube pain not covered by thoracic PVB with great results.

Chest drain-related pain not relieved by thoracic PVB, TEA or selective intercostal nerve blocks is a common problem following thoracic surgery. A possible explanation is ‘unblocked nociceptive signals from the long thoracic nerve (LTN), the phrenic nerve, the thoracodorsal nerve, the vagus nerve, and incompletely blocked intercostal nerves.’ The SAP block is not equivalent to thoracic PVB, TEA or intercostal nerve blocks but complements these by blocking only the lateral cutaneous branches of the intercostal nerves and offering a solution to chest drain related pain.

In addition to the absence of autonomic blockade which results in haemodynamic stability, the SAP block eliminates the risk of pleural puncture and serious injury to the spinal cord. In addition, the anatomy on ultrasound is simple to identify, with shallow needle placement allowing for easy block administration.

The analgesia provided by the SAP block has been found to be comparable to TEA for acute post-thoracotomy pain by Khalil et al.

Continuous erector spinae plane (ESP) block

Forero et al have used the ultrasound guided ESP block to manage chronic thoracic neuropathic pain, acute surgical pain and as rescue analgesia after failed thoracic epidural post-thoracotomy.

When performing the ESP block, local anaesthetic is injected into the tissue plane deep to erector spinae muscle but superficial to the transverse processes and inter-transverse connective tissues. This local anaesthetic penetrates anteriorly to block the spinal nerves. Due to the confines of the erector spinae tissue plane,
extensive craniocaudal spread of local anaesthetic is promoted, resulting in good analgesia.6

This block is simple to perform using ultrasound, provides extensive analgesia from a single injection and poses reduced risk of pleural puncture and epidural spread.6 Safety is enhanced by the absence of neural and vascular structures within the erector spinae plane.6

Caution should still be exercised in patients with coagulopathy.6 Further research is being conducted to establish efficacy and optimal dosing for both single-shot and continuous blocks.6

Conclusion

Thoracic incisions are indicated for a wide variety of cardiothoracic and non-cardiothoracic procedures. The strategy for postoperative analgesia requires a multimodal approach with regional techniques at the forefront.

References

Extracorporeal Membrane Oxygenation (ECMO)

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This is a review of the underlying basic concepts of cardiopulmonary bypass and mini-cardiopulmonary bypass, with a focus on the complications related to cardiopulmonary bypass and whether these complications can be reduced with the use of mini-bypass techniques.

Keywords: conventional cardiopulmonary bypass, mini-cardiopulmonary bypass, comparison, complications

Extracorporeal membrane oxygenation (ECMO) is a form of cardiopulmonary bypass. It is an artificial means of supplying oxygen, removing CO₂ and/or providing cardiac output. Due to significant advancements in intensive care, perfusion technology, anticoagulation, circuit, pump and membrane engineering, modern ECMO is considered to be relatively safe and easy to implement. However, ECMO for respiratory disease still carries with it a high mortality risk (more than 50%) and therefore in most circumstances it is indicated only if the current respiratory disease process has a more than 80% mortality risk. There is sparse literature on the use of ECMO in the non-cardiac theatre, but it has also been used with success electively and emergently in various situations. It is important to appreciate the current evidence-based indications and guidelines for the use of ECMO, the basic ECMO circuit, and finally the anaesthetic considerations regarding procedures related to, or while on, ECMO.

Indications for the use of ECMO in adults

The results of the CESAR trial and the use of ECMO during the H1N1 epidemic in 2009 have stimulated much progress in the development of ECMO research programmes, excellence centres and registries worldwide. However, there is controversy regarding the indications for ECMO in adult patients. Table I summarises the current Extracorporeal Life Support Organisation (ELSO) recommended indications for ECMO in the adult patient population.

Indications for the use of ECMO in paediatrics

ECMO use in the paediatric population for various indications has seemingly resulted in greater survival than in adult patients. According to the ELSO registry, 83% of neonates with a predicted mortality of > 80% survived with the use of ECMO. Infants with meconium aspiration had a 93% survival rate while patients with Table I. Current ELSO recommended indications and contraindications for ECMO in adult patients

<table>
<thead>
<tr>
<th>Organ failure</th>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>Respiratory failure</td>
<td>• Hypoxic respiratory failure with:</td>
<td>• (All relative)</td>
</tr>
<tr>
<td></td>
<td>▫ CONSIDER WHEN: PaO₂/FiO₂ &lt; 150 on FiO₂ &gt; 90% or Murray score of 2–3</td>
<td>▫ On mechanical ventilation with high settings (FiO₂ &gt; 90%, Pplat &gt; 30 cmH₂O) for 7 days or more</td>
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<tr>
<td></td>
<td>▫ INDICATED WHEN: PaO₂/FiO₂ &lt; 100 on FiO₂ &gt; 90% or Murray score of 3–4</td>
<td>▫ Severe neutropenia</td>
</tr>
<tr>
<td></td>
<td>▫ Despite optimal care &gt; 6 hours</td>
<td>▫ Recent/expanding CNS haemorrhage</td>
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<td></td>
<td>▫ CO₂ retention with Pplat &gt; 30 cmH₂O</td>
<td>▫ Non-recoverable co-morbidity (major CNS damage/terminal malignancy)</td>
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<tr>
<td></td>
<td>▫ Severe air leak</td>
<td>▫ Advanced age</td>
</tr>
<tr>
<td></td>
<td>▫ Need for intubation in patient on a lung transplant list</td>
<td></td>
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<tr>
<td></td>
<td>▫ Immediate cardiac/respiratory collapse (PE/blocked airway, unresponsive to optimal care)</td>
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<tr>
<td>Cardiac failure</td>
<td>• Cardiogenic shock</td>
<td>• Absolute</td>
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<tr>
<td></td>
<td>▫ acute MI, myocarditis, peripartum CMO, decompensated chronic heart failure, post cardiotomy shock</td>
<td>▫ Unrecoverable heart, not a candidate for transplant</td>
</tr>
<tr>
<td></td>
<td>▫ ECMO seen as a bridge to:</td>
<td>▫ Advanced age</td>
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<tr>
<td></td>
<td>▫ Recovery</td>
<td>▫ Chronic organ dysfunction (emphysema, CKD, cirrhosis)</td>
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<tr>
<td></td>
<td>▫ Transplant</td>
<td>▫ Prolonged CPR without adequate</td>
</tr>
<tr>
<td></td>
<td>▫ Implantable circulatory support</td>
<td>▫ Poor compliance with cardiology management</td>
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<tr>
<td></td>
<td></td>
<td>• Relative</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ Contraindication for anticoagulation, advanced age, obesity</td>
</tr>
</tbody>
</table>
congenital diaphragmatic hernia had the lowest survival rate at 62%. The reason for the apparent survival benefit over a wide range of indications and pathologies in paediatrics is largely unknown. However, it may be that ECMO is difficult to study if compared against conventional support and that many of the older adult trials were designed with ECMO as a “rescue therapy”, hence selecting out patients that would have a poor outcome in any case.

Nevertheless, there indications for ECMO in the paediatric population are considered to be supported by more substantial evidence than the adult population. Table II lists the current ELSO-recommended indications for ECMO in paediatric patients.

South African recommendations and indications for ECMO
ECMO is a costly modality, and in developing countries such as South Africa, is considered a limited resource. However, published South African recommendations largely mirror international ELSO guidelines. Table III lists the current recommendations and indications for ECMO from a South African perspective as delineated by Richards.

Extracorporeal cardiopulmonary resuscitation (E-CPR)
Initiation of ECMO during cardiopulmonary resuscitation (E-CPR) has been receiving significant attention in the recent literature.

---

### Table II. ELSO-recommended indications for ECMO in paediatric patients (Current August, 2016)\(^9\)\(^11\)

<table>
<thead>
<tr>
<th>Organ failure</th>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory failure</strong></td>
<td>Neonates</td>
<td>• Severe respiratory failure, refractory to medical management with a potentially reversible aetiology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Indicated by</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ Oxygenation index (O.I) &gt; 40 for &gt; 4 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ O.I &gt; 20 with lack of improvement (&gt; 24 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ Severe hypoxic respiratory failure with acute decompensation (Pao₂ &lt; 40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ Progressive respiratory failure and/or pulmonary hypertension with evidence of RV dysfunction or continued high inotrope requirements</td>
</tr>
<tr>
<td></td>
<td>Infants (≥ 30 days) to children (&lt; 18 years)</td>
<td>• Potentially reversible respiratory failure within the first 7 days</td>
</tr>
<tr>
<td></td>
<td>Cardiac Failure</td>
<td>Neonates to children (&lt; 18 years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Early postoperative cardiac failure (unable to come off bypass)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In ICU: refractory shock (to vasopressors/inotropes)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiac arrest from any cause (with response to CPR, with no return of circulation &gt; 5 mins)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Myocardial failure unrelated to surgery: e.g. myocarditis, cardiomyopathy, drug ingestions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Elective support for high risk surgical procedures</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>▫ Primary pulmonary hypertension</td>
</tr>
</tbody>
</table>

### Table III. South African recommendations for ECMO (Adapted from Richards)\(^12\)

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Indications – respiratory failure</th>
<th>Indications – cardiac failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Non availability of trained multidisciplinary team with access to a specialised intensive care, cardiothoracic and vascular surgical services.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pulmonary oedema from myocardial dysfunction, unless bridging to transplant or acute myocarditis from which recovery is expected.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Exacerbations of COPD with respiratory failure.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Multiple organ failure from severe sepsis or SIRS.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pneumocystis jiroveci pneumonia requiring ventilation.</td>
<td></td>
<td></td>
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<tr>
<td>• Severe co-morbid illness that will impact significantly on life expectancy (e.g. incurable malignant disease or liver failure).</td>
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<tr>
<td>• Inadequate recruitment and/or diuresis/dialysis in the presence of fluid overload.</td>
<td></td>
<td></td>
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<tr>
<td>• Any potentially irreversible condition.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Technical difficulty associated with the procedure.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Where systemic anticoagulation is contraindicated.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Immunosuppression not likely to recover rapidly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Patients mechanically ventilated for &gt; 7 days.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Age &gt; 75 years.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Primary ARDS with refractory hypoxaemia: e.g. severe pneumonia (particularly viral, but any pneumonia without multiple organ failure), pulmonary contusion, gas inhalation, aspiration, smoke inhalation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Status asthmaticus or reversible airway obstruction not able to be ventilated conventionally or rapidly ameliorated.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pulmonary embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Post cardiac surgery failure to come off cardiopulmonary bypass.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bridge to cardiac transplantation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Acute myocarditis.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pulmonary hypertension (after pulmonary endarterectomy or following surgery on congenital heart defects).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
According to the most recent ELSO guidelines on the subject—"The American Heart Association guidelines for CPR recommend the consideration of ECMO to aid CPR in patients who have an easily reversible event and have had excellent CPR."

All contraindications to ECMO use in general apply to its use in the case of E-CPR. In addition, unsuccessful CPR with no return of spontaneous circulation or poor perfusion (due to poor CPR) for longer than 30 minutes is considered a contraindication.

It is recommended that patients receiving E-CPR should also be cooled for 48–72 hours to augment neurological protection.13

**Types of ECMO support and ECMO circuits**

ECMO circuits contain the following essential components (demonstrated in Figure 1):

- Drainage cannula
- Return cannula
- Pump (usually centrifugal)
- Membrane oxygenator (with an oxygen/air blend gas input)
- Heat exchanger (to manage temperature)
- Conduit tubing – can be heparin bonded

There are two basic types of ECMO support:

- **Veno-arterial (VA):** Typically suited for respiratory and circulatory support. Examples where VA-ECMO would be employed are post-cardiac surgery, septic shock, massive pulmonary embolus, post-CPR or in patients with cardiomyopathy. Central drainage and return cannulae can be sited in the above situations through a sternotomy, in the right atrium/SVC/IVC and aorta respectively. However, central cannulation is usually reserved for post-cardiac surgery ECMO due to the ease of access. Peripheral cannulae are sited in most other instances, with the drainage being from the internal jugular or femoral vein and the return cannula placed in the femoral or carotid arteries (neurologically, infants tolerate ligation of one carotid artery more than older children).

- **Veno-venous (VV):** This is usually used for sole respiratory support. Examples where VV-ECMO would be used are: meconium aspiration syndrome, drowning, hyaline membrane disease, viral pneumonias or chemical pneumonitis. Peripheral cannulae are sited for VV-ECMO, with the drainage and return cannulae being placed in the internal jugular or femoral vein. A dual-lumen single cannulae is now most commonly placed for VV ECMO. This is a single cannula that is percutaneously placed in the right internal jugular vein, with the distal tip in the IVC (the drainage orifice) and the return orifice facing the tricuspid valve.

Although VA ECMO restores cardiac output as the pump is started, VV-ECMO will restore RV function in cases of acute cor pulmonale secondary to acute hypoxaemic pulmonary hypertension (e.g. in ARDS). This in turn will improve left ventricular cardiac output.

**When to remove a patient from ECMO**

Once there are indications that lung or heart functioning is improving (e.g. improving lung compliance or reduction in inotrope requirements), ECMO flow or oxygenator FiO₂ will be decreased. If the cardiorespiratory function remains stable...
off ECMO support, ECMO will be resumed and a planned discontinuation of ECMO will ensue.

Anaesthetic considerations

The anaesthesiologist is part of a multidisciplinary team managing a patient planned for, or on, ECMO. Like all other members of the team, the anaesthesiologist responsible must be appropriately trained and experienced to deal with patients on ECMO. It has been shown that the best outcomes for patients on ECMO are achieved if every member of the team has the necessary training or experience to manage this highly specialised group of patients. There are local and international courses and training programmes available to this end.

The anaesthesiologist may be called upon to: 1) anaesthetise the patient for initiation of ECMO; 2) transport a patient already on ECMO; 3) anaesthetise the patient for a procedure while on ECMO; or 4) anaesthesia for liberation from ECMO and vessel repair after decannulation. It is not within the scope of this article to discuss all of these scenarios in detail. However, a discussion on anaesthesia for ECMO initiation follows.

General anaesthetic considerations for placing patients onto ECMO

Patients requiring ECMO have severe cardiac and/or respiratory failure and are already on significant cardiorespiratory support. These patients are usually in the intensive care units (ICUs) of hospitals and are undergoing multiple mechanical and pharmacological support modalities.

The degree of physiological derangement and the risk of transport are the major concerns facing the anaesthetist when dealing with such patients.

Patients with respiratory disease presented for ECMO initiation have very little respiratory reserve with most patients being on very high ventilator settings. Non-conventional ventilator modes such as adjustable pressure release ventilation (APRV) or high frequency oscillatory ventilation (HFOV) are commonly used. Similarly, patients with cardiac disease presented for ECMO initiation are on high-dose inopressor infusions, and some centres still use an intraaortic balloon pump as an adjunctive measure in these cases. It must be remembered that severe respiratory disease can cause acute or chronic right ventricular failure, and these patients also often require high-dose inopressor infusions. Severe organ failure of this nature requiring high levels of support indicates that transient disconnection from the ventilator or from an inopressor infusion may result in rapid deterioration requiring emergent resuscitation. Therefore considerable attention needs to be given to the careful handling of tubing, cabling, power plugs, securing devices and straps to ensure that any accidental disconnection does not occur.

It is evident that transport of the patient to theatre will carry a high risk of disconnection and subsequent failure of organ support. It is this author’s opinion that these patients are best initiated on ECMO in the ICU. However, any discussion with regards to site of ECMO initiation must be had with the perfusionist and cannulating physician (usually a cardiothoracic surgeon). The perfusionist may have space or equipment issues in the ICU which would be less of a problem in theatre, such as the availability of various pieces of perfusion equipment and additional gas supply points. The surgeon may prefer theatre in cases of difficult vessel anatomy where a percutaneous approach is not possible; or in cases where on-table fluoroscopy is required. In these cases ECMO placement may be quicker and easier in theatre, with a lower rate of potential complications. Indeed, the anaesthetist may prefer theatre as it is a more comfortable and familiar environment with specialised monitoring such as capnography readily available. Once all relevant members of the multidisciplinary team are consulted, these factors must be balanced against the risk of moving the patient from ICU to theatre.

Preoperative assessment and optimisation must be carried out rapidly, and there are often only a few hours in which to do this. Standard history, often available from the ICU notes as well as family members of the patient, and systemic examination must be carried out. Particular attention needs to be given to examining existing venous and arterial access; doses of cardio-active drug infusions; ventilator settings; size and depth of endotracheal tube; depth of sedation and doses of sedative or analgesic infusions if present. A detailed neurological and cardiorespiratory examination needs to be carried out and documented. Large bore intravenous access is recommended, as sudden haemorrhage is a significant possibility.

Special investigations should be focused toward optimising coagulation parameters and cardiorespiratory support. Full blood count, international normalised ratio (INR) and thromboelastography (TEG) will assist in directing the appropriate ordering and administration of blood and blood products perioperatively. An arterial blood gas allows the calculation of the oxygenation index, and rapid evaluation of electrolyte and acid-base derangements.

A mobile chest x-ray can confirm the position of the endotracheal tube and central venous lines. In addition an x-ray can exclude large pleural effusions or pneumothoraces.

Echocardiography is especially useful, as both cardiac function and anatomy can be rapidly assessed. Of particular importance is the exclusion of congenital shunts, abnormal valvular function and pericardial collections. It is evident that patients with cardiogenic shock requiring ECMO will have depressed biventricular function. However, patients with respiratory disease frequently have high pulmonary artery pressures with markedly depressed right ventricular function.

The echocardiography probe can also be used to quickly evaluate for the presence of alveolar collapse, consolidation, pleural effusions and pneumothorax. A linear ultrasound probe can be used to mark the surface anatomy of large vessels, such as the internal jugular vein or carotid artery, to assist the cannulating physician.

While the ECMO circuit is being prepared and primed by the perfusion team and other preparation measures are being taken, coagulation parameters, cardiorespiratory function, electrolyte and acid-base status should be optimised as much as possible in the short time available. Unnecessary equipment should
be removed from the patient's cubicle and emergency drugs, airway and vascular access equipment should be prepared and checked. In addition to routine ECG, non-invasive blood pressure and oxygen saturation monitoring, invasive blood pressure measurement is essential. Temperature monitoring and capnography are very helpful if available. Near-infrared spectroscopy cerebral perfusion monitoring should be employed especially if carotid artery cannulation is being performed. Occasionally the patient would need to be moved to a theatre bed brought into the ICU. This would usually be to facilitate fluoroscopy. Once again, great care needs to be taken to avoid life-threatening disconnections during patient movement.

Induction of anaesthesia may not be necessary, as these patients are often already receiving infusions of sedative and analgesic agents. Most commonly combinations of ketamine, midazolam, propofol or fentanyl are employed. Small boluses or adjustments of infusion rates of these drugs should be used to maintain anaesthesia titrated against haemodynamic stability. Neuromuscular blockade, with boluses or infusions of intermediate-acting drugs, is often necessary to ensure that optimal ventilation and surgical conditions are maintained. If in theatre, volatile anaesthesia should be avoided due to its depressant effects on cardiovascular function and hypoxic pulmonary vasoconstriction. It is essential to note that various pharmacokinetic and pharmacodynamic alterations will influence drug dosing, and a slow titration strategy should be employed.

After the endotracheal tube is properly secured, the patient is usually placed in a slight anti-Trendelenburg position with a pillow or bag under the shoulders, for internal jugular vein cannulation. The correct size and depth of the cannulae will be decided upon by the surgeon.

Heparin should be administered as a bolus 2–3 minutes prior to cannulation at a dose of between 75 to 100 IU/kg. An activated clotting time (ACT) and activated partial thromboplastin time (aPTT) should be performed prior to and after heparin administration. A heparin infusion should be commenced within 60–90 minutes at a rate of 25–50 IU/kg/hour. ACT for cannulation should be in the range of 250–300 seconds, and for maintenance should be in the range of 180–250 seconds.

Once cannulation is performed, the ECMO circuit will be connected and pump blood flow will be commenced. ECMO pump flow should be set at 100–150 ml/kg/minute. FIO2 of 100% should be set on the membrane oxygenator oxygen flowmeter and the gas flow or sweep should be set equal to the ECMO pump flow rate. The ECMO pump flow rate will be adjusted to perfusion parameters such as serum lactate, and the gas flow rate will be adjusted to PaCO2 during the course of the ECMO run.

Significant haemodynamic changes can occur during the period immediately after cannulation. Prior to cannulation the patient may be on high doses of inopressor agents. During cannulation, blood pressures may fall due to acute haemorrhage. This can be treated with a rapid bolus of isotonic crystalloid or blood. Immediately on initiation of ECMO, mean arterial pressures increase significantly requiring a cessation or marked reduction of inopressor support. During VV-ECMO, this is most likely due to improved oxygen delivery to the myocardium and reduced pulmonary vascular resistance. In the case of VA-ECMO, myocardial recovery is not expected to be that rapid, and it is most likely due to a direct increase in intra-aortic pressure from the arterial return cannula. Inotropic agents should be stopped during VA-ECMO to reduce myocardial strain.

On exposure of the patient's circulation to the artificial plastic tubing and membrane, a release of inflammatory mediators occurs. The resultant vasodilation and drop in systemic vascular resistance causes a drop in circulating effective blood volume and preload. Mean arterial pressures fall as a consequence. This phenomenon can occur within 15–30 minutes of initiation of ECMO. Volume should be replaced with blood to an Hb of 10 g/dl, or isotonic crystalloid. Vasopressor agents should be considered to reduce the potential for fluid overload. ECMO circuit markers of an increased volume requirement include “shuddering” vibration of the circuit; a fall in pump flow rate despite constant revolutions per minute; and a fall in pre-oxygenator circuit pressures.

Echocardiography can guide haemodynamic management after ECMO institution. Important potential complications to exclude after ECMO initiation are pericardial tamponade, left ventricular distention and improper cannulae placement.

Once on ECMO, ventilation should be kept on lung protective settings. The following settings are recommended: PEEP between 8–10 cmH2O; tidal volume of 4–6 ml/kg; driving pressure (plateau minus PEEP) less than 15 cmH2O; and FIO2 under 40%.

On initiation of ECMO, exposure of blood to ambient temperature via the circuit tubing and oxygenator can cause a decrease in body temperature. In neonates and children, this is especially significant, as the proportion of blood volume exposed to ambient temperature at any one time is larger than adults. A fall in body temperature can cause life-threatening arrhythmias or coagulation abnormalities. To avoid this problem, it is recommended that a water heat exchanger is utilised routinely on the circuit. Other conventional means of temperature management should also be considered, for example, convective warm air blankets.

Further intensive care management of the patient should be led by an intensivist experienced in the management of patients on ECMO.

Conclusion

ECMO is an organ support modality becoming increasingly commonplace in the management of cardiorespiratory failure. The anaesthetist plays an important role as part of the multidisciplinary team involved in the management of patients for ECMO initiation, on ECMO or for liberation from ECMO. These patients have significantly deranged physiological changes and are heavily dependent on organ support modalities. Anaesthetists managing such cases need to be appropriately trained and experienced in order deal with the challenges posed in these scenarios.
References:


Anaesthetic considerations for inhaled and ingested foreign bodies in children: What? Where? When?

A Z Bhettay

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Introduction

Young children are naturally curious and learn by exploration, often putting objects into their mouths and other orifices. Toddlers lack the neuro-motor coordination for proper swallowing, and the molars necessary to grind food boluses into more innocuous pieces. Additionally, they tend to move around while eating. These factors render them vulnerable to aspiration of food particles.1 Data from local studies report that foreign body (FB) ingestion is the fifth most common cause for admission to paediatric trauma units.2 Asphyxiation due to an inhaled FB lodged in the tracheobronchial tree remains a leading cause of death in children under four years of age.3

Epidemiological data

In the absence of neurodevelopmental delay, most children are under the age of four, with a peak incidence between 1–2 years. Poverty, overcrowding, number of children in the household, young maternal age, low maternal education status and single parent households, all conditions that abound in certain strata within our society, are associated with greater risk.4

Typology of FBs

Generally, objects may be organic or non-organic (metal or non-metal). Complications arise from objects causing mechanical obstruction with or without pressure necrosis, sharp objects causing internal penetrating trauma, and corrosive objects causing mucosal injury and perforation with leakage of contents and potentially catastrophic infection. Organic materials, nuts especially, cause more chemical inflammation. In Africa, the coin is the most commonly ingested object. Round objects are more dangerous as they can cause complete obstruction. The most dangerous ingested objects are lithium button batteries.

Anaesthetic considerations for removal of inhaled foreign bodies

Preoperative

History and examination

The presentation is largely dependent on the type of FB, where it is located, and time elapsed since the incident. Children may be asymptomatic and completely comfortable, or present in extremis with imminent respiratory arrest. Up to 45% of patients may have no findings on clinical examination.5 The suggestion is to adopt a ‘What? Where? When?’ approach.

What? In the younger age group and in the neurodevelopmentally delayed, the most commonly aspirated or ingested materials are food particles. In older children, non-organic matter is more prevalent.

Where? There are multiple potential sites of impaction (see Figure 1).
Objects lodged in the larynx or trachea are usually large and bulky, and can cause significant airway obstruction. Fortunately, they are far less common. Occasionally objects are thin and angular, and can then be missed resulting in diagnostic delay. The mortality for aspirated FBs in the upper airways remains high at around 45%, and even those that survive have a 30% chance of developing hypoxic encephalopathy. A small number of organic FBs fragment and lodge in different parts of the airway.

<table>
<thead>
<tr>
<th>Location</th>
<th>% (rounded off)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larynx</td>
<td>3</td>
</tr>
<tr>
<td>Trachea + carina</td>
<td>13</td>
</tr>
<tr>
<td>Right lung (total)</td>
<td>60</td>
</tr>
<tr>
<td>Main bronchus</td>
<td>52</td>
</tr>
<tr>
<td>Lower lobe bronchus</td>
<td>6</td>
</tr>
<tr>
<td>Middle lobe bronchus</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Left lung (total)</td>
<td>23</td>
</tr>
<tr>
<td>Main bronchus</td>
<td>18</td>
</tr>
<tr>
<td>Lower lobe bronchus</td>
<td>5</td>
</tr>
<tr>
<td>Bilateral</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 2. Location of aspirated foreign bodies in children. (Reproduced with permission. Van As, et al.)

Most aspirated FBs lodge in the right bronchial tree, causing obstruction (see Figure 2).

There are four types of bronchial obstruction that may ensue:

- Bypass-valve effect – partial obstruction occurs during inspiration and exhalation. The chest radiograph (CXR) is usually normal.
- Check-valve effect – obstruction occurs on exhalation. The CXR may show hyperinflation or emphysema of the ipsilateral lung.
- Ball-valve effect – partial obstruction by object which intermittently prolapses into and obstructs the bronchus.
- Stop-valve effect – complete bronchial obstruction with no movement of air. This leads to segmental collapse of the distal lung.

Symptoms vary considerably depending on the location of the FB.

<table>
<thead>
<tr>
<th>Location</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larynx + trachea</td>
<td>Acute airway distress, hoarseness, stridor,</td>
</tr>
<tr>
<td></td>
<td>dyspnoea</td>
</tr>
<tr>
<td>Bronchi</td>
<td>Cough, wheeze, haemoptysis, dyspnoea,</td>
</tr>
<tr>
<td></td>
<td>respiratory distress</td>
</tr>
<tr>
<td>Lower airway</td>
<td>Usually asymptomatic unless secondary infection</td>
</tr>
</tbody>
</table>

**When?** Unless acute asphyxiation is caused by a large object lodged in the upper airway, which results in urgent presentation, patients can present late. If the delay is significant, morbidity and lung disease may be present. Recurring pneumonia, not responding to conventional antibiotic therapies may be elicited on history. Thirty percent of cases are misdiagnosed as infective, as children present with fever, cough and other signs and symptoms suggestive of pneumonia. Other symptoms may be non-specific and include hoarseness, dyspnoea, stridor, croupy cough, haemoptysis, wheezing or drooling.

The incidence and severity of complications is directly proportional to the chronicity of the retained FB. Bronchitis, tracheitis, distal atelectasis and pneumonia occur commonly. Chronic or recurrent infection can lead to bronchiectasis. Chronic obstruction can lead to localised emphysema. Prolonged inflammation caused by the presence of a FB can cause granulomatous tissue formation, possibly requiring further intervention.

**Special investigations**

- CXR – posteroanterior (PA) and lateral. Although only 10–15% of aspirated FBs are radio-opaque, the CXR may show secondary pathology. It is normal in 30% of patients.
- If a laryngotracheal FB is suspected, PA/lateral neck radiograph may reveal subglottic swelling and laryngeal stenosis, especially if present for > 24 hours.
- High resolution spiral computerised tomography (CT) can be considered in stable patients.
- Virtual bronchoscopy is a new imaging modality that uses reconfigured axial images obtained during CT, generating an endoscopic perspective of the trachea and bronchi.

There is some controversy in the literature as to whether a negative result with CT/virtual bronchoscopy would preclude bronchoscopy. Larger studies are needed to provide more clarity. Clinicians should be cognisant of the radiation and contrast load.

Early diagnosis and management improves outcomes. Removal of inhaled FBs is facilitated by rigid bronchoscopy, still the gold standard, under general anaesthesia. Where airway patency is threatened, rigid bronchoscopy must be embarked upon as an emergency. Where patients are stable, procedures may be delayed until daylight hours, or until the child is fasted to decrease the risk of aspiration as the airway will not be fully protected during the procedure.

Premedication can be considered, but with care to avoid excessive sedation which may worsen airway obstruction. Consider the use of an anti-sialagogue like glycopyrrolate to reduce secretions.

**Intraoperative**

The surgical and anaesthetic plans should be clearly defined by both teams. The goal should be a smooth, coordinated, sharing of the child’s airway with a combination of optimal oxygenation, ventilation, and surgical exposure, resulting in retrieval of the foreign body. Bronchoscopic removal has a high success rate (> 95%) and low complication rate (around 1%). Thoracotomy is rarely indicated. Numerous unsuccessful attempts may result in the FB being pushed more distally, making retrieval even more difficult. The experience of the anaesthetist and the endoscopist is critical in ensuring a good outcome and minimising complications.

Good communication between surgeon and anaesthetist is of paramount importance during shared airway surgery. Although the induction technique of choice is often based on
the experience of the anaesthetist or institutional practice, most deem it prudent to maintain spontaneous respiration to prevent converting partial obstruction to complete obstruction. This, however, appears to be a rare phenomenon, and largely theoretical. Sevoflurane has emerged as the induction agent of choice. Liberal topicalisation with local anaesthetic under direct vision, preferably via a laryngo-tracheal atomiser, is a useful adjunct.

Many different anaesthetic techniques have been employed to facilitate removal while minimising complications and operating time. The cumulative evidence doesn't provide a clear superior option, although a recent meta-analysis showed that when controlled ventilation was employed, a lower incidence of laryngospasm and shorter operating time resulted. A study evaluating risk factors for hypoxaemia during FB removal found that manual jet ventilation (MJV) was associated with the lowest incidence of hypoxaemia, when compared to spontaneous and controlled ventilation. A retrospective review found a higher incidence of adverse events – laryngospasm, coughing, breath holding, bronchospasm and patient movement – in patients who received Propofol and Remifentanil compared with Propofol and Sevoflurane. When comparing Dexmedetomidine in spontaneously ventilating patients to MJV with Fentanyl and Propofol, no difference in adverse events, success rates or haemodynamic changes between groups was found, but patients who received Dexmedetomidine required longer stays in the post-anaesthesia care unit.

Intraoperative complications include hypoxia (most common), hypercarbia, laryngospasm, disintegration or dislodgement of the FB, haemorrhage, pneumothorax, pneumomediastinum (due to tracheal or bronchial laceration), hypoxic brain damage and cardiac arrest. Disintegration is more likely with organic FBs. Dislodgement of the FB due to manipulation by the endoscopist can cause severe airway compromise, resulting in an inability to ventilate with severe hypoxia. The main consideration in this scenario is tracheal obstruction, which requires immediate removal of the FB or advancing the FB into the same bronchus initially lodged in. If vocal cord movement precludes removal, Suxamethonium should be considered.

After successful removal of the FB it is prudent to repeat the bronchoscopy, as up to 5% of patients may have additional FBs in-situ, and to assess for airway injury. In patients with a prolonged history, antibiotics may be required to treat secondary infection. This should be guided by cultures taken at the time of the bronchoscopy. Corticosteroids can reduce inflammation and airway oedema, but no clear guidelines exist advocating for a single dose vs a course of steroids.

Postoperative

Severe laryngeal oedema or bronchospasm may require reintubation or tracheostomy. A CXR is mandatory to exclude pneumothorax or pneumomediastinum. The postoperative destination should be individualised and depends on the preoperative state and intraoperative course.

Ingested foreign bodies

In contrast to adults, 98% of all FB ingestion in children is accidental. In the South African context, the number of cases of ingested FBs requiring surgical intervention is considerably higher when compared to international studies, although the need for management guidelines has been highlighted.

The most common site of impaction for ingested FBs found on CXR is the proximal oesophagus, followed by the stomach, distal duodenum and distal oesophagus, in descending order. Symptoms include vomiting, drooling and dysphagia, although few patients are symptomatic at time of presentation.

In recent years, there has been a dramatic increase in morbidity and mortality caused by the ingestion of button batteries (BBs). Newer batteries are composed of lithium, have a higher voltage, and are larger in diameter. BBs are ubiquitous, found in hearing aids, watches, remote controls and games. Newer batteries carry three-fold greater risk of injury, but even ‘dead’ ones carry sufficient charge to cause substantial damage. Lithium BB ingestion is associated with high complication rates and high mortality, justifying emergency endoscopic removal.

The mechanisms of injury include leakage of contents, pressure necrosis or electrical discharge. In the stomach's acidic environment, batteries can disintegrate, releasing alkaline solutions – sodium and potassium hydroxide – which cause liquefaction necrosis, mucosal disintegration and subsequent perforation. Heavy metal poisoning is a rare complication caused by the breakdown of mercury batteries. The most common mechanism of injury involves electrical discharge, which is extremely dangerous. Electric current flows through the surrounding tissue, generating hydroxide radicals in the mucosa. Within 30 minutes, the pH increases from seven to 13 at the negative pole of the battery, resulting in caustic injury. Within 15 minutes, necrosis occurs within the lamina propria of the oesophagus. After 30 minutes, the necrotic area extends to the outer muscular layer. Continued injury can occur for days to weeks even after removal of the battery.

Death caused by the formation of an aorto-enteric fistula has been known to occur weeks later. This is a dreaded complication with a very high mortality, and should be the chief concern in any patient presenting with coffee-ground vomitus or haematemesis, even post-endoscopic removal. Classically, patients are under the age of five years, have ingested multiple large BBs, and present with haematemesis. Impaction at the level of the aortic arch, battery size greater than 20 mm, and prolonged time since impaction are other factors that should elicit the greatest concern.

Other complications include tracheoesophageal fistula (47.9%), oesophageal perforation (23.3%), oesophageal strictures (38.4%), vocal cord paralysis from recurrent laryngeal nerve injury (9.6%), mediastinitis, pneumothorax, cardiac arrest and death.
Management of these cases requires a multi-disciplinary approach, involving emergency medicine physicians, paediatric gastroenterologists, interventional radiologists and cardiologists, paediatric surgical sub-specialities and anaesthesia. Rapid risk assessment and mobilisation of the appropriate resources is crucial in optimising outcomes.

CXR helps to distinguish the more innocuous coin from the dreaded BB. The characteristic ‘halo’ sign diagnostic of a BB should be sought, as well as the ‘step off’ sign, between the positive and negative nodes (see Figure 3).

CT angiogram can diagnose aortic injury, for which there should be a high index of suspicion if the point of impaction is mid-oesophageal. Magnetic Resonance Imaging is a useful tool for evaluating the extent of the injury, both at the initial presentation, and for ongoing surveillance. Consideration should be given to removing ingested button batteries in the cardiac catheterisation laboratory, under fluoroscopic guidance and arteriography, if aortic injury is suspected.

The most common method employed for removal of ingested FBs is endoscopy. With the airway secured, anaesthesia for endoscopy is significantly less challenging than that for aspirated FBs. In the absence of life-threatening complications associated with certain ingested objects, most complications are mild and can be managed conservatively. These include oesophageal ulcers, mucosal injury, tears in the oesophageal wall and stricture formation.

The management of BBs that have passed through the oesophagus is under debate. Previous guidelines recommended a period of observation, but more recent guidelines suggest endoscopy for evaluation of injury and possible removal in high-risk patients (see above).

**Conclusion**

Ingestion or aspiration of FBs is common in the paediatric age group, causing significant morbidity and mortality. Child accident preventative programmes need to adopt a multi-pronged strategy aimed at reducing the number of children affected. Anaesthesia for these children can be challenging, with considerable potential for complications. The literature does not provide consensus on anaesthesia techniques, but does advocate for the presence of a skilled and experienced anaesthetist and endoscopist. A multidisciplinary approach is advocated, and good communication is essential.

**References**

Anaesthesia for audiology brainstem response testing in children with autism spectrum disorder

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Introduction

Audiology brainstem response (ABR) testing is used to examine the integrity of the conductive and neuronal auditory pathways in children presenting with developmental delay. Testing needs to be done with a quiet, co-operative patient preferably under normal sleeping conditions in a sound-proof booth. In infants and children, especially those with associated behavioural problems, this may mean that sedation or even general anaesthesia will be necessary to adequately complete testing.

A 2015 audit of the ABR service at Chris Hani Baragwanath Academic Hospital found that the rate of co-morbidities in these children was high with the most common co-morbidities being autism spectrum disorder (ASD), with or without attention deficit and hyperactivity disorder (ADHD), epilepsy, cerebral palsy, or a diagnosed syndrome.

This review will cover aspects related to the most common co-morbid conditions found in ASD children presenting for ABR testing and the effect that different anaesthetic agents may have on the evoked potentials obtained. The author also presents a possible approach to managing these children.

Autism spectrum disorder

ASD is a neurodevelopment disorder which presents with deficits in social communication, repetitive behaviours and some sort of sensory hypersensitivity. These children have restricted interests and struggle with normal emotional and physical expression. The term ASD has recently been reviewed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) to include autistic disorder, high functioning autism, Asperger syndrome, pervasive developmental disorder and atypical autism. The incidence of ASD is estimated at around 1% of the population and is more common in males especially in children with higher IQ.

The exact aetiology is unknown but is thought to be due to a combination of genetic and neural developmental factors. Emerging evidence suggests that in some children with ASD there may be a link with some biochemical and metabolic problems. Mitochondrial dysfunction, increased lactate, B-vitamin complex deficiency, increased oxidative stress and membrane lipid abnormalities may be of concern perioperatively.

Autism is heterogenous in its presentation and no two children with ASD will have the same features. The condition is defined based on behavioural symptoms and diagnostic criteria and includes the following:

- difficulty with social communication and reciprocity
- restrictive and repetitive behaviours
- symptoms that are present from early in life

Significant functional impairment must be present for the diagnosis to be made and all other causes must have been excluded. The Childhood Autism Rating Scale (CARS) may be used to identify children who need further testing. It consists of 15 questions asked of the caregiver pertaining to the child's behaviour. Each question is equally weighted and can be scored from 1, indicating normal age-appropriate behaviour, to 4, indicating severely abnormal behaviour. A score of 36–60 indicates moderate to severe autism.

The difficulty these children experience with communication ranges from struggling with the use of everyday language to having no verbal skills at all. They may also find physical and non-verbal communication challenging. Eye contact may seem threatening to some and provoke intense anxiety in others. Ritualistic behaviour patterns with the need for familiar routines and environments are an attempt to control the confusing world around them. A small change in their daily routine can be extremely unsettling and aggravate changes in behaviour which may be detrimental to both the child and others.

The inability to process sensory inputs is included under the DSM criteria of repetitive behaviour. These children may be hypo- or hyperresponsive to stimuli which may involve any of their five senses. This can be difficult to manage perioperatively: the use of certain stimuli that evoke pleasure may be used to distract these children while basic non-painful procedures are carried out but a bright, noisy hospital room with unfamiliar faces and sounds can elicit unmanageable anxiety and fear.
Management of ASD may be pharmacological or non-pharmacological. Drugs used may include long-acting antipsychotic medications like risperidone. These agents are associated with hypotension and arrhythmias under general anaesthesia. It is recommended that clozapine be stopped perioperatively and the patient changed to a shorter-acting drug. Clozapine is associated with agranulocytosis, hyperthermia, cardiac conduction problems and significant hypotension under general anaesthesia (GA). Caution should be exercised when discontinuing these drugs as side-effects include dystonia, dyskinesia, delirium and psychosis with sudden withdrawal. Consultation with the child’s psychiatrist is mandatory.1

Non-pharmacological strategies used in ASD are usually a combination of psychological, behavioural, developmental, therapy-based and sensory-motor.

Other than the essential features noted above, children with ASD often have associated problems that have implications for the anaesthetist.1,3,4 Additional intellectual disability may make communication even more challenging. Both gross and fine motor co-ordination can be impaired with apraxia (difficulty in planning their next movement) and hypotonia being common findings. These children may have an odd gait and appear clumsy.

Patients may also be on pharmacological treatment for anxiety or sleep disorders. Benzodiazepines, antihistamines, alpha-2 agonists and melatonin may be used by patients and drug interactions need to be considered before formulating an anaesthetic management plan.

Seventy percent of children with ASD will have at least one associated psychiatric disorder and 40% will have two or more. ADHD and epilepsy are amongst the most common comorbidities seen with prevalence rates of around 30% and 20% respectively.1,3 These conditions have their own anaesthetic considerations and are discussed below.

**Attention deficit and hyperactivity disorder**

ADHD is characterised by inattention, impulsivity and hyperactivity.6,7 The incidence is reported as between 2–20% in school-aged children. The cause is unknown but there have been associations shown between ADHD and genetic predisposition, prematurity, low birth weight, maternal smoking, parental alcoholism and social/family problems. The pathophysiology is linked to central nervous system neurotransmitter imbalance or dysfunction.7

Potential problems associated with the perioperative management of patients with ADHD may be due to increased levels of anxiety preoperatively, severe agitation during induction and emergence, postoperative behavioural changes and anaesthetic drug interactions with medications prescribed.6,7 Tait et al describe the first prospective trial done that looked at a cohort of ADHD patients presenting for elective ambulatory surgery under general anaesthesia.6 They showed that these patients were more likely to be uncooperative at induction and display exaggerated postoperative maladaptive behaviour. Their premedication regimens, induction and maintenance drugs as well as perioperative opioid use were the same as the control group.

Treatment for ADHD is multimodal and can be divided into pharmacological and non-pharmacological strategies. Non-pharmacological therapies involve intensive family and individual counselling and education, school remediation and behavioural interventions to help patients and their families deal with the condition.

Pharmacological strategies are divided into CNS stimulants and CNS non-stimulants.7 The medications used are effective in controlling symptoms and improving overall function. Most of the treatment options increase CNS levels of dopamine and noradrenaline leading to increased neurotransmission.

**CNS stimulants:**
- **Methylphenidate**
- **Amphetamines**

**CNS non-stimulants:**
- **Tricyclic antidepressants**
- **Monoamine oxidase inhibitors**
- **Alpha-2 agonists**
- **Atomoxetine (noradrenaline re-uptake inhibitor)**
- **Modafinil (atypical dopamine re-uptake inhibitor)**
- **Bupropion (noradrenaline re-uptake inhibitor and nicotinic receptor antagonist)**

**Potential drug interactions**

**Methylphenidate** is most commonly prescribed. It is structurally similar to the catecholamines and acts as a noradrenaline and dopamine re-uptake inhibitor. It is metabolised to inactive metabolites in the liver which are then excreted via the kidneys. Concerta is the trade name for the extended release formula which minimises fluctuations between peak and trough drug levels during the day. Common side-effects include anorexia, weight loss and sleep disturbances.

Drug interactions associated with general anaesthesia include cardiovascular instability, dose adjustments required for minimum alveolar concentrations (MAC) values for the volatile agents, postoperative nausea and vomiting (PONV) and decreases in the seizure threshold in at-risk patients.

Preoperatively, oral midazolam used in regular doses for premedication has been shown to be less effective in patients taking methylphenidate. Ketamine use perioperatively is associated with increased PONV and dehydration. Clonidine, when used as a premed, is associated with less PONV, has an anaesthetic sparing effect, blunts haemodynamic responses to stimuli and decreases the incidence of shivering.

Intraoperatively, patients taking CNS stimulants have a blunted ability to respond to hypotension because of decreased endogenous catecholamine stores and down regulation of receptors. They exhibit increased baseline heart rates, are at higher risk for the development of arrhythmias and require increased MAC levels to maintain an adequate depth of anaesthesia. Careful titration of anaesthetic agents is needed.
to avoid large swings in haemodynamic variables and depth of anaesthesia monitors such as Bis or entropy should be used.

One of the biggest concerns with patients on CNS stimulants is the increased risk of seizure activity perioperatively. Anticonvulsants need to be continued and certain drugs avoided. Ketamine, tramadol and pethidine may all increase the risk of seizures in these patients.

**Epilepsy**

Epilepsy is defined as paroxysmal, abnormal cerebral electrical discharges associated with clinical signs and is one of the most common chronic neurological conditions diagnosed. It is twice as common in children as in adults and may be progressive. The incidence ranges from 0.5–2% and varies with age, sex, race and socio-economic status. There is also an association with mental retardation, cerebral palsy, and behavioural disorders.

Seizures may be primary (idiopathic) or secondary to a host of other conditions.

Secondary causes may be divided into pre-, peri- or postnatal events ranging from inborn errors of metabolism and chromosomal disorders to prematurity and biochemical abnormalities such as neonatal hypoglycaemia or hypocalcaemia. Infectious diseases remain an important cause especially in developing countries.

The classification of seizures is divided into partial (focal) or generalised.

- **Partial seizures**
  - Excessive neuronal discharges originate from one point of a cerebral hemisphere.
  - May be simple or complex depending on whether there is an associated depressed level of consciousness.
  - May progress to a generalised seizure.
  - The presentation of partial seizures will depend on the area of the cortex involved and may present with motor, sensory, autonomic or psychological signs and symptoms.
- **Generalised seizures**
  - Represent bilateral symmetrical brain activity and involve the thalamic tracts in the generation of diffuse, bilateral discharges.

They may present only with transient depressed level of consciousness, as in absence or petit mal seizures, or generalised muscle contractions which may be tonic, clonic or grand mal seizures which involve a combination of tonic and clonic movements.

There is usually always an impaired level of consciousness associated with generalised seizures.

The pathophysiology of epilepsy is thought to be related to the loss of gamma-aminobutyric acid (GABA) mediated post-synaptic inhibition associated with the development of new neuronal connections and the increased release of the excitatory neurotransmitter glutamate. This, coupled with the presence of pacemaker cells which contain abnormal calcium currents leads to abnormal firing of neurons in affected areas of the brain. The harmful consequence of this abnormal activity is termed excito-toxicity: the increased depolarisation of neurons and activation of excitatory amino acid receptors leads to an influx of calcium. The high intracellular calcium levels eventually lead to cell necrosis and apoptosis resulting in loss of neuronal cells and toxicity.

Treatment for epilepsy is individualised for each patient and is based on seizure type and severity. Management strategies include treatment of predisposing factors, dietary, pharmacological and surgical resection or callosotomy. Dietary and pharmacological treatments are discussed below.

**Dietary management**

Dietary strategies are used to help control seizures in patients with intractable symptoms and unacceptable side-effects on anti-epileptic drugs (AEDs.) The use of a ketogenic diet has been shown to decrease seizure severity and frequency. A normal diet has a fat:carbohydrate (CHO) and protein ratio of 0.3:1 with about 35% of daily calories coming from fat. A classical ketogenic diet has a fat:CHO and protein ratio of 4:1 with 90% of daily calories coming from fat. Because of the high rates of non-compliance with this diet in children, a revised diet of fat:CHO ratio of 1:1 with 65% of calories from fat has been shown to be as effective with better compliance. Important side-effects of a ketogenic diet to consider when planning anaesthesia include poor growth in children < 1 year, renal calculi, long bone fractures, abnormal liver enzymes, abnormal lipid profile, hypoproteinaemia and ketoacidosis.

**Table I.** Commonly used anti-epileptic drugs and their side-effects pertaining to anaesthesia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-life (hours)</th>
<th>Mechanism of action</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin</td>
<td>12–24</td>
<td>Sodium channel blocker</td>
<td>Enzyme induction, megaloblastic anaemia, highly protein bound</td>
</tr>
<tr>
<td>Sodium Valproate</td>
<td>6–10</td>
<td>Sodium channel blocker</td>
<td>Enzyme induction, thrombocytopenia, hepatotoxicity, highly protein bound</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>4–12</td>
<td>Sodium channel blocker</td>
<td>Enzyme induction, pancytopenia, cholestasis, hyponatraemia, highly protein bound</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>12–96</td>
<td>GABA agonist, AMPA blocker</td>
<td>Enzyme induction, megaloblastic anaemia, highly protein bound</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>18–50</td>
<td>GABA agonist</td>
<td>Sedation, CNS depression</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>5–7</td>
<td>Calcium channel blocker</td>
<td>Sedation, breakdown blocked by sodium valproate</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>24</td>
<td>Sodium channel blocker</td>
<td>GI disturbances, sedation, dizziness</td>
</tr>
<tr>
<td>Topiramate</td>
<td>26</td>
<td>Unknown, sodium channel blocker, GABA, agonist</td>
<td>Insignificant normal anion gap metabolic acidosis, enzyme inhibition</td>
</tr>
</tbody>
</table>

**References:**

2. Partial seizures
3. Generalised seizures
4. The classification of seizures is divided into partial (focal) or generalised.
5. Seizures may be primary (idiopathic) or secondary to a host of other conditions.
6. Secondary causes may be divided into pre-, peri- or postnatal events ranging from inborn errors of metabolism and chromosomal disorders to prematurity and biochemical abnormalities such as neonatal hypoglycaemia or hypocalcaemia. Infectious diseases remain an important cause especially in developing countries.
7. The classification of seizures is divided into partial (focal) or generalised.
8. They may present only with transient depressed level of consciousness, as in absence or petit mal seizures, or generalised muscle contractions which may be tonic, clonic or grand mal seizures which involve a combination of tonic and clonic movements.
9. There is usually always an impaired level of consciousness associated with generalised seizures.
**Pharmacological management**

The aim of treatment with AEDs is control of seizures on monotherapy with minimal to no side-effects. Prognosis is usually good with 70% of patients achieving control for five years or more. Fifty percent of patients that have their anti-epileptic drugs discontinued appropriately will remain symptom free. The most commonly used AEDs and their significant effects with respect to anaesthesia are represented in Table I.

The prevention of seizures perioperatively is paramount. AEDs should be continued up to the time of the planned procedure and restarted as soon as possible afterwards. Most drugs have a long half-life so a missed dose is not usually critical. Many of the AEDS do not have parenteral preparations and for those patients with intractable symptoms or a prolonged nil per mouth period, a perioperative treatment plan should be agreed upon with the child’s neurologist before the procedure. Premedication in these children may prove beneficial as hyperventilation from anxiety may decrease the seizure threshold. Caution must be used when administering sedative drugs as some of the AEDs have enzyme induction effects which increase dose requirements and others have an additive sedative effect. All agents used must be individualised per patient depending on their presentation, chronic medications and level of anaesthesia required for the procedure.

Status Epilepticus is a medical emergency that should be recognised and treated promptly. It is a rare event perioperatively but must be considered if there are tonic-clonic seizures, loss of consciousness or tongue biting under sedation or delayed emergence, unexplained haemodynamic changes, increases in oxygen consumption or increases in end tidal CO2 under general anaesthesia.

**Status Epilepticus**

**Definition:** Continuous seizure activity lasting > 30 minutes or intermittent seizure activity lasting > 30 minutes during which consciousness is not regained.

**Emergency management**

**ABC**

- Airway
- Breathing – 100% O2
- Circulation – IV access
- Don’t Ever Forget Glucose! – check and correct hypoglycaemia

**First-line therapy**

- IV Benzodiazepines – Lorazepam (0.1mg/kg) or Diazepam (0.1mg/kg)

**Second-line therapy if seizures not terminated within 10 min**

- IV Phenytoin (15–17 mg/kg) by slow infusion (rate < 50 mg/ min)

**Intubation and ventilation to maintain normal PaO2 and PaCO2**

- Rapid sequence induction should be performed (propofol is an acceptable substitute for thiopentone)

Fluid resuscitation to maintain adequate systemic blood pressure and cerebral perfusion pressure.

If seizures are not controlled after 30 minutes with second-line therapy, consider propofol or low-dose thiopentone infusion anaesthesia preferably under EEG control. Alternatives include phenobarbital.

Remember – muscle relaxants stop the seizure movements, but not the abnormal cerebral activity, therefore in the paralysed patient, anti-convulsants are also essential.

**Auditory brainstem response testing**

ABR testing is useful clinically as a measure of hearing sensitivity and to examine the functional integrity of eighth cranial nerve (CN VIII) and the auditory brainstem neurones. It is reliable, reproducible and non-invasive. Auditory brainstem responses are elicited by stimulating the auditory pathway with acoustic signals while electrodes on the scalp measure the response. ABRs are separated out from the background electroencephalograph (EEG) using averaging and amplification techniques. It is made up of a series of peaks in waveforms occurring within 10 milliseconds of the stimulus which is usually a click administered through headphones in one or both ears. The waves obtained represent the different areas of the pathway being examined: Waves I and II originate from CN VIII and waves III–V depend on the neural functioning of the cochlear nucleus through the lateral lemniscus.

In order for interference with testing to be minimised, the patient needs to remain still throughout the procedure. Various anaesthetic techniques have been used to facilitate testing. Spontaneous respiration in a sedated patient is preferred as this minimises interference. The administration of general anaesthesia in the operating room (OR) has been shown to decrease the number of waveforms obtained with delays in latencies and decreases in amplitudes of the ABRs. The causes of diminished test results in the OR are due to both equipment and patient factors. Electromagnetic and background noise interference is higher in the OR and changes in patient blood oxygenation levels, blood pressure and decreases in body temperature all have a negative effect on the ABR obtained. Interpretation of ABR results in the OR is challenging but achievable should a GA be required to optimise patient safety.

The ideal setting for ABR testing is in a sound proof booth to minimise interference. This is usually in the audiology department far away from the familiar theatre environment. The SASA guidelines for the safe use of procedural sedation and analgesia for diagnostic and therapeutic procedures in children should always be followed when performing sedation in a remote location. A reliable oxygen source, suction unit, emergency drugs/equipment and devices for advanced airway management must be immediately available. Monitoring must include standard ASA monitors and capnography.

The sedation technique chosen should ideally use agents that don’t interfere with ABR waveforms, have a rapid and predictable onset of action and have a short duration of action with minimal respiratory and cardiovascular effects. Emergence and
awakening should be prompt to minimise recovery times and return the patient to their baseline level of functioning as soon as possible.

Table II. The effect of commonly used anaesthetic agents for sedation and general anaesthesia on auditory brainstem-evoked potentials14,15,17

<table>
<thead>
<tr>
<th>Anaesthetic Agent</th>
<th>Amplitude</th>
<th>Latencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halogenated volatile agents (0.5–1.0 MAC without N2O)</td>
<td>Decrease</td>
<td>Increase</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Decrease</td>
<td>No effect</td>
</tr>
<tr>
<td>Propofol</td>
<td>Minimal decrease</td>
<td>No effect</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Increase</td>
<td>Minimal increase</td>
</tr>
<tr>
<td>Opiates</td>
<td>Minimal decrease</td>
<td>Minimal increase</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>No effect</td>
<td>No effect</td>
</tr>
</tbody>
</table>

A recommended approach to children with ASD presenting for ABR testing

Preprocedure

Early identification of these patients is crucial so that the child’s needs can be given due consideration from admission to discharge. The child, caregiver and staff need to be prepared timeously. Non-threatening but necessary procedures such as measuring the weight, height and basic vitals of the child should be done before the day of admission, as a part of a familiar routine and preferably in an environment that is familiar to them e.g. their regular paediatrician’s office.

The caregivers know their children best and should be consulted before the day of admission as to what stimuli the patient will respond to. This includes both positive and negative responses. A proposed checklist to be filled out by the caregiver is shown in Figure 1:

Admission procedures should be minimised by getting necessary forms filled out at the hospital before the day of the procedure or at home. Waiting and preprocedure fasting times should be as short as possible. Depending on the needs of the child and if the hospital has the facility, it may be necessary to bring the child in via a separate corridor into a quiet room where no other patients or staff have access.

Preoperative assessment should be thorough and focus on any co-existing medical conditions that may influence anaesthetic management. Birth history, associated syndromes, behavioural problems, symptoms of snoring or chronic upper airway obstruction and a history of epilepsy need to be specifically elicited from the caregiver and investigated. A detailed history of special diets and medications must be asked. As shown in the text above, the most important concerns regarding medications perioperatively are the potential for drug interactions and side-effects of treatment the patients may be taking. For ABR testing, all chronic medications should be continued on the day of the procedure preferably given more than two hours before the child is sedated and with the minimal amount of volume possible to satisfy fasting guidelines.

It may be difficult to examine these patients and care must be taken not to come across as threatening. Many children with ASD and normal intelligence will be cooperative as long as they know what is expected of them. Visual information cards and videos have shown to be effective in preparing these children.1,5 Allowing comfort items to be brought in, especially those that hold a special interest, can be very useful distractors. Minimising sensory inputs is important to limit sensory hypersensitivity: examining the child in a quiet, semi-dark room with the minimal number of staff necessary can be helpful in keeping them calm. A focused examination looking for airway abnormalities, evidence of upper or lower respiratory infections, hypotonia and obstructive sleep apnoea should be carried out efficiently to minimise examination time.

Because ABR testing is non-invasive and usually accomplished with minimal sedation, blood results are not usually required prior to induction. However, it is recommended that these children have the appropriate laboratory testing done to check for side-effects of their chronic medication before undergoing any surgical procedures.

Administration of premedication is recommended but can be challenging and patients may refuse. Knowing what foods and drinks the child normally likes and using them to disguise the drug is useful. Evidence is lacking as to which premedication is best. Using a drug that you are comfortable with is always best. The application of EMLA® cream to potential drip sites is useful but should be abandoned if it causes the patient unnecessary distress. The use of physical restraint should be avoided at all times. If there is serious risk of injury and the procedure is not urgent, the procedure should be postponed and

Figure 1. Proposed pre-operative checklist for caregivers
an alternative plan discussed. If restraint is unavoidable, consent must be obtained from the caregiver and preferably trained staff should be involved.

For premedication, oral midazolam 0.5 mg/kg is effective with minimal side-effects but may not be enough when used as a single agent especially if the child is on CNS stimulant drugs.

Ketamine 5–7 mg/kg PO may be added or used as an alternative in children with moderate to severe autism who are uncooperative or intellectually impaired. Intramuscular ketamine 3–5 mg/kg is a reliable choice when the use of oral medication is not possible or ineffective. Side-effects include disorientation, emergence delirium, hyper-salivation and PONV.

A retrospective study by Lubisch et al showed that the alpha-2 agonist dexmedetomidine at 2–5 mcg/kg can be successfully used PO to obtain adequate sedation in these patients. Side-effects are minimal and parent satisfaction was greatly improved with the use of dexmedetomidine/midazolam combination when compared to chloral hydrate and phenobarbital. Clonidine 5 mcg/kg PO has also been shown to induce adequate sedation for EEG studies in autistic children. Intranasal dosing of the alpha-2 agonists is usually not possible in these children.

Because ketamine has multiple side-effects, it should be viewed as second-line for premedication with midazolam and alpha-2 agonists as first-line. Once the patient is calm and cooperative, IV access should be obtained.

**Maintenance of sedation**

Maintenance of sedation during the ABR testing can be achieved with a number of different techniques. Additional dosing may not be required depending on the drug and dose used for premedication. The goals of the sedation technique chosen should be to provide adequate depth of sedation (Ramsey score 3–4) with minimal haemodynamic changes, adequate oxygenation, maintenance of control of airway reflexes and fast recovery times.

A combination of propofol and ketamine in a 4:1 dilution is effective and safe. An initial dose of 0.5–1 mg/kg can be used to achieve a Ramsey sedation score of 3–4. A maintenance infusion of 50–100 mcg/kg/min titrated appropriately may be used to achieve adequate levels of sedation.

Intravenous dexmedetomidine 1 mcg/kg combined with IV ketamine 1 mg/kg causes adequate levels of sedation for ABR testing for at least 40 minutes when combined with midazolam for premedication. A single IV dose of each drug at the beginning of the procedure is usually sufficient.

Effective antiemetic medication and adequate IV hydration are recommended during the procedure as many autistic children will refuse oral medication afterwards. This will also facilitate early removal of the intravenous cannula which will probably not be tolerated once the child is awake.

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**Ramsey Sedation Assessment Scale**

<table>
<thead>
<tr>
<th>Levels:</th>
<th>Awake</th>
<th></th>
<th>Asleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient anxious or agitated or both</td>
<td>1</td>
<td>A brisk response to a light glabellar tap</td>
<td>4</td>
</tr>
<tr>
<td>Patient cooperative, oriented and tranquil</td>
<td>2</td>
<td>A sluggish response to a light glabellar tap</td>
<td>5</td>
</tr>
<tr>
<td>Patient responds to commands only</td>
<td>3</td>
<td>No response</td>
<td>6</td>
</tr>
</tbody>
</table>

**Recovery**

Children with ASD often become agitated and distressed on emergence from anaesthesia or sedation. It can be difficult for healthcare workers to differentiate between pain, anxiety, nausea and emergence delirium. The child should be allowed to recover in a quiet, semi-lit room with caregivers and comfort items standing by. Early removal of the intravenous cannula is recommended in those patients who seem to be recovering well. Early discharge home and return to a familiar routine is ideal if at all possible.

**Conclusion**

Children with ASD are a challenging group of patients for the anaesthetist. The perioperative environment is entirely contrary to their unique needs and can be a source of extreme anxiety and stress for child, caregiver and medical staff alike. They often have significant co-morbidities that necessitate careful anaesthesia assessment and planning in the pre-, intra- and postoperative periods.

ABR testing is clinically useful in these patients as it can differentiate causes of delayed development and ultimately allow for progressive treatment options to improve how these children interact with the world around them.

Educating healthcare workers and hospital management about ASD can go a long way to improving the perioperative experience for all concerned. Being imaginative and making small changes to the environment and how we communicate with these children can go a long way to improving how we care for them.

**References**

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Anaesthesia for craniosynostosis surgery

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Introduction

Anaesthesia for craniosynostosis surgery is complex and poses numerous challenges to the anaesthesiologist. Evaluation of these patients for surgery needs to be part of a multidisciplinary team involving anaesthesia, plastic surgery, neurosurgery and paediatric intensivists.

Rudolf Virchow in 1851 first described the relation between facial dimorphism and craniosynostosis and the fact that the arrest of skull growth occurs perpendicular to the fused suture line. This effect is responsible for the common deformities associated with specific suture line involvement.1

Craniosynostosis occurs because of premature fusion of skull suture lines. The majority of cases (+/- 80%) occur as an isolated event in an otherwise normal child and the remaining (+/- 20%) occur as part of a known syndromic condition. Isolated craniosynostosis often only involves one suture line (most...
commonly the sagittal suture) and is not associated with other congenital abnormalities. Their aetiology as far as is known is non-genetic and most probably relates to some physical intrauterine factor which restricts skull growth (multiple pregnancy or uterine abnormality). Other suspected contributing factors are hyperthyroidism in the mother, warfarin or valproate use during the pregnancy and if the mother smokes. Syndromic craniofacial abnormalities may be associated with craniosynostosis and the common ones include, Apert, Crouzon, Muenke, Pfeifer and Saethre-Chotzen. These syndromes are associated with specific abnormalities in genes coding for fibroblast growth factor receptors so that when fibroblast growth factor binds to the abnormal receptor for a prolonged time, premature signalling occurs for immature bone cells to differentiate early and cause suture lines to fuse. Inheritance is autosomal dominant although the majority are new mutations from unaffected parents. The overall incidence of craniosynostosis is approximately 1:2 000 to 1:3 000 live births.

Paul Tessier in 1967, a plastic surgeon, pioneered corrective surgery for these patients, thought previously to be impossible. He described how bones of the skull in infants could be removed, remodelled and put back as a free graft and survive. This field has continued to grow with important advances in surgical as well as anaesthetic techniques to make these types of surgeries safe for children to undergo.

The three clinical features associated with cranial dysostosis are craniosynostosis, midface regression and exorbitism. Common skull deformities are described with craniosynostosis depending on which suture lines have closed prematurely. Premature closing of the sagittal suture results in scaphocephaly with a broad skull. Turricephaly is as a result of or an elongated skull. Bilateral coronal suture fusion results in plagiocephaly with an asymmetrical distorted skull. The most common of the syndromic craniofacial abnormalities resulting in craniosynostosis are Crouzon's and Apert syndromes. Crouzon's syndrome is the most common to be associated with craniosynostosis. The suture lines usually affected are the coronal sutures resulting in brachycephaly. It occurs with a frequency of 1:25 000 live births with an autosomal dominant inheritance. In addition to the skull abnormality these patients also have midface hypoplasia with nasal obstruction and exorbitism. Many (up to 55%) have hearing loss and up to 33% have fusion of cervical spines C2/3 which can make airway management and intubation difficult. They are usually mentally normal. Surgery for the craniosynostosis usually occurs before one year of age and midface extraction surgery at around four to five years.

Apert's is the next most common syndrome associated with craniosynostosis. Apert's syndrome is often associated with mental retardation, midface hypoplasia with or without cleft palate, nasal abnormalities, and syndactyly and hearing abnormalities as a result of chronic middle ear infections. Similarly to Crouzon's the craniosynostosis is corrected before a year of age with midface corrections happening at four to five years of age.

Surgical correction of craniosynostosis is necessary for cosmetic as well as medical reasons and these include management of raised intracranial pressure, to allow normal brain growth as well as eye protection in severe exorbitism and potential blindness. Numerous sources in the literature have sought to seek a link between severe craniosynostosis and mental developmental difficulties including associations with learning difficulties, hyperactivity and attention deficit disorders. Most of these associations are, however, anecdotal.

The timing of surgery needs to be carefully considered. Raised intracranial pressure (ICP) by itself may dictate when surgery will be done but in otherwise normal children it is a balance between earlier surgery at a young age before six months and the increased anaesthetic-related risks. Early surgery may also increase the risk of re-operation. In older children the bones are harder and more difficult to remodel as well as bones losing their ossification properties versus less anaesthetic risks. The optimal time is somewhere between six months and one year of age which still provides advantages of early surgery with less anaesthesia-related risks. The Johannesburg craniofacial unit operates at six to twelve months of age unless raised intracranial pressure dictates otherwise.

Surgical options

Surgical correction addresses the fused sutures so as to allow normal brain growth and attempts to correct the areas of compensatory overgrowth so that the skull can remodel into normality. Treatment options include:

1. **Strip craniectomies**

   These procedures are performed mainly for sagittal stenosis and are performed at a young age (< 6 months) and rely on rapid brain growth to remodel the calvarium. A high stenosis rate has been found with only 29% returning to normal. This procedure is often combined with helmet moulding therapy.

2. **Spring assisted craniectomies**

   Springs are inserted across the osteotomy defect created in an attempt to open the bi-parietal narrowing and allow rapid brain growth to remodel the skull. The springs are removed after six months. As with strip craniectomy alone the results are less positive than calvarial remodelling.

   Strip craniectomy is a less invasive procedure with less blood loss and shorter hospital stay but at the expense of a higher stenosis rate and poorer resolution of the deformity. Endoscopically assisted osteotomies are being performed in some centres and this is the procedure of choice in a young (< 3 months) syndromic patient with raised intracranial pressure.

3. **Total calvarial remodelling and forehead advancement**

   This is the more definitive procedure performed after six months of age for multi-sutural synostosis. This procedure corrects both the fused sutures as well as correcting the skull deformity. This procedure is more invasive and involves removal of most of the skull in patients with multi-sutural fusion. The removed skull is then reconstructed with wires,
2. Intra-operative concerns and management

1. Pre-operative assessment

The majority of patients presenting for surgery for craniostenosis are normal children with premature fusion of the skull sutures. The majority of these children do not have raised ICP or other comorbid conditions. The syndromes associated with facial synostosis need a more careful assessment and in particular issues relating to raised intracranial pressure, the airway, the respiratory system and obstructive sleep apnea (OSA).

Maxillary hypoplasia, nasal obstruction and exorbitism may make mask ventilation difficult. Intubation may also prove a challenge if these children have cervical spine abnormalities.

A recent study has shown that children with Apert’s syndrome have a 6.1% respiratory complication rate with these procedures and a recent respiratory infection renders them more likely to develop intraoperative respiratory complications.2

The midface hypoplasia and choanal atresia predispose these children to OSA with increased risk of airway obstruction at the time of induction or in the postoperative period. Examination of the tonsils and adenoids may need to be done in children with severe OSA and the need for tonsillectomy and adenoidectomy assessed before the craniofacial surgery.

Preoperative assessment of anaemia and the management with iron supplements or erythropoietin may be indicated. In addition, a coagulation and biochemical screen should be performed and two units of fresh leucodepleted blood ordered for theatre.

2. Intra-operative concerns and management

a) The airway and positioning

The majority of these children have normal airways and pose the same concerns as with any other child. Children with facial synostoses may prove a far greater challenge. Midface hypoplasia may cause difficulty with bag mask ventilation and airway adjuncts such as oropharyngeal, nasopharyngeal airways need to be close at hand as well as video laryngoscopes and fibre optic intubation devices in case the need arises. Gaseous inductions are generally the preferred technique with the establishment of intravenous access as soon as the child is deep enough. When difficulty is anticipated it is often prudent to have a second anaesthetist available. In children undergoing forehead advancement procedures in the supine position a non-reinforced tube can be used bearing in mind that kinking of the tube under the drapes is a real possibility. Many authors advocate the use of preformed Ring, Adair and Elwyn (RAE) tubes in these circumstances. I do not use preformed tubes as the risk of endobronchial intubation is higher in infants and correcting this once the patient is draped may prove disruptive to the surgery and is often difficult to remedy. Children with multisutural fusions undergoing total calvarial remodelling are generally done in the prone position on a specially designed foam mattress (Figure 2) or on a horseshoe frame. The foam mattress allows for greater exposure of the entire skull and also prevents movement of the head and body during the procedure.

b) Temperature

It is important to increase the theatre temperature slightly (23–24 degrees Celsius) particularly at the start of the procedure whilst the patient is being induced and invasive lines inserted. Fluid and convection warmers need to be used from the beginning to prevent heat loss as these procedures are lengthy and the head and brain are exposed.

c) Monitoring

The largest bore peripheral intravenous line should be placed after inhalational induction and care taken to ensure that the connections are secure and that the cannula is properly in the vein. During the procedure access to the drip site will be limited so monitoring for leaks and a drip that has dislodged becomes difficult.

An arterial line is mandatory to monitor blood pressure as well as providing a port for frequent blood sampling. The placement of a central line in many texts is not deemed
essential, however I always insert a 3 lumen central line for monitoring and fluid management. My preferred site is the right internal jugular vein. The femoral vein can also be used if internal jugular cannulation is not possible. These lines are always placed under ultrasound guidance. As fluid loss and central blood volume status is difficult to assess in these patients, trends in central venous pressure and arterial pressure together with metabolic changes detected on blood gas analysis are used to guide fluid therapy. Central venous pressure is not always accurate in determining fluid responsiveness but I have found trends very useful particularly in these infants that have normal cardiorespiratory function where the surgery does not involve the thorax or abdomen. Arterial waveform analysis with intermittent positive ventilation (IPPV) has become an acceptable tool to determine fluid responsiveness in adults, however there is conflicting data as to its accuracy in infants and children. Tachycardia is also not a useful indicator of hypovolaemia in major craniofacial surgery. Blood is administered through the peripheral line and not the central line so that dilution of a potentially high potassium and citrate can occur before it returns to the heart. I have found intraoperative urine output measure to be a very poor guide of fluid status.

A precardial Doppler has been used to detect venous air embolism particularly during osteotomy and removal of the orbital bandeau. Faberowski et al have shown an incidence of venous air embolism (VEA) of 82.6% using precardial Doppler. Of importance is that they found that the majority of episodes detected were clinically not significant. I do not use precardial Doppler monitoring but take care to minimise the occurrence by ensuring paralysis and IPPV and ensuring that the patient does not become hypovolaemic.

d) Haemorrhage and strategies to minimise blood loss and transfusion

Complex craniofacial surgery is associated with the potential for massive blood loss. Van Uittert et al looked at 44 patients undergoing craniosynostotic corrections and found a mean estimated perioperative blood loss of 55 ml/Kg (blood loss estimates were only reported in 27 cases). Williams et al found that only five of the 27 cases in their study undergoing major craniofacial surgery had an estimated blood loss in excess of 100 ml/Kg. Blood loss is generally gradual but significant throughout the procedure and it is important to appreciate times when blood loss may be rapid. Blood loss may be rapid when periosteum is lifted off the bone and when craniotomies are performed to remove skull bones. Removing bone can be a tedious and lengthy process as the neurosurgeon needs to be meticulous so as not to breech dural sinuses which can result in a dramatic and rapid blood loss. Most studies report the use of homologous blood transfusion in almost all cases of complex craniosynostosis repair.

Independent risk factors for increased requirements for homologous blood transfusion are a young age and low weight, duration of surgery (> 5 hours) and a low preoperative haematocrit. This increased requirement may result in an increased donor exposure and transfusion of other blood products at a young age. A dedicated team with a set routine, and an increased volume of cases has been shown to reduce blood loss, duration of surgery and length of hospital stay.

Reducing blood loss and therefore exposure to donor antibodies has become a major focus in complex craniofacial surgery. The risks associated with homologous blood transfusion are well known such as haemolytic reactions, transfusion-related acute lung injury, infection and the complications of massive transfusion such as coagulopathy, electrolyte and acid base disturbances. In adult patients strategies to minimise blood loss and transfusion are well established, however many of these have serious limitations in infants undergoing major craniofacial surgery. Good surgical technique, positioning, temperature regulation, a normal metabolic state, the use of anti-fibrinolytics and a rational transfusion protocol are the mainstay in this population group to reduce the need for homologous blood. If time permits, preoperative optimisation of haematocrit with good nutrition and the use of recombinant erythropoietin may be feasible. Recent adult data showing a possible increase in thrombotic complications, increased risk of stroke, hypertension, renal disease and serious cardiac complications have limited its use in the paediatric population. Cell saving techniques are becoming more feasible with the development of cell savers that require small initial volumes for processing. If this type of equipment is used, changes in draping techniques need to be adopted for effective collection of blood. Studies by Dahmani et al and Carver et al have shown a reduction from two units of packed cells to one unit after the introduction of cell saving.

Preoperative autologous donation and normovolaemic dilution are not commonly used as these patients have small blood volumes and usually are just recovering from the low haematocrits of infancy. Preoperative donation in infancy is also not always feasible as these children need to come to hospital for numerous donations which often require sedation or anaesthesia.

The use of an anti-fibrinolytic such as tranexamic acid (TXA) has been shown in numerous studies to be effective in reducing blood loss with these procedures. No data in children exists as to the efficacy ofaminocaproic acid. Tranexamic acid is cheap, easy to administer and seems to have a low incidence of adverse effects. The adverse effects that have been described in the literature are with large doses (> 100 mg/kg) and include seizures and thrombotic events. Dosing schedules quoted in studies vary from an initial bolus of 10–100 mg/kg and a continuous infusion of 1–10 mg/kg/hour. Goobie et al studied 23 patients aged two months to six years, one group receiving TXA as a bolus (50 mg/kg) and then an infusion of 5 mg/kg for the duration of the surgery. The control group received 0.9% saline. The mean total blood loss in the TXA group was 65 ml/kg vs 119 ml/kg with postoperative losses being 3 and 12 ml/kg respectively. All their patients did, however, receive blood...
transfusion. These authors suggest that tranexamic acid effects at the tissue level may outlast its half-life and exhibit effects well into the postoperative period by possibly an unexplained mechanism at the tissue level. In a meta-analysis done by Song et al with four studies and 138 patients included, they concluded that TXA can significantly reduce blood loss and transfusion of packed red blood cells (PRBCs) in children undergoing major craniofacial surgery, however in a subgroup analysis on randomised controlled trials the efficacy of TXA on reducing blood loss compared to controls was not significant. When large blood losses are replaced with crystalloid and PRBCs, dilution coagulopathy seems to be the major cause of bleeding. Williams, in their study, showed that coagulopathy only became a real problem in those infants that bled more than 100 ml/kg or approximately 1.2 times the blood volume. If fresh frozen plasma (FFP) is deemed to be necessary as per laboratory testing or clinical evidence, it is prudent to use the same donor from whom PRBCs are obtained. This would mean ordering FFP before surgery with the potential of wastage if not used or inappropriate use simply because it was available. Haas et al have shown that the use of fibrinogen concentrate was effective in decreasing perioperative blood loss without the need for FFP. High cost may be a disadvantage, however saving the patient a transfusion of other blood products with its attendant allo-immunisation may outweigh the cost. Vitamin K, activated factor VII, DDAVP have all been used to augment coagulation. The risks attached to the use of these agents always needs to be taken into account.

e) Metabolic and electrolyte disturbances

Metabolic and electrolyte disturbances occur for a number of reasons. Infants starved for a prolonged period of time may start off with a metabolic acidosis. Significant blood loss with replacement of crystalloid and PRBCs may lead to metabolic and electrolyte disturbances. Transfusion of 0.9% saline will result in a hyperchloremic acidosis and transfusion of PRBCs may result in electrolyte disturbances such as hyperkalaemia from packed cells stored for more than two weeks and hypocalcaemia from citrated blood. Packed cells stored for more than two weeks may have a potassium concentration greater than 40 mmol/l.

Choi et al, looking at metabolic disturbances, found a median base deficit of -9, with 39% of patients having a base deficit of less than 10 recorded with the maximum base deficit occurring at the end of the procedure in the majority of cases. Twenty-five percent of cases had a base deficit of lower than -4 at the time of arterial line insertion. The median time for this to correct was 9.25 hours. The degree of metabolic disturbance has been found to correlate with the amount of PRBCs, colloid or crystalloid given intraoperatively. Cladis et al described an incidence of hyponatraemia on reviewing 72 records of 30.6% in children undergoing cranial vault remodelling. Hyponatraemia was associated with increased preoperative intracranial pressure, blood loss, females and in patients receiving hyponatraemic intravenous fluids postoperatively. The mechanism is unclear but it has been suggested to be related to the syndrome of inappropriate anti-diuretic hormone (ADH) secretion and cerebral salt wasting syndrome.

f) Nausea and vomiting

An audit done by Hughes et al showed that 60% of children vomited in the first 24 hours. Vomiting may be deleterious as it will increase bleeding, raise intracranial pressure and may cause cerebral spinal fluid leaks. Ondansetron and dexamethasone have both been shown to be effective in this patient population and should be used routinely.

Anaesthetic technique

No anaesthetic technique has been shown to be superior to another in long-term outcomes. The routine at the Johannesburg craniofacial unit is as follows:

The children and parents are admitted on the day before surgery and seen by the paediatric intensivist and the anaesthesiologist. Routine blood screens are ordered (haemoglobin and white cell count, urea and creatinine and electrolytes, C-reactive protein and coagulation profile) and two units of fresh adult leuco-depleted PRBCs are ordered for theatre.

On the morning of surgery the availability of an ICU bed is confirmed and the patient brought to theatre. Blood is checked for correct identification. A gas induction with sevoflurane is performed, peripheral IV access obtained and the child paralysed with a long-acting non-depolarising muscle relaxant (Pancuronium 0.1 mg/kg). Intubation is performed with a straight reinforced cuffed ETT and the position is fixed using a combination of stretchy pink elastoplast and a ‘tegaderm’ dressing. A pressure-controlled ventilation mode is usually preferred. An oro-gastric tube is passed.

A 3 lumen central venous line is placed in the right internal jugular vein under ultrasound guidance and a radial arterial line is inserted. An arterial blood gas is immediately sent off for analysis. If circumstances dictate, a femoral long line is inserted instead.

Antibiotics, 5HT3 receptor blocker and dexamethasone are administered. Tranexamic acid is given prior to the commencement of surgery with an initial bolus of 15 mg/kg and an infusion of 5 mg/kg till completion of surgery. The head is shaved; a temporary tarsorrhaphy performed to protect the eyes and an indwelling urinary catheter is placed as well as a rectal thermometer.

The patient is then positioned on the foam mattress (Figure 2) in the prone position for total calvarial remodelling or placed supine on a gel head ring if forehead advancement and limited calvarial remodelling is to be done. Fluid warmers and forced air convection warmers are used from the beginning and temperature kept as near normal as possible throughout the procedure.

Ringers lactate and PRBCs are administered according to need. A combination of blood pressure readings, CVP measurements, systolic pressure variation and metabolic parameters on arterial blood gas are used to determine fluid requirements and fluid responsiveness. On average the crystalloid volume infused
during the procedure is 40–50 ml/kg and 20–25 ml/kg of PRBCs. Volumes larger than this may occasionally be required in difficult surgical cases. FFP, platelets and other blood products are not routinely ordered and in almost all cases are not needed if fresh PRBCs are used. Good communication between surgeons and anaesthesiologist is essential particularly when bleeding occurs. The unsuspecting anaesthetist can very quickly get behind on fluids as these children have requirements much higher than expected. Analgesia is provided with fentanyl boluses 5–8 ug/kg as needed and with morphine 0.1 mg/kg once all the bone is removed and bleeding is under control. A dexmetetomidine infusion is started intraoperatively at a rate of 0.4 to 0.6 ug/kg/hour which is continued into the postoperative period. Serial blood gases are done to determine metabolic status, haemoglobin and blood glucose and electrolyte levels.

The total theatre time is usually between 5–6 hours with actual surgical time between 3.5 and 4.5 hours. At the conclusion of surgery the muscle relaxant is reversed once temperature is normal and an acceptable metabolic state is achieved. Similar to what Choi et al found, most patients have a base deficit of between -4 and -8 at the end of the procedure and are extubated with these values. The majority of our patients are extubated and placed on nasal oxygen. Dexmetetomidine is continued in the postoperative period to ensure a calm, non combative patient. This is essential so as to avoid bleeding, raised intracranial pressure and damage to the skull. It is my experience that these children require a larger infusion rate of dexmetetomidine than adults and I often have to supplement with another sedative in the early stages of recovery.

**Conclusion**

Complex craniofacial surgery presents numerous challenges to the paediatric anaesthesiologist. These range from managing difficult airways in syndromic children to coping with large blood volume loss in infants and small children. Exposing these children to allo-immunisation with blood and blood products may be problematic in later life so all efforts to minimise this exposure should be made. Many of the blood conservation techniques used in adults are not always feasible in these children so preoperative optimisation of haematocrit, meticulous surgical technique, careful positioning, temperature and metabolic control together with the use of anti-fibrinolytic agents and an institutional protocol for transfusion triggers forms the mainstay of limiting transfusion of homologous blood and blood products. Advances in cell saving have now made it a viable option in small children where it is available. One must also not neglect dealing with parenteral anxiety and a detailed preoperative counselling of the parents is required.

**References**

Anaesthesia for thoracoscopy in paediatric patients

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Modern equipment and surgical techniques have enabled endoscopic procedures in smaller patients, making thoracoscopy a possibility for a variety of diagnostic and therapeutic procedures, even in very young patients.1,2 (Table I)

To understand the perioperative anaesthetic requirements of paediatric patients for video-assisted thoracoscopic surgery (VATS), a review of the physiology of one-lung ventilation in the lateral decubitus position and techniques of lung isolation are imperative. A review of the general considerations of paediatric anaesthetic practice fall outside the scope of this review, but should be kept in mind during VATS procedures in children.

Pulmonary physiology of one-lung ventilation in children1,3

Several factors cause ventilation-perfusion mismatch in patients undergoing anaesthesia and one-lung ventilation (OLV) in the lateral decubitus position (LDP). Anatomical and physiological differences in children compared to adult patients further predispose these patients to hypoxaemia during such procedures.

In the awake, upright adult, the right lung receives 55% and the left lung 45% of the total lung blood flow. Perfusion favours lower (dependent) parts of the lung due to gravitational effects. In terms of ventilation, dependent lung areas are on the steep, high compliant part of the alveolar volume-transpulmonary pressure curve with ventilation favouring these parts of the lungs, matching ventilation with perfusion.

When the patient is still awake, but positioned in the LDP, gravity increases blood flow to the dependent lung with an average of 40% blood flow to the non-dependent lung and 60% to the dependent lung (disregarding the slight differences between the left and right lungs). Ventilation now also favours the dependent lung. This is due to a vertical gradient in pleural pressure (Ppl) and because the dome of the lower part of the diaphragm is pushed higher into the chest by the abdominal contents compared to the upper part, resulting in a more curved shaped lower diaphragm with enhanced contraction and further increase in ventilation to the dependent lung.

When the patient is anaesthetised and OLV commences, in the absence of confounders or inhibitors of hypoxic pulmonary vasoconstriction (HPV), the absence of ventilation to the non-dependent lung results in HPV with a 50% reduction of blood flow to the non-dependent lung (which now receives 20% of blood flow) and subsequent 50% increase in flow to the dependent lung (which now receives 80% of blood flow). Inhalational anaesthetic agents reduce the effect of HPV so that the reduction in blood flow to the non-dependent lung is approximately 40% with 1 MAC isoflurane (compared to 50% in the absence of vapours). The final blood flow is approximately 24% to the non-dependent (non-ventilated) lung and 76% to the dependent (ventilated) lung in the anaesthetised patient during OLV in the LDP.

During OLV in the LDP, the use of muscle relaxants prevents the diaphragm from contracting, and the effect of the curved bottom part of the diaphragm on ventilation is lost. Under anaesthesia the dependent lung (which is being ventilated) moves to a lower,

<table>
<thead>
<tr>
<th>Table I. Indications for video-assisted thoracoscopic surgery (VATS) in children1,2</th>
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<tbody>
<tr>
<td><strong>Lungs:</strong></td>
</tr>
<tr>
<td>• Biopsy of pulmonary tissue</td>
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<tr>
<td>• Pulmonary resections (wedge resections to lobectomies)</td>
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<tr>
<td>• Closure of recurrent pneumothorax</td>
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<td>• Diagnosis of broncho-pleural fistula</td>
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<tr>
<td><strong>Pleura:</strong></td>
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<tr>
<td>• Decortication of empyema thoracis</td>
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<td>• Pleurodesis</td>
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<tr>
<td><strong>Trachea:</strong></td>
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<tr>
<td>• Trachea-oesophageal fistula repair</td>
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<tr>
<td><strong>Mediastinum:</strong></td>
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<td>• Thymectomy</td>
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<tr>
<td>• Posterior mediastinal neurogenic tumour resection</td>
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<tr>
<td>• Excision of mediastinal cysts</td>
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<tr>
<td><strong>Major vessels:</strong></td>
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<tr>
<td>• Ligation of patent ductus arteriosus</td>
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<tr>
<td><strong>Heart:</strong></td>
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<tr>
<td>• Pericardectomy</td>
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<tr>
<td><strong>Oesophagus:</strong></td>
</tr>
<tr>
<td>• Heller’s myotomy</td>
</tr>
<tr>
<td>• Oesophageal resections</td>
</tr>
<tr>
<td><strong>Diaphragm:</strong></td>
</tr>
<tr>
<td>• Repair of congenital diaphragmatic hernia</td>
</tr>
<tr>
<td><strong>Spine and nerves:</strong></td>
</tr>
<tr>
<td>• Fusions and corrections</td>
</tr>
<tr>
<td>• Thoracic sympathectomy</td>
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<tr>
<td>• Drainage of abscess</td>
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less compliant part of the alveolar volume-transpulmonary pressure curve resulting in a reduced functional residual capacity (FRC). Muscle relaxants also reduce FRC which is often further reduced by the mediastinum resting on the dependent lung, weight of the abdominal contents pushing more into the thoracic cavity of the dependent lung and poor positioning impeding expansion of the dependent lung. Ventilation may be further decreased due to pre-existing pulmonary disease or pooling of secretions in the dependent lung.

The above effects lead to ventilation-perfusion (V/Q) mismatch and susceptibility to hypoxaemia during OLV. The supine position (for orthopaedic and other procedures) enhances the mismatch due to the loss of gravitational effect. Blood distributes to both lungs, whereas ventilation only occurs in the ventilated lung during OLV. The matching of ventilation and perfusion is now even more dependent on HPV.

Paediatric pulmonary physiology\[4-7\] predisposes to further mismatch and an increased tendency towards hypoxaemia during OLV in the LDP. The FRC is reduced in paediatric patients and oxygen consumption is 6–8 ml.kg\(^{-1}\).min\(^{-1}\) compared to 3.5 ml.kg\(^{-1}\).min\(^{-1}\) in adults, both resulting in a smaller oxygen reserve and susceptibility to desaturation during OLV in children. In adults, placing the sick lung in the non-dependent position (as is the case during surgery on the sick lung) offers considerable advantages to V/Q matching. This is not the case in small children due to a variety of factors. The compressible rib cage of the infant cannot fully support the dependent lung, resulting in atelectasis during tidal breathing. Due to their smaller size, the hydrostatic pressure gradient between the two lungs in the LDP is less in small children than in adults, resulting in a less pronounced increased perfusion to the dependent lung in the LDP. As a result of the compressible nature of the infant lung, the FRC is closer to the residual volume (RV) and airway closure can occur even during tidal breathing. The dependent diaphragm in adults has a mechanical advantage due to the increased abdominal pressure gradient, resulting in increased ventilation in the dependent lung. This pressure gradient is absent in infants.

Apart from the physiological effects, anatomical considerations further result in a higher susceptibility to hypoxaemia. Smaller diameter airways necessitate smaller diameter tubes with higher resistance to airflow and an increased tendency to block. Shorter airways result in easier displacement of airway devices.

**Techniques of lung isolation in children**\[1-2,4-5,8,9\]

Although VATS can be performed during two-lung ventilation with CO\(_2\) insufflation and retraction of lung tissue from the operating field, OLV is highly desirable. There are several techniques for OLV in children, each with advantages and disadvantages (Table II). The age and size of the child will determine the devices available for use (Table III).

1. **Single-lumen endotracheal tube**

A conventional single lumen endotracheal tube (ETT) may be placed in the ipsilateral mainstem bronchus. Half a size smaller than for tracheal use is selected. When intubating the left mainstem bronchus, the bevel of the ETT is rotated through 180° and the patient’s head turned to the right. To place the ETT in the right mainstem bronchus, it is simply advanced deeper than for endotracheal use. The ETT is advanced until breath sounds disappear on the operative side. Placement may be assisted or confirmed with a fibre optic bronchoscope (FOB) passed through or alongside the ETT. Fluoroscopy-guided placement has also been described. When a cuffed tube is used, the distance from the proximal part of the cuff to the tip of the ETT should not exceed the length of the bronchus in order to prevent obstruction of the contralateral bronchial opening or trachea. An uncuffed tube may result in inadequate seal with failure of lung collapse and risk of contaminating the healthy lung. Suctioning of the operative lung is not possible and in small children with short bronchi, the risk of occlusion of the upper lobe bronchus is high. Independent intubation of both main bronchi with small ETTs have been described where one ETT is placed, after which the second ETT is advanced over a FOB into the other bronchus. This allows independent ventilation of the two lungs but is difficult to place, can potentially cause trauma and the thin lumens cause high airflow resistance and propensity for obstruction.

2. **Balloon-tipped bronchial blockers**

Bronchial blockers (BB) can be used for a variety of paediatric ages (Tables III and IV). Fogarty embolectomy catheters (Edward Lifesciences, Irvine, CA, USA) are placed with FOB guidance and completely seal the bronchus with good lung isolation. Their closed tips preclude suctioning and continuous positive airway pressure (CPAP) to the operative lung. The use of end-hole catheters (Arrow International Corp, Redding, PA) could overcome these problems. They are placed by first inserting a single-lumen ETT into one bronchus, advancing a guidewire through the tube, removing the tube and railroading the catheter over the guidewire. An FOB is then placed in the trachea alongside the catheter. Suctioning is possible (the lumen is too small to suction secretions but suctioning aids in lung collapse) and CPAP is possible to the operative lung. The Arndt Endobronchial Blocker* (Cook Critical Care, Bloomington, IN, USA) can be used for children older than two years (ETT ≥ 4.5). A three-port adapter accompanies the blocker and attaches to the ETT. The blocker is passed through one of the adapter lumens, the FOB through the second and the third is connected to the anaesthetic breathing circuit. The blocker is hooked around the FOB and advanced under vision.

<table>
<thead>
<tr>
<th>Embolotomy catheters</th>
<th>Arndt bronchial blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Photo: Newtech™ medical devices catalogue)</td>
<td>(Photo: Cook Medical catalogue Arndt_Blocker_Balloon_444114_P_002)</td>
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<tr>
<td>(Permission for use granted by Cook Medical, Bloomington, Indiana)</td>
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</tbody>
</table>
3. Univent tube

The Univent tube (Fuji Systems corporation, Tokyo, Japan) comprises a conventional ETT with a second lumen containing a small tube with a balloon tip which is advanced into a bronchus to serve as a blocker. The blocker lumen can be used for suctioning and insufflation of oxygen. Because the blocker is attached to the ETT, displacement is less likely than with other blockers. The blocker channel does, however, occupy a sizable portion of the cross-sectional area of the device which increases resistance to airflow. The device is placed in the same way as a conventional ETT, after which it is rotated through 90° so that the blocker sits on the appropriate side. The tube is secured and the blocker is advanced either blindly or under FOB guidance.

Univent tube (Photo: Sharn Anesthesia catalogue)

4. EZ blockers

The Rusch® EZ-Blocker™ (Teleflex International Corp, USA) is a BB catheter with a bifurcated distal end with an inflatable balloon at the end of each leg. It is placed through a conventional ETT. While inside the ETT, the legs are in close proximity, but deploy when exiting at the bottom of the ETT to form a Y-shape. Each leg enters one of the main bronchi and the two colour-coded balloons are independently inflated. A multiport is supplied with one port for the blocker, one for the FOB and the third connects to the breathing circuit. Cuff inflation is done under FOB guidance. The blocker is only available in one size with a 7Fr catheter (2.33 mm in diameter) and passes through ETT tubes ≥ size 7.

EZ-Blocker™ (Photo: Teleflex incorporated catalogue)

5. Double lumen tubes

Double lumen tubes (DLTs) (Mallinckrodt Medical, Inc, St Louis, MO, USA for 28-41 Fr and Rüsch, Duluth, GA, USA for 26 Fr) consist of two cuffed tubes of unequal length moulded together with the shorter tube ending in the trachea and the longer tube in either bronchus. The tube is placed through the vocal cords and the stylet is removed before it is rotated 90° towards the appropriate side and advanced until resistance is met. Placement is verified by auscultation ± FOB. The smallest available size is a 26 Fr which can be used in children from eight years of age.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single lumen tube in main bronchus</td>
<td>• Relatively easy to place&lt;br&gt;• Cost-effective&lt;br&gt;• No special equipment required&lt;br&gt;• Can use through tracheostomy tube</td>
<td>• Poor seal if uncuffed (inability to deflate lung and possibility of soiling)&lt;br&gt;• Easily occludes upper lobe bronchus&lt;br&gt;• Unable to suction operative lung&lt;br&gt;• No CPAP possible to operative lung&lt;br&gt;• Slow conversion from OLV to two-lung ventilation and vice versa</td>
</tr>
<tr>
<td>Separate single lumen tube in each bronchus</td>
<td>• Independent ventilation of two lungs&lt;br&gt;• Suction possible</td>
<td>• Technically difficult&lt;br&gt;• Trauma&lt;br&gt;• Small lumens (resistance to airflow, block easily)</td>
</tr>
<tr>
<td>Closed-tip bronchial catheters (Fogarty)</td>
<td>• Good seal&lt;br&gt;• Relatively easy placement</td>
<td>• Inability to suction operative lung&lt;br&gt;• No CPAP possible to operative lung&lt;br&gt;• Tracheal occlusion if dislodges proximally&lt;br&gt;• Slow lung collapse</td>
</tr>
<tr>
<td>End-hole bronchial blocker catheters (BB)</td>
<td>• Can be used when single lumen ETT already in place&lt;br&gt;• Good seal&lt;br&gt;• Good lung collapse&lt;br&gt;• Suctioning possible&lt;br&gt;• CPAP possible&lt;br&gt;• No need to replace ETT at end of procedure&lt;br&gt;• Selective lobar blockage possible&lt;br&gt;• Can use through tracheostomy</td>
<td>• Tracheal occlusion if dislodges proximally&lt;br&gt;• Slow conversion from two-lung to OLV&lt;br&gt;• Independent lung management difficult or impossible (suctioning, FOB inspection, split lung ventilation in ICU)&lt;br&gt;• Easily displaces</td>
</tr>
</tbody>
</table>
Perioperative management of paediatric patients for VATS

Preoperative evaluation

Preoperative workup for thoracoscopy should be similar to the workup for thoracotomy since these patients will also be anaesthetised, might be in the LDP and will most probably be exposed to OLV. The focus of the workup is on pulmonary and cardiac reserve and function. A full history and examination is followed by special investigations which should routinely include a haematocrit, haemoglobin, serum-electrolytes and a chest X-ray. Pulmonary function tests (in older children), ECG and computerised tomography (CT) scans are done as indicated by the patient’s specific pathology.

Patients should be optimised according to their pathology (mediastinal masses could be shrunk by radiation or chemotherapy) and their general condition should be optimised with adequate nutrition, chest physiotherapy, bronchodilator therapy, antibiotics, steroid supplementation and blood transfusion as indicated. As conversion to open thoracotomy is always a possibility and major vessel injury could occur, blood should be ordered on standby.

Anxiolytic premedication could be considered in children without respiratory compromise and could include midazolam.
0.3–0.5 mg.kg\(^{-1}\) p.o or a suitable alternative. Antiemetics and H\(_2\)-antagonists should be administered in patients at risk of aspiration. Fasting times resemble guidelines for routine surgery.

**Intraoperative management**

Monitoring should include ECG, pulse oximetry, non-invasive blood pressure monitoring (NIBP), capnography, temperature monitoring and urinary output in longer cases. Neuromuscular and depth-of-anaesthesia monitoring are convenient optional modalities, the latter being especially useful when a total intravenous technique is chosen.

Large-bore peripheral lines should be placed in the event of conversion to thoracotomy or massive bleeding. The literature regards arterial lines mostly as optional or indicated by specific pathological conditions, but the author prefers them in all patients undergoing OLV for both blood gas and electrolyte analysis and continuous blood pressure monitoring. When end-tidal CO\(_2\) (ETCO\(_2\)) levels drop, a continuous blood pressure trace will differentiate between airway compression and compression of the heart or major vessels. When a central venous pressure catheter is indicated (for drug administration or central venous pressure monitoring), the catheter should be placed on the side of the thoracotomy to prevent the eventuality of bilateral pneumothoraces.

Patient positioning should take meticulous care of pressure points as well as optimization of the effect of gravity on perfusion and subsequent matching of ventilation and perfusion. In the LDP, potential pressure points are the dependent eye and ear, acromion process, olecranon, ribs, iliac crest, greater trochanter, condyles and malleoli. To optimise perfusion to the dependent lung (the ventilated lung) in the LDP, the patient needs to be perfectly perpendicular to the bed. Slight ventral or dorsal tilt will decrease the gravitational effect and reduce perfusion. When placing a patient in the LDP, the dependent arm is perpendicular to the body, the dependent knee flexed, padding placed under the ankles, between the knees, under the hip (for protection of the greater trochanter and iliac crest), behind the olecranon and between the arms. The dependent eye and ear should be free, the neck supported and in line with the body and a chest roll (just distal to the axilla) in place. The abdomen should be allowed unobstructed movement.

Anaesthetic technique (local anaesthesia, regional anaesthesia or general anaesthesia) will depend on the age and pathology of the child. Local anaesthesia is rarely an option but could be considered in older children for short procedures without intrathoracic surgical manipulation or in moribund patients, especially where spontaneous breathing is paramount. Such patients are, however, often not able to withstand the required lung collapse for thoracoscopy in which case local anaesthesia is not a viable option. Regional techniques include epidural, paravertebral block or multi-level intercostal blocks, often supplemented with a stellate ganglion block to suppress the cough reflex.

For general anaesthesia, induction and maintenance are possible with inhalational or intravenous drugs. The effect of each drug on HPV (Table V) and cardiac output should be considered in addition to the pathology and general condition of the patient. The decision to extubate the patient in theatre or ventilate postoperatively, will also influence the choice of drugs. Muscle relaxants are commonly used, except in instances where spontaneous ventilation is mandatory, as is mostly the case with anterior mediastinal masses. A balanced anaesthetic with opioids and inhalants is probably advisable (see below). Nitrous oxide should be avoided when gas insufflation is used as it can enhance gas embolism. This is less of an issue when CO\(_2\) is used (solubility of nitrous oxide and carbon dioxide are similar), but nitrous oxide is still best avoided.

OLV is achieved with one of the methods previously described. Especially in smaller children where lung isolation is impossible or suboptimal, CO\(_2\) insufflation into the operative hemithorax facilitates lung collapse. At this point displacement of intrathoracic contents and tension pneumothorax can cause significant cardiovascular compromise due to increased left ventricular afterload or decreased venous return reducing cardiac output. Insufflation can also lead to bradycardia due to increased vagal tone caused by activation of pulmonary stretch receptors. Therefore, insufflation rate should not exceed 1 litre/minute and insufflation pressure should be between 4–6 mmHg. Insufflation of CO\(_2\) directly into lung parenchyma is possible and could lead to sudden increase in ETCO\(_2\), subcutaneous emphysema and gas embolism. CO\(_2\) is used for insufflation because it is more soluble in blood than O\(_2\) or air and poses a smaller risk for embolisation.

Methods described to monitor for gas embolism include transoesophageal echocardiography (detects 0.1 ml of gas), precordial Doppler (detects 0.5 ml) and capnometric end tidal nitrogen monitoring (for air embolism but not useful in detecting CO\(_2\) emboli). ETCO\(_2\) monitoring is also useful to detect gas embolism. CO\(_2\) insufflation could lead to hypothermia in small children and meticulous temperature management is mandatory.

Hypercarbia during VATS is more common in young children than in adults. Possible causes include hypoventilation, CO\(_2\) insufflation and malpositioning of airway devices.

Hypoxaemia during OLV is not uncommon and several management strategies are described (see Table VI). Specific variables influence oxygenation during OLV and should be optimised in the event of hypoxaemia. These are pulmonary shunt fraction (Qs/Q\(_T\)), haemoglobin concentration and the ratio between oxygen consumption and cardiac output (VO\(_2\)/Q\(_T\)). Reducing Qs/Q\(_T\) is achieved by optimising HPV in the non-dependent lung while minimising pulmonary vascular resistance in the dependent lung. This is mainly achieved by good lung isolation and selecting drugs with minimal effect on HPV. Haemoglobin should be optimal for patient age. Cardiac output should be optimal but injudicious use of inotropes will be contra-productive as increased Q\(_T\) could increase pulmonary artery pressure and reduce HPV and inotropes can directly reduce HPV. Inhalational agents will decrease VO\(_2\) but will also reduce Q\(_T\), negating the positive effect on oxygenation. It is therefore probably advisable to use a balanced anaesthetic technique with opioids and inhalants at concentrations of < 1 MAC, limiting the reduction in Q\(_T\). Inhalants are good bronchodilators and their half-life is short, permitting extubation.
in theatre. Further strategies to manage hypoxaemia during OLV include increasing $F_O_2$, maintaining adequate tidal volume (too low will cause atelectasis in the dependent lung with subsequent intrapulmonary shunt and hypoxaemia and too high (> 10 ml/kg) will increase pulmonary vascular resistance in the dependent lung and will force blood to the nondependent lung which will also increase intrapulmonary shunting), apply positive end-expiratory pressure (PEEP) to the dependent lung and apply intermittent two-lung ventilation. Continuous positive airway pressure (CPAP) to the non-dependent lung is probably not advisable during thoracoscopy as this might compromise visibility.

Table V. Effects of drugs on hypoxic pulmonary vasoconstriction

<table>
<thead>
<tr>
<th>Minimal effect on HPV</th>
<th>Reduces HPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane &lt; 1 MAC</td>
<td>Vasodilators (nitroglycerine, dobutamine)</td>
</tr>
<tr>
<td>Opioids</td>
<td>Beta-agonists (salbutamol)</td>
</tr>
<tr>
<td>Propofol</td>
<td>Inhalants if &gt; 1 MAC</td>
</tr>
<tr>
<td>Ketamine</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td></td>
</tr>
</tbody>
</table>

HPV = hypoxic pulmonary vasoconstriction; MAC = minimum alveolar concentration

Table VI. Strategies to manage hypoxaemia during one-lung ventilation

- Check ETT tube positioning
- Suction airway
- Check cardiac output
- Check haemoglobin
- Consider drug effects on HPV – Table V
- Increase $F_O_2$
- Optimise tidal volume
- PEEP to dependent lung (5 cmH2O)
- No CPAP during VATS
- Intermittent two-lung ventilation

ETT = endotracheal tube; HPV = hypoxic pulmonary vasoconstriction; $F_O_2$ = inspiratory fraction of oxygen; PEEP = positive end expiratory pressure; CPAP = continuous positive airway pressure; VATS = video-assisted thoracoscopic surgery.

Analgesic requirements for VATS are less than for thoracotomy because of smaller incisions without splitting of serratus anterior and latissimus dorsi muscles and spreading of ribs. Chest drains are, however, painful and pleural procedures require more than simple analgesia. Analgesia is often achieved with paracetamol, nonsteroidal anti-inflammatory drugs, and intravenous opioids supplemented by local infiltration of the port sites or intercostal nerve blocks. Neuromax local anaesthetic agents or opioids are reserved for open procedures.

Apart from ventilation and perfusion challenges, intraoperative complications could include dysrhythmias, re-expansion pulmonary oedema and massive bleeding. Vigilance on the part of the anaesthetist is paramount.

Postoperative care

Postoperative care for thoracoscopic procedures is not different from thoracotomies. Analgesia and chest physiotherapy are important and early chest radiographs should be done to exclude pneumothorax or severe atelectasis. The perioperative team should focus on early detection and management of postoperative complications, including bleeding, lung herniation through the chest wall, Horner syndrome, persistent air leak, respiratory complications (atelectasis and pneumonia) and infection (wound infection, abscess or empyema).

Thoracoscopy in children is less invasive than thoracotomy, but due to their smaller size with associated physiological and equipment difficulties, this is often more challenging than anaesthesia for thoracoscopy in adults. Paediatric thoracic anaesthetists should be well versed in the physiology of OLV and LDP as well as the various types of equipment available for lung isolation in children.

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References
Mediastinoscopy in paediatric patients

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Mediastinal pathology presents a diagnostic and therapeutic dilemma that requires management from a multidisciplinary team, often consisting of members of various specialties, including an anaesthetist, surgeon, radiologist, oncologist and intensivist.1 Discourse and planning are paramount.

Anatomy of the mediastinum

The mediastinum is divided into a superior and inferior part, the division being an imaginary line extending from the sternomanubrial junction to the T4 vertebra. The inferior part is further divided into three parts. Of these three parts, the anterior mediastinum lies posterior to the sternum, anterior to the pericardium, superior to the diaphragm, inferior to the superior mediastinum and medial to the parietal pleurae. The middle mediastinum is bordered anteriorly by the anterior margin of the pericardium, posteriorly by the posterior border of the pericardium, laterally by the mediastinal pleura (parietal pleura) of the lungs, superiorly by the superior mediastinum and inferiorly by the diaphragm, whereas the posterior mediastinum is situated posterior to the pericardium and great vessels, anterior to the T4–T12 vertebrae, superior to the diaphragm, inferior to the superior mediastinum and lateral to the parietal pleurae.1

Presentation of mediastinal tumours

In children under the age of two years, most tumours are benign and the incidence of malignancies increases above this age.1 Different types of malignant tumours are found in the three different parts of the inferior mediastinum. In children, the most common anterior mediastinal tumours are lymphoma (Hodgkin and non-Hodgkin), thymoma and teratoma.1 In the middle mediastinum lymphoma is the most common with tumours of neuronal tissue most frequently found in the posterior mediastinum. The clinical presentation depends on where the tumour is situated and which structures are compressed (see Table I).

Techniques of mediastinoscopy

Mediastinoscopy was first described by Harken2 in 1954, followed by the development of the suprasternal approach by Carlen3 and his colleagues in 1959 and the anterior mediastinotomy approach by Chamberlain4 in 1966. By permitting minimally invasive access to the mediastinum, mediastinoscopy is utilised to obtain biopsies of mediastinal lymph nodes and masses in order to facilitate tissue diagnosis for staging and treatment purposes.1 It is therefore mainly a diagnostic procedure.

Superior (cervical) mediastinoscopy is not commonly used in children,6 although its safe use has been reported in children older than one year.7 The technique utilises a small transvers incision in the suprasternal notch, with advancement of the scope through the pretracheal fascia into the mediastinum and down towards the carina. The scope is therefore inserted...
anterior to the trachea and posterior to the aortic arch and lies in close proximity to several major vessels in the mediastinum. Although this technique is advantageous due to its minimally invasive nature, it affords the surgeon only limited access to lymph nodes in the superior mediastinum up to the level of the carina (anterior and lateral para-mainstem bronchial, anterior subcarinal, anterior and lateral paratracheal lymph nodes) and allows poor access to the aortocapulmonary window. Successful biopsy of the thymus has been done through this route.

The anterior mediastinotomy (also called anterior mediastinoscopy), of which the Chamberlain’s procedure is one example, is a surgical technique where the second or third intercostal space is incised lateral to the sternum to allow access to the anterior mediastinum, right paratracheal area and aortocapulmonary window, where biopsies of lymph nodes and anterior mediastinal masses can be obtained.

Middle and posterior mediastinal masses are biopsied through thoracoscopy or thoracotomy.

**Contraindications to superior mediastinoscopy**

Absolute contraindications to superior mediastinoscopy are listed as anterior mediastinal masses, inoperable tumours, previous recurrent laryngeal nerve injury, severely debilitated patients, ascending aortic aneurysms and previous mediastinoscopy (due to adhesions) while relative contraindications mentioned include severe tracheal deviation, cerebrovascular disease, superior vena cava syndrome and descending thoracic aortic aneurysm.

**Anaesthetic implications of mediastinal masses**

Patients booked for superior mediastinoscopy usually present with mediastinal lymph nodes but no anterior mediastinal masses (as these are contraindications to the procedure). Those for Chamberlain’s procedure may present with a range of symptoms from asymptomatic to severe respiratory or cardiovascular compromise. Patients with mediastinal masses may present with superior vena cava (SVC) syndrome and are at risk of compression of the heart, the great vessels or the tracheobronchial tree (often below the level of an endotracheal tube), especially under anaesthesia (see below). Anaesthetic risk is increased in patients with a narrowing of the trachea or bronchi on computerised tomography (CT) scan to < 50% of predicted cross-sectional area. Symptoms like dyspnoea are good predictors of the degree of obstruction, with a good correlation between severity of symptoms and cross-sectional area of the airways.

The compression effects of mediastinal tumours place these patients at severe risk of decompensation under anaesthesia. During general anaesthesia, especially with the use of muscle relaxants and positive pressure ventilation, lung volume is reduced due to a loss of inspiratory muscle tone and the loss of the tethering effect of the expanded lung on the airway, which is normally present during spontaneous ventilation. There is a reduction in the normal transpulmonary pressure gradient which distends the airway during spontaneous inspiration, leading to further reduction in airway caliber. Whereas the diaphragm moves in a caudad direction during spontaneous inspiration, pulling the airways open, it moves cephalic at end-expiration during positive pressure ventilation, resulting in further airway compromise. Gravity pulls the tumour onto the great vessels and tracheobronchial tree. These effects are exaggerated in small children due to the increased cartilages component of their ribs which results in an increased compliance of the chest wall and an inability of the chest wall to support the tumour which then compresses major structures in the mediastinal cavity. The small child already has small diameter airways with high airway resistance. Poiseuille’s teaches that during laringoscopy in a tube, resistance is inversely proportional to the radius to the power of four. During positive pressure ventilation, laringoscopy is disrupted and during subsequent turbulent flow, the pressure gradient that drives gas flow is proportional to the density of the gas. Heliox, a mixture of oxygen and helium (helium has a lower density than air) has been used successfully in a child with a mediastinal mass during anaesthesia with a laryngeal mask and spontaneous breathing. Due to the above pathophysiological reasons, spontaneous ventilation is preferred in patients with mediastinal masses. The oxygen demand in children is higher than in adults and the functional residual capacity (FRC) of the child is reduced, predisposing to faster desaturation. The addition of CPAP during spontaneous ventilation could maintain the FRC.

Two possible disadvantages to spontaneous breathing during superior mediastinoscopy are firstly the possibility that the child might move in the absence of a muscle relaxant, with subsequent injury to any of the vital structures adjacent to the scope and secondly the possibility of air embolism, as this procedure is done in the head-up position to reduce engorgement of blood vessels and the operative site is therefore above the heart. The tip of the mediastinoscope is located intrathoracically and therefore directly exposed to pleural pressure, making the possibility of venous air embolism likely when venous bleeding occurs. Spontaneous breathing will enhance this risk due to the generation of negative intrathoracic pressure during inspiration.

**Perioperative management of patients for mediastinoscopy**

The preoperative preparation of the child should aim at optimising respiratory and cardiovascular function. In patients with mediastinal masses, the nocturnal sleeping position of the child (likely position to cause least compression of major structures) should be determined. A thorough history and clinical examination aim to detect SVC syndrome, tracheobronchial compression, compression of the heart or great vessels, involvement of the myocardium, cardiac tamponade and other complications of mediastinal masses as well as complications generally associated with malignancies or chronic disease. It should be remembered that wheezing is often the only sign of tracheobronchial compression in small children. A peripheral lymph node should always be sought. This could be used for biopsy under local anaesthesia with sedation and will spare the patient a general anaesthetic with the associated risks. The child should also be assessed for contraindications for the procedure. Special investigations include a full blood count with platelet count, renal function and electrolytes. Blood gas analysis should be done per indication. Imaging should include...
a chest X-ray and a contrast-enhanced CT scan to determine the size of the mass or lymph node involvement. Magnetic resonance imaging (MRI) scans may be better able to determine nerve plexus and blood vessel involvement and are especially indicated in patients with iodine allergy or in thyroid tumours. Transsthoracic echocardiography can assess the involvement of cardiac structures and supply dynamic information about ventricle compression, SVC compression and compromise of the pulmonary outflow tract. Some authors advocate the usefulness of lung function tests in the supine and sitting positions in older children, which may reveal distortion of the expiratory flow rate in intrathoracic obstruction, distortion of inspiratory flow rate in extrathoracic obstruction and equal reduction in inspiratory and expiratory flow rates in fixed lesions. Others argue against the usefulness of lung function tests in the work-up of patients with mediastinal masses due to their poor correlation with the degree of obstruction.

The need for biopsies are often urgent, as some common Hodgkin lymphomas display a doubling time of 12 hours. If the tumour is large with significant cardio-respiratory compromise, steroids and/or irradiation are suggested in order to shrink the tumour and reduce its compression effects. Although this might compromise the integrity of the tissue and reduce the likelihood of a proper tissue diagnosis, studies have shown that adequate tissue diagnosis is possible, especially if a section of the tumour is shielded from radiation.

Standard nil per os guidelines are adhered to, prophylactic antibiotics prescribed or administered in theatre and blood products ordered on standby. Sedative premedication is probably best avoided in patients with cardiovascular or respiratory compromise.

The preferred position then is the one determined preoperatively as the patient’s preferred nocturnal sleeping position, failing which, the lateral decubitus positions (especially the left lateral decubitus) or prone position should be trialed.

Standard American Society of Anesthesiologists (ASA) monitoring is applied. Capnography allows early detection of airway compression or cardiovascular collapse and temperature monitoring is mandatory, especially in small children. Depth of anaesthesia monitoring permits an adequate anaesthetic plane during maintenance with intravenous agents or in compromised patients where excessive inhalational agent concentration might further suppress cardiovascular function. Neuromuscular transmission monitoring might prevent postoperative residual muscle relaxant effects, but is probably more important in adult patients with myasthenic effects of mediastinal malignancies. Urinary catheterisation is usually not indicated due to the short nature of the procedure.

In patients with mediastinal masses, intravenous access should be obtained while the patient is awake if at all possible, to allow for intravenous administration of emergency drugs if cardiovascular or respiratory collapse ensue. Two large-bore lines should be inserted in preparation of possible massive bleeding. In the presence of SVC syndrome, these should be inserted in the lower limbs due to the slow circulation of blood in the SVC distribution and the possibility of further engorgement with fluid administration. Central venous cannulas are not routinely inserted, but should it be warranted in a patient with SVC syndrome, the preferred site is the femoral vein. In other instances, the central venous catheter is placed on the side most likely to develop a pneumothorax caused by the surgical procedure. If placed in the right radial artery during superior mediastinoscopy, the arterial line tracing may disappear or display false low readings, when the innominate artery is occluded. Although this is a way of monitoring the patency of the innominate artery (to prevent cerebrovascular damage), it is preferable to insert the arterial line on the left (in order not to lose the trace) and to place a second saturation probe (apart from the one used to monitor saturation which should be on the left) on the right hand for monitoring the innominate artery.

Local anaesthesia is not indicated in the majority of paediatric patients. Older children or moribund younger patients could be considered for local anaesthesia with sedation. In comparison with general anaesthesia, this has the beneficial effects of being safer in terms of cardiovascular and respiratory function, often reduces theatre times and enables early detection of pneumothorax and recurrent laryngeal nerve injury. In adults and much older children, awake fibre optic intubation with spontaneous ventilation could be attempted.

Flexible bronchoscopy might precede mediastinoscopy and anaesthesia should be planned accordingly. Induction of anaesthesia should be done in a semi-fowler or sitting position in the presence of symptomatic mediastinal masses and should aim at maintaining spontaneous respiration and cardiovascular function. The use of inhalational agents or ketamine have been described. It must be kept in mind that ketamine stimulates the formation of secretions which might further increase airway
resistance in small or obstructed airways and necessitates the co-administration of an anticholinergic agent. Ketamine may also cause cardiovascular collapse in chronically ill patients with depleted catecholamine stores.26 Where muscle relaxants will be omitted, spraying of the vocal cords with lignocaine might aid the blunting of the intubation response and might reduce intraoperative coughing,9 but might result in postoperative aspiration due to inhibition of sensory innervation of the supraglottic airway.27 Intravenous induction is permitted in children with intravascular access in the absence of mediastinal masses. Intubation should be done with care in patients with head and neck engorgement to avoid airway bleeding. A reinforced (armoured) tube should be used in patients with mediastinal masses in order to prevent the mass from occluding the airway and for superior mediastinoscopy to prevent the surgeon from occluding the tube while working in close proximity with the patient’s head. Endotracheal tubes should be carefully secured to prevent dislodgement by the surgeon, especially during superior mediastinoscopy.26 Maintenance of anaesthesia23 should aim at spontaneous respiration in patients with mediastinal masses and could again be accomplished with inhalational agents or ketamine. Inhalational or intravenous techniques are used in patients where positive pressure ventilation is permitted. Nitrous oxide (N₂O) is best avoided due to the possible risk of procedure-related pneumothorax which will expand in the presence of N₂O. The use of muscle relaxants is optional but advisable during mediastinoscopy in the absence of compressing lesions, in order to afford the surgeon optimal operating conditions and to prevent sudden patient movement with injury to vital structures, especially during superior mediastinoscopy. The focus of intraoperative care should be on the early identification and management of complications11 caused by the surgical technique (especially during superior mediastinoscopy) or the disease process (especially during anterior mediastinoscopy).

During anterior mediastinotomy the visibility is better with less likelihood of injury to anatomical structures, but patients often present with complications of mediastinal masses. During superior mediastinoscopy, the scope is placed adjacent to a number of vital structures and massive bleeding from any of the major vessels (innominate artery, innominate vein azygos vein, aorta, bronchial artery, pulmonary artery etc) is possible. Massive bleeding requires emergency sternotomy or thoracotomy. In the instance of SVC injury, additional intravenous access should be obtained in the lower limbs.18 Other possible intraoperative complications include pneumothorax, innominate artery compression, oesophageal injury, tumour seeding, chilothorax or air embolism. Intraoperative dysrhythmias are possible due to pressure on the heart or great vessels, pulling on mediastinal structures, pericardial or pleural effusion, or myocardial involvement of the malignancy. Negative pressure pulmonary oedema may follow deep inspiratory efforts against obstructed airways which generate large negative pressures (mainly seen in adults).

Due to the minimally invasive nature of mediastinoscopy, intra- and postoperative analgesic requirements are limited to balanced pharmacological analgesic regimens in conjunction with local infiltration of wound sites.

Following both superior mediastinoscopy and anterior mediastinotomy, patients are mostly extubated in theatre. Patients with mediastinal masses should be nursed in the head-up position in the postoperative period in order to reduce venous engorgement, and monitored closely for complications.11,17 They may experience worsening of obstruction caused by swelling or increase in turbulent air flow due to pain, coughing, tachypnoea or anxiety.18 The incidence of postoperative respiratory complications is proportional to the size of the tumour. Following superior mediastinoscopy, bleeding caused by blood vessel injury might manifest in the postoperative period. Postoperative hemiparesis may follow intraoperative carotid artery compression, while recurrent laryngeal nerve injury may cause vocal cord paralysis with stridor or airway compromise and phrenic nerve injury may result in respiratory compromise. Any of the two mediastinoscopy sites might be complicated by infection.

In summary, the anaesthetic plan for both superior and anterior mediastinoscopy is determined by the underlying pathology and the selected route of surgical access. Vigilance and adaptability are crucial as clinical conditions can change rapidly. Good planning and sound knowledge of the pathology and surgical techniques are therefore paramount.

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**References**


The obese parturient

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Introduction

The prevalence of obesity worldwide is increasing. In the United States (USA) the prevalence of obesity was found to be 35.0% among men and 40.4% among women by the National Health and Nutritional Examination Survey during 2005–2014.1 Maternal pre-pregnancy obesity has increased from 17.6% in 2003 to 20.5% in 2009 according to a survey in the USA in 20 states.2 Maternal obesity is associated with increased rates of gestational diabetes, pre-eclampsia, operative delivery, long-term risks to the foetus and increased mortality in both mother and foetus (Table I).3,4

Table I. Complications associated with maternal obesity in pregnancy

<table>
<thead>
<tr>
<th>Maternal complications</th>
<th>Respiratory:</th>
<th>Cardiovascular:</th>
<th>Musculoskeletal:</th>
<th>Gastrointestinal:</th>
<th>Endocrine:</th>
<th>Other:</th>
<th>Foetal:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dyspnoea</td>
<td>Hypertension/Pre-eclampsia/Eclampsia</td>
<td>Low-back pain</td>
<td>Gastroesophageal reflux</td>
<td>Gestational diabetes mellitus</td>
<td>Risk of Caesarean delivery</td>
<td>Prematurity</td>
</tr>
<tr>
<td></td>
<td>Obstructive sleep apnoea</td>
<td>Congestive heart failure</td>
<td>Immobility</td>
<td>Fatty liver</td>
<td>Dyslipidaemia</td>
<td>Wound infections</td>
<td>Stillbirth</td>
</tr>
<tr>
<td></td>
<td>Hypoventilation</td>
<td>Thrombo-embolism</td>
<td>Osteoarthritic knees and hips</td>
<td></td>
<td></td>
<td></td>
<td>Neural tube defects</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Macrosomia</td>
</tr>
</tbody>
</table>

| Weight gain during pregnancy |

Obesity is usually defined using the Body Mass Index (BMI) where BMI is equal to weight/height² (kg/m²). Normal weight is defined as a BMI of 18.5–24.9 kg/m², overweight as a BMI 25–29.9 kg/m² and obesity as a BMI more than 30 kg/m².7

The Institute of Medicine in the USA recommends that women should try and limit weight gain during pregnancy, as shown in Table II. This should be determined according to the pre-pregnancy weight.8

Table II. Recommended weight gain during pregnancy

<table>
<thead>
<tr>
<th>Pre-pregnancy BMI (kg/m²)</th>
<th>Recommended weight gain (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5</td>
<td>12.5–18</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>11.5–16</td>
</tr>
<tr>
<td>25–29.9</td>
<td>7–11.5</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>5–9</td>
</tr>
</tbody>
</table>

Anaesthetic considerations in the obese parturient

There is an increased risk in providing anaesthesia for obese parturients as compared to normal weight parturients. The combination of physiological changes and obesity may affect the anaesthetic management of these patients. Obese patients often pose a diagnostic challenge. The changes in the airway, respiratory and cardiovascular systems are important to note.7 Placement of monitors, intravenous access and provision of labour analgesia, neuraxial anaesthesia or general anaesthesia for Caesarean section have an increased technical difficulty in performing and pose a higher risk in caring for the obese parturient.5,8

Airway

A failed tracheal intubation in the general public occurs in around 1:2 500 patients, however in the obstetric patient the risk increases to 1:280 patients. In the obese parturient the risk may increase to 1:3 for having a difficult or failed intubation.5 Mask ventilation may also be more difficult.7 The increased risk of aspiration of gastric content in the pregnant patient should also be taken into consideration. Results from the 4th National Audit Project of the Royal College of Anaesthetists and The Difficult Airway Society on major complications of airway management in the United Kingdom (NAP 4) report indicated that airway problems in the obstetric population were reported in four cases, all were for out-of-hours emergency Caesarean sections, and two had a BMI > 35 kg/m².7

Maltby et al10 found no statistical difference between obese surgical patients that ingested 300 ml of clear liquid two hours
before surgery compared to those fasted for six hours. Similar results were found by Juvin et al.\textsuperscript{11} and Wong et al.\textsuperscript{12} Obese patients without other co-morbid conditions should follow the standard starvation guidelines. Labour itself does prolong gastric emptying, and should a general anaesthetic be necessary for a Caesarean section, a rapid sequence induction and intubation should be performed.\textsuperscript{7}

A comprehensive airway examination focussing on Mallampati score, mouth opening and range of neck movement should be done before embarking on any anaesthetic for an obese parturient. Changes in the airway are due to fat deposition in the neck, back and airway in obese patients and pregnancy induced soft-tissue changes like enlarged breasts.\textsuperscript{7,13} Factors associated with difficult laryngoscopy include: short sternomental and thyromental distance, increased neck circumference, limited neck and jaw movement, receding mandible and prominent teeth.\textsuperscript{6}

**Respiratory system**

Changes include displacement of the diaphragm in a cephalad position due to the enlarging uterus, as well as a reduction in the functional residual capacity (FRC). This can be significant enough to cause the closing capacity to exceed the FRC during tidal breathing. Furthermore, oxygen consumption and minute ventilation increases. Hypoxaemia and rapid desaturation can ensue due to this.\textsuperscript{14} Obstructive sleep apnoea may be present, however there is no validated screening tool specific to pregnancy. Postoperative complications are more common, including atelectasis and hypoxaemia. All these contribute to an increased risk for in-hospital death.\textsuperscript{5}

**Cardiovascular changes**

Normal pregnancy changes in the cardiovascular system include increase in stroke volume, heart rate, cardiac output and pulse pressure. All of which may be poorly tolerated in the obese patient. Aorticval compression may be exacerbated in these patients. Obesity related cardiovascular diseases (hypertension, ischaemic heart disease, diabetes mellitus and congestive heart failure) may be aggravated. Obesity is a risk factor for developing peripartum cardiomyopathy.\textsuperscript{5,7} There should be a low threshold for echocardiographic examination.

**Anaesthetic management**

**Pre-labour considerations**

Ideally all obese pregnant patients should have an anaesthetic evaluation before labour. This will help identify risk factors and aid in proper planning and preparation to minimise complications during labour and possible surgical intervention.\textsuperscript{6} Multidisciplinary meetings between obstetricians, anaesthetists, midwives and nursing staff should be held with regard to need for additional operating tables, monitoring, and postoperative care.\textsuperscript{13} It has been demonstrated that despite an antenatal anaesthetic consultation most obese pregnant women remained unaware of the risks of obesity in pregnancy.\textsuperscript{15}

Accurate blood pressure measurements are required during neuraxial analgesia and anaesthesia, it is important to select the correct size non-invasive blood pressure cuff. Often in the morbidly obese patient this is not possible and invasive blood pressure monitoring should be utilised. Peripheral venous and central venous access may be very difficult to place; ultrasound guidance may be useful in this regard.\textsuperscript{13}

**Labour analgesia**

There is an increased risk of foetal macrosomia and labour difficulties (shoulder dystocia, prolonged labour, labour induction and augmentation), with increased risk of more painful contractions. Early placement of a functioning labour epidural catheter is advised. This can then be used should there be the need to convert to Caesarean section.\textsuperscript{7}

Despite the advantages of labour epidurals, the placement of an adequately working epidural catheter can be challenging. Reasons for this include difficulty identifying anatomical landmarks and increase in depth of epidural space. Jordan et al.\textsuperscript{16} found that almost 75% of morbidly obese pregnant patients required multiple attempts in placing an epidural. The midline can be difficult to identify, but having the patient seated may be beneficial.\textsuperscript{7} Other risks include catheter dislodgement and migration. Leaving a longer length of catheter in the epidural space may increase the risk of having a one-sided block.\textsuperscript{13}

The use of ultrasound to identify the midline may be useful but its use in identifying the structures of the vertebral column may be limited in the morbidly obese patient. The use of a combined spinal epidural (CSE) may be advantageous in this population, as it provides fast onset analgesia, but there is the risk of developing a post-dural puncture headache (PDPH). PDPH has been postulated to have a decreased incidence in obese patients as compared to normal weight parturients, but a retrospective record review by Miu et al.\textsuperscript{17} from 2014 found the incidence of PDPH not to differ significantly between obese versus non-obese parturients. Should PDPH be present, the performance of an epidural blood patch as part of the management may be more difficult.\textsuperscript{13}

**Choice between neuraxial vs general anaesthesia for Caesarean section**

There are risks and complications involved with both neuraxial and general anaesthesia techniques. Some recommendations to consider before surgery are shown in Table III.

**Table III. Recommendations pre-, intra- and postoperatively in obese parturients\textsuperscript{18}**

- Cardiac evaluation (baseline ECG, possible cardiology consultation, echocardiogram)
- Broad-spectrum antibiotics 20–30 min before skin incision (2 g Cefazolin)
- Ensure that the operating table is adequate for weight, may need extra table, or special obese operating table, additional theatre personnel
- Consider availability of blood products as necessary due to increased risk of intra- and postpartum haemorrhage
- Pneumatic compression stockings should be considered intra- and postoperatively
- DVT prophylaxis (BMI > 40 kg/m²)
- Early ambulation
Regional anaesthesia

Regional anaesthesia is advantageous due to avoidance of intubation and decreased risk of aspiration, but it can be technically challenging owing to the changes in anatomy. For the morbidly obese parturient, single-shot spinal, epidural and CSE have all been used successfully. The dose of local anaesthetic for single-shot spinal should not be reduced, unless the patient is shorter than 1.5 m tall. Placing a catheter for an epidural or CSE has the benefit of providing prolonged anaesthesia and analgesia should surgery be difficult or longer in duration.

In a retrospective study by Vricella et al from 2008, 142 morbidly obese, 251 obese and 185 normal weight patients coming for Caesarean section were investigated with regards to outcome of the anaesthetic. Complicated placement (5.6%), failure to establish (2%) and insufficient duration (4%) of block was found in morbidly obese patients who had regional anaesthesia. Overall complication rate was 8.4% in the morbidly obese group.

Continuous spinal anaesthesia and double catheter techniques have been described for the super morbidly obese patients, but these are technically very difficult to perform, with the added risk of PDPH.

General anaesthesia

There is a greater morbidity and mortality associated with general anaesthesia for the morbidly obese parturient. The incidence of inability to visualise the vocal cords is twice as high in obese parturients. The airway changes, risk of aspiration and difficulty in intubating has been discussed above.

Strategies to overcome the risks involved with general anaesthesia includes the following:

- Having senior anaesthetic help available.
- Following standard starvation guidelines.
- Pulmonary aspiration prophylaxis including sodium citrate, H₂-antagonists and performing a rapid sequence induction.
- Placing the patient in a ‘ramped’ position by placing folded towels or pillows under the chest and head, in order to ensure that the external auditory meatus and the sternal notch are in a horizontal plane, which aligns the oral, pharyngeal and tracheal axes.
- Adequate pre-oxygenation. This is done with a tight fitting mask, breathing 100% oxygen for five minutes or four maximal inspiration breaths.
- Availability of rescue airway devices (supraglottic airway devices, intubating laryngeal mask airways), video laryngoscopy devices (CMAC), fibre optic bronchoscopes and surgical access devices (cryothyrotomy sets).
- Following difficult airway algorithms, e.g. The Obstetric Anaesthetist’ Association and The Difficult Airway Society (OAA/DAS) guidelines for management of difficult and failed tracheal intubation in obstetrics.
- Possible use of transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) to overcome desaturation and apnoea during induction, however no literature could be identified investigating the use of THRIVE in the pregnant population. The OAA/DAS guidelines for the management of difficult and failed tracheal intubation in obstetric patients suggest the use of nasal oxygenation, but the method is not clearly described.
- Extubation should occur in a semi-upright position when the patient is fully awake and alert. The use of supplemental oxygen is advocated.

Postoperative care

A review of maternal deaths in Michigan from 1985–2003 revealed 855 pregnancy-associated deaths, where eight were anaesthesia related and seven had contributing factors from anaesthesiology. Five of these deaths were in the postoperative period, due to hypoventilation or airway obstruction. During 2006–2010, in Wisconsin, among pregnancy-related deaths, 12% were overweight and 65% were obese.

Postoperative complications such as hypoxaemia, atelectasis and pneumonia, deep vein thrombosis and pulmonary embolism, post-partum cardiomyopathy, pulmonary oedema and infective complications are more common in the obese parturient.

Most of these complications can be prevented by good postoperative care, including good analgesia and thromboprophylaxis and vigilance to prevent hypoxia and respiratory depression. Multimodal analgesia should be provided, including nonsteroidal anti-inflammatory agents and local anaesthesia. Sedating agents and opioids should be used judiciously. Providing adequate analgesia enables early mobilisation and improves respiratory function, which in turn aids prevention of deep vein thrombosis. Despite these measures, additional thromboprophylaxis should be provided for these patients. Patients with obstructive sleep apnoea may require postoperative supplemental oxygen or continuous positive airway pressure.

Conclusion

The prevalence of obesity in increasing. Obese patients have an increased risk of co-morbidities, complications and mortality. A thorough preoperative airway, respiratory and cardiac assessment is essential. Proper preparation before labour analgesia or Caesarean section and good postoperative care may help to reduce complications.

References

5. Gupta A, Faber P. Obesity in pregnancy. CEACCP. 2001;11(4).


Laryngospasm is a common and serious respiratory complication in anaesthetic practice which can be fatal if not diagnosed and treated timeously. This review will look at the definition, epidemiology, mechanism, risk factors, clinical presentation, differential diagnosis, prevention, treatment and complications of laryngospasm.

**Definition**

Literature provides multiple definitions for laryngospasm. Some clinical definitions regard laryngospasm as any unwanted muscular response of the larynx that produces partial or complete obstruction of the larynx, while from an anatomical point of view, laryngospasm is seen as prolonged closure of the larynx in association with a ball-valve mechanism involving the intrinsic laryngeal muscles.

**Epidemiology**

The reported incidence of laryngospasm differs vastly. The overall incidence is said to be 0.87%. The paediatric incidence is quoted as 1.7% by Olsson and 0.1% by Burgoyne with a higher incidence in infants of 2.82%. The reported incidence probably depends on the case mix of the reporting hospital, experience of the anaesthetist (higher incidence amongst junior personnel or when substantial interruption of clinical work has occurred) and the lack of consensus on the definition of laryngospasm. Underreporting probably also skews data, as reporting is not compulsory in all centers and cases managed timeously often resolve quickly and remain unreported. It is likely that the incidence has declined with the use of propofol total intravenous anaesthesia and modern, non-irritant inhalational agents.

**Mechanism**

Laryngospasm is a protective airway reflex. The afferent leg of the reflex involves mechanos-, chemo- and thermoreceptor stimulation of the supraglottic airway which results in activation of the internal branch of the superior laryngeal nerve. The sensory nerve supply to the subglottic airway is via the recurrent laryngeal nerve. Reflex adduction of glottic muscles follows through a vagal efferent pathway. The recurrent laryngeal nerve supplies all the intrinsic laryngeal muscles other than the cricothyroid muscle (which is supplied by the external branch of the superior laryngeal nerve). Laryngospasm is mediated through the lateral cricoarytenoid and thyroarytenoid muscles (adductors of the glottis) and the cricothyroid muscle (tensor of the vocal cords). Vagal nerve mediated apnoea, bronchoconstriction and bradycardia often accompany laryngospasm. Laryngospasm occurs on two anatomical levels (Figure 1). False vocal cord closure with simultaneous anterior movement and backwards tilt of the arytenoids and posterior movement of the base of the epiglottis firmly close the larynx. The true vocal cords close at a lower level and posterior to the false vocal cords. Their closure is not mandatory for laryngospasm to occur, as is evident from the fact that laryngospasm is possible in bilateral vocal cord paralysis. Hypoxia and hypercapnia eventually decrease brainstem impulses to the superior laryngeal nerve, resulting in decreased intensity of glottic closure and spontaneous cessation of laryngospasm as hypoxia and hypercapnia worsen. Dangerous complications may however ensue (see below), and laryngospasm is best treated timeously.

![Figure 1a: Normal airway anatomy](Photo credit: Daniel Simpson)
Causes and risk factors

Laryngospasm is usually caused by either airway stimulation (blood, secretions, foreign objects) or a light plane of anaesthesia resulting in inadequate central nervous system depression of airway reflexes.8

Risk factors can be divided into three categories (see Table I)

a. Anaesthesia-related factors

Insufficient depth of anaesthesia at induction or emergence is probably the most common cause of laryngospasm. When blood or mucus accumulate in the airway or suction catheters or laryngoscope blades are inserted into the airway at this point, laryngospasm is frequently elicited. Sodium thiopentone does not blunt the airway responses and, compared to propofol, the incidence of laryngospasm is increased.9 Ketamine per se does not cause laryngospasm, but its tendency to increase secretions may indirectly result in spasm.10 Intravenous maintenance of anaesthesia with propofol causes less laryngospasm than sevoflurane, probably due to the ability of propofol to blunt airway reflexes.11 Of the inhalants, the highest incidence is seen with desflurane, then isoflurane, enflurane and lastly sevoflurane and halothane (equal incidence).12,13 Sugammadex has been reported to cause tight glottic closure around two minutes after administration, which correlates with train-of-four ratios in excess of 0.9. This reportedly resolved after 2-3 minutes with the application of positive end-expiratory airway pressure (PEEP).14,15 The use of laryngeal mask airways (LMA) is listed as an independent risk factor for laryngospasm, but studies do not state what proportion of patients were done with LMA, whether they were breathing spontaneously or assisted or whether the LMA was removed deep or awake.4 Other studies found that laryngospasm occurred more on induction when LMAs were used and more on extubation when endotracheal tubes were used.16

b. Patient-related factors

The incidence of laryngospasm is higher in children and especially small babies.17 Upper respiratory tract infections cause airway hyperactivity, increasing the risk of laryngospasm. This hyperactivity lasts 6 weeks after the infection.18 More laryngospasm occurs in American Society of Anesthesiologists (ASA) class 3 and 4 patients compared to those of class 1 and 2, but emergency surgery does not seem to independently increase the risk of laryngospasm.19 The incidence is increased in children with airway anomalies,20 as well as in adult patients with anatomically long uvulas21 or a history of choking during sleep.22 Chronic smoking also increases airway reflex sensitivity and smokers are advised to abstain from smoking for at least 48 hours prior to surgery.23 Passive smoking also increases airway reactivity. Gastroesophageal reflux is another risk factor for laryngospasm.24

c. Surgery-related factors

The type of surgery influences the incidence of laryngospasm. Tonsillectomy and adenoidectomy probably have the highest incidence with others like appendectomy, cervical dilation, hypospadias surgery and skin grafts also displaying an increased risk.1

In thyroid surgery, laryngospasm may occur either secondary to superior laryngeal nerve injury or due to hypocalcaemia following iatrogenic parathyroidectomy.25,26 Oesophageal surgery could cause laryngospasm via stimulation of the distal afferent oesophageal nerves.26

Presentation of laryngospasm (see Table II)

Two clinical entities are commonly distinguished – partial laryngospasm (chest movement with stridor and limited bag movement disproportional to breathing attempts) and complete laryngospasm (silent chest movement, no bag movement and no ventilation possible).6,27 The literature is however divided on the

<table>
<thead>
<tr>
<th>Anaesthesia-related</th>
<th>Insufficient depth of anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Airway irritation with inhalational agents, blood, etc.</td>
</tr>
<tr>
<td></td>
<td>Sodium thiopentone (does not blunt airway responses)</td>
</tr>
<tr>
<td></td>
<td>Ketamine induced secretions</td>
</tr>
<tr>
<td></td>
<td>Desflurane, isoflurane, enflurane in awake patients</td>
</tr>
<tr>
<td>Sugammadex</td>
<td>LMA &gt; ETT (on induction)</td>
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<tr>
<td>ETT &gt; LMA (on extubation)</td>
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<table>
<thead>
<tr>
<th>Patient-related</th>
<th>Children</th>
</tr>
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<tr>
<td></td>
<td>Upper respiratory tract infections</td>
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<td></td>
<td>ASA class ≥ III</td>
</tr>
<tr>
<td></td>
<td>Children with airway anomalies</td>
</tr>
<tr>
<td></td>
<td>Chronic smoking (including passive smoking)</td>
</tr>
<tr>
<td></td>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td></td>
<td>Long uvula; history of choking at night</td>
</tr>
</tbody>
</table>

| Surgery-related    | Airway surgery (Tonsillectomy and adenoidectomy) |
|--------------------| Appendectomy |
|                    | Genitourinary surgery (hypospadias, cervical dilatation) |
| Thyroid surgery (SLN injury; hypocalcaemia secondary to iatrogenic parathyroidectomy) | Oesophageal surgery |

LMA = laryngeal mask airway; ETT = endotracheal tube; ASA = American Association of Anesthesiologists; SLN = superior laryngeal nerve.
existence of “partial laryngospasm”. Some present endoscopic evidence that, during closure of the true vocal cords, passage of some air could occur through the posterior commissure, resulting in stridor which should not be seen as partial laryngospasm and only false cord closure is viewed as laryngospasm. True cord closure is possible prior to false cord closure (laryngospasm) or after laryngospasm has resolved. Laryngospasm is regarded as silent and stridor as a clinical sign of broken laryngospasm.26 Other clinical signs of laryngospasm include a lack of airflow at the mouth or nose, intercostal retraction, tracheal tug, paradoxical breathing and late signs including desaturation, bradycardia and cyanosis.26 In adults, severe strain against a closed glottis is often evident from engorged neck veins and vigorous movement of the body, resembling severe coughing efforts, albeit silent. In babies, desaturation is often the first or only sign (personal observation). Capnographic evidence of laryngospasm entails a lack or severe decrease in end-tidal CO2 (ETCO2).

Table II: Presentation of laryngospasm
- Chest movement with limited airflow at the mouth or nose and limited bag movement
- Silence or stridor
- Body movements; engorged neck veins
- Intercostal retraction
- Tracheal tug
- Paradoxical breathing
- Desaturation
- Bradycardia
- Cyanosis
- Absence of ETCO2 on capnography

ETCO2 = End-tidal carbon dioxide

Differential diagnosis (see Table III)
The differential diagnosis probably resembles the differential diagnosis of vocal cord dysfunction29 and will include anaphylaxis, angioedema, tracheal stenosis, vocal cord polyps or other tumours, foreign bodies in the airway, vocal cord paralysis, laryngomalacia and tracheomalacia. Breath holding and reflex apnoea (especially in children) due to the Hering-Breuer reflex occur on over-inflation of the lungs. This will worsen when sustained high inflation pressure is administered to the airway, as is often the case during treatment of laryngospasm.30 Vocal cord dysfunction (VCD), also known as paradoxical vocal cord motion (PVCM), is a condition where vocal cords paradoxically adduct during inspiration leading to stridor, wheezing and dyspnea. This occurs during emotionally stressful times and is a possible cause of postoperative stridor or laryngospasm. Treatment includes benzodiazepines and reassurance.30 Residual muscle relaxants or opioids cause loss of upper airway tone with occlusion of the pharynx by the tongue. This should be excluded when stridor occurs in the recovery room. Although bronchospasm usually results in expiratory wheezing and not inspiratory stridor, bronchospasm and laryngospasm often co-exist, especially when triggered by airway stimulation during light plains of anaesthesia. Bronchospasm should therefore be excluded once laryngospasm has ceased.

Table III: Differential diagnosis of laryngospasm

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Anaphylaxis</td>
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<tr>
<td>Angioedema</td>
</tr>
<tr>
<td>Tracheal stenosis</td>
</tr>
<tr>
<td>Vocal cord polyps or tumours</td>
</tr>
<tr>
<td>Foreign bodies in the airway</td>
</tr>
<tr>
<td>Vocal cord paralysis</td>
</tr>
<tr>
<td>Laryngomalacia</td>
</tr>
<tr>
<td>Tracheomalacia</td>
</tr>
<tr>
<td>Breath holding or reflex apnoea</td>
</tr>
<tr>
<td>Vocal cord dysfunction (VCD)</td>
</tr>
<tr>
<td>or paradoxical vocal cord motion (PVCM)</td>
</tr>
<tr>
<td>Loss of upper airway tone</td>
</tr>
<tr>
<td>Bronchospasm</td>
</tr>
</tbody>
</table>

Prevention (see Table IV)
The incidence of laryngospasm is lower in the hands of experienced anaesthetists.3 The use of premedication to decrease laryngospasm is controversial. Anticholinergic drugs reduce secretions and therefore reduce laryngeal irritation, but they display some undesirable side-effects. Their use should probably be limited to use in conjunction with ketamine or in patients known with increased secretions. Benzodiazepines decrease upper airway reflexes and may reduce laryngospasm. Although it will not prevent laryngospasm, some authors feel that N2O should be omitted during preoxygenation as to ensure optimal oxygen reserve in case of laryngospasm or other difficulties.51 Inhalational induction should be done with a non-irritating agent like sevoflurane or halothane and the patient should be in a deep anaesthetic plane prior to intravenous cannulation and airway instrumentation.28 Some suggest waiting two minutes after loss of the eyelash reflex in children before the intravenous line is placed,32 while others emphasize that a deep anaesthetic plane is a clinical diagnosis and not definable by a time interval.31 Similarly, oropharyngeal airways should never be inserted while a patient is in a light plane of anaesthesia, even if airway obstruction occurs. The airway should rather be opened by a cautious jaw-thrust manoeuvre. Propofol induction and maintenance could cause less laryngospasm than sevoflurane.11

Exubation should either occur at a deep level of anaesthesia or in a patient who is fully awake; both techniques have advantages and disadvantages.26 Some advocate the “no touch” technique where the patient is left unstimulated with the airway device in situ until fully awake.31 Others extubate while the lungs are fully inflated in order to reduce the adductor response of the larynx and to force the patient to exhale upon extubation, expelling secretions and reducing larynx irritation.54

Some studies have shown intravenous lignocaine (1 mg.kg−1) to be effective in preventing post-extubation laryngospasm, while others were unable to demonstrate a benefit.35,36 Glottic topicalization with 2% lignocaine at 4 mg.kg−1 showed some benefit.27 The potential danger of this practice is postoperative aspiration of blood or secretions if the airway is devoid of sensation. Intravenous MgSO4 (15 mg.kg−1) after intubation effectively decreased extubation laryngospasm, probably by increasing the anaesthetic depth and decreasing laryngeal muscle tone.38 In cats, inhaling 5% CO2 for 5 minutes prior to extubation reduced laryngospasm, probably because the drive to exhale the CO2 overrides the laryngospasm reflex.29
Diagnose laryngospasm

Call help

Remove stimulus if possible (LMA)

Apply CPAP; FiO₂ = 1

Open airway (gentle jaw thrust)

Degree of laryngospasm?

Not improved

Contraindication to suxamethonium?

Propofol 0.5 mg.kg⁻¹ IV

Atropine 20 µg.kg⁻¹ IM (children)

Suxamethonium 4 mg.kg⁻¹ IM

IV access

Improvement?

No

Yes

CPR

Continue anaesthetic/emergence

LMA = laryngeal mask airway; CPAP = continuous positive airway pressure; FiO₂ = inspiratory fraction of oxygen; IV = intravenous; IM = intramuscular; CPR = cardiopulmonary resuscitation.

Figure 2: Personal treatment algorithm of the author.
CO₂ is of course not routinely available in theatre, and no human studies exist. The partial success of acupuncture⁴⁰ is another interesting observation, but most anaesthetists are not skilled acupuncturists.

### Table IV: Possible strategies to prevent laryngospasm

<table>
<thead>
<tr>
<th>Strategy</th>
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</thead>
<tbody>
<tr>
<td>Experienced anaesthetist</td>
</tr>
<tr>
<td>Anticholinergic premedication</td>
</tr>
<tr>
<td>Sedative premedication</td>
</tr>
<tr>
<td>Propofol induction (rather than thiopentone, ketamine or inhalants)</td>
</tr>
<tr>
<td>Deep plane of anaesthesia prior to IV cannulation, airway instrumentation or surgical stimulation</td>
</tr>
<tr>
<td>Propofol maintenance (rather than sevoflurane)</td>
</tr>
<tr>
<td>Deep or fully awake extubation</td>
</tr>
<tr>
<td>Extubate following maximal inspiration</td>
</tr>
<tr>
<td>Intravenous lignocaine</td>
</tr>
<tr>
<td>Intravenous magnesium sulphate</td>
</tr>
<tr>
<td>Acupuncture</td>
</tr>
<tr>
<td>Inhaled CO₂ (cats)</td>
</tr>
</tbody>
</table>

IV = intravenous; CO₂ = carbon dioxide

### Treatment (see Tables V and VI and Figure 2)

Most treatment guidelines concur that the first steps in the treatment of laryngospasm should include removing the stimulus, calling for help (to have extra hands to draw up drugs), applying a jaw thrust maneuver and 100% oxygen. Controversy surrounds some of the aspects of treatment. As part of removing the stimulus, some believe that the airway should be suctioned and examined for foreign bodies.⁴¹ Personal experience has taught that this is firstly very difficult as jaw clenching often occurs at this point and inserting a suction device into the throat during a light plane of anaesthesia might stimulate further spasm of the larynx. Suctioning and inspection of the airway should probably only occur after deepening the anaesthetic plane or administering a muscle relaxant. A laryngeal mask should however be removed if possible if this was the initial trigger. This is also often only possible after pressure on the “laryngospasm notch” (see below) or pharmacological treatment of the spasm. Suctioning should only be done under vision and very cautiously following oropharyngeal surgery. Some authors list, as first line treatment of laryngospasm, the insertion of an oropharyngeal or nasopharyngeal airway.⁴² This is contested by others because the patient is probably in a light plane of anaesthesia and inserting an object into the airway might worsen the spasm.⁵ Also, an oropharyngeal airway should never be inserted after oropharyngeal surgery, as this might dislodge sutures or cause wound trauma. In these cases, laryngospasm should be treated without delay, as coughing and straining will increase venous pressure and cause bleeding. Deepening the anaesthetic is commonly accepted as a treatment option for laryngospasm, but some list the use of inhalational agents, even in complete obstruction.²⁸ It might be argued that inhalational agents will not reach the airway during complete laryngospasm, and deepening the plane of anaesthesia during complete laryngospasm is only possible with intravenous agents like propofol 0.25–0.8 mg.kg⁻¹,ⁱ,⁷ which is successful in more than 75% of cases. Positive pressure ventilation as a treatment option is also controversial. Some regard this as imperative²⁸ while others question its potential for breaking a tight laryngospasm and regard the practice as dangerous due to the potential of stimulating stretch receptors if the patient accidently inhales, causing reflex apnoea.³ Gastric insufflation with splinting of the diaphragm might also follow these high pressures.²⁸,⁴³ Gentle manual assistance of breathing could be beneficial. Some mention gentle chest compressions as a treatment option,⁴⁴ but this study is criticised⁴⁵ for amongst others methodology and treatment delay while compressions are done. Short-acting opioids like alfentanil can be used, but will probably cause apnoea and less optimal intubating conditions than suxamethonium.⁴⁵ Guidelines concur that in the less than 25% of cases where propofol is not successful, suxamethonium should be used. Suggested intravenous dosages range from 0.1–3 mg.kg⁻¹. Propofol is initially preferred over suxamethonium because of the latter’s possible interaction with non-depolarizing muscle relaxants, range of contra-indications and possibility of suxamethonium apnoea. Suxamethonium should however be administered before severe hypoxia ensues, as its administration under these conditions may result in bradycardia and cardiac arrest. It is recommended for the same reason, that suxamethonium be preceded by atropine 0.02 mg.kg⁻¹ in children.²⁸ The use of suxamethonium in extubation laryngospasm might follow shortly after the administration of neostigmine, in which case it should be remembered that pseudocholine esterase is also inhibited by neostigmine and the breakdown of suxamethonium might be prolonged.⁴⁶

When laryngospasm occurs in the absence of intravenous access, the use of suxamethonium via the peripheral intramuscular (deltoid or quadriceps muscles) or intralingual route (4 mg.kg⁻¹ in both instances), will have an onset of action of 295 seconds and 265 seconds respectively. It is recommended that both submental and peripheral intramuscular injection sites be massaged post-injection as it could reduce the onset of action to 133 seconds.⁴⁷ The intranasal route resembles the intravenous route in dosage and onset time. The intra-oral intralingual route, could cause bleeding and hematoma formation and may complicate airway management. Mask ventilation is also interrupted while injection occurs. The submental route is therefore advisable. These non-intravenous routes might have a slower onset of action than the intravenous route, but muscle relaxation occurs sooner in the larynx than in peripheral muscles, enabling airflow much quicker than the quoted onset times for non-intravenous suxamethonium.⁴⁸ The duration of action of intramuscular suxamethonium will however be prolonged to 15–30 minutes, compared to its six- to ten-minute duration via the intravenous route.⁴⁹ Most non-depolarizing muscle relaxants are not suitable for intramuscular use in laryngospasm, both due to their unacceptably slow onset of action via this route (mivacurium and atracurium > 10 minutes) and tissue irritation (atracurium).⁴⁹ Only rocuronium is deemed to have an acceptable onset of action via the intramuscular route,⁵⁰ keeping in mind that rocuronium burns intraneously and probably intramuscularly and could momentarily trigger further laryngospasm.⁵¹ One study describes the use of intramuscular vecuronium (0.2–0.3 mg.kg⁻¹) in 12 patients.⁵² This was not for laryngospasm but rather for routine intubation in conjunction with ketamine. Intubation was possible within 3–5 minutes. This is similar to the 4 minutes quoted for intramuscular rocuronium (1 mg.kg⁻¹ and 1.8 mg.kg⁻¹ in children < 1 year and > 1 year of age respectively).⁴⁹ Laryngospasm will probably cease even sooner. Intramuscular rocuronium is therefore an alternative to suxamethonium in patients with burns or other contraindications to suxamethonium in the absence of...
intravenous access. The duration of action will however exceed 60 minutes.50 The immediate reversal of both rocuronium and vecuronium is possible with sugammadex,23 but intravenous access needs to be established. Although intramuscular administration was tolerated in rabbits,34 no human studies exist and no data is available on the intramuscular route for sugammadex (personal communication with the manufacturing company). Sugammadex has also been implicated as a possible cause of laryngospasm (see above).

Five cases of post-extubation laryngospasm were reportedly treated with doxapram (1.5 mg.kg⁻¹ intravenously)35 and 2 cases with nitroglycerin (4 µg.kg⁻¹ intravenously)36. The mechanism of action of doxapram is possibly the stimulation of respiratory drive but nitroglycerine is known to act on smooth muscle and this might not explain laryngeal muscle (skeletal muscle) relaxation.

Two non-pharmacological treatment options have been described. The first is well known but often applied incorrectly. Larson described a technique where pressure is applied to the “laryngospasm notch”. This is often erroneously interpreted as pressure on the angle of the jaw or ramus of the mandible. The correct technique is the application of pressure with the middle fingers on a point bordered anteriorly by the ascending ramus of the mandible adjacent to the condyle, posterior by the mastoid process and superior by the base of skull. The operator presses firmly inwards and in a cephalad direction (in the direction of the styloid process, as cephalad as possible) with the middle fingers while performing a jaw thrust manoeuvre with the thumbs and index fingers to open the airway and maintain a thorough mask seal. The mechanism of glottic relaxation is not well understood, but probably results from pain-induced autonomic nervous systems effects.44 The second technique is superior laryngeal nerve block to prevent post-extubation laryngospasm.37,38

<table>
<thead>
<tr>
<th>Table V: Treatment options for laryngospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removal of stimulus</td>
</tr>
<tr>
<td>Calling for help</td>
</tr>
<tr>
<td>Jaw thrust maneuver</td>
</tr>
<tr>
<td>Stimulation of the laryngospasm notch</td>
</tr>
<tr>
<td>100% Oxygen</td>
</tr>
<tr>
<td>Deepen the plane of anaesthesia (propofol, opioids, inhalational agents – partial laryngospasm)</td>
</tr>
<tr>
<td>Positive pressure ventilation</td>
</tr>
<tr>
<td>Gentle chest compressions</td>
</tr>
<tr>
<td>Suxamethonium (preceded by atropine in children) or rocuronium (see algorithm)</td>
</tr>
<tr>
<td>Other (doxapram, nitroglycerine, superior laryngeal nerve block)</td>
</tr>
</tbody>
</table>

| Table VI: Dosages and onset of action of different routes of muscle relaxants in laryngospasm |
|---------------------------------|-----------------|-----------------|
| Agent              | Route     | Suggested dose | Onset of action |
| Suxamethonium       | Intravenous | 0.5 mg.kg⁻¹    | 30–60 s         |
|                    | Interosseous | 0.5 mg.kg⁻¹    | 30–60 s         |
|                   | Intramuscular | 4 mg.kg⁻¹    | 4 min           |
|                   | Intralingual | 4 mg.kg⁻¹    | 4 min           |
| Rocuronium          | Intravenous | 1 mg.kg⁻¹     | 90 seconds      |
|                    | Intramuscular | 1.2 mg.kg⁻¹ | 4 min           |
|                    |              | 1.8 mg.kg⁻¹ in infants | 4 min |

s = seconds; min = minutes; mg = milligram; kg = kilogram

Complications

Laryngospasm can be fatal if left untreated. Cardiac arrest, bradycardia, pulmonary aspiration and oxygen desaturation have been reported.20 Post-obstructive negative pressure pulmonary edema is another concern. This occurs when patients generate a large negative pressure when inhaling against a closed glottis.7 Complications following the treatment of laryngospasm is also possible. This includes the extensive list of side-effects of suxamethonium, hypotension of propofol and trauma caused by high pressure ventilation and intubation attempts with a closed glottis.

Laryngospasm is a treatable condition which can result in serious morbidity and mortality. Vigilance, good decision-making skills and thorough education, possibly through simulator training and algorithms, are vital for timely diagnosis and treatment of laryngospasm.

Interests: No interests are declared.

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References:


Epilepsy and anaesthesia

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Definitions

Seizure: an episode of abnormal excessive neuronal discharge due to an imbalance between excitatory and inhibitory neurotransmission and resulting in clinical manifestations of a particular pattern.

Epilepsy: a brain condition characterised by an enduring predisposition or tendency to developing recurrent, unprovoked seizures and including the neurobiologic, cognitive, psychological and social consequences of the condition.

Status epilepticus: a medical emergency characterised by continuous seizure activity for ≥ 5 minutes or recurrent seizure activity without full neurological recovery between each seizure.

(PLEASE REVIEW EMERGENCY MANAGEMENT OF STATUS EPILEPTICUS WHICH IS NOT COVERED IN THESE NOTES)

Aetiology

• Genetic, e.g. benign familial neonatal epilepsy, juvenile myoclonic epilepsy
• Structural, e.g. tumours, trauma, intracranial haemorrhage
• Metabolic, e.g. inborn errors of metabolism, porphyria
• Immune, e.g. autoimmune encephalitis
• Infectious, e.g. meningitis, brain abscess, HIV, tuberculosis, neurocysticercosis, etc.
• Unknown (previously termed idiopathic)

Classification

Focal seizures

• Previously termed partial seizures.
• Seizure activity limited to one hemisphere of the brain.
• May occur with or without altered consciousness or awareness. Partial seizures occurring with altered consciousness or awareness are termed dyscognitive seizures.
• Focal seizures may evolve to include both hemispheres in which case they are termed focal to bilateral (previously secondary generalised) seizures.

Generalised seizures

• Seizure activity involving both hemispheres of the brain.
• These are described in terms of the pattern of the clinical manifestations observed as being tonic, clonic, tonic-clonic, myoclonic, atonic or absence in nature.

Anaesthetic considerations

1. Preoperative

Patients with epilepsy may present for emergency management of status epilepticus or neurosurgical procedures aimed at diagnosing or controlling epilepsy such as cortical mapping, cortical electrode placement or implantation of anti-seizure devices. More commonly, however, patients with epilepsy present for elective or emergency surgical procedures unrelated to epilepsy. As always, a thorough preoperative assessment includes taking a history, performing a physical examination and reviewing special investigations. Of particular importance, the anaesthesiologist must determine the clinical pattern of seizures in order that seizure activity may be readily identified and treated in the perioperative period.

<table>
<thead>
<tr>
<th>History</th>
<th>Type of epilepsy</th>
<th>Clinical pattern of seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cause of epilepsy</td>
<td>Underlying medical conditions</td>
</tr>
<tr>
<td></td>
<td>Seizure history</td>
<td>Seizure control/last seizure</td>
</tr>
<tr>
<td></td>
<td>Seizure precipitants</td>
<td>Episodes of status epilepticus</td>
</tr>
<tr>
<td>Anticonvulsant medication</td>
<td>Other medical or surgical</td>
<td>Drugs including doses</td>
</tr>
<tr>
<td></td>
<td>therapies</td>
<td>Last dose/next dose</td>
</tr>
<tr>
<td></td>
<td>Implanted anti-seizure devices</td>
<td>Plan to minimise dose interruptions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adverse effects or complications of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>medication</td>
</tr>
</tbody>
</table>
Prevention of seizures during the perioperative period depends largely on maintaining the ‘chain of therapy’ by minimising the duration of preoperative starvation and ensuring correct doses of anticonvulsant medication are given at the correct time. Consideration should be given to administration of a benzodiazepine premedication as well as timeous reinitiation of anticonvulsant medication postoperatively. Nausea and vomiting may interfere with oral intake causing treatment interruptions and should be aggressively prevented and treated. Antiemetic agents known to cause extra-pyramidal side effects should be avoided. Should a patient be unable to take orally in the days following surgery, intravenous substitutes should be prescribed and therapeutic drug monitoring commenced. Not all anticonvulsant medications are available in intravenous preparations. It is valuable to contact the hospital pharmacy preoperatively in order to establish the availability of intravenous preparations or appropriate substitutes.

2. Intraoperative

Do anaesthetic agents cause seizures?

Most anaesthetic agents have been shown to be either pro- or anti-convulsant, however, several anaesthetic agents have been shown to be both pro- and anti-convulsant depending on the circumstances under which they are used. The dose response is unpredictable and depends on patient factors, dosages and drug interactions.

What are the effects of anticonvulsants on anaesthesia?

Almost all anticonvulsants have some CNS sedating effects reducing anaesthetic requirements and placing patients at risk of delayed emergence and prolonged sedation in the postoperative period. Aconvulsive status epilepticus should be on the list of differential diagnoses for all patients with delayed emergence following general anaesthesia. Consideration should be given to regional or local anaesthetic techniques where possible. This is especially true for patients with poorly controlled epilepsy.

Most anticonvulsants (carbamazepine, phenytoin and phenobarbital) are inducers of the hepatic P450 cytochrome oxidase enzyme system resulting in several drug interactions:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
<th>Metabolism</th>
<th>Efficacy</th>
<th>Risk Halothane Hepatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halothane</td>
<td>↑</td>
<td>↓</td>
<td></td>
<td></td>
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<tr>
<td>Aminosteroid muscle relaxants</td>
<td>↑</td>
<td>↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic opioids</td>
<td>↑</td>
<td>↓</td>
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</table>

Through their effect on the hepatic P450 cytochrome oxidase system, anticonvulsants may also decrease plasma concentrations of many other medications of relevance to the anaesthetist including amiodarone, β adrenoceptor blocking agents, calcium channel blocking agents and warfarin. These potential drug interactions should be kept in mind when encountering patients on multiple chronic medications.

How does one diagnose seizure activity under anaesthesia?

The typical clinical manifestations of seizure activity are often absent in patients under general anaesthesia. This is especially true for those patients who have received muscle relaxants. The clinical signs reflect autonomic instability and include hypertension, tachycardia, cardiac arrhythmias, sweating, temperature derangements, poor glycaemic control, electrolyte derangements, metabolic acidosis, neurogenic pulmonary

<table>
<thead>
<tr>
<th>Induction agents</th>
<th>Seizure threshold increase</th>
<th>Seizure threshold decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopentone (infusion&gt;bolus)</td>
<td></td>
<td></td>
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<tr>
<td>Propofol</td>
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<td></td>
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<tr>
<td>Midazolam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam, etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaesthetic gases and vapors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoflurane</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desflurane</td>
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<tr>
<td>Nitrous oxide</td>
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<td></td>
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<tr>
<td>Enflurane</td>
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<tr>
<td>Sevoflurane (esp. paediatric patients with ↑F,sevo and ↓P,CO₂)</td>
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<tr>
<td>Muscle relaxants</td>
<td></td>
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<tr>
<td>Benzylisoquinolones (atracurium metabolite: laudanosine)</td>
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<tr>
<td>Analgesics</td>
<td></td>
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<tr>
<td>Alfentanil</td>
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<tr>
<td>Remifentanil</td>
<td></td>
<td></td>
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<tr>
<td>Morphine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine (metabolite: nor-pethidine)</td>
<td></td>
<td></td>
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<tr>
<td>Local anaesthetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(All agents cross the blood brain barrier and have potential to cause seizures, esp. in toxic doses.)</td>
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</tbody>
</table>
Due to their non-specific nature, a high index of suspicion is required for patients presenting with these signs under anaesthesia.

3. Postoperative

Following anaesthesia, all patients should be monitored in the recovery room until they are fully recovered and fulfill criteria for recovery room discharge. Patient safety is of paramount importance. As such, patients should be recovered on stretchers with secure sides to prevent falls from height. Patients with epilepsy should be discharged from the recovery room with reliable vascular access for use should a seizure occur postoperatively. In addition, recovery room and ward availability of benzodiazepines and other anticonvulsants should be ensured.

Patients with well controlled epilepsy may be considered for day case procedures provided they are adequately supervised and have easy access to the emergency department should a problem arise. If there is any doubt, overnight postoperative admission for observation is recommended.

References
Neonatal eye surgery

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Introduction
As the primary organ of vision, the eye is an embryological extension of the nervous system. As a result, it shares many common anatomical and physiological properties with the brain. The globe itself occupies about one fifth of the orbital volume, the remainder of the space being taken up by extraocular muscles, fascia, fat, blood vessels, nerves and the lacrimal gland. Ophthalmic procedures are commonly divided into intra- and extra-ocular surgeries. Intra-ocular procedures encompass those performed on or within the globe, while extra-ocular surgeries are those involving the tissues surrounding the globe, within the orbit. This distinction has important anaesthetic implications.

Types of Surgeries
While elective ophthalmic surgery is common in the paediatric population, the relative complexity and risk of neonatal anaesthesia and potential threat to the developing brain preclude surgery in the neonatal period unless a delay in intervention will worsen outcome.

Ophthalmic procedures requiring anaesthesia in the neonatal population most commonly include cataract extraction, treatment of congenital glaucoma, examination under anaesthesia and treatment of retinopathy of prematurity.

Infants and children frequently present for the following surgeries: strabismus, trauma and lacrimal, vitreo-retinal and oculo-plastic surgeries.

Anaesthetic Implications
Apart from the anaesthetic concerns and considerations relating to all neonates undergoing anaesthesia, there are some specific implications for ophthalmic surgery:

Pre-operative assessment
While most children scheduled for ophthalmic surgery are ASA class I or II, eye abnormalities in the neonatal population are more frequently manifestations of multisystem disorders. Particular attention should be paid to the possibility of concomitant chromosomal or metabolic disorders, as well as a history of exposure to congenital infection or premature birth.

Airway management
Although the airway is not strictly shared, draping of the surgical field frequently restricts access to the airway. It is therefore recommended that neonates be intubated and ventilation controlled, except for the shortest of procedures.

Furthermore, a number of syndromes in which there can be major difficulties with intubation are associated with cataracts, glaucoma or squints. These include the mucopolysaccharidoses, the craniosynostosis disorders (e.g. Crouzon’s, Apert’s and Pfeiffer’s syndromes) and the craniofacial syndromes (e.g. Goldenhar, Treacher–Collin and Smith–Lemli–Opitz). The Hallerman–Strieff syndrome, although rare, may present for cataract surgery in the neonatal period and invariably is associated with a particularly difficult airway. Stickler’s syndrome, which is associated with early retinal detachment and glaucoma, is a progressive connective tissue disorder that has some of the features of the Pierre Robin sequence; it can also present intubation problems. Difficulties in airway management in these patients should be anticipated and necessitate a clear plan of action prior to initiating anaesthesia.

Intra-ocular pressure
Normal intra-ocular pressure (IOP) is 10–22 mm Hg. The factors that affect IOP are essentially the same as those that affect intracranial pressure. The main factors involved in the regulation of IOP are the choroidal, aqueous and vitreous volumes together with external pressure. Sudden changes in intra-ocular pressure may affect measurements, or result in expulsion of ocular contents or haemorrhage. The following strategies should be employed in an attempt to maintain innate pressures:

- Choroidal volume: As venous drainage from the eye is valveless, any cause of raised venous pressure will impede aqueous drainage via the Canal of Schlemm. A 15° head-up tilt should be employed to reduce IOP, while coughing, straining and retching should all be avoided. Mean arterial pressure and PaCO₂ should also be maintained constant.
• Vitreous and aqueous volumes may be affected by the use of osmotic diuretics and carbonic anhydrase inhibitors, but are generally of little significance to anaesthesia.

• External pressure: Direct pressure should be avoided. Increase in tone of the extra-ocular muscles will increase IOP. Depolarizing muscle relaxants, such as suxamethonium, therefore, cause an increase in IOP. The rise produced by suxamethonium is maximal at 2 minutes after administration and lasts for 5 minutes. Pretreatment with non-depolarizing muscle relaxants to prevent this effect has been advocated but is of unproven value.2

Accurate measurement of IOP is essential in the case of suspected glaucoma. Currently available anaesthetic agents, with the exception of ketamine, reduce IOP. The extent of this reduction is unknown and not reproducible, even in the same individual. This effect can lead to misleading readings of IOP, which has a detrimental effect on treatment.2 Ketamine has been shown to cause only a transient rise in IOP, which can be eliminated with the use a benzodiazepine as premedication.2 A falsely high reading is preferable to a missed diagnosis.

Cardiorespiratory reflexes

The oculo-cardiac reflex (OCR) is defined as a 10–30% decrease in heart rate from baseline.1 Increased IOP (pressure on the globe) or traction on the extra-ocular muscles, particularly the medial rectus, or less commonly trauma or pain, invoke a bradycardia via the trigemino-vagal pathway. Interruption of the stimulus usually results in resolution but if left untreated, it may quickly progress to asystole. Other arrhythmias such as nodal rhythms and ventricular fibrillation can also occur.1 Intravenous atropine 20 μg/kg or glycopyrrolate 10 μg/kg at induction of anaesthesia or presentation of a bradycardia will block the OCR. These can be repeated at any time during surgery if the OCR recurs, so it is important to have the drugs available and ready to use if bradycardia ensues. The reflex can also be counteracted by application of topical local anaesthetic eye drops such as tetracaine, or by blocking the afferent limb of the reflex with a peribulbar block, which is not commonly used in paediatric patients due to the risk of globe perforation.5

OCR has been shown to occur less commonly with sevoflurane than with halothane, but is more likely with the use of rocuronium than atracurium.4,5 Hypercarbia doubles the incidence of significant bradycardia, so controlled ventilation should be employed. In older children, postoperative nausea and vomiting (PONV) has been shown to be more likely to occur in paediatric patients who experience OCR during surgery.6

Extraocular muscles manipulation can also provoke an oculorespiratory reflex (ORR) which results in reduction in tidal volume and respiratory rate.7 Consequent hypercarbia and hypoxemia may occur, which in turn increase the risk of OCR.5 The ORR shares the same afferent pathways as the OCR which relays to the brainstem respiratory control centre, while the efferent pathways are mediated by the phrenic nerves.

Another related reflex, the blepharocardiac reflex (BCR) may be elicited by stretching of the eyelid muscle during the placement of an eyelid retractor.2 Similar pathways and treatment to the OCR are postulated. Investigation into a similar pathway in Sudden Infant Death Syndrome infants indicates that a vagal hypersensitivity may be, in part, hereditary.9

Bacterial endocarditis prophylaxis

The majority of ophthalmic procedures do not produce a bacteraemia, the exception being any instrumentation of the nasolacrimal ducts. Those undergoing such surgeries with a susceptible cardiac lesion should receive appropriate prophylaxis.

Pharmacological implications

• Effect of drugs used by surgeons: Topical mydriatic agents are frequently administered preoperatively for pupillary dilatation. Should the effect be insufficient, a repeat dose may be given intraoperatively. While usually well-tolerated, severe side-effects such as hypertension and pulmonary oedema may ensue, especially if injected subconjunctivally.

• Anaesthetic drugs that may influence surgical concerns:
  ▫ Propofol, thiopentone: IOP reduced by 20–30%
  ▫ Inhalational agents: IOP reduced by 20–30%
  ▫ Opioids: Minimal to no effect on IOP
  ▫ Ketamine: Minor rise in IOP, marked if dose greater than 5 mg/kg, can be eliminated by premedication with benzodiazepine
  ▫ Non-depolarising muscle relaxants: Minimal to no effect on IOP
  ▫ Depolarising muscle relaxants: Marked rise in IOP, sustained for 5–7 minutes, can be reduced by pre-treatment with non-depolariser
  ▫ Nitrous oxide: no effect on IOP, may diffuse into surgically-created gas bubble – avoid in vitreoretinal surgery.

Analgesia

While pain is a subjective experience, infants and even premature neonates possess the basic pathways and nociceptors necessary for pain perception.10 Most ophthalmic operations performed in neonates, however, are not particularly painful, and only simple analgesia in the form of paracetamol and non-steroidal anti-inflammatory drugs, with or without the use of local anaesthetic, is necessary.2

Postoperative apnoea

Immature respiratory control predisposes neonates to apnoea, oxygen desaturation and bradycardia.11 Risk factors include a postconceptual age of less than 50 weeks in a term infant or 60 weeks in a prematurely-born infant, a history of apnoeic episodes, concomitant anaemia, hypothermia, sepsis, metabolic derangements and the presence of cardiac anomalies, as well as exposure to general anaesthesia, muscle relaxation and opiates. Apart from modifying those risk factors where possible, pharmacological prophylaxis can be given in the form of Caffeine 10 mg/kg or Aminophylline 5 mg/kg per os two hours
preoperatively. Postoperatively, infants should be transferred to a monitored environment, with a minimum of an apnoea detection mat until they are at least 24 hours apnoea-free.

**Retinopathy of Prematurity**

Retinopathy of prematurity (ROP) is a proliferative disorder of the immature retinal vasculature.\(^7\) Classified into five stages, the most severe can result in retinal detachment and total and irreversible blindness if left undetected and/or untreated.

The normal retina begins to vascularise at about sixteen weeks gestation and is usually complete one month after birth (or 44 weeks postconceptual age). This process is mediated by high levels of Vascular Endothelial Growth Factor (VEGF) in a relatively low oxygen (intraterine) environment. Exposure to increased oxygen concentration, whether under normal circumstances (term healthy infant birth) or supplemental (premature infant with underdeveloped cardiorespiratory system), VEGF production decreases and retinal development slows. Insufficient vascularisation of the developing retina conversely results in a localised hypoxia, which precipitates the release of factors stimulating new and abnormal blood vessel growth.\(^8\)

Similarly, Insulin-like Growth Factor (IGF-1) prevents normal vessel growth when insufficient, but promotes unchecked neovascularisation in excess. It is thought that fluctuations in arterial oxygenation place the infant at a higher risk than the amount and duration of oxygen delivery.

Apart from premature birth, other risk factors for ROP include multiple births, maternal preeclampsia, intraterine growth restriction, mechanical ventilation, need for blood transfusion, the presence of a patent ductus arteriosus, intraventricular haemorrhage, pulmonary insufficiency, male gender\(^9\) and infants conceived through assisted reproductive therapy.

**Conduct of Anaesthesia**

These infants frequently present for anaesthesia, for both diagnostic and therapeutic purposes. Screening is mandatory in all high risk patients. Commonly performed in a clinic setting, the use of an eye speculum is the most common source of pain.

Treatment options include cryotherapy or laser photocoagulation (modality of choice) in its less severe stages, and vitreoretinal surgery when more severe.\(^10\) Infants frequently require repeat interventions every 10–14 days. While surgical intervention will require a general anaesthetic with controlled ventilation, laser- and cryotherapy can be performed under various anaesthetic techniques. Baring in mind the complexity of neonatal anaesthesia and the risk to the infant both intra-and postoperatively, the following options are available:

- **Local anaesthesia:** topical anaesthesia and a mydriatic agent are applied to the eyes one to two hours prior to intervention.

  The infant is then fed and swaddled and it is hoped that the infant will sleep through/tolerate the procedure awake. While certainly providing the safest conditions from a postoperative point of view, failure of this technique results in an unstarved child, rendered unsuitable to progress to sedation or general anaesthesia.

- **Sedation:** this can be performed in theatre or in a remote setting. Various combinations of drugs can be used. This technique carries the same risks as a general anaesthetic with less control and increased propensity to complication. It is not recommended.

- **General anaesthesia:** This should be performed in a fully-equipped and prepared theatre environment. A mask and spontaneous ventilation technique can be employed if the procedure is anticipated to be particularly short. The shared work space can complicate matters should difficulties arise or if the procedure goes on longer than anticipated. As a result, the safest modality would be to intubate the infant and control ventilation for the duration of the procedure. It should be borne in mind that oxygen fluctuations are thought to be the greatest modifiable contributor to the process and fractional inspired oxygen content sufficient to maintain oxygen saturation of 88–92% should be targeted. General anaesthesia will marginally increase intervention time relative to the other options and necessitates the availability of theatre space, but is the preferred modality if resources allow.

**References**

Conventional cardiopulmonary bypass and mini-cardiopulmonary bypass

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This is a review of the underlying basic concepts of cardiopulmonary bypass and mini-cardiopulmonary bypass, with a focus on the complications related to cardiopulmonary bypass and whether these complications can be reduced with the use of mini-bypass techniques.

Keywords: conventional cardiopulmonary bypass, mini-cardiopulmonary bypass, comparison, complications

Introduction

The concept of a mechanical method of taking over the function of the heart and lungs dates back to the work of Von Frey in 1885, but the technique required the discovery of heparin in order to become feasible. The earliest successful open heart operation took place in 1953, when John Gibbon repaired an atrial septal defect in a young woman. In 2005, according to the American Heart Association,¹ nearly 500 000 coronary artery bypass grafts and nearly 110 000 heart valve replacement surgeries were performed using cardiopulmonary bypass in the United States alone.

Principles of conventional Cardiopulmonary Bypass (c-CPB)²

In essence, blood from the patient, via one or two venous catheters (usually in the right atrium or the superior and inferior vena cavae), drains by means of a gravity siphon into a venous reservoir. The blood then passes through an oxygenator, a pump and an arterial filter, and is then returned to the aorta of the patient via an aortic catheter.

Oxygenators

All oxygenators now used are of a membrane type – the membranes can be flat or spiral and are composed of polypropylene, which has micropores (0.05–0.3 μm), or silicone, which is a ‘true’ membrane. Polypropylene membranes allow leakage of plasma over time with prolonged bypass.

Gas exchange with extra-corporal oxygenators occurs with the same physical principles (convection, diffusion, chemical reaction) as natural gas exchange does, but they are always less efficient than functional lungs because the diffusion distances are greater (200 μm vs 10 μm) and the surface area is considerably less (1.7–3.5 m² vs 70–100 m²).

Blood Pumps

Blood flow across pumps follows Hagen-Poiseuille’s law:

\[
\text{Blood flow} = \frac{\text{Pressure gradient} \times \text{Tube radius} \times \pi \times 8}{\text{Fluid viscosity} \times \text{Tube length}}
\]

Roller pumps are commonly used – a length of polyvinylchloride (PVC) tubing is compressed against a curved metal backing plate by two rollers located on the ends of two rotating arms. This allows constant delivery of blood volume, even with minor variations in afterload (resistance). Roller pumps are positive displacement devices and are occlusive – the tubing is partially occluded with each cycle of the rotating arms.

Other components of the c-CPB circuit

Heat exchangers allow manipulation of the temperature of the perfusate and of body temperature.

A cardioplegia roller pump delivers a potassium rich solution to the coronary circulation in order to arrest the heart in diastole.

Cardiac drainage roller pumps are used for active removal of blood from heart – the “aortic sucker” and the “left ventricular vent”. This blood is often returned into the bypass circuit without washing or filtration.

Deleterious effects of c-CPB

While c-CPB is necessary for many “open heart” operations, the rate of postoperative morbidity and mortality in patients undergoing c-CPB is relatively high – up to one third of patients undergoing coronary revascularization have undesired
effects including cardiovascular instability, arrhythmias, renal dysfunction, lung dysfunction and cerebral dysfunction. The 30 day mortality after cardiopulmonary bypass is usually quoted as 1.5–2 %.

**Haemodilution**

The average priming volume (to remove air and wet the surfaces of the tubing) of a conventional adult c-CPB circuit is approximately 2 000 ml. The circuit can be primed with a balanced crystalloid solution, colloids, blood, plasma, or with a combination of these fluids.

In practice, this means that there is always haemodilution of the patient’s blood, particularly if the circuit is primed with crystalloid. While the associated reduction in fluid viscosity improves flow through the pump, the resultant decrease in haemoglobin concentration, together with the potential risk of large amounts of intra- and postoperative blood loss, causes an increased risk of blood transfusion perioperatively.

The incidence of transfusion intra and post cardiac surgery varies considerably, but up to 50% of patients undergoing cardiac bypass require blood products. It is also well established that morbidity and mortality increases when haematocrit levels fall below 19% on bypass and when blood transfusion is required after cardiac surgery. Blood transfusion itself is associated with an increase in in-hospital mortality, increased use of intra-and postoperative intra-aortic balloon pumps, increased risk of bleeding and strokes, and an increased risk of repeat CPB runs.

**Haemolysis**

The action of the occluding roller pumps causes mechanical damage to red blood cells, resulting in free haemoglobin and the levels of this rise proportionately with the length of bypass time. Free haemoglobin is associated with an increased risk of renal dysfunction.

**Activation of the systemic inflammatory response**

The inflammatory response occurs in the presence of stress and is necessary for recovery. It is therefore not limited to patients undergoing c-CPB. However, there is strong evidence that both open heart surgery and c-CPB techniques can provoke a marked Systemic Inflammatory Response Syndrome (SIRS) that involves all components of the inflammatory and coagulation systems. This SIRS is believed to be the cause of much of the postoperative morbidity and mortality associated with CPB because it causes temporary and permanent organ dysfunction (cerebral, renal, lung, cardiovascular).

No consensus has yet been reached on the exact pathophysiology of this SIRS. The cause is almost certainly multi-factorial, with the reaction divided into ‘early’ and ‘late’ phases.

The early phase probably results from contact of blood with non-physiological surfaces (the polyvinylchloride tubing of the CPB circuit, air in the venous reservoir), causing contact activation of both cellular components, such as endothelial cells, neutrophils, lymphocytes and platelets, as well as humoral components, such as the clotting factors, complement and activation of fibrinolysis.

Activation of complement has been shown to be linked to postoperative morbidity.

The late phase reaction is possibly related to an ischaemia-reperfusion type injury, to the presence of endotoxaemia, to coagulation disorders and to heparin-protein reactions.

Late phase SIRS reactions involve leucocyte dependant and leucocyte independent pathways, with neutrophil-endothelial reactions, formation of reactive oxygen species, cytokines and arachidonic acid metabolites. The sources of endotoxaemia are diverse, but there is usually significant splanchnic vessel vasoconstriction during c-CPB, with increases in intestinal permeability.

Induction of Nitric Oxide Synthetase (NOS), and the resultant elevated nitric oxide levels caused by bypass, has been implicated in the development of the vasoplegic syndrome that can occur post-bypass.

**Factors that influence the inflammatory response to c-CPB include:**

- Preoperative factors, such as renal dysfunction and diabetes – it is postulated that the inflammatory response is different and that oxidative stress is increased in diabetics.
- Perioperative haemodynamic factors that are postulated to influence the SIRS are low cardiac output states, splanchnic hypo-perfusion, anaesthesia drugs and techniques, and lung management strategies during CPB.
- Surgical factors that play a role in the SIRS associated with cardiac surgery include the type of incision or approach of the surgery; the duration of surgery and the use of the cardiotomy sucker with return of mediastinal blood (potentially containing fat and debris) to the circulating blood.
- The factors related to the c-CPB circuit itself that are believed to be responsible for the SIRS include biomaterial dependant factors, such as the tubing of the extra-corporeal circuit, the oxygenator and damage to blood components caused by pumps. Biomaterial independent factors include the type of priming solution, the volume and type of the cardiotopia, the presence of non-pulsatile blood flow, and the return of fat and debris containing blood from vents into the circulation.
- Postoperative factors such as the type and length of mechanical ventilation and organ support strategies probably also contribute to the reaction.

According to Durandy, the aim of interventions regarding the SIRS should be to modulate the systemic inflammatory response so that excessive inflammation is controlled, while preserving a level of inflammation necessary for host defences and healing.

**Myocardial Damage**

Myocardial ischaemic and reperfusion injuries are associated with the use of CPB. In particular, levels of Platelet Activating Factor are increased and this is implicated in compromised haemodynamic function post-bypass.

**Interventions that can potentially limit the complications of CPB**

- The use of off-pump surgery and minimally invasive surgical techniques.
- Drugs that limit inflammation have been studied. At present, no single intervention on its own demonstrates strong evidence for limiting adverse outcomes as a result of manipulation of the systemic inflammatory response.¹¹

A Cochrane database review¹² revealed no clinical benefit on mortality, cardiac or pulmonary outcomes with the use of corticosteroids, although there is also little evidence of harm.

Many other pharmacological attempts to limit SIRS, including Complement C5 inhibitors, propofol, neutrophil elastase inhibitors, propionyl-carnitine, intensive insulin therapy, nitric oxide donors, preoperative aspirin and fluvosatine have not conclusively shown to provide any clinical benefit.

- CPB (Perfusion) related strategies

Many studies of the perfusion related strategies to reduce complications due to c-CPB are limited by small sample sizes and differing end point selections. Overall, clinical benefits are difficult to prove.¹²,¹³

1. The use of biocompatible (usually heparin coating) of c-CPB circuits has become routine.
2. Leucocyte depleting filters and ultrafiltration of the perfusate have been shown to have some benefit in small children undergoing CPB but not in adults.
3. Pericardial blood processing or discarding of mediastinal blood does reduce inflammatory markers in some studies but, as usual, the clinical benefit is not so easily proven.
4. Miniaturized Cardiopulmonary Bypass Circuits (Mini-cardiopulmonary bypass).

**Miniaturized Cardiopulmonary Bypass Circuits (Mini-cardiopulmonary bypass)**¹⁴

Mini-cardiopulmonary bypass (m-CPB) refers to a variety of novel adjustments to c-CPB circuits that have a common, shared philosophy that includes:

- The use of a centrifugal pump instead of a roller pump. Centrifugal pumps use a vane impeller within a plastic casing that is magnetically coupled at the base to an electric motor, which, when rotated rapidly, generates a centrifugal force which is transmitted to the blood within the pump. This is then converted into kinetic energy, producing flow. Centrifugal pumps are therefore not occlusive and cause less damage to cellular components in the blood. They are, however, afterload dependant to a greater degree than roller pumps.
- Elimination of the venous reservoir in order to reduce circuit length, with the aim of limiting haemodilution and decreasing the volume and surface area of the circuit in contact with the blood. This requires that venous blood must be actively drained from the body.
- Cardioplegia is usually given via a separate roller pump that is connected to the arterial side of the CPB circuit.
- The mediastinal blood does not return to the circuit but is processed via cell salvage techniques and infused separately.

<table>
<thead>
<tr>
<th>Differences between c-CPB and m-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-cardiopulmonary bypass</td>
</tr>
<tr>
<td>Venous cannula, usually one.</td>
</tr>
<tr>
<td>Size 29 F, multistage, longer length</td>
</tr>
<tr>
<td>Rigid and less prone to collapse but requires careful placement as it extends down into the inferior vena cava</td>
</tr>
<tr>
<td>Venous line drainage: ½ inch.</td>
</tr>
<tr>
<td>Use of active kinetic drainage (suction) to drain blood, which has to be tailored to the individual patient’s ‘collapse’ pressure.</td>
</tr>
<tr>
<td>A venous air filter is required because of risk of aspirating air.</td>
</tr>
<tr>
<td>Venous reservoir not present. Circuit is therefore closed and extra volume cannot be added.</td>
</tr>
<tr>
<td>Blood from the operating field is not returned to the bypass circuit; instead it returns to a cell salvage system, where it can be processed and returned to the circulation intravenously.</td>
</tr>
<tr>
<td>Arterial side: Gas-micro emboli (GME) detector and filter required</td>
</tr>
<tr>
<td>Prime volume 700–800 ml (adult). Significant reduction in circuit blood contact surface area: 1.4–2 m²</td>
</tr>
<tr>
<td>Biocompatible coating (usually heparin)</td>
</tr>
</tbody>
</table>

**Advantages of m-CPB**

**Reduction of haemodilution**

It is generally accepted that blood transfusion requirements in adults¹⁵ are up to 33% less with m-PCB compared to c-CPB, almost certainly as a result of the decrease in priming volume. In low body weight neonates,¹⁶ m-CPB was also associated with lower blood transfusion rates and a lower incidence of post-operative extra-corporeal membrane oxygenation (ECMO) support. On bypass, when haematocrit levels were similar, there was no difference in oxygen delivery between the two systems.

Mini-CPB was also associated with less desaturation³ as measured by cerebral oximetry and with better neurocognitive function in adults at time of discharge, but a meta-analysis⁶ of nine randomised control trials revealed no difference in overall morbidity and mortality between c-CPB and m-CPB.

**Haemolysis**

CCPB¹⁶,¹⁷ was associated with an increase in free haemoglobin levels and a decrease in leucocyte count as compared to m-CPB. Retrospective analyses comparing m-CPB with c-CPB reveal that m-CPB was associated with a shorter intensive care stay, a lower incidence of atrial fibrillation and ventricular arrhythmias, a lower postoperative serum creatine and bilirubin level, and less
postoperative blood loss; but in-hospital mortality did not differ between the two groups

**Reduction of the Inflammatory Response to Bypass**

A review of the literature reveals that six out of fourteen randomised controlled trials that attempted to assess the effect of m-CPB on markers of inflammation showed clinical significance in that inflammatory markers were reduced; however, there was no clear linkage between suppression of inflammation and clinical outcome.

Generally speaking, the literature in this regard is poor and meta-analysis is limited by small sample sizes and differing endpoints (traditional endpoints such as death or stroke versus suppression of inflammation) so that, at present, the evidence base is insufficient to recommend clinical practice with regard to use of m-CPB to reduce inflammation with the aim of improving clinical outcomes.

What is apparent in all the trials comparing m-CPB with c-CPB is that m-CPB is as safe as c-CPB.

**Myocardial protection**

Cardiac specific enzymes suggestive of myocardial damage were noted in a study to be lower in patients undergoing m-PCB as compared to conventional bypass.¹⁴,¹⁵

**Limitations of m-CPB**

- Mini-CPB requires increased technical prowess, awareness, participation and co-operation from the members of the cardiac team for success. There is a relatively long learning curve for surgeons, perfusionists and anaesthetists for using m-CPB, with many studies estimating that at least fifty bypass runs are required to gain competence.

- There is a risk of micro air bubble formation as a result of venous drainage by suction. Spontaneous formation of microbubbles is associated with excessive negative pressure in the venous limb of the circuit! This can be transmitted to the left side. In one study,¹⁸ the measured volume of arterial air bubbles in an m-CPB was 1522 ± 654 μl compared with 4.1 ± 2.5 μl for c-CPB. Mini-CPB requires a special GME filter on the arterial side of the m-CPB circuit.

- Managing volume status can be challenging because the perfusionist cannot add to or use the venous reservoir to compensate for inadequate venous return. Blood lost from the operating field is salvaged, processed and must be returned intravenously. Some surgeons using m-CPB still prefer to use c-CPB when performing complex procedures with considerable risks of bleeding, and most of the trials using m-CPB are performed for coronary artery bypass grafting procedures.

- At Charlotte Maxeke Academic Hospital, the current cost of a conventional oxygenator is approximately R5 600 and the cost of conventional tubing for the CPB circuit is approximately R4 000. The cost of the oxygenator in the m-CPB circuit is approximately R10 000 and the tubing and filters cost about R15 000. (Personal communication)

**Mini-Cardiopulmonary Bypass vs Conventional Cardiac Bypass: Which technique is superior?**

In a best evidence review,¹⁵ 144 papers were found on the comparison of c-CPB to m-CPB.

Of these, fourteen articles, with a database of 100 patients, were believed to show the best evidence to answer the clinical question of which technique was superior.

The results were as follows:

<table>
<thead>
<tr>
<th>No of Studies (n = 14)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Reduced haemodilution</td>
</tr>
<tr>
<td>7</td>
<td>Reduced transfusion requirements</td>
</tr>
<tr>
<td>2</td>
<td>Reduced fresh frozen plasma requirements</td>
</tr>
<tr>
<td>3</td>
<td>Reduced Intensive Care Stay</td>
</tr>
<tr>
<td>3</td>
<td>Reduced postoperative blood loss</td>
</tr>
<tr>
<td>3</td>
<td>Improved renal function</td>
</tr>
<tr>
<td>4</td>
<td>Better Cardiac Output Index</td>
</tr>
<tr>
<td>6</td>
<td>Reduced inflammation markers</td>
</tr>
</tbody>
</table>

**Conclusion**

Cardiopulmonary bypass has become an essential adjuvant to cardiac surgery but is associated with significant morbidity related to haemodilution of blood volume, damage to blood cell components, myocardial damage, and activation of the systemic inflammatory response with associated organ dysfunction.

Mini-CPB is more expensive and complex to run, although the literature shows that it is at least as safe as c-CPB.

Mini-CPB shows considerable potential for limiting the degree of haemodilution and haemolysis associated with bypass. There appears to be some evidence that that inflammatory response associated with bypass is reduced and some of the shorter term adverse outcomes associated with this do appear to be improved with its use. As yet, the overall morbidity and mortality associated with CPB appears to be similar with both types of bypass techniques. However, the evidence base for these assumptions is limited.

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1. www.health247.com; www.texasheart.org>Topics>Proceed


Posterior fossa surgery

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This is a review of the underlying basic concepts of cardiopulmonary bypass and mini-cardiopulmonary bypass, with a focus on the complications related to cardiopulmonary bypass and whether these complications can be reduced with the use of mini-bypass techniques.

Keywords: conventional cardiopulmonary bypass, mini-cardiopulmonary bypass, comparison, complications

Introduction

Posterior fossa surgery, because of the location of the fossa, its contents and its volume, and the duration of surgery, presents the surgeons and the anaesthesiologists with unique and significant problems. The most common surgical procedures done are tumour excisions, correction of congenital and acquired craniovertebral junctional anomalies, e.g. Arnold-Chiari malformation, and surgical procedures to relieve pressure on the brainstem, e.g. evacuation of cerebellar haematomas, and decompressive craniotomy to relieve pressure on the brainstem. About 60% of all childhood brain tumours and about 20% of adult brain tumours originate in the posterior fossa.

Anatomical considerations

The base of the skull is divided into anterior, middle and posterior fossae. The posterior fossa is the largest and the deepest. The bony structures comprising the floor of the posterior fossa are: sphenoid, occipital, temporal and the mastoid angle of the parietal bone. There are two dural reflections in the posterior fossa, the tentorial cerebelli, which form the roof of the fossa separating it from the cerebral hemispheres. Between the anterior medial part of the right and left is an oval opening, the tentorial incisura, which allows the brainstem to pass through from the middle to the posterior cranial fossa.

The venous drainage of the whole cranium passes through the sinuses of the posterior fossa. The important venous sinuses in the posterior fossa are the right and left transverse sinuses which join the sagittal sinus and the straight sinus to form confluence sinuses which leave the posterior fossa to continue as internal jugular veins.

Contents of the posterior fossa

The lower part of the midbrain, Pons, Upper Medulla Oblongata, Cerebellum, Reticular Activating System, 3rd to 12th cranial nerves nuclei and many efferent and afferent fiber tracts that connect the brain with the rest of the body, the aqueduct of Sylvius and the 4th ventricle.

Important foramina in the posterior fossa

- Foramen magnum: the fossa communicates with spinal canal via this foramen. Structures passing through are: spinal roots of the Accessory nerve, meningeal branches of the upper cervical nerves C1 to C3, meninges, and vertebral arteries ascending to supply the posterior part of the brain.
- Jugular foramina: internal jugular vein, glossopharyngeal, vagus nerve, accessory nerve
- Hypoglossal canal: hypoglossal nerve
- Internal acoustic meatus: facial nerve, vestibular nerve, nervus intermedius.

Surgical pathology

With reference to the 4th ventricle, the posterior fossa can be divided into anterior and posterior compartments. Histologically, all nervous system tumours can be broadly divided into three groups: primitive neuroectodermal tumours (which occur in the brain, the sympathetic nervous system and the eye, e.g. medulloblastomas, etc.), glial tumours (which arise from the supportive tissue of the brain or glia, e.g. astrocytomas and gliomas), and metastatic tumours.

Pathophysiology

The location of the tumour in a particular area may give rise to a unique syndrome confined in that area, e.g. midline syndrome, cerebellar hemisphere syndrome, ponto-cerebellar angle syndrome and brainstem syndrome. Depending on the location of the tumour, patients may present with a large variety of clinical symptoms.

Intracranial Hypertension Syndrome is amongst the first elements of diagnosis. Even a slight increase affects the brain function in two ways: firstly, decrease in cerebral perfusion...
pressure leading to ischemia; secondly, it may cause herniation of the brain substance, particularly the cerebellar tonsils and nervous paths of the brainstem, impairing the brainstem’s vital functions coordinated at this level.8

**Significance of posterior fossa procedures**

- Vital structures within the posterior fossa.
- Confined space of the posterior fossa: even a relatively small lesion, haemorrhage or oedema in the vital areas may exaggerate the neurologic consequences of the mass effects of lesion; hydrocephalus due to obstruction of CSF flow through aqueduct of Sylvius leads to increased ICP.
- Location and anatomy of the lesions complicating surgical access requiring unusual positions.
- Relatively long duration of surgery in extreme positions.
- Increased propensity for development of hydrocephalus and/or Venous Air Embolism (VAE).

**Operating positions**

An ideal operating patient position should facilitate surgical access without compromising patient safety. Choosing one position over the other may be influenced amongst others by the following:

- location of the tumour
- patient age
- preexisting diseases and the patient’s physical status, particularly in reference to cardiovascular and pulmonary stability and airway manageability
- method of surgical approach
- technical possibilities of monitoring.

Regardless of the position chosen, particular attention should be paid in positioning, as many problems can be avoided with careful positioning and padding of vulnerable parts.

**Supine position**

In this position there is maximum rotation (up to 45 degrees can be achieved) to the contralateral side and head up tilt or reverse Trendelenburg to improve venous drainage. It is used for access of the lateral structures of the posterior fossa.

**Disadvantages:**

- It is associated with reduced venous return from the brain with a possible increase in ICP.
- Extreme lateral rotation for a prolonged period can cause macroglossia and peripheral nerve damage.

**Prone position**

Oldest and the most commonly used in posterior fossa surgery. It facilitates easy and optimal surgical access for both midline and lateral posterior fossa structures.

**Disadvantages:**

- Amount of blood loss is much higher than in sitting position, especially if abdominal compression has not been avoided.
- Difficult access to airway.
- Blindness can result from: pressure on the globe of the eye, or ischemic optic neuropathy or retinal artery thrombosis associated with prolonged procedures in prone position in the absence of direct pressure on the eye and conjunctival edema.
- Venous pooling sufficient to lead to hypotension especially in the elderly debilitated patients.
- Incompatibility with cardio pulmonary resuscitation.
- Danger of necrotic lesions of the face areas and other points of support due to uneven pressure distribution when head rests are used.

**Lateral position**

It is used for unilateral positions, it improves surgical access by gravitational retraction of the cerebellum and drainage of the CSF and blood from the operating field.

**Park-bench:** modification of the lateral position where the patient is positioned semi-prone with head rotated and neck flexed with brow facing the floor. This gives greater access to the midline structures when compared to lateral position and in selected patients it avoids the need for the prone position.

**Disadvantages:**

- Peripheral nerve damage: brachial plexus injury if the arm is pulled caudally to gain access to the retromastoid area, or nerve compression on the dependent side from pressure on the axillary or peroneal nerve at the knee.
- Venous engorgement and macroglossia.

**Sitting position**

It provides optimal surgical access, particularly for the midline structures and the cerebellar pontine angle.

**Contraindications:**

**Absolute contraindications**

- Documented right to left intracardiac shunt, which would facilitate systemic embolization of air.
- Ventriculo-atrial shunt as air entry from the ventricles during surgery may migrate into the atrium.

**Relative contraindications**

- Include presence of Patent Foramen Ovale, uncontrolled hypertension, extremes of age, severe autonomic neuropathy, severe hypovolemia, severe hydrocephalus, impaired cardiac function, degenerative diseases of cervical spine, significant cardiovascular disease.

**Advantages:**

- Respiratory system: promotes favorable changes in ventilator mechanics:
  - Lower airway pressure, ease of diaphragmatic excursion
  - Improved ability to hyperventilate.
- Although there is an increase in FRC, redistribution of blood due to gravity negates the effects of optimal oxygenation. There is no evidence of improved pulmonary function after sitting position.
• Cardiovascular system: it promotes drainage of blood and CSF with decrease ICR, intraoperative bleeding and transfusion requirements.

• Surgery: better surgical exposure, less tissue traction, less cranial nerve damage and a more complete resection of the tumour possible.8

• Monitoring: increase access to the ETT and thorax for monitoring, easy access to arms and other extremities for monitoring of fluid and blood administration and sampling.

• Visualization of face for observation of motor responses during cranial nerve stimulation.

Disadvantages and complications associated with sitting position:

• Hypotension and cerebral hypo-perfusion

The hydrostatic effect of gravity produces a decrease in systemic arterial pressure because of venous pooling in the lower extremities.10 This may be aggravated by the depressant and the vasodilatory effects of anaesthesia, which may reduce the compensatory response to hypotension, such as an increase in heart rate and an increase in systemic vascular resistance, accentuated by advanced age and associated comorbidities. Intermittent positive pressure ventilation may contribute to this hypotension by reducing the venous return.

The impact of a decrease in Mean Arterial Pressure due to gravitational effects and anaesthesia may cause a decrease in cerebral perfusion pressure (CPP) leading to an increased risk of cerebral ischemic damage. For each 2.5 cm increase in vertical height of the head above the level of the heart, there is a 2 mmHg reduction in MAP.10

• Quadruplegia with cervical spinal ischemia

Flexion of head on the neck causes stretching of the spinal cord at C5 level (mid cervical) or a prolonged focal pressure on the spinal cord; regional cord perfusion may be compromised particularly during episodes of significant hypotension resulting in ischemic damage to the spinal cord.

Blood pressure should be measured at the level of the head because blood pressure measured at the level of the heart will grossly under estimate the perfusion pressure for the brain. For each 2.0 cm increase in vertical height of the head above the level of the heart, leads to a 1.5 mmHg reduction in MAP.10

• Pneumocephalus

It occurs when air enters the brain or spaces around the brain after dural incision.10 If the volume is large, and this is accompanied by other factors that cause cerebral oedema, tension pneumocephalus may occur with possible brain herniation.

Possible causes: various techniques used to reduce the volume of the brain may encourage air entry into the intracranial space and when the cranial cavity is closed the brain expands, the air is compressed causing a mass effect with elevated ICP.10,11 The condition is worsened by intraoperative use of N2O.

- contraction of intravascular blood volume associated with acute haemorrhage
- intraoperative slow continuous gravitational drainage of CSF in sitting position can result in accumulation of air in subdural space.10

It can present in the postoperative period as a delayed recovery, neurologic deficit, headache, confusion, agitation or convulsions.

Treatment: high O2 flow reduces pneumocephalus; in severe cases, neurosurgical treatment.

• MacroGLOSSIA

Extreme flexion of head with the chin resting on the chest during prolonged surgery; prolonged presence of an oral airway leads to obstruction of venous and lymphatic drainage of the tongue, airway obstruction, hypoxemia and hypercapnia in the postoperative period, particularly in children.5

• Venous Air Embolism (VAE)

VAE is a potentially life threatening complication associated with all surgery in the steep head up position. The incidence of VAE varies from 25–75% during surgery in sitting position depending on the sensitivity of the monitoring used.1 However, it is thought to be lower in children because the dural venous pressures are higher than in adults.12 It is more likely to occur when the surgical site is above the level of the heart. The other predisposing factor is the presence of open and noncollapsible venous channels as it may occur with major dural venous sinuses and diploic veins.11,13

In the sitting position, the site of surgery is above the level of the heart and this results in a negative venous pressure at the level of the surgical wound (subatmospheric). A pressure gradient is established which facilitates the open veins to entrain atmospheric air into the circulation, resulting in VAE.11 In adults the lethal volume is thought to be between 200–300 ml or 3–5 ml/kg.14 Dehydration exacerbates the low venous pressure and increases the risk of air entrainment.5

Clinical features of VAE depend on the rate and volume of air entrained. The spectrum of manifestation includes cardiovascular and respiratory disturbances:

Cardiac manifestations:

Massive air embolism produces abrupt and catastrophic haemodynamic changes due to a large embolus obstructing the outlet of the right ventricle with a sudden onset of right heart failure and cardiac arrest.14 This is a rare event. More commonly, the slow entrainment of air may produce little or no respiratory or haemodynamic compromise. However, as air is cleared to the pulmonary circulation, pulmonary vascular resistance, pulmonary artery and right atrial pressures increase, resulting in right sided heart failure, decreased left ventricular filling pressures and decreased cardiac output.5 Tachyarrhythmias and myocardial ischemia may ensue.

Respiratory manifestations:

The pulmonary vascular obstruction increases dead space ventilation, resulting in a decrease in end tidal carbon dioxide with an increase in arterial carbon dioxide tension.
Hypoxemia may result from partially obstructed pulmonary vasculature and the local release of vasoactive substances.

How to minimize the risk

Use of Trendelenburg tilt and leg elevation to minimize the gradient between the surgical field and the right heart and optimise hydration.

Reduction of risk for development of VAE includes liberal use of bone wax, vigilance, avoidance of N2O and maximisation of intravascular space.

Acute treatment of VAE

The surgical team should be notified to identify open sinuses which should be immediately closed surgically or covered with saline soaked swabs to prevent further air entrainment and any suspected air entry point sealed with bone wax.

Increase venous pressure:

If possible the surgical field should be positioned below the level of the heart (trendelenburg). Jugular venous pressure compression may be considered as it reduces air entrainment but should be used with caution as it increases ICP and decreases CSF because of the simultaneous compression of the carotid artery. Use of PEEP (CONTROVERSIAL). It may greatly increase the risk of hypotension in a patient who is already intravascularly depleted. It will raise venous pressure, but also raise right atrial pressure and the possibility of opening a functionally closed foramen ovale, predisposing the patient to paradoxical air embolism. May be considered when all other attempts at preventing continuous VAE have failed. Discontinue N2O if in use.

Support cardiovascular system:

Volume, Inotropes, vasopressors

Monitoring modalities for VAE

• Pre-cordial Doppler ultrasound: it is sensitive and noninvasive (can detect 0.05 ml of air/kg or 0.015 ml/kg/min). The drawback is the interference with the use of cautery. The Capnography: it is convenient and available on most anaesthetic machines – a change of 2 mmHg of EtCO2 can be an indicator of VAE.

• Mass spectrometry (End-tidal nitrogen detection): more sensitive than EtCO2.

• Pulmonary artery catheter: can detect a rise in right heart pressures – most invasive and less sensitive than the Doppler.

• Pulse oximetry, clinical vigilance, oesophageal stethoscope, ECG – changes occur later.

• Transoesophageal echocardiography: more sensitive but invasive and expensive.

Choice of anaesthetic technique

Anaesthetic goals are to facilitate surgical access, minimize nervous tissue trauma and maintain respiratory and cardiovascular stability.

Preanaesthetic assessment

Basic principles for assessment of general health for any neurosurgical operation. This would include:

• Signs and symptoms relating to complications from the posterior fossa lesion, cranial nerve palsies, localizing lesion for the brain stem, and cerebellar and craniovertebral junctional abnormalities which may influence airway management.

• Review of imaging of the brain to assess location and size of the lesion, presence of hydrocephalus or increased ICP.

• Sedatives and narcotics should be used cautiously, if needed. The consequences of respiratory depression like hypoxia and hypercarbia in a patient with low intracranial compliance may be disastrous.

• The induction of anaesthesia and intubation should be gentle and smooth; the blunting of laryngoscopy and intubation response is standard practice.

• The significance of the disturbances, such as hyperdynamic response to laryngoscopy and intubation, is much higher in patients with posterior fossa pathology due to decrease intracranial compliance leading to an increased ICP and possible ischemia or herniation with brainstem compression.

Maintenance of anaesthesia

The selection of the appropriate anaesthetic agents in neurosurgery depends on the risk factors inherent to the patient and the procedure.

Drugs used for maintenance should be able to provide the following:

• Brain relaxation

• Reduction of CMRO2

• Cerebral protection

• Stable systemic and cerebral hemodynamics stability with ease of titration

• Preservation of cerebral autoregulation

• Minimal effect on ICP

• Rapid awakening at the end of the procedure

• Minimal effect on electrophysiological monitoring during surgery

• Maintenance of vascular reactivity to CO2

Tiva vs inhaled anaesthetics (ia)

Neuroprotection is the cornerstone of anaesthetic management in neurosurgery. Two modalities are commonly used in neurosurgery. Both modalities were found to have neuroprotective properties.

Total Intravenous Anesthesia (TIVA)

For our discussion it refers to a use of hypnotic, e.g. propofol, in combination with an opioid, e.g. remifentanil, for anaesthesia induction and maintenance.

Propofol favourable features:

• interacts with GABA receptors

• rapid onset of action and offset
• neuroprotective effect during cerebral ischemia
• lowering ICP, CBF, cerebral metabolism and cerebral oedema effect
• improving cerebral perfusion pressure and MAP
• anticonvulsant properties
• preservation of autoregulation and vascular reactivity.

Limitations of TIVA:
• need an experienced anaesthetist
• propofol use may lead to accumulation which may delay emergence
• prolonged propofol infusion has been associated with development of rhabdomyolysis, lactic acidosis and renal failure
• it may induce a substantial reduction of cerebral blood volume, leading to complications
• relatively expensive.

Currently, TIVA is used more frequently in neurosurgery because of the fast onset of action and the ability to monitor neuronal structures continuously using intraoperative neurophysiological monitoring techniques.

A combination of TIVA and a low dose of sevoflurane has been used in some studies with success.

Inhaled anaesthetics (IA) (Sevoflurane/Isoforane) favourable features
• Reduced excitotoxicity
• Increased physiologic stability

The effect is mediated by their GABA agonist and NMDA antagonist activity and also to glutamate reduction. At a dose of 1 MAC there is a balance between the drop in CMR and the increase in CBF.

No significant difference was found between TIVA and sevoflurane in the incidence of postoperative nausea and vomiting (PONV) in a study done on patients who underwent an infratentorial surgery. However, a systematic review done later showed more PONV and greater use of anti-emetics in patients treated with sevoflurane as compared to propofol; this was supported by a meta-analysis done in patients who had undergone elective craniotomy, which showed a lower incidence of PONV in patients managed with propofol.

In patients with adequate intracranial compliance, the use of an IA dose equal or less than 1 MAC has been shown to have minimal interference with autoregulation of cerebral blood flow, cerebral blood volume and ICP. Generally, in patients with normal intracranial compliance, the effect of IA on brain haemodynamics is negligible.

TIVA is preferred in patients with an altered flow/metabolism ratio, unstable ICP, expansive or large lesions.

Electrophysiological monitoring

The brainstem has a concentration of nerve structures and minor damage to them may result in devastating complications. Intraoperative neurophysiological monitoring plays a major role in continuous monitoring of neuronal integrity and function of the neuronal structures at risk during the surgical procedure by facilitating early detection of changes in the brain prior to irreversible damage. It is indicated for monitoring of cranial nerve functions for microvascular decompression and tumors of the posterior fossa, thus minimizing the risk of permanent damage to the nerves. Evoked potentials monitoring includes somatosensory evoked potentials and motor evoked potentials.

Brainstem auditory evoked potentials are valuable intraoperatively for the detection of auditory nerve and brainstem dysfunction, when hearing is at risk and when there is potential danger of damage to the brainstem. Electrophysiological monitoring (EMG) is also used extensively during operative cases to assist in identifying structures and to minimise facial weakness when dissecting near cranial nerves V and VII. Neuromuscular blocking agents may need to be avoided during the period of monitoring.

Effect of anaesthesia on electrophysiological monitoring

All neuromuscular blocking agents cause depression of evoked potentials and prolongation of latencies. They are therefore best avoided during electrophysiological monitoring.

Other intraoperative problems

Cardiovascular instability

Surgical stimulation of the floor of 4th ventricle, lower pons, upper medulla and the cranial nerve nuclei may cause hypertension, bradycardia, tachycardia and arrhythmias. Cardiovascular disturbances that occur during surgery may be a warning that the surgeon is too close to the vital structures and a brief interruption of surgery may be enough to address the problem, otherwise pharmacological agents can be used.

Potential for large blood loss

This may be influenced by the skill of the surgeon, the location of the tumour, the vascularity of the mass and the involvement of the sinuses

Emergence

The blunting of extubation response is standard practice. Awakening allows immediate postoperative neurological assessment. When preoperative consciousness is intact, the surgery relatively uneventful, it is recommended that the patient be awakened in the operating room.

If, however, the pre-surgery consciousness is impaired, surgery is prolonged and difficult with frequent traction on the brain stem, there may be a danger of apnea and or decreased sensorium with diminished airway reflexes or perioperative problems (e.g. cerebral oedema, haemodynamic instability), delayed awakening is recommended, with the patient remaining intubated and allowed to awaken slowly after a period of monitoring and continued ventilation.

Postoperative period

Ventilated patients may need intracranial pressure monitoring probe as deteriorating mental status cannot be used for postoperative monitoring.
For extubated patients, close monitoring of vital signs and repeated neurological examination is needed.

Sedation, analgesia and PONV prophylaxis are important considerations.

References

The anaesthetist’s role in the endoscopy suite

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Introduction
The anaesthesiologist’s role in the endoscopy suite is twofold:
1. Provide safe and comfortable sedation or anaesthesia to the patients who may present to us on an endoscopy list
2. Provide acceptable conditions for the endoscopist to perform their work.

With advances in endoscopy, our role is becoming increasingly more challenging. New and more invasive procedures (which previously have been done by surgeons in an operating theatre) are being done in the endoscopy suite. Consequently, we are being presented with patients with co-morbidities who may, overall be sicker; presenting for more invasive procedures, which take longer than standard endoscopy; and who expect to be discharged home on the same day.

Topic to be discussed further includes:
1. Advances in endoscopy
2. Dangers of sedation and how to avoid them
   a. Hypoxia
   b. Hypercarbia
3. Pharmacology
   a. New sedation drugs
   b. Antispasmodics
   c. Adverse drug reactions
4. Disease processes commonly associated with patients presenting for endoscopy
   a. Visceral hypersensitivity
   b. Aortic stenosis
   c. Neuroendocrine tumours
   d. Obesity
   e. Renal failure
   f. Liver failure

1. Advances in Endoscopy

There have been major advances in the field of gastrointestinal endoscopy in the last 20 years, both in the diagnostic and especially in the therapeutic arena.

a. Gastroscopy and colonoscopy

   DIAGNOSTIC

   Colonoscopy has been shown to be very effective in detecting precancerous colonic polyps. With the implementation of screening programs, the patients presenting for screening colonoscopy will increase.

   THERAPEUTIC

   • There have been many advances in upper gastrointestinal endoscopy, concerning the management of bleeding. Techniques employed may include the use of clips, injection and glue.
   • Strictures in the upper and lower gastrointestinal tract may be stented.
   • Mucosal lesions in the upper and lower gastrointestinal tract may be resected endoscopically. This is known as endomucosal resection. These procedures take longer than the standard endoscopic procedure.

b. Endoscopic retrograde cholangiopancreatography (ERCP)

   ERCP requires screening and is therefore often done in a remote location in the radiology suite. It is done in the prone position. Patients often have obstructive jaundice and usually require antispasmodics (see later).

c. Endoscopic ultrasound (EUS)

   DIAGNOSTIC

   EUS can be employed for use in the upper and lower gastrointestinal tract. It can be used to define and examine sub-mucosal lesions as well as peri-luminal structures such as the pancreatic, posterior mediastinal and para-aortic lymph nodes. These lesions can then also be sampled, via fine needle aspiration through the endoscope.

   THERAPEUTIC

   • EUS can be used to drain fluid collection or abscesses in the pancreas or any other area abutting the gastrointestinal tract.
• Coeliac plexus blocks for cancer palliation can also be performed via EUS.

d. Double balloon endoscopy (DBE)

DBE can be performed via the upper and lower gastrointestinal tract. DBE is employed to access the small bowel for diagnostic and/or therapeutic purposes. DBE is a very time-consuming procedure.

2. Dangers of sedation and how to avoid them

a. Hypoxia

Most of the sedative drugs depress the respiratory system. The art of sedation involves giving enough drugs to sedate but not enough to cause hypoxia. There is no magic formula for this, but rather an "intelligent" feel one develops with experience.

However, if one is worried about hypoxia; remember the benefits of preoxygenation and supplemental oxygen. Adequate preoxygenation fills the functional residual capacity (residual volume plus expiratory reserve volume) with oxygen. In the average adult, this equates to 2300 ml. Oxygen consumption (VO₂) in the average adult is 250 ml. Therefore, if the average adult is rendered apnoeic, it will take approximately 9 minutes 12 seconds before the patient becomes hypoxic. This period of time is more than adequate for a standard gastroscope and can provide more margin of error in those patients with less reserve (e.g. obese patients).

b. Hypoventilation and hypercarbia

Hypoventilation and subsequent hypercarbia is dangerous in patients with pulmonary hypertension and especially those with poor right ventricular function. Hypercarbia can set these patients spinning into a downward spiral of worsening pulmonary hypertension, exacerbation of hypoxia and hypercarbia and worsening right ventricular function.

Once there is right ventricular dilatation, consequences are:

• Increase in wall tension, which increases myocardial oxygen demand as well as decreasing ventricular perfusion.
• Functional tricuspid regurgitation, which leads to right ventricular volume overload and further annular dilatation and right ventricular remodeling.
• Ventricular asynchrony, which leads to a decrease in right ventricular stroke volume and under-filling of the left ventricle.

All these factors can lead to a marked decline in cardiac output and myocardial ischaemia that can set up a vicious cycle which can be impossible to rectify. These patients can be very tricky to sedate as mere hypoventilation and not apnoea can set up this vicious cycle.

Capnography offers an earlier indication of hypoventilation compared with pulse oximetry and is better than visual assessment alone. There are pitfalls with pulse oximetry. These arise because at the upper limit of the oxyhaemoglobin dissociation curve, large changes in partial pressure of oxygen result in small changes in oxygen saturation. This is especially true in patients receiving supplemental oxygen as this shifts the oxyhaemoglobin curve to the left. In addition, pulse oximetry readings can be delayed by up to 50 seconds depending on cardiac output and peripheral vasoconstriction.

Capnography therefore should be considered in procedures requiring moderate or deep sedation and in any patient in whom hypoventilation would be a problem.

Respiratory volume monitors (RVMs) monitor ventilation in nonintubated patients and may prove to be useful in the future. RVMs operate by detecting thoracic impedance through electrodes placed over the patient’s chest, enabling real-time calculations of respiratory rate, tidal volume and minute ventilation.

3. Pharmacology

a. New Sedation Drugs

REMIMAZOLAM

Remimazolam is a short-acting GABA A receptor agonist that has organ-independent metabolism. Preclinical animal studies showed that remimazolam had a more rapid onset and shorter duration of action than midazolam. Because of its organ-independent metabolism and rapid and predictable onset and recovery profile, remimazolam may have advantages over other currently available benzodiazepines. Its drawback, however, is that, as with the other benzodiazepines, it has a respiratory depressant effect.

FOSPROPOFOL

Fospropofol is a water-soluble prodrug of propofol. It is metabolized in vivo by tissue alkaline phosphatases to liberate propofol, phosphate and formaldehyde. After intravenous injection it has a lower peak concentration and a slower decline in drug concentration than propofol. This prodrug formulation overcomes the disadvantages of the lipid-based formulations, the complications of lipid infusion, and the risk of fluctuations in propofol levels due to bolus injection.
**METHOXYFLURANE**

Methoxyflurane is an agent formerly used as a volatile anaesthetic but with strong analgesic properties. It is available in South Africa as Penthrox®. It is packaged as a single-use inhaler. Methoxyflurane is added to a propylene wick within a small chamber, and is vaporized as the patient inhales. There is a dilutor hole on the inhaler that the patient can cover to increase the inhaled concentration of methoxyflurane. The inhaler has a charcoal activated carbon chamber in which exhaled vapour is adsorbed to minimize environmental contamination.7

Nguyen has compared methoxyflurane with a combination of midazolam and fentanyl for colonoscopies.8 They concluded that methoxyflurane is a feasible drug for colonoscopy and as effective as conventional drugs. It has a shorter recovery time, is not associated with respiratory depression and it does not influence success and polyp detection.

Problems with methoxyflurane include that it is contraindicated in renal failure or impairment. 8

**Antispasmodics**

**HYOSCINE**9

Hyoscine is also known as scopolamine and distributed as buscopan®. It has antimuscarinic and anticholinergic effects. Therefore, the side effects include tachycardia, dry mouth, paralysis of visual accommodation and urinary retention. Hyoscine is contraindicated in patients with atrial tachyarrhythmias, congestive cardiac failure, coronary artery disease and mitral stenosis. However, the duration of action of hyoscine is short, therefore these effects are unlikely to be of concern except in severe disease.

Other contra-indications include myasthenia gravis, glaucoma, megacolon, gastrointestinal stricture and prostatic hypertrophy.

**GLUCAGON**9

Glucagon is a naturally occurring hormone produced by the α cells of the islets of Langerhans in the pancreas. Intravenous glucagon causes gastrointestinal smooth muscle relaxation by an incompletely elucidated mechanism. Glucagon causes hyperglycaemia with a reactive hypoglycaemia occurring about 2 hours after administration. So it should be used with caution in diabetic patients.

**Adverse drug reactions**

**MIDAZOLAM**10

Paradoxical reactions or disinhibition reactions may occur with midazolam. Paradoxical reactions are characterised by increased talkativeness, emotional release, excitement, excessive movement and even hostility and rage. Risk factors include: male gender, previous unsuccessful sedation, heavy drinking, smoking, upper endoscopy; and a higher dose of midazolam. The reported incidence in adult patients is 1.4%. Flumazenil may be used to treat the paradoxical reaction.

**PROPOFOL**11

The administration of propofol may be associated with generalized tonic-clonic seizures, focal motor seizures, increased tone with twitching and rhythmic movements, opisthotonus and involuntary movements. This is a rare adverse event and further investigation is required to elucidate the exact incidence and mechanism.

4. Disease processes commonly associated with patients presenting for endoscopy

a. **Visceral hypersensitivity**

Irritable bowel syndrome (IBS) is one of the most common gastrointestinal disorders. It is characterized by abdominal pain and disturbed defaecation that cannot be explained by structural or biochemical abnormalities. Increased sensitivity to stimuli arising from the gut wall (visceral hypersensitivity) contributes to the abdominal pain.12 Patients with coeliac disease exhibit increased rates of neuropsychiatric disturbances and visceral hypersensitivity. These patients may require higher amounts of both opioids and midazolam compared with age- and gender-matched controls.6

b. **Aortic stenosis**

There is an association between chronic gastrointestinal bleeding and calcific aortic stenosis. This is known as Heyde syndrome after Edward Heyde, who first described it in 1958. The pathogenesis is due to an acquired type IIA von Willebrand syndrome and angiodyplasia.13

Aortic stenosis is associated with high shear stress, which elevates von Willebrand factor-cleaving metalloprotease activity. This leads to proteolysis of von Willebrand factor and increases interactions between von Willebrand factor and platelets, leading to degradation of von Willebrand factor.

The management of Heyde Syndrome is multidisciplinary. Unfortunately, the treatment for conventional von Willebrands disease (octreotide, vasopressin, Factor VIII) is ineffective in the acquired form of the disease. Oestrogen-progesterone preparations and thalidomide may be helpful. Blood transfusions and endoscopic interventions are used as a bridge to valve replacement. Bioprosthesis should be considered in a patient older than 65 years and it also precludes the need for anticoagulation. Trans catheter aortic valve implantation is a feasible alternative.

c. **Neuroendocrine tumours**14

Neuroendocrine tumours (NETs) are malignant growths that arise from neuroendocrine cells. They most
commonly occur in the gastrointestinal tract (48%), lung (25%) and pancreas (9%). Neuroendocrine cells can produce hormones such as serotonin, which can produce symptoms of flushing and diarrhea.

NETs may be found incidentally or may be suspected when they produce clinical symptoms from secreted hormones. These are termed “functioning” tumours. Most NETs, however, are “nonfunctioning”.

Carcinoid syndrome, characterized by flushing, diarrhea and valvular heart disease, occurs when hormones produced by NETs reach systemic circulation. This usually happens when liver metastases are present, allowing for bypass of the hepatic metabolism, which would normally inactivate the hormones.

Endoscopic ultrasonography is the most sensitive test for diagnosis of pancreatic NETs.

d. **Obesity**

Patients with a higher body mass index (BMI) have a higher prevalence of gastrointestinal diseases such as gallbladder disease, oesophageal and colon cancer. In addition, obesity is associated with hypertension, hyperlipidaemia, diabetes, stroke, osteoarthritis, sleep apnoea, restrictive lung disease and pulmonary hypertension.

Obese patients are anecdotally believed to be at higher risk for procedural sedation, but this is not extensively backed up by the medical literature.

Pharmacokinetics (specifically binding, elimination and volume of distribution) is also difficult to predict in obese patients. Higher adipose mass, a reduction in total body water, higher glomerular filtration rate and normal hepatic clearance, which may lead to higher sedative dose requirement and thus increased sedation risks.

As with obesity, it is thought that obstructive sleep apnoea (OSA) may increase the risk of cardiopulmonary unplanned events during endoscopy, but this is not backed up by medical literature. The ASA guidelines recommend that capnography should be used for monitoring of ventilation in patients with OSA.²

e. **Renal failure**

Midazolam and fentanyl have been safely used for sedation in renal failure patients on dialysis.²⁶

Oral sodium phosphate bowel preparations (e.g. picolax®, picoprep®, coloprep®) should be avoided in patients with chronic kidney disease or any patient who is taking drugs, which may affect renal perfusion such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or non-steroidal anti-inflammatories.²⁷ Polyethylene glycol (moviprep® or cleanprep®).

f. **Liver failure**²⁸

Diagnostic and/or therapeutic endoscopy is frequently necessary in patients with chronic liver disease on an elective and emergent basis. Liver dysfunction can reduce the clearance of sedative drugs eliminated by hepatic metabolism or biliary excretion and plasma protein binding. Chronic liver disease is also associated with a reduction in drug-metabolizing activities of enzymes such as CYP450.

Midazolam has delayed clearance in patients with cirrhosis, probably due to reduced conjugation ability of the liver and/or decreased portal blood flow. Midazolam can exacerbate subclinical hepatic encephalopathy in patients with cirrhosis and Child-Pugh scores A or B.

Propofol use in patients with chronic liver disease has a shorter biological half-life and a lower risk of inducing hepatic encephalopathy

**Conclusion**

There has been a rapid advancement in the field of endoscopy with better imaging and the ability to do more invasive procedures. In addition, new endoscopes have been introduced in practice, such as EUS and DBE, enabling endoscopists to do procedures never done before. This has made our job as anaesthesiologists all the more challenging.

A study performed in Australia showed that patients presenting for gastrointestinal endoscopy under anaesthetist-based sedation at public hospitals had a high-risk profile. In addition, the incidence of significant unplanned events was 23% and the 30 day-mortality was 1.2%.¹⁹ This serves to remind us not to be complacent when we are faced with an endoscopy list. Unfortunately, sedation remains more of an art than a science. There is no perfect recipe or protocol that will work for all patients. Competency usually only comes with experience and exposure.

**References**


Inadvertent burns in theatre

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Keywords: burns in theatre, accidental burns and surgery, closed claims analysis, cautery burns

Introduction

The incidence of inadvertent patient burns in the operating theatre is fairly low with a paucity of reports in the literature. Inadvertent burning of a patient is traumatic and often catastrophic, not only to the affected patient but equally to the surgical team members. Burns in the operating room environment are caused by electrical current, chemical irritants, induction burns due to magnetic resonance (MRI), contact burns, and inhalation burns.1,2 Physical scars, emotional trauma and prolonged hospital stay are inevitable, depending on the extent of the injury. Doctor-patient relationships often become disrupted with legal consequences to the relevant practitioners. The awareness of the possibility of burns during surgery has to be increased by emphasising the causes, warning signs, and recommendations to prevent patient burns.3

Incidence and extent

Kressin analysed the American Society of Anaesthesiologists (ASA) Closed Claims Project database, reporting the database fraction of inadvertent operating theatre burns to be 2%. The commonest cause in this analysis is hot intravenous bags or bottles in contact with skin (35%); 23% of burns were caused by patient warming devices, and electrocautery was responsible for 19% intraoperative burns. The latter includes both cautery induced fires and electric ground pad/plate skin burns.4,5,6

Other causes for inadvertent skin or mucosa burns include laser devices (mostly airway), pulse oximeter finger probe and electrocardiogram lead burns during magnetic resonance imaging, defibrillator paddle burns, and two rare cases of burns due to hot surgical instruments.4,5

Location of inadvertent burns

The trunk or axilla is the commonest site for inadvertent burns, caused commonly by hot intravenous fluid bags used in the positioning of patients for invasive line placement or aiding patient warming. The ASA Closed Claims Registry identified the said site in 28% of burns. The buttocks, thighs, and feet were involved in 21% of burn claims which were, in 61% of claims,
Aetiology of inadvertent burns

Skin heated to 45°C for 2 hours produced first-degree burns, while 3 hours’ exposure produced complete epidermal necrosis.7 Burns inflicted inadvertently in the operating theatre are due to surface contact, convection, electric, chemical, radiant heat, inhalation, and magnetic resonance induced.

1. Conduction (surface contact)

Surface contact burns mostly occur in the operating theatre due to hot intravenous fluid bags used for patient positioning when placing of invasive lines, alternatively for optimal surgical positioning. Wrapping of hot fluid bags with substantial layers of surgical drape prior to placement is essential in avoiding contact burns. Using room temperature bags is advised to eliminate the possibility of an inadvertent contact burn.

2. Convection (forced air warming devices)

Incorrect usage of forced air warming devices is a major cause of burns in theatre. Burns are extremely rare and even non-existent with the correct usage of this patient warming modality. Postoperative burns caused by the incorrect use of forced warm air devices are well-described in patients with functional regional or neuraxial blocks.9 Numerous cases are described in the literature due to “hosing” with forced air warming devices.10 The correct use of the prescribed dissipating blankets, as prescribed by the relevant manufacturer, prevents burns.

3. Electrical

The incidence of recognisable burns due to aberrant/leakage currents is an estimated 0.1%.11 Burns are often not identified immediately after surgery but only days afterwards. Burns can be misdiagnosed as pressure sores, chemical contact reactions, or an allergic response to a disinfectant solution or even a drug reaction.

The technical principles underlying diathermy include a high frequency current (0.4-3 MHz) entering of the body via the small surface work electrode (diathermy probe/knife) and exiting via the neutral electrode (ground plate). The current density at the work electrode (small contact surface) rises to +1000 °C.11 The ground plate contact area has to be large in order to limit the current density, therefore limiting heat production to a minimum.

Heat generation (Q) increases proportionally with the square of the current intensity (I), duration of the current (t) and the patient resistance (R):11,12:

\[ Q = I^2t \times R \quad \text{where } R = \text{length of the current path} \]

Factors responsible for inadvertent diathermy-induced burns include a decreased neutral plate contact area or the existence of an additional, lower resistance patient ground area. The latter includes patient contact with conductive metal, e.g. operating table, via direct contact or via conductive fluid (electrolyte, cleaning solutions). Commonly found pooling areas for cleaning solutions include the buttocks, scapulae, and interscapular area including lower posterior neck.

Fire burns sparked by electrocautery use (cautery fires) is typically found in conjunction with highly flammable agents used for skin cleansing. The majority of cautery fires in the ASA Closed Claims Analysis were encountered during plastic surgery and monitored anaesthesia care. The majority of fire burns were encountered in the facial area. Highly flammable agent usage with the open administration of oxygen (facial mask, nasal prongs) was found to be a common scenario.4

Recommendations regarding the safe application of neutral electrodes are:11

Application site

Avoid application on:
- bony protuberances
- obese body regions
- metal implants
- scar tissue

Preparation of application site

- clean application area, remove traces of grease
- remove hair
- wait for cleaning agents to evaporate before placement

Positioning

- check expiry date of disposable ground plates
- prevent gel from drying; open just before use
- do not cut the ground plate to desired size
- avoid air or bubbles between plate and skin
- prevent cleaning solution to come in contact with ground plate
- do not touch the contact surface of the electrode before or during placement
- recheck contact after movement of the patient

Alarm control

- test alarms
- do not ignore alarm warnings
- limit high frequency output (> 400 W is excessive)

Removal

- remove slowly to prevent skin damage
- never pull on the connecting cable
- never reuse/reapply a disposable ground plate

4. Chemical

Prepping and degreasing agents may be toxic to the skin or react chemically with other substances, producing an exothermic reaction with skin destruction. Removal of the natural protective lipid layer of the skin with degreasing agents makes the skin vulnerable to chemical irritants. Chemical injury may look similar to thermal injury and makes
skin more exposed to heat and friction injury. Isopropyl alcohol in combination with certain soaps, in combination with pressure or mild heat from a warming blanket is known to cause skin injury. Skin exposure to unanesthetised heat-sensitive items sterilised with ethylene oxide can be extremely irritating, especially when skin is moist.4

Prepping has to be conducted with great care, at all times. A collection of fluid beneath the patient or tourniquet must be prevented. Chemically and/or electrocautery burns are inevitable when a preventative attitude is not customary.

5. Radiant heat

Heat radiant devices are known to cause patient burns. Malfunctioning or wrongly applied radiating heaters (e.g. too close to skin) is a common source of burns. High density operating lights can cause skin burns in the absence of heat filters. Oximeter probe burns are not unknown due to probe temperature that can be as high as 44°C. The time threshold for skin injury at this temperature is 6 hours. This may be less in the elderly, neonates, and patients with more sensitive skin.4 Overhead radiant heating devices must be used with caution, limiting exposure time in conjunction with sensor feedback servo control.

6. Magnetic resonance (MR) induced

A thermal injury can occur where skin is in contact with monitoring cables or sensor (e.g. ECG skin electrodes or cables, pulse oximeter sensor) or an MR accessory, e.g. surface coil. The MR environment induces currents in a conductor. Currents are induced by two magnetic fields, that is the pulsed magnetic-gradient field and the pulsed radio-frequency field. These fields fluctuate and the changing magnetic flux lines intercept an electrically conductive loop, inducing an electromotive force. Heating results from the current flowing through the loop. The loop's resistance determines the magnitude of the current. Precautions can be taken to minimize the likelihood of burns, such as not looping sensor cables and using high-resistance graphite electrodes and cables. An electrical conduction path can be eliminated by using the specified monitoring equipment, and placing the cables and sensors away from the radio frequency coil.8

Burns in the MR suite can be prevented by adhering to the following basic principles:9

- Use electrically non-conducting paths, e.g. fiber-optic cables and plastic tubing or high-resistance paths (carbon ECG leads), according to the manufacturer's instructions.
- Do not loop cables.
- Place the sensor as far away as possible from the radio-frequency coil, and run the cables away from the coil whenever possible.
- Ensure that electrical insulation on sensors and cables is intact and prevent bare metal surfaces touching the patient.
- Keep cables off the patient and run it over blankets.
- Remove all unused sensors, cables, and surface coils.
- Instruct conscious patients to call out if they experience a warming sensation.

Patient factors

Decreased blood flow to skin at risk may predispose to inadvertent burns due to decreased dissipation of heat in the following circumstances:

- Vasculopathy
- Tourniquet usage
- Low cardiac output states
- Peripheral vasoconstriction
- Hypothermia

Procedure to follow after inadvertent burn occurrence

Do not assume the cause of a burn but investigate all possible aetiologies and mechanisms. Finding the cause is essential in preventing future incidents. A description of procedures to follow investigating all possible causes of inadvertent burns in theatre is available.6,11,12 Contemporaneously noting investigation procedures followed and the state of the relevant equipment is essential. This includes patient data, all risk factors, and perioperative occurrences. Colour photographing of lesions immediately after identifying a possible burn is essential for future reference. Burns often have the immediate appearance of an electrical or thermal cause but may, after a while, reveal to have a chemical origin.3

Explanation to the patient regarding the possible mechanism(s) is essential and responsibilities have to be taken. A treatment plan is proposed to the patient in conjunction with the most appropriate specialised discipline(s). Inadvertent patient burns are not acceptable and awareness has to be fostered amongst all doctors and staff in theatre, including knowledge of risk factors and early patient examination after surgery.

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The postoperative management of a supraventricular tachyarrhythmia

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Introduction

Cardiac arrhythmias are a major contributor to morbidity and mortality in the perioperative period.1,2 Postoperative arrhythmias are common1 and the incidence of arrhythmias following major non-cardiac surgery has been reported between 4% and 20%, depending on the type of surgery or arrhythmia.3 Atrial fibrillation is the most common arrhythmia encountered following major non-cardiothoracic surgery.3

The occurrence of supraventricular tachyarrhythmia (SVT) may affect postoperative hospital and ICU stay, as well as mortality.3,5 Several authors reported a mortality of 20–50% in patients with new arrhythmias.3,6,7 Although the arrhythmia may rarely be the cause of death, the arrhythmia may have been triggered by the underlying condition.3,6,7

Classification of supraventricular tachyarrhythmias

Supraventricular tachyarrhythmias (SVTs) are paroxysmal tachyarrhythmias that are initiated and maintained in the atrial or atrioventricular (AV) nodal tissue.2,4 The classification of SVTs may be simplified according to regularity of rhythm into regular and irregular SVTs.

Regular SVTs
- Sinus tachycardia
- Atrioventricular nodal re-entrant tachycardia (AVNRT)
- Atrioventricular re-entrant tachycardia (AVRT)
- Atrial flutter
- Focal atrial tachycardia
- Wolf-Parkinson-White syndrome

Irregular SVTs
- Atrial fibrillation (AF)
- Multifocal atrial tachycardia (MAT)

Keywords: Postoperative arrhythmia, supraventricular tachyarrhythmias, perioperative supraventricular tachyarrhythmias

Predisposing factors for postoperative SVTs

Supraventricular tachyarrhythmias may be a warning sign, which may be overshadowing correctable life threatening conditions.10

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Figure 1: Classification of SVT

- Narrow QRS complex (<120 ms)
  - Regular
    - P wave visible
      - P:QRS>1
        - Atrial flutter
        - Atrial tachycardia
      - P:QRS=1
        - Long RP interval (>70 ms)
          - AVNRT
        - Short RP interval (<70 ms)
          - AVNRT
          - Atypical AVNRT
          - Atrial tachycardia
  - P wave invisible
    - AVNRT
    - Atypical AVNRT
    - Atrial tachycardia
  - Atrial fibrillation
    - Atrial flutter with variable AV block
    - Atrial tachycardia with variable AV block
    - Multifocal atrial tachycardia

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The most common reversible conditions, and which should be corrected before considering pharmacological antiarrhythmic therapies, are:

- Hypoxaemia
- Hypercarbia
- Acidosis
- Hypotension
- Electrolyte imbalances
- Mechanical irritation: Chest tube
- Hypothermia
- Adrenergic stimulation
- Proarrhythmic drugs
- Micro/macro shock
- Cardiac ischaemia

Management of postoperative SVTs

The management of postoperative SVTs requires a comprehensive approach. Firstly, the problem is recognized, an arrhythmia is diagnosed and the physiological effect on the patient is assessed. Assess clinical condition – the heart rate will typically be ≥ 150/min if tachyarrhythmia is present. A cascade of adverse physiological phenomena may precipitate SVT in the postoperative period. Reversible aetiologies should be identified and treated before antiarrhythmic therapy is instituted, unless the patient is haemodynamically unstable. If the patient is haemodynamically unstable, immediate synchronised direct current cardioversion is required to prevent the life threatening complications of ventricular rate control is the next priority in a patient who develops SVT and does not require immediate cardioversion. The advantages of slowing ventricular rate during SVT are: prolongation of diastole enhancing left ventricular filling, which enhances stroke volume and improves haemodynamic stability. The other advantage of rate control is the reduction of myocardial oxygen consumption and therefore lowering risk of ischaemia.

Rate control is achieved with one of a variety of AV nodal blockers. These are agents with class II or IV activity.

Beta blockers: esmolol 500 mcg/kg over 1 minute then 50–300 mcg/kg/min titrated to effect, with repeat boluses in between each dose increase or metoprolol 2 – 5 mg over 2 minutes, which can be repeated in 10 minutes up to three doses. Esmolol has ultra-rapid elimination, rendering it easily titratable. Both IV verapamil and diltiazem are calcium channel blockers effective for acute treatment of SVT in haemodynamically stable patients. They are less easily titrated than esmolol but provide rapid slowing of the ventricular rate in SVT in minutes. Diltiazem 0.25 mg/kg IV bolus over 2 minutes followed by an infusion of 5–10 mg/h or verapamil at a dose of 0.075–0.15 mg/kg IV bolus over 2 minutes. If the abovementioned pharmacological treatment is ineffective or not feasible, synchronised cardioversion is recommended.

Sinus tachycardia

Physiological sinus tachycardia may result from causes such as fever, dehydration, anaemia, and heart failure. Tachycardia usually resolves with treatment of the underlying causes.

Atrioventricular nodal re-entrant tachycardia

AVNRT results from a re-entrant circuit involving anterior and posterior inputs to the AV node. The treatment of AVNRT follows the general management of regular SVT described earlier. The initial management involves slowing of the AV node conduction using vagal manoeuvres, and adenosine if vagal manoeuvres fail to slow the heart rate. This is followed by pharmacological therapy with IV beta blockers, diltiazem or verapamil in haemodynamically stable patients. Synchronised cardioversion is recommended in haemodynamically unstable patients or where pharmacological therapy is ineffective or not feasible. IV amiodarone is also recommended where IV beta blockers or calcium channel blockers are ineffective or not feasible.

Atrioventricular re-entrant tachycardia

AVRT uses an accessory pathway that bypasses the AV node, which may have anterograde conduction from the atria to ventricle or retrograde from ventricle to atria. Three types of arrhythmias may be seen as a result: a regular narrow complex

The review will focus on the acute management of SVTs in the postoperative period. The initial acute management goal is to establish haemodynamic stability. The haemodynamic instability entails hypotension (systolic blood pressure < 80 mm Hg), loss of consciousness, signs of shock, cardiac ischaemia or acute heart failure. The patient is haemodynamically unstable, immediate synchronised direct current cardioversion is required to prevent the life threatening complications of hypoperfusion. The initial shock of 50–100 J (biphasic) for narrow irregular tachyarrhythmias is used. Ensure the patient is adequately sedated prior to delivering a shock. Even though the response to cardioversion may be transient, a brief period of sinus rhythm may provide valuable time to correct reversible causes of SVT or instituting pharmacologic therapies.

Regular narrow complex SVT

In haemodynamically stable patients, acute conversion of regular narrow complex SVTs is attempted with vagal manoeuvres as the first line of treatment. These include Valsalva manoeuver or carotid massage. IV adenosine is recommended as a first line medication due to a rapid onset and short half-life. Adenosine 6 mg rapid IV bolus administered over 1–2 seconds followed by rapid saline flush. If there is no response within 1–2 min, a 12 mg rapid IV bolus may be given. Administration of adenosine is associated with potential adverse effects including: transient AV block, flushing, chest pain, hypotension and dyspnea. Patients should be warned of these potential adverse effects prior to administration.

Both IV verapamil and diltiazem are calcium channel blockers effective for acute treatment of SVT in haemodynamically stable patients. They are less easily titrated than esmolol but provide rapid slowing of the ventricular rate in SVT in minutes. Diltiazem 0.25 mg/kg IV bolus over 2 minutes followed by an infusion of 5–10 mg/h or verapamil at a dose of 0.075–0.15 mg/kg IV bolus over 2 minutes. If the abovementioned pharmacological treatment is ineffective or not feasible, synchronised cardioversion is recommended.
**Tachycardia** (orthodromic), a regular broad complex tachycardia (antidromic) or an irregular broad complex tachycardia (AF with rapid anterograde conduction via the accessory pathway).2 The regular narrow complex AVRT follows the same management as regular SVTs.16

**Atrial flutter**

The management of atrial flutter also begins with ascertaining whether the patient is haemodynamically stable or not. If the patient is haemodynamically unstable, the treatment strategy begins with synchronised DC cardioversion, followed by rate control with IV amiodarone. In haemodynamically stable patients, the acute management involves rate control with IV beta blockers, IV diltiazem, IV verapamil or IV amiodarone.16

**Focal atrial tachycardia**

Focal atrial tachycardia is regular atrial rhythm originating outside the sinus node, either within the left or right atrium.2 The management begins with the use of IV adenosine for haemodynamically unstable patients, with synchronised DC cardioversion if adenosine is ineffective or not feasible. In haemodynamically stable patients and the diagnosis of focal atrial tachycardia established, IV beta blocker, IV diltiazem or IV verapamil may be used, which may be followed by IV amiodarone or IV ibutilide, if ineffective. If the diagnosis is not established, IV adenosine is administered followed by IV amiodarone or IV ibutilide if ineffective.16

**Irregular narrow complex SVT**

The acute management of irregular narrow complex SVT also begins with assessment of haemodynamic status and correction of reversible causes. The management goal is rate control.2

**Atrial fibrillation**

The cornerstone of management of AF is rate control and anticoagulation.20,21 Atrial fibrillation does not involve the AV node in a re-entrant pathway and so AV nodal block by adenosine will only produce transient slowing of the ventricular rate; therefore rate control with beta blockers or calcium channel blockers is the first line treatment.10

Rate control with beta blockers (esmolol or metoprolol) is recommended. These agents are negatively inotropic and should not be used in patients with severe left ventricular impairment. Diltiazem and amiodarone are recommended for heart rate control in patients with left ventricular impairment.2

Amiodarone is recommended by the ACC/AHA/HRS for use as a rate-controlling agent for patients intolerant of or unresponsive to other agents.20 Postoperative AF predisposes patients to stroke and thromboembolism. Patients with persistent AF should be risk stratified and anticoagulated as soon as it is safe in the postoperative period.2,22

**Multifocal atrial tachycardia**

Multifocal atrial tachycardia is commonly associated with underlying medical conditions, for example pulmonary disease, pulmonary hypertension, valvular heart disease and coronary artery disease.19 Treatment of the precipitant takes precedence, as the condition is usually transient and tends to resolve when the underlying medical condition improves.2 Cardioversion is rarely successful in MAT,2,16 and management often involves conduction slowing at the AV nodal level to control heart rate.16 Verapamil has been shown to be effective in patients with MAT without ventricular dysfunction, sinus node dysfunction or AV block. Beta blockers can also be used to treat MAT without respiratory decompensation or AV block.16

**Conclusion**

This review covered the acute management of SVTs focusing mainly on those presenting as narrow complex. SVT may on certain occasions present as a broad complex tachycardia due to conduction via an accessory pathway or a bundle branch block. Regular broad complex tachycardia should be treated as ventricular tachycardia, unless it is an SVT with aberrant conduction or antidromic AVRT.2

**Conflict of interest**

The author declares that he has no financial or personal relationship(s), which may have inappropriately influenced the writing of this paper.

**References**


Background: An adverse outcome during the administration of an anaesthetic may result in morbidity or mortality, the latter providing the most fundamental measure of the safety of anaesthesia. Perioperative deaths due to anaesthesia have not been documented in Gauteng Province, South Africa, since 1955. This study was to document these deaths for comparison with previous South African and overseas studies.

Objectives: 1. To investigate the prevalence of perioperative deaths, particularly anaesthesia associated deaths due to both general and regional anaesthesia, in the Charlotte Maxeke Johannesburg Academic Hospital during the period 2000–2004. 2. To examine and comment on current legislation and the causes or possible risk factors involved in the perioperative deaths that were studied.

Methods: This was a retrospective longitudinal descriptive clinical audit.

Results: The Anaesthetic Contributory Death (ACD) rate at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) was 0.4 per 10 000, which is an improvement on the 2.1 per 10 000 seen in a pilot study in that hospital in 1999 and is a slight improvement on the 0.7 per 10 000 at Groote Schuur Hospital in the Western Cape by 1987.

Conclusions: The ACD rate in this hospital is low; it may not improve any further, as human error cannot be totally eliminated from anaesthetic practice.

South African law does not specify a time period from the start of the anaesthetic during which a perioperative death may be classified as an ACD. This is poorly understood by the medical fraternity and general public. An improved reporting system is recommended, with education at all levels, including anaesthetists, surgeons in all specialties, nursing staff, administrators and patients.

Clinical anaesthesia has been described as a state of “physiological trespass” and “an indispensable adjunct to the surgical management of disease.” The more injury and disease have encroached on the body’s physiological milieu, the less can anaesthetic encroachment per se be tolerated, and the more does the clinical anaesthetist’s margin of error accordingly shrink.

At times, this poses important risk to our patients.

Since the promulgation of the National Health Act of 2003, legislation in South Africa mandates that patients (health care users) be informed of the following: the range of diagnostic procedures and treatment options available and the benefits, risks, costs and consequences associated with each option. This legislation also states that the information must be communicated in a language that the user understands and in a manner that takes into account the literacy of the user (patient). Thus, anaesthetic risk needs to be discussed with each patient prior to receiving an anaesthetic.

In order to determine the risks and consequences of anaesthesia, multiple factors must be considered. There are those risks due to the anaesthetic itself, the risks of the surgery, and also the patient’s co-morbid diseases, which may pose serious risks in their own right. Ultimately, these risks may combine into major or minor morbidity (complications) or mortality (death).

In South Africa we do not have adequate reporting structures to quantify anaesthetic associated mortality, let alone anaesthesia-associated morbidity. This is despite the latter’s importance, particularly from the patient’s perspective. It is also becoming increasingly important to include outcomes that affect economic issues, quality of life and patient satisfaction.

Rates of death due solely to anaesthesia are sometimes difficult to ascertain and studies reporting these rates use varying definitions of such deaths. What is clear is that anaesthetic related mortality is rare. In previous studies in South Africa, mortality is estimated to have ranged from 1 per 2 anaesthetics in the very early days, (these were deaths in which anaesthesia played a “role”) to 1.1 per 10 000 anaesthetics, where anaesthesia was considered solely responsible for the patient’s death.

The first historically reported death due to anaesthesia was Hannah Greener who died due to aspiration on induction with chloroform. The anaesthetic was given to her by the surgeon, Mr. Meggison, who was going to “remove the nail from the great toe of her right foot.”
Since then, numerous studies have been published internationally on anaesthesia mortality rates. These studies are often very difficult to compare for the following reasons:

- There are no agreed definitions of what constitutes anaesthesia mortality;
- There is no agreement over how much of the perioperative period to include (studies vary from 24 hours to 2 years);
- The number of years to be covered by a particular study is frequently not clear.

As a result, one cannot compare mortality rates to assess whether mortality from anaesthesia is improving. Each study needs to be looked at individually.

Derrington and Smith reviewed studies of anaesthetic risk, morbidity and mortality in 1987, and found numerous audits and studies on “anaesthetic deaths”. The time perspective in these studies – in other words, the time that the death occurred in relation to the start of the administration of the anaesthetic ranges from 24 hours to 30 days. For example, in 1978 Harrison looked at deaths within 24 hours of the administration of the anaesthetic, whilst in 1963 Clifton and Hotten looked at deaths within 24 hours of the administration of the anaesthetic, or of which the administration of an anaesthetic has contributed.76  whilst in 1963 Clifton and Hotten looked at deaths within 24 hours of the administration of the anaesthetic, or of which the administration of an anaesthetic has contributed.

In South Africa, the Medical, Dental and Supplementary Health Services Professions Act of 197413 states that “the death of a person whilst under the influence of a general anaesthetic or local anaesthetic, or of which the administration of an anaesthetic has been a contributory cause, shall not be deemed to be a death from natural causes, as contemplated in the Inquest Act, 1959 (Act 58 of 1959), or the Births, Marriages and Deaths Registration Act, 1963 (Act 81 of 1963).” This statement has been amended in the Health Professions Amendment Act of 200714 to read as follows: “the death of a person undergoing, or as a result of, a procedure of a therapeutic, diagnostic or palliative nature, or of which any aspect of such procedure has been a contributory cause, shall not be deemed to be a death from natural causes, as contemplated in the Inquest Act, 1959 (Act 58 of 1959), or the Births, Marriages and Deaths Registration Act, 1963 (Act 81 of 1963).”

What was not clear with the original act (of 1974) was the definition of when a patient is no longer “under the influence” of an anaesthetic, a matter that still needs to be defined. Likewise, the phrase “as a result of a procedure of a therapeutic, diagnostic or palliative nature, or of which any aspect of such procedure has been a contributory cause” needs to be clearly and specifically defined. What is clear, however, is that South African legislation does not state a time limit for recovery after the start of an anaesthetic or procedure. Thus, a patient who suffers a cardiac arrest under anaesthesia with consequent hypoxic brain damage, and dies 2 years later, should still be classified as a death to which the anaesthetic contributed. The consequences are that the death is unnatural in such a circumstance, requiring a medicolegal post-mortem and inquest. This is a fact often ignored by anaesthetic and surgical colleagues, as well as by many South African health facilities. It relies largely on the “voluntary cooperation” of anaesthetists and surgeons.

### Methods

Before commencement the study was approved by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand; permission to access records was granted by the hospital CEO.

For the purposes of this study, but not in keeping with previous studies2,4,6,8 the following definitions were used:

An **anaesthesia associated death** (AAD) is a death occurring after the induction of a general or regional anaesthetic, or after the failure of a patient, conscious before, to regain consciousness after anaesthesia, regardless of the time that has elapsed since the start of the anaesthetic.

An **anaesthetic contributory death** (ACD) is a similar death, but due solely to the anaesthetic. The ACDs therefore form a sub-group of the AADs.

The 24-hour cut-off period after commencement of the anaesthetic was also not used.

The study period was from the 1st January 2000 to 31st December 2004. All patients who died during or after surgery during the specified time were studied. They are referred to as perioperative deaths. Data were obtained predominantly from the records in the records store room in the Department of Anaesthesia, and supplemented by central hospital records. The denominator figures were obtained from the operating theatre statistics. Data collected included demographics, American Society of Anesthesiologists (ASA) grading, surgery category, premedication, pre-operative workup, anaesthetist level, type of anaesthesia, airway management, anaesthetic record keeping, adverse event, and where and when the death occurred.

Anaesthetist level (of experience and training) was defined as follows: registrar, senior registrar (minimum of 3 years of experience and a primary examination for the FCA) and specialist.

Based on all of the information available, deaths were classified as caused by the anaesthetic (AAD), and whether it was solely due to the anaesthetic (ACD). If there was any doubt about the latter, the death was classified as an AAD.

Statistical analysis was with SAS for Windows (version 9.1, SAS Institute Inc, Cary NC, USA). The statistical methods used were: descriptive statistics – frequencies and prevalence ratios; analytical statistics – for categorical analysis the Chi-square test and Fisher’s exact test, depending on the numbers per category cell. When a cell number was too low for the Chi-square test to be appropriate, a combination of categories, based on logic, was used. Statistical significance was accepted at p < 0.05.

### Results

There were 465 perioperative deaths recorded during the 5-year study period. Overall findings from the study are listed in Table 1. The majority of cases (89%) were emergencies, 85% were in the ASA 4 and 5 categories and 66% were trauma patients.
A high proportion of patients (75%) were not worked up preoperatively, probably because so many were emergencies, many of them ASA 5 trauma patients, who were rushed through to the operating theatre while being resuscitated.

Thirty-six percent of the patients (150 trauma and 11 from the other categories) did not receive a hypnotic agent as part of the anaesthetic. Many received only a muscle relaxant and a small dose of opiate; some were apparently too sick to even tolerate an opiate. What is unclear in this "no anaesthetic" group is whether they received any hypnotic agents "pre-casualty" or preoperatively, since at the time that these statistics were being generated, some paramedics administered small to moderate doses of hypnotic agents such as midazolam to patients. Nevertheless, it is still important to note the high number of patients who were "analgosed" and paralysed, but not "anaesthetised" with either a volatile or intravenous hypnotic.

Almost all patients (98%) had endotracheal intubation; only 24% had a rapid sequence induction. This is an unexpected, since 89% were emergencies, and it would be expected that most of these patients would have received a rapid sequence induction. However, it is likely that many of the ASA 4 and 5 trauma patients were intubated either in casualty, or at the trauma scene, thus obviating the need for intubation in the operating theatre and explaining the low number of rapid sequence inductions recorded.

Statistically significant relationships between ASA categories and the following variables were found, all at p < 0.0001: preoperative workup, anaesthetist "level", whether an anaesthetic (hypnotic agent) was administered or not, whether a rapid sequence induction was performed, when an adverse event occurred, when a patient died in relation to the start of the anaesthetic, where a patient died, the surgical category and whether there was trauma or not. There was weaker significant effect of airway problems (p = 0.013) and no significant effect for the anaesthetic record. Anaesthetic record keeping was suboptimal, with records not appended to the GW7/24 forms.

The total perioperative deaths, numbers within trauma or other surgical groups are listed in Table 2. There was an average of 3 ACD/AADs per year during the 5-year study period. Of these 15 cases, 4 may be considered ACDs, where the anaesthetic directly caused the patient’s death. Thirteen out of the 15 were adults, two were children; seven were males, eight were females; six were ASA 2; five were ASA 3 and there were four ASA 4 patients. One third of the patients who died from an anaesthetic associated (AAD) cause, died more than 24 hours after the start of the anaesthetic. Four of these deaths were directly attributable to the anaesthetic (ACD), and all four died more than 24 hours after the start of the anaesthetic. Two of the patients were cardiac surgery patients, both anaesthetised by specialists. The "other" two patients received spinal anaesthetics. All 4 cases were either ASA 2 or 3. Two patients had an adverse reaction to an intravenous drug or fluid. Three out of the 4 died > 24 hours after the start of the anaesthetic; 2 died at 7 and 10 days respectively.

A breakdown of the 4 ACDs is illustrated in Table 3.

The prevalence rate for all causes of perioperative deaths per 10 000 per year was calculated ((death category/total cases)*10 000). The yearly rates for all deaths are compared with the AAD and ACD rates in Table 4. The prevalence of AAD and ACD is very low in comparison with all of the causes; the prevalence of ACDs for the entire 5 years is 0.4 per 10 000.

**Discussion**

It is likely that "human error" played a role in some, if not all of these ACDs, and at least two of the four had well-known and treatable complications, namely anaphylaxis and a high spinal. In both of these cases the anaesthetic was given by a senior registrar. As Davies and Strunin commented in 1984:\(^15\) "when the problem is due to the anaesthetic, most mishaps result from the failure of the anesthetist to recognize or cope with a problem."

The data available in published articles and official reports thus far indicate that the risk of death attributable to anaesthesia has probably declined over the years.\(^10,16\) The reasons for this are not entirely clear. They may include new monitoring modalities, new anaesthetic drugs and changes in the anaesthesia workforce. However, no study has shown improved outcomes with any one of these, including the advent of pulse oximetry.\(^16\) This limitation supports the need for ongoing audits and peer review of all of the complications relating to anaesthesia, with death being at one extreme.

Deaths due to anaesthesia or procedure-related deaths with anaesthesia as the primary cause are still not clearly defined in South Africa. Harrison’s study included patients who died within 24 hours of the start of induction of anaesthesia, and he comments that he used this definition for convenience. However, as is illustrated in this study, three of the ACDs would not have been included in the study, if Harrison’s definition had been used. Patients may suffer hypoxic brain damage as a result of an anaesthetic misdemeanor, remain unconscious, and die months later. They should still be reported as procedure-related deaths.

Until deaths due to anaesthesia are notifiable (as with maternal deaths\(^17-20\)), and all those who administer anaesthesia are suitably educated and trained, there will not be accurate anaesthetic mortality statistics in South Africa. Therefore, audits of what we do and how we are doing at it will continue to be inaccurate. Debriefing and structured peer review needs to occur after all ACDs. A correlation between the clinical and post mortem causes of death would be very useful.\(^21\)

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**References**


Anaesthetic considerations for children with malignancies

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Introduction

It is estimated that one in 408 children worldwide will be diagnosed with cancer before the age of 15. In Western countries, cancer is the second most common cause of death in children aged 5–14 years, after accidents.

In South Africa, the five most common childhood cancers are:
1. leukaemia (25.4%) - most of these are ALL
2. lymphomas
3. brain tumours
4. nephroblastomas
5. soft tissue sarcomas

These cancers are treated with chemotherapy, radiation therapy, surgery, bone marrow transplantation, or a combination of these modalities. The aim of combination therapy is to achieve better results while limiting drug toxicity.

Children may present for surgical and thus anaesthetic interventions at many points through their disease and treatment. They may present for diagnostic procedures, like MRI scans, lumbar punctures, bone marrow sampling, and lymph node or tumour biopsies. They then present during their treatment for port insertions, intrathecal chemotherapy, and surgery for tumour excision. When assessing and treating these children, the anaesthetist needs to actively consider the following:

1. the effects of the malignancy itself (both physical effects, e.g. masses, and effects on other organ systems, such as myelosuppression)
2. toxicity of therapy (often masked in the ill child)
3. coexisting illnesses, including sepsis
4. psychosocial vulnerability

As leukaemia is seen so often, and is treated with all the drugs that can cause toxicity, it deserves a brief mention.

Almost 80% of childhood leukaemias are acute lymphoblastic leukaemia (ALL). ALL is characterized by the overproduction and accumulation of lymphoid precursors, immature white blood cells (WBC) called lymphoblasts, in the bone marrow. These cells can then spread to other organs. The production of normal red blood cells (RBC), WBC and platelets is inhibited. ALL is commonly seen in children of 2–5 years of age, who present with signs and symptoms relating to the underproduction of normal marrow components (fever, infection, fatigue, headache, bruising, bleeding) or the infiltration of other organ systems with the abnormal cells (lymphadenopathy, hepatosplenomegaly).

Leukaemias are more common in children with congenital abnormalities, including Noonan syndrome, neurofibromatosis and Fanconi's anaemia. Children with Down syndrome have a 10–20 times higher risk of developing acute leukaemia than non-syndromic children.

Cure rates for newly diagnosed ALL approach 85%. ALL is typically treated with high dose prednisone, daunorubicin, vincristine, L'asparaginase, and intrathecal hydrocortisone, methotrexate and cytarabine. Acute myeloid leukaemia (AML) is treated with high dose cytarabine, daunorubicin and etoposide, as well as intrathecal cytarabine.

A systems-based approach when looking for the effects of the malignancy and treatment should hopefully identify areas of concern, bearing in mind that certain complications can be subclinical and be unmasked during times of physiological stress, such as surgery and anaesthesia. An excellent in depth review of this subject can be found in Latham and Greenberg's three-part review in Paediatric Anaesthesia in 2010.

1. The effects of the malignancy

(ii) Airway

While oral tumours are rare, tumours compressing structures lower down the airways are not.

Anterior mediastinal masses are commonly seen in children with non-Hodgkin's lymphoma (NHL), T-cell ALL, and Hodgkin's, where up to 50% of children may have a mediastinal mass at presentation. Signs and symptoms, where present, relate to the compression of major vascular and respiratory structures.
(superior vena cava (SVC) syndrome or superior mediastinal syndrome). A high index of suspicion in children with these malignancies is important as up to 50% of masses are asymptomatic at presentation, making a good history and examination essential. Signs and symptoms include:

1. **cardiovascular:**
   a. symptoms: chest pain, syncope, nausea, headache
   b. signs: SVC obstruction, cyanosis, facial swelling, dilated upper body veins

2. **respiratory:**
   a. symptoms: wheeze, cough, dyspnea, hoarse voice, dysphagia
   b. signs: stridor, orthopnoea

Compression and distortion of airway structures like the carina, trachea and bronchi are of particular concern because they are so compliant in children. The severity of symptoms does not correlate well with the degree of compression, with the exception of stridor, which has been shown to correlate significantly with anaesthetic complications. All children with an anterior mediastinal mass presenting for surgery should have diagnostic imaging, which may include CXR, CT/MRI and echocardiography. Children with > 50% compression of the trachea are at high risk of respiratory complications during anaesthesia. It should be ascertained if their symptoms are positional (may be relieved by turning laterally).

These tumours can be shrunk with high dose steroids and radiation. The problem is in the patient who needs a tissue diagnosis before treatment can be started, as preoperative irradiation and steroids have traditionally been described as having the potential to alter the tumour cell histology. This has been shown to not always be the case, and in the symptomatic child, preoperative treatment and tumour shrinkage should be seriously considered.

The second option is to perform the surgery (e.g. lymph node biopsy) under local anaesthetic. This may not be feasible in small or uncooperative children. Beware the “gentle sedation” as it carries significant risks, including loss of the airway.

If general anaesthesia is required, the child should be induced in a position in which they are comfortable (usually head up or lateral), spontaneous ventilation should ideally be maintained, and they should be extubated awake. If IPPV is used, it should be demonstrated that the child can be adequately ventilated before a muscle relaxant is given. Postoperative ICU facilities should be available and a fiberoptic bronchoscope and rigid bronchoscope should be available in theatre. There should be good team communication and plans in place in case of cardiorespiratory compromise.

(iii) **Respiratory**

While primary lung tumours are rare in children, respiratory compromise is not. Abdominal tumours can cause splinting and reduced FRC, cancers may be associated with pleural effusions, and pneumonias are common as a result of immunosuppression. Most respiratory complications are due to treatment.

(iv) **Haematological system**

Myelosuppression is a common complication of childhood cancer, manifesting with the signs and symptoms of low red cell, white cell and platelet counts. Hyperleukocytosis can occur in AML and can cause clumping of white cells blasts with resultant hyperviscosity and intravascular sludging, leading to hypoxia, infarction and haemorrhage. Thrombophilia and thrombosis are also seen, especially in children with sarcomas or haematological malignancies.

2. **Toxicities of treatment**

A full review of the pharmacology of chemotherapeutic agents is beyond the scope of this lecture, and is comprehensively covered in Latham and Greenberg’s article and others. A systems-based approach is presented here.

(i) **Airway**

Oral mucositis has been described as the most painful part of a child’s chemotherapy journey. It is associated with high-dose chemotherapy and radiation to the head and neck. Irradiation can also cause soft tissue fibrosis, which may cause limited mouth opening, neck extension, and fibrosis and narrowing of airway structures.

Cases of severe mucositis have been associated with difficult intubation and with airway bleeding and oedema. The airway may be friable and prone to injury. At the same time, airway trauma can cause sepsis in neutropaenic children with mucositis and needs to be avoided. In cases where children have received radiation to the head and neck, particularly in the past, smaller endotracheal tubes may be required due to airway stenosis and retarded growth.

(ii) **Cardiac**

The anthracyclines doxorubicin and daunorubicin, frequently used in the treatment of childhood cancer, are the main culprits to watch out for. A prospective cohort study from Pakistan demonstrated that 14% of children developed cardiac dysfunction within a month, and 25% within a year of starting treatment with the anthracyclines. In addition, 6.4% died due to severe cardiac dysfunction. It seems that younger patients are particularly at risk, with studies describing some degree, often subclinical, of cardiac dysfunction in 18–57%, and long-term follow-up studies demonstrating cardiac toxicity in 70% of patients previously treated with anthracyclines. Toxicity can present early, with symptoms and signs of a cardiomyopathy, but often presents late, when the damage is progressive. Other effects include myocardial depression and ischaemia, hypotension, arrhythmias (including SVT and heart block) and myocarditis.
Cardiotoxicity is dose dependent, and it seems that doxorubicin is worse than daunorubicin. Damage is probably caused by oxygen free radical-mediated cytotoxicity and results in impaired left ventricular reserve and contractility with long-term myocardial fibrosis. Diastolic dysfunction has also been demonstrated. Cardiac damage is worse with concomitant chest radiation, which causes damage both to heart muscle and to valves, particularly mitral and aortic, resulting in incompetence.

There is controversy as to how often patients should be screened. Guidelines published in 1992 recommend screening at least 3 weeks after the last dose and a week before the next dose of anthracycline therapy, but this routine screening has not been shown to change management. In our limited-resource setting, patients usually have a baseline echo before starting treatment and then as dictated by their clinical condition. This lack of regular screening mandates a good history-taking and examination before anaesthesia, with a preoperative echo where clinically indicated. The concern is that our clinical skills may miss more than 50% of patients with early chemotherapy-induced heart failure, meaning we need to maintain a high index of suspicion and vigilance. It would seem prudent to minimize myocardial depressants and negative inotropes.

Childhood cancer survivors should ideally be followed up with screening echos every 2 to 5 years, as an increased risk of cardiac death has been demonstrated in adults who were exposed to anthracyclines as children.

(iii) Respiratory

Chemotherapeutics can cause a range of pulmonary toxicity that can manifest as pneumonitis, pulmonary oedema or fibrosis. The signs of pulmonary fibrosis may be insidious and include a dry cough, dyspnea, fever and basal crackles. The two worst culprits are bleomycin and methotrexate. Children can clinically present with either restrictive or obstructive lung disease.

Bleomycin deserves special mention:

Bleomycin is an antibiotic used as chemotherapy for the treatment of germ cell tumours and Hodgkin lymphoma, as well as intravesionally for the sclerotherapy of lymphatic and venous malformations or persistent pleural effusions. It is metabolized by enzymes that are not present in the skin or lungs, which is why that is where side effects are seen.

The most serious side effect is that of pulmonary toxicity. Bleomycin accumulates in the lung and causes inflammation and damage to endothelial cells and alveolar epithelial cells, impairing alveolar barrier function. The mechanism is not well understood but involves reactive oxygen species. This causes a range of disease processes, from subclinical lung function abnormalities to life threatening and disabling pulmonary fibrosis. Described pulmonary disease includes bronchiolitis obliterans organizing pneumonia (BOOP), eosinophilic hypersensitivity, and interstitial pneumonia (most common), which may progress to fibrosis. Some degree of pulmonary reaction is said to occur in 10% of adult patients, with 1% of these dying of pulmonary fibrosis. The onset usually starts a few months after finishing treatment. Risk factors include younger age, higher cumulative systemic bleomycin dose (> 400 U/m²), and combination treatment with other chemotherapeutic agents and radiation.

The perioperative use of high FiO₂ has been implicated in accelerating lung damage in patients being treated with systemic bleomycin, likely due to increased free radical production. It is recommended that FiO₂ be kept to the lowest sensible limit for these children, while avoiding hypoxia. Of note, there have been no reported cases of pulmonary fibrosis following intravesional bleomycin sclerotherapy (e.g. a lymphatic malformation), likely because the systemic doses of bleomycin are not high enough.

Several skin changes have been reported in patients receiving bleomycin therapy. As with the lung changes, this is probably because bleomycin is not metabolized in the skin. Reported skin reactions include flagellate erythema, Raynaud’s, hyperkeratosis, nailbed changes, plantopalmar desquamation and hyperpigmentation.

There have been a couple of reports of abnormal pigmentation developing around ECG sticker points following intravesional bleomycin injection. The changes seem to be inflammatory mediated and increase with heat. It is recommended that if intravesional bleomycin is being used, ECG dots be placed in places where residual hyperpigmentation is less visible, such as the axillae and soles of the feet. Skin precautions such as those used for epidermolysis bullosa are not necessary.

Radiation therapy also causes lung damage that can progress from interstitial pneumonitis to pulmonary fibrosis.

(iv) Kidney

Several agents have been implicated in causing nephrotoxicity, including cisplatin, carboplatin, ifosfamide, methotrexate, cyclophosphamide and radiation therapy.

A U&E should be checked prior to surgery. Take care to maintain renal perfusion and avoid nephrotoxic agents. Exercise caution when using NSAIDS in children with dehydration or pre-existing renal dysfunction.

The most dramatic cause of acute renal failure is tumour lysis syndrome (TLS): TLS occurs when rapidly dividing large volume tumours, e.g. the acute leukaemias, lymphoblastic lymphomas and B cell lymphomas (including Burkitts lymphoma) are treated with cytotoxic agents. The chemotherapy causes rapid cell death and tumour breakdown, with an efflux of potassium, phosphate, and uric acid, causing these children to develop acute renal failure and a hyperkalaemia metabolic acidosis, which may be fatal. This is considered an oncological emergency and needs to be managed immediately. TLS has been described as being triggered by steroid therapy, intraoperative tumour manipulation, pyrexia, chemotherapy, radiation, and has been described as occurring spontaneously. While originally described in haematological malignancies, cases of TLS have also been seen in patients with solid tumours, such as Wilms tumours and embryonal tumours.

There are several cases described in the literature of children developing TLS in the perioperative period. In some cases, the
Dexamethasone induces apoptosis of B cells, including monoclonal lymphoma and ALL cells. It causes rapid cytoreduction, especially in the case of previous chemotherapy. It is thus recommended that dexamethasone be avoided as a routine antiemetic in children with malignancies, and that a high index of suspicion for perioperative TLS be maintained and supportive care started immediately if TLS is suspected.

Emergency management includes:

- aggressive hydration with normal saline and diuresis to avoid obstructive uropathy
- reducing the potassium:
  - insulin 0.1 U/kg with 50% dextrose 2 ml/kg
  - calcium gluconate 100 mg/kg or calcium chloride 10–20 mg/kg
  - iv salbutamol
- treating the acidosis (Sodium bicarbonate 1–2 mmol/kg)

Dialysis and inotropic support may be required and the child should be transferred to ICU as soon as possible.

(v) GIT

The side effects of chemotherapy include nausea and vomiting, diarrhoea, mucositis, stomatitis and enterocolitis. Radiation can damage the microvasculature of the gut and cause perforations, stenoses, enteritis and adhesions. As a result, children may present with electrolyte imbalances, dehydration, malabsorption and malnutrition. Antiemetics should always be given with chemotherapy.

(vi) Haematological system

Myelosuppression is a common dose limiting effect of many chemotherapeutic agents, particularly methotrexate, cyclophosphamide, ifosfamide, vincristine and the anthracyclines. It leads to anaemia, thrombocytopenia and neutropenia.

Anaemia occurs in over 80% of children with cancer. It may be managed with erythropoietin or transfusion. If transfusion is required, it should be with leucodepleted and irradiated products. It is recommended that the child’s haematologist/oncologist be contacted before electively transfusing patients.

Platelet transfusion, where required, is not innocuous. The data on platelet transfusion thresholds in these children is not clear, but it is suggested that a platelet count above 40 000 is adequate for surgery if no other coagulopathy is present. For bone marrows, a platelet count of 20 000 is said to be sufficient, and a count of 10 000 for an LP appears to be safe. A platelet count above 100 000 is recommended before neurosurgery. A transfusion of 10 ml/kg of platelets should cause the platelet count to rise by 50–100 000.

Leukopaenia and specifically neutropenia contribute to significant morbidity (up to 30%) and mortality (1%) in children with cancer, due to infections and sepsis. Care should be taken to minimize their contact with children and staff with other infections, such as respiratory infections, chicken pox and gastrointestinal infections. These children should be placed on a theatre list before any known infective cases.

Central lines and ports should be accessed using strictly aseptic techniques. Hands should be washed before accessing the line and gloves worn before cleaning the hub with a chlorhexidine-containing wipe. At the end of the procedure, the line should be flushed to ensure that there are no residual drugs in the line or connectors.

(vii) Endocrine

Steroid therapy may cause features of Cushing’s and impaired glucose control. There are concerns about these children being able to mount an adequate stress response in the face of long standing steroid treatment, and a replacement dose of 1–2 mg/kg of hydrocortisone might be appropriate for major surgery. However, in children at risk for TLS this should be discussed with their oncologist first, as discussed above.

3. Coexisting illnesses

Coexisting illnesses to look out for include infection, especially pneumonia with respiratory failure, hyperviscosity and thromboembolic phenomena, and complications of bone marrow or stem cell transplantation including GVHD.

4. Psychosocial vulnerabilities

Children with cancer and their families are a particularly vulnerable patient population. These children are more likely to be diagnosed with depression, anxiety, PTSD and behavioural problems than their healthy peers. They may have had numerous procedures and developed their own coping mechanisms to deal with them. They may have particular preferences around induction (iv vs inhalational) or specific rituals they need to follow prior to a procedure. It is worth asking what these are and what premedication has or has not worked in the past.

These children have usually experienced numerous episodes of pain of varying degrees – either from their surgeries or from the cancer itself (both from the tumour and metastases). They may have significant analgesic requirements.

Summary

Childhood cancer is common. The most common of these are the leukaemias, which have a high cure rate but are treated with all the agents that cause multiple organ system toxicities. A child’s treatment regime should be available and read before embarking on anaesthesia and surgery. The child should be examined with special focus on the above organ systems, bearing in mind that subclinical cardiac and respiratory dysfunction are common and may be unmasked under anaesthesia and the stress of surgery. Preoperative blood and imaging tests should be performed where clinically indicated.
Take home tips:

- Avoid dexamethasone as an antiemetic
- Avoid unnecessary hyperoxia in children treated with bleomycin
- Avoid nephrotoxic agents and NSAIDs in children with any renal dysfunction
- Ensure organ perfusion – optimize cardiac output and oxygen delivery
- Maintain a good relationship with your haem-onc colleagues.

The child with cancer is physiologically, psychologically and pharmacologically vulnerable, and should be treated as such. And so should their families.

References
(those marked in bold are recommended reading)

2. Personal communication, Dr J Geel. 2017.
Can you sedate a child for a dental procedure?

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Dental procedures may be uncomfortable, painful or simply scary to any patient. This is a particular problem for young children. Because the resource of general anaesthesia in a theatre setting is so limited, the option of procedural sedation and analgesia (PSA) in the dental rooms is widely used. Apart from the shortage of actual theatre space; cost, time and dentist comfort are also major drivers. Performing dental work under general anaesthesia in theatre adds significantly to the total financial cost of treatment. As specialist anaesthetists are relatively scarce, these dental room sedations are often performed by non-anaesthetists and in up to 43% of cases, by the dentist themselves. So the question is not “Can you sedate a child for a dental procedure?” but “Should you?” and if yes, then, “How should it be done?”

Paediatric dental room sedation is being done globally. Several tragic case reports have emerged from the USA, mostly where dentists have been the sole operator providing both sedation and dental care. There is ongoing debate in the USA of where the divide lies between anaesthesia and dental scopes of practice.

In South Africa, in 2015, Bham F et al. performed an audit of dental chair sedation practice in Gauteng. Following random sampling, 213 dental practitioners were interviewed. Of these, a total of 94 (44.1%) routinely practice paediatric dental chair PSA. This group of 94 practitioners were asked to complete an online survey, to which 52 (55.9%) responded. Bham F et al. found the following:

• Overall PSA rate 44.1%.
• Patients mostly 1–5 years old. (76.6% of patients < 6 years of age).
• Minimal to moderate sedation targeted most of the time.
• Midazolam the most frequently used agent. Sometimes supplemented with Nitrous Oxide (N₂O).
• In 28.1% of cases ≥ 3 agents were used.
• A pre-sedation assessment was done in 83% of cases.
• Informed consent was obtained in 75.6% of cases.
• In 41.3% of cases no monitoring was used at all.
• In 41.3% of cases the dentist was the sole operator sedationist and dentist.
• In 43.2% of cases no emergency drugs were at hand.
• In 19.6% of cases no emergency or resuscitation equipment was at hand.

These results are staggering and terrifying. They show extreme non-compliance with South African Society of Anaesthesiologists (SASA) sedation guidelines, and in the words of Dr De Wet of the Society of Sedation Practitioners of South Africa (SOSPOSA): “This is exactly how sedation should not be done.”

In 2000, Charles Cote et al. did a critical incident analysis of contributing factors to adverse sedation events in paediatrics. They obtained data from 3 sources:

1. Food and Drug Administration (FDA) voluntary reports between 1969 and 1996.
2. US Pharmacopoeia (USP) drug event reports from a similar period.
3. Survey results from a group of over 1 300 USA practitioners surveyed.

Where possible, the cases were divided into hospital based vs. non-hospital based locations. They admit that under-reporting may have influenced their results, but did identify a total of 118 sedation cases across the full spectrum of paediatric sedation where adverse events occurred, from these 3 sources. Of these, in 95 cases, the adverse event was purely sedation related. This number seems low but the outcome for these 95 cases was that 51 died and 9 suffered permanent neurological damage. While the incidence of respiratory depression was equal in the hospital vs. the non-hospital group, other results were all greater in the non-hospital setting:

<table>
<thead>
<tr>
<th></th>
<th>Non-hospital setting</th>
<th>Hospital setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory events</td>
<td>= 80%</td>
<td>= 80%</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>53.6%</td>
<td>14%</td>
</tr>
<tr>
<td>(as 2nd complication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>25%</td>
<td>7%</td>
</tr>
<tr>
<td>(as 3rd complication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td>57.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>resuscitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or permanent</td>
<td>92.8%</td>
<td>37.2%</td>
</tr>
<tr>
<td>neurological injury</td>
<td></td>
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</tbody>
</table>
The 35 patients who did not die or suffer permanent neurological injury had all been monitored with pulse oximetry as opposed to the other cases, where no documented monitoring could be ascertained.

Of these 95 patients, 32 (33.7%) had received sedation for dental procedures, showing that across the full spectrum of possible reasons to administer paediatric sedation, dental procedures carry the highest risk.

Cote et al. reached the following conclusions:
1. The non-hospital setting carries a higher risk and is associated with poorer resuscitation and rescue chances.
2. Poor monitoring and poor responses to abnormal monitor readings are associated with poorer outcomes.
3. Pre-sedation assessments were often inadequate or omitted.
4. Poorer outcomes correlated more frequently with single operator sedationists and where an independent observer was not present.
5. Medication errors in paediatric dosing were common.
6. Inadequate recovery procedures were associated with poorer outcomes.

In 2000, Charles Cote et al. also looked at the medications involved when adverse events occurred during paediatric sedation in these same 95 cases mentioned above. Looking at the 60 patients who suffered death or permanent neurological injury they found the following relationships:

<table>
<thead>
<tr>
<th>Incidence of death or permanent neurological injury</th>
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</thead>
<tbody>
<tr>
<td>Type of drug used</td>
</tr>
<tr>
<td>Route of drug administration</td>
</tr>
<tr>
<td>Drug overdose</td>
</tr>
<tr>
<td>Drug combinations</td>
</tr>
<tr>
<td>N₂O added to other sedative agents</td>
</tr>
<tr>
<td>Giving sedative to parent to administer at home or en route to the clinic</td>
</tr>
<tr>
<td>Non-medical sedationist or single operator sedationist</td>
</tr>
<tr>
<td>Discharging patients home too early before sedative(s) had worn off</td>
</tr>
</tbody>
</table>

A review of the closed malpractice insurance claims for dental related anaesthesia and PSA events, of two liability carriers during the period 1993 to 2007, by Chicka et al. in 2012 uncovered 17 claims. Of these, one patient had received a general anaesthetic, three received local anaesthesia alone, and the remaining 13 all had sedation. 53.6% of patients suffered death or permanent neurological damage. The average patient age was 3.6 years old. In 6 of the 13 sedation cases the dentist had been the sole operator sedationist and dentist. 71% of the sedation mishaps occurred in dental rooms. In 12 of the 13 sedation related incidents no monitoring had been used. Again it is monitoring, single operator sedationist/dentists and office based sedation that stand out as risk factors.

In 2013, Helen Lee et al. looked at media reports from 2 databases, during the period 1980 to 2011, to find deaths related to paediatric dental sedation or general anaesthesia. The media databases used were the Lexis-Nexis Academic search engine and the Raven Maria Blanco foundation website. They specifically did not look at any outcome other than death (i.e. neurological damage or other adverse outcomes were excluded) and admit that under-reporting probably affected the accuracy of their numbers. Still, some interesting trends did emerge. A total of 44 deaths were found in these media reports. 41 of the patients were completely healthy prior to the event and all the deaths were believed to have been largely preventable. Three patients had pre-existing medical conditions which were not picked up during a pre-sedation assessment. Lee found that:
- 21/44 (47.7%) of cases occurred in dental rooms.
- In 25/44 (56.8%) of cases the dentist had been a sole operator.
- Most patients initially suffered a respiratory arrest which was subsequently followed by a cardiac arrest.
- Sources of error were found to have been:
  - Inadequate or no pre-sedation assessment done.
  - Medication errors.
  - Inadequate or no monitoring used during sedation.
  - Inadequate resuscitation equipment availability and poor staff training in resuscitation skills.

In 2016, Nathan Reuter and colleagues from the Department of Oral Health Practice at the University of Kentucky, USA, published a systematic review of death related to dental treatment in general. They found dentistry itself to be very safe, with the mortality rate for pure, non-sedated dentistry to be less than 1 death per 10 million patients. However, as soon as PSA is added to the picture, this mortality rate jumps to around 1 death per 350 000 patients. In fact, Reuter et al. found 94% of all dentistry related deaths to be anaesthesia, sedation or medication error linked. They found the following associations:
- A strong association between death and either the absence of an anaesthetist altogether, or when single service providers did the sedation as well as the dentistry; also between the levels of training which the sedationists possessed if they were indeed present.
- A strong association between death and deeper levels of sedation being used.
- Inadequate monitoring was a causal risk factor in most deaths.
- Poor emergency procedure implementation in these lethal cases.
- Children under 5 years were most at risk. (All were usually normal, healthy children pre-procedure).
- Causes of respiratory related deaths were predominantly from airway obstruction due to:
  - Foreign body aspiration
  - Angioedema
  - Hypersensitivity reactions
  - Spasm and asphyxia
Bellolio et al. did a systematic review and meta-analysis of 13883 PSA sedations done for children requiring minor procedures in the emergency department in 2016. In contrast to studies which involve dental procedures, where death or permanent neurological damage is the focus, this meta-analysis revealed no deaths at all, and in fact found respiratory complications to be very rare. These were 34 cases of laryngospasm, of which only one required intubation. This re-emphasizes the particular risk which PSA for dental procedures does carry.

PSA for dental anaesthesia is particularly fraught. The greatest challenge is the shared airway. Minimal to moderate sedation is generally planned, but there is always the risk of accidental oversedation. The level of stimulation will fluctuate, making it difficult to maintain the sedation level constant without inadvertently slipping too far into the next level of sedation. Applying topical anaesthesia prior to inserting intravenous lines and dental local anaesthesia injections will help to avoid requiring a deeper sedation plane during these interventions. The use of N₂O alone may be sufficient when there is no stimulation, but generally fails as soon as any painful or deep stimulation is given. The dentist must understand that having the patient in the correct plane of sedation means that the patient should still move. This will probably happen unexpectedly, either spontaneously, but especially to painful stimuli. Aspiration of foreign bodies, blood or irrigation water is also a real danger and apart from Mendelsohn’s syndrome, this may provoke laryngospasm and bronchospasm. The dentist must use the minimum amount of water to cool their drill and suction pedantically. Even with minimal to moderate PSA, most young children are still not able to tolerate sitting in the dental chair for very long. Often, only short, limited procedures are possible for these patients under PSA.

SASA has published updated guidelines for paediatric PSA in 2016. These guidelines cover the full ambit of PSA for all procedures in children, not only those presenting for dental procedures. SOSPOSA fully endorses these guidelines and is lobbying for the implementation of training and accreditation for sedationists in South Africa.

Sedation end-points are described as follows:

1. **Minimal sedation.** (Anxiolysis) Cognitive function is impaired but the patient responds normally to verbal commands. Ventilatory and cardiovascular function is unaffected.

2. **Moderate sedation.**
   - The patient has a depressed level of consciousness but still responds purposefully to verbal commands or light touch.
   - The patient maintains his/her own airway and breathing.

3. **Deep Sedation.**
   - This forms part of the spectrum of general anaesthesia and may only be practised by practitioners with anaesthesia training.
   - Deep sedation is also known as “monitored anaesthesia care”.
   - The patient has a depressed level of consciousness but responds purposefully to repeated or painful stimuli, i.e. not merely a reflex withdrawal to pain.

   The patient may not be able to maintain his/her own airway or breathing, which may require intervention by the sedationist.

4. **General anaesthesia.**
   - The patient has a depressed level of consciousness from which he/she cannot be roused, even with painful stimuli.
   - The patient may not be able to maintain his/her own airway or breathing.

While minimal to moderate sedation is generally aimed for during PSA, it is important that the sedationist is always capable of rescuing a patient who inadvertently progresses to a deeper level of sedation.

In the SASA sedation guidelines, a further distinction is made between simple or standard sedation and advanced sedation. SASA endorses single operator sedationists for the use of simple or standard sedation but requires a separate sedationist as soon as the use of advanced sedation is planned. Even with single-operator sedation, however, a separate observer must be present to monitor the patient. Simple sedation does also require that all safety equipment, monitoring and rescue protocols are in place. Non-fasted patients may be offered simple or standard sedation. Patients presenting for advanced sedation must all be fasted according to standard anaesthesia fasting guidelines. Fasting guidelines are currently a topic of debate in the literature. For now, however, the SASA guidelines remain 6 hours for solids and formula feeds, 4 hours for breast milk and 2 hours for clear fluids.

**Simple or standard sedation.**

A single agent is used. This may be:
- Administered by an oral or transmucosal route.
- A single titrated intravenous dose of midazolam.
- Inhaled N₂O in 50% oxygen.

**Advanced sedation.**

- Any drug combination using more than one agent.
- An intravenous bolus injection or continued transfusions.
- Inhaled N₂O in < 50% oxygen or any other inhaled agents.

The SASA guidelines emphasize the importance of careful patient selection prior to performing PSA:

1. Only ASA I & II patients should be offered PSA. It is important to remember that an ASA II patient may deteriorate acutely and be ASA III on the day of the procedure, so a thorough pre-sedation assessment is warranted.
2. All patients < 5 years of age must be sedated by practitioners trained specifically in PSA for young children.
3. All PSA practitioners must have completed life support training.
4. Children suffering from an acute upper respiratory tract infection should be postponed until after this has resolved.
5. Children < 1 year of age and all ASA III or higher patients should be referred to a specialist anaesthetist or highly experienced and trained paediatric sedationist. These patients should probably undergo their procedure in a hospital setting and not undergo an office-based procedure.
The importance of a thorough pre-sedation assessment cannot be over-emphasized. Apart from identifying underlying medical conditions, a thorough focussed airway assessment must be done and the ability to communicate with the patient ascertained. It is important to ensure that the child will be able to co-operate and tolerate minimal to moderate sedation for the procedure.

Documentation must include:

- Informed consent.
- The pre-sedation assessment.
- The sedation chart outlining drugs administered and observed vital signs.
- Post-procedure observations.
- Home instructions.

Examples of all these documents are included in the SASA guidelines document. All the conditions required for safe day case procedures must also be adhered to.

Short-acting sedative agents are generally recommended and where applicable, antidotes must be available in the emergency drug armamentarium. Supplemental analgesia should not be forgotten. The SASA guideline document includes a full description of suitable agents for PSA.

Before office based PSA is commenced, a clear plan for emergency management and transfer to a hospital setting must be in place. Emergency equipment and drugs required for rescuing a patient who proceeds to a deeper level of sedation, or who suffers an unanticipated complication, must be directly available. A full list of these is available in the SASA guidelines document.

The SASA guidelines for monitoring of minimal and moderate sedation include:

1. Level of consciousness (University of Michigan Sedation Scale).
2. Breathing, ventilation and airway patency.
3. Heart rate and rhythm.
5. Oxygen saturation.

In patients with an underlying cardiovascular disease undergoing moderate sedation, the additional use of an electrocardiogram (ECG) is advised.

Capnography is not mandatory for moderate sedation but is recommended for deep sedation according to the SASA guidelines. There is always the risk of moderate sedation inadvertently progressing to deep sedation, however. It is also worth remembering that pulse oximetry is a lag monitor. Jenifer Lightdale et al. of Children’s Hospital in Boston, Massachusetts, did a randomised, controlled trial of microstream capnography during moderate sedation in 2005, challenging the guideline to monitor with pulse oximetry only. They looked at the incidence of hypopnoea and apnoea diagnosed by observing chest movement and pulse oximetry vs capnography and their results were as follows for patients sedated with identical sedation protocols:

<table>
<thead>
<tr>
<th>Hypopnoea detection rate</th>
<th>Apnoea detection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest wall observation and pulse oximetry</td>
<td>3% detected</td>
</tr>
<tr>
<td>Capnography</td>
<td>56% detected</td>
</tr>
</tbody>
</table>

These results beg the question; “Are we simply not seeing the apnoea or hypopnoea episodes with our current observation methods?”

The addition of supplemental oxygen in particular, may mask the desaturation which would otherwise present when monitoring by pulse oximetry alone.

In conclusion, paediatric PSA for dental procedures is already being widely done in our country, unfortunately often to poor safety standards, as can be seen from the Bham F et al. study. Paediatric dental PSA is potentially extremely dangerous, but the pitfalls and practice guidelines are quite clear. Education, accreditation and implementation of the SOSPPOS and SASA guidelines will hopefully go a long way to enhance safety for a practice which will likely remain popular, given the resource constraints we face.

References:

2. De Wet; SASA refresher course lecture, March 2017.
Anaesthesia in pregnancy for non-obstetric surgery

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This is a review of the maternal and foetal concerns with respect to non-obstetric surgery during pregnancy, with a focus on anaesthetic management of such surgery and on teratogenicity.

Introduction

Patients presenting for non-obstetric surgery during the course of their pregnancy present a challenge to attending physicians. The anaesthetic management is complicated by the need to balance the anaesthetic requirements of the mother against avoiding harmful effects of the anaesthetic on the growing foetus. When a mother needs surgery during pregnancy, a multidisciplinary team approach is necessary to assess the correct timing and approach to surgery. To date, no anaesthetic drug has been shown to be harmful to the human foetus when used appropriately, but it would seem wise to minimise placental transfer of drugs. The anaesthetic considerations should also include assessment of the surgical disease process, teratogenicity, physiological changes of pregnancy, types of anaesthesia, foetal monitoring and tocolysis.

The American College of Obstetricians and Gynecologists (ACOG) Practice Guidelines Committee acknowledges that there are no data to allow for specific recommendations in this group of patients because of the difficulty of conducting clinical trials.

Epidemiology

0.75% to 2% of pregnant women require non-obstetric surgery during pregnancy. In the United States of America, approximately 75 000 women annually have non-obstetric surgery during their pregnancies.

The incidence of non-obstetric surgery is most common during the first trimester, with 42% of such surgeries occurring then. Thirty-five percent of surgeries occur during the second and 23% in the third trimester. The incidence of surgery is probably higher during the first trimester because some women are not aware of their pregnancy.

Appendicitis, cholecystitis, ovarian disorders, trauma and malignancy during pregnancy are the most common conditions requiring non-obstetric surgery during pregnancy. Less common causes of surgery during pregnancy may include decompensated cardiac lesions such as mitral stenosis and neurosurgical conditions (ruptured aneurysm/space occupying lesions).

Timing of surgery

Emergency procedures should proceed regardless of the trimester of pregnancy and a pregnant woman should never be denied indicated surgery regardless of the trimester. However, when considering good foetal outcome, we know that the timing of exposure to anaesthesia and drugs is critical. The decision to proceed to surgery should be made by a multidisciplinary team involving anaesthetists, surgeons, obstetricians and neonatologists.

In a study that investigated pregnancy outcome and non-obstetric surgery, the overall miscarriage rate was 5.8%. In surgery in the first trimester of pregnancy, the miscarriage rate was 10.8%. The first trimester is associated with the period of foetal organogenesis (between 3–8 weeks) and thus also associated with all the concerns of foetal malformations.

The third trimester or advanced stages of pregnancy pose problems of operating around the growing uterus and the possibility of irritating the uterus, resulting in preterm labour. Lower abdominal procedures and the presence of peritonitis have been found to be associated with preterm labour.

Semi-elective procedures should be done during the second trimester and purely elective surgery should wait for the patient to be six weeks postpartum. However, conservative/medical management of symptomatic cholelithiasis was associated with an increased risk of recurrence – 38% of patients treated medically had recurrence of symptoms.

Anaesthetic considerations for non-obstetric surgery during pregnancy

The aim of anaesthetic and perioperative management is to ensure maternal safety, avoid foetal loss and to deliver a healthy baby.
Understanding of the physiological changes of pregnancy is essential for maternal safety during anaesthesia, particularly after 20 weeks gestation. The hormonal and physiological changes of pregnancy are designed to cope with the oxygen and nutritional demands of the developing foetus, but may pose a challenge for airway management, and positioning of the patient for surgery. Precautions must be taken to ensure safety of the mother.

Knowledge of the pharmacological profiles of anaesthetic drugs and the placental transfer of drugs is key to avoidance of adverse outcomes in the foetus.

**Foetal considerations and safety**

Most patients presenting for non-obstetric surgery are concerned about the risk of the anaesthetic and surgery to the developing foetus. To ensure foetal safety, the anaesthetic management must include maintaining uteroplacental perfusion by avoiding maternal hypotension, acidosis and hypoxia.

A study evaluating pregnancy outcome following non-obstetric surgery during pregnancy that included 12 452 patients, found that maternal mortality is very rare (0.006%); the miscarriage rate was 5.8%; the incidence of preterm labour was 3.5% and the incidence of elective termination following non-obstetric surgery was 1.3%.

Appendectomy was associated with a higher rate of surgery-induced labour (4.6%), with foetal loss in 2.6% of patients. The incidence of foetal loss increased to 10.9% when peritonitis was present.6

Normal physiological changes that occur in pregnancy that impact on anaesthesia management are noted in Table I.

**Teratogenicity**

Teratogenicity is defined as an observation of any significant change or form of a child secondary to prenatal treatment with an external agent, such as a drug. Therefore, any drug that the patient takes has the potential to disturb the development of the embryo and may result in malformation.

Prior to anaesthesia and surgery, most patients will need information regarding anaesthetic drugs and their possible teratogenic effects and it is the duty of the anaesthetist to provide them with current information in order for them to be able to give informed consent before surgery.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Change during pregnancy</th>
<th>Normal pregnancy values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crdiovascular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>Increases 1-20 bpm</td>
<td>75-95 bpm</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>Increases 30-50%</td>
<td>6-8 l/min</td>
</tr>
<tr>
<td>Mean arterial blood pressure</td>
<td>Decreases 10 mmHg in midtrimester</td>
<td>80 mmHg</td>
</tr>
<tr>
<td>Systematic vascular resistance</td>
<td>Decreases 10-15%</td>
<td>1200-1500 dynes/s/cm²</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume</td>
<td>Increased 40%</td>
<td>700 ml</td>
</tr>
<tr>
<td>Minute ventilation</td>
<td>Increased 40%</td>
<td>10.5 l/min</td>
</tr>
<tr>
<td>Expiratory reserve volme</td>
<td>Decreased 15-20%</td>
<td>550 ml</td>
</tr>
<tr>
<td>Functional residual capacity</td>
<td>Decreased 20-25%</td>
<td>1350 ml</td>
</tr>
<tr>
<td><strong>Blood gas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>Unchanged</td>
<td>7.4-7.45</td>
</tr>
<tr>
<td>pCO₂</td>
<td>Decreased</td>
<td>27-32 mmHg</td>
</tr>
<tr>
<td>pO₂</td>
<td>Increased</td>
<td>100-108 mmHg</td>
</tr>
<tr>
<td>HCO₃</td>
<td>Decreased</td>
<td>18-21 mEq/l</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood volume</td>
<td>Increased 30-50%</td>
<td>4500 ml</td>
</tr>
<tr>
<td>Erythrocyte volume</td>
<td>Increased 10-15%</td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Decreased</td>
<td>32-34%</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>Increased</td>
<td>5000-15 000/mm³</td>
</tr>
<tr>
<td>Factors I, II, V, VII, IX, X and XII</td>
<td>Increased</td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Increased</td>
<td>&gt; 400 mg/dl</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal blood flow</td>
<td>Increased 50-60%</td>
<td>700 ml/min</td>
</tr>
<tr>
<td>Glomerular filtration rate</td>
<td>Increased 60%</td>
<td>140 ml/min</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>Decreased</td>
<td>&lt; 0.8 mg/dl</td>
</tr>
<tr>
<td>Serum urea nitrogen</td>
<td>Decreased</td>
<td>&lt; 13 mg/dl</td>
</tr>
</tbody>
</table>

BPM: Beats per min.

Source: Women’s Health © 2009 Future Medicine Ltd
Some studies have concluded that virtually every drug used in anaesthesia can be found to possess teratogenic characteristics in some species, under some set of circumstances, at some particular point in time, during pregnancy. Despite years of animal studies and observational studies, no anaesthetic drug has been shown to be clearly dangerous to the human foetus and there is no optimal anaesthetic technique. The search for a clear answer is hampered by lack of human studies and no animal model perfectly mimics human pregnancy.\(^1\)\(^2\)

Teratogenicity probably depends on some of the following:
- Anatomy and physiology of the placenta: the human placenta is very different from that of animals which makes extrapolation from animal studies not practical.
- Pharmacokinetic profile of the drug: more lipid soluble drugs cross the placenta and can result in ‘trapping’ of the drug in the placenta.
- Time of exposure is crucial: the first 15 days of pregnancy seem to be a period with an ‘all or none phenomenon’ with regard to teratogenicity, with the pregnancy either lost or preserved, while most of the major congenital malformations were most likely to occur from exposures between days 13 and 60.\(^9\)

The two drugs that have been mostly implicated in anaesthesia are nitrous oxide and benzodiazepines.

**Effect of nitrous oxide on DNA synthesis:**

\[ \text{Homocysteine} \xrightarrow{\text{THF}} \text{S-Methyl} \xrightarrow{\text{Folic acid}} \text{THF} \xrightarrow{\text{DNA synthesis}} \text{Methionine} \xrightarrow{\text{Methionine synthase}} \text{THF} \xrightarrow{\text{DNA synthesis}} \text{N,0} \]

**Nitrous oxide** inhibits methionine synthetase and thereby inhibits vitamin B\(_12\) and folate metabolism. The inhibition of folate metabolism interferes with DNA synthesis and may be harmful to the foetus. Exposure to > 50% nitrous oxide for prolonged periods has been shown to be teratogenic in animal studies. However, no effects have been demonstrated in women after brief exposure. Rowland et al conducted a study that concluded that women exposed to unscavenged nitrous oxide for prolonged periods had more abortions and decreased fertility than those who were not exposed.\(^10\)\(^11\)

A subsequent Swedish study of more than 5 000 women failed to implicate nitrous oxide in adverse foetal outcome,\(^5\) but it would seem best to avoid using it in modern anaesthetic practice as there is a large range of drugs with a better safety profile.

**Benzodiazepine** use during pregnancy was associated with cleft palate and cardiac abnormalities in earlier studies.\(^12\) A single dose of benzodiazepine does not appear to be a problem but repeated and prolonged use is.\(^13\)\(^14\)

In summary, most of the commonly used induction agents, opioids, muscle relaxants and volatile agents can be safely used in clinical concentrations.

### Table II. Teratogenic drugs\(^1\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Possible congenital abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Foetal alcohol syndrome</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Premature closure of ductus arteriosus</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Spontaneous abortions, abruptio placenta</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Cleft palate, heart and facial defects</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Abortions</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>Cardiac, CNS, facial and thymus defects</td>
</tr>
<tr>
<td>Warfarin</td>
<td>CNS defects, spontaneous abortions and haemorrhage</td>
</tr>
<tr>
<td>Lithium</td>
<td>Cardiac, kidney and thyroid defects</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Congenital facial abnormalities</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Neonatal renal failure</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Limb abnormalities</td>
</tr>
</tbody>
</table>

### Table III. FDA pregnancy categories of drugs

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Controlled studies in pregnant women show no risk in first trimester</td>
</tr>
<tr>
<td>B</td>
<td>Animal studies show no risk, unconfirmed risk in humans</td>
</tr>
<tr>
<td>C</td>
<td>Animal studies show risks but benefits outweigh risks</td>
</tr>
<tr>
<td>D</td>
<td>Evidence show risk to human foetus, benefits outweigh risks</td>
</tr>
<tr>
<td>X</td>
<td>Animal and human studies show harm, risks outweigh benefits</td>
</tr>
</tbody>
</table>

**Anaesthetic management**

There is no ideal anaesthetic technique and the anaesthetic choice should be guided by the indication, site and nature of surgery. Regional and nerve block techniques are preferred over general anaesthesia where feasible, in order to minimise the transfer of drugs across the placenta. Doses of local anaesthetics for neuraxials need to be reduced during pregnancy and any resultant hypotension must be appropriately managed. There is no definite proof or data showing definite superiority of regional over general and both have been safely used during pregnancy.

The preoperative assessment should be used to discuss and reassure the patient about her concerns (miscarriage, preterm and teratogenicity). The attending obstetrician and paediatrician must be notified and gestational age should be noted.

Important issues in the anaesthetic management include:
- Preoperative evaluation of the airway in view of pregnancy related airway changes that increase difficulty in airway management. Adequate preoxygenation prior to induction is recommended to avoid hypoxia in the presence of the reduced Functional Residual Capacity and the increased oxygen consumption.
- Blood investigations required will be determined by the type of surgery and the disease process.
- Aspiration prophylaxis from 14 weeks gestation is advisable.
- Avoid aortocaval compression from 20 weeks gestation by positioning the patient with lateral tilt.
• Adequate ventilation, aiming for normocarbia to avoid foetal acidosis. Hypercarbia and hypocarbia both reduce placental blood flow.

• Avoid any reductions in uteroplacental circulation. Prolonged maternal hypoxia causes uteroplacental vasoconstriction and decreased uteroplacental perfusion, which can result in foetal acidosis and death. Maternal blood pressure must be maintained because a decrease in maternal blood pressure decreases placental perfusion.

• Prophylactic glucocorticoid administration 24–48 hours preoperatively for lung maturity in case of preterm labour.

• Anaesthetic drugs: most anaesthetic drugs have been safely used during pregnancy. Plasma cholinesterase levels are reduced up to 35% during pregnancy but recovery from succinylcholine is not usually prolonged because of the increased volume of distribution and relative resistance to succinyl choline associated with pregnancy. MAC values of inhalational anaesthetics are reduced in pregnancy and lower levels of these agents may be required. Atropine may be preferred over glycopyrrolate to counteract the effects of neostigmine because neostigmine crosses placenta while glycopyrrolate does not.

• Prophylactic tocolysis.

• Foetal monitoring.

**Foetal heart monitoring**

Continuous foetal heart rate should be done, when feasible, from 18–22 weeks of gestation and uterine activity can also be monitored, depending on the site of surgery.

The ACOG state that the decision for foetal monitoring should be individualised and, if used, should depend on the gestational age, type of surgery and available facilities of the institution.3

**ACOG guidelines for foetal monitoring**

In the case of a previable foetus, it is sufficient to ascertain foetal heart rate (FHR) by Doppler before and after the procedure.

In the case of a viable foetus, a minimum of FHR and contraction monitoring before and after the surgical procedure should be done, in order to assess foetal wellbeing and absence of contractions.

Electronic FHR monitoring should be used during a surgical procedure when

- A viable foetus is present.
- It is physically possible to use the monitor.
- A healthcare provider with obstetric knowledge is available and willing to intervene during the procedure for foetal indications.
- The patient has given informed consent for emergency Caesarian section delivery.
- The nature of the surgery is such that it can allow interruption or alteration for Caesarian section delivery.

FHR variability can be monitored from 25–27 weeks gestation; however, because most drugs cross the placenta they can reduce FHR variability under general anaesthesia.

Foetal bradycardia is more concerning during surgery as it may be a reflection of foetal distress or compromise (hypoxaemia). Other factors that may reduce FHR variability include maternal acidosis, hypotension and hypothermia.

**Tocolysis**

Efficacy of most of the agents used for tocolysis is unproven and the significant side-effects of the drugs need to be considered before their use.

Prophylactic administration of tocolytic agents is controversial and should be limited to those patients who require uterine manipulation intraoperatively and those patients undergoing lower abdominal and pelvic procedures.11 Patients who have appendicitis and peritonitis have an increased incidence of foetal loss.6

If a patient develops preterm labour, treatment options include use of magnesium sulphate, calcium channel blockers, β-mimetics, prostaglandin inhibitors (indomethacin) and nitrates.16 Indomethacin is no longer recommended after 28 weeks because it causes premature closure of the PDA.

**Laparoscopy**

Laparoscopy is no longer considered to be contraindicated during pregnancy. The surgical approach should be determined by the skills of the surgeon, surgical needs and the availability of equipment. Concern with laparoscopy in the past has been about associated foetal trauma, foetal acidosis with CO₂ insufflation and increased intra-abdominal pressure which resulted in decreased cardiac output and reduced uteroplacental perfusion.

Reedy et al conducted a retrospective study comparing laparotomy and laparoscopy for non-obstetric surgery during pregnancy. No difference between the two groups was found regarding the incidence of preterm labour, the birth weight of the babies, growth restrictions, malformations and foetal losses.17

Rollins et al investigated their own practices during two different time periods and concluded laparoscopic cholecystectomy and appendectomy had increased greatly with no associated adverse foetal outcome.18

**Important factors for maternal laparoscopy**:

- Use open technique to enter the abdomen.
- Monitor ETCO₂ to avoid maternal hypercarbia (30–34 mmHg).
- Use low pressure pneumoperitoneum (10 cmH₂O).
- Limit extent of Trendelenburg or reverse Trendelenburg positions.
- Try and maintain uterine displacement.

Although the laparoscopic approach can be used during any trimester of pregnancy, it is technically difficult during the last trimester because of the growing uterus.
Postoperative management

• Continue monitoring the patient for contractions and foetal heart rate to ensure safety of the foetus. The obstetrician should review the patient at this stage. If the pregnancy is maintained for one week after the surgery, the pregnancy is considered ‘safe’.

• Provision of adequate analgesia is important. Peripheral nerve blocks and epidural are preferable. Opioids can be used to control postoperative pain but the drug of choice is paracetamol. Avoid using nonsteroidal anti-inflammatories because of the risk of side-effects in the foetus, including oligohydramnios, premature closure of the ductus arteriosus, necrotising enterocolitis and intraventricular haemorrhage.

Conclusion

Non-obstetric surgery during pregnancy is not common, but it appears to be safe if careful attention is paid to maintaining uteroplacental circulation and minimising placental drug transfer during anaesthesia and if surgery is performed at the correct time. Successful maternal and foetal outcome depends upon expert surgical and anaesthetic management of the disease process.

References

3. ACDG committee opinion no 696, 2017 on non-obstetric surgery during pregnancy.
Anaesthesia for cleft lip and palate surgery

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“Dignity begins with a smile” by Nicholas Serra, Operation Smile

Introduction

Worldwide, cleft lip and palates (CLP) are one of the most common craniofacial abnormalities requiring surgical treatment in the early years of life. Cleft lip and palate can impact a child’s appearance, speech, teeth, eating, hearing and ability to develop socially. Cleft lip and palate can be successfully treated using a comprehensive team approach including presurgery support and long-term postsurgery care.

Prevalence

Internationally the prevalence of cleft lip ranges between 1:300–1 200 live births and for cleft palate 1:2 500 live births but these vary based on ethnicity and country. The prevalence in South Africa is about 1.4:1 000 live births in Caucasians and 0.4:1 000 live births in Africans.

CLP is more common in males. Isolated CP is more common in females.

Classifications (See Picture)

<table>
<thead>
<tr>
<th>Table I. Types of abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral cleft lip</td>
</tr>
<tr>
<td>Unilateral cleft lip and palate</td>
</tr>
<tr>
<td>Bilateral cleft lip and palate</td>
</tr>
<tr>
<td>Cleft palate alone</td>
</tr>
</tbody>
</table>

Cleft lip (CL)

Cleft lip occurs in the upper lip and is either unilateral (left side more common) or bilateral. The defect may be:
- Complete (extends across the whole lip and into the nostrils)
- Incomplete (ranges from small indentations to large defects)

Cleft palate (CP)

Cleft palate occurs in the soft palate and may extend into the hard palate and is either a unilateral or bilateral fissure.

The defect may be:
- Complete (both primary and secondary palates are affected)
- Incomplete (affects only the secondary palate)

CP may occur with CL but CP without CL is aetiologically and embryologically a distinct entity.

Embryology

CLP occurs because of palatal growth defects during the first trimester. The window of opportunity for fusion to occur is relatively short, and suggested theories for failure of fusion include mechanical obstruction by tongue position, structural hypoplasia or primary breakdown. Clefts of the lip and alveolus can be diagnosed reliably at the routine 18–20 week antenatal ultrasound scan, allowing for earlier preparation of support services and counselling of parents. Clefts of the palate are not easily seen by ultrasound and can only be excluded by examination of the palate after delivery.

Aetiology

The aetiology is unknown but is multifactorial. Both genetic and environmental factors play a role. There is also a strong hereditary role. Some cases result from mechanical obstruction. There is also an association with teratogen exposure such as smoking, maternal alcohol use, anticonvulsant drugs (phenytoin and benzodiazepines) and other drugs such as salicylates and cortisone. Increased paternal age also plays a role.
<table>
<thead>
<tr>
<th>Syndrome name(s)</th>
<th>Features</th>
<th>Anaesthesia implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthrogryposis Multiplex congenita</td>
<td>Limb contractures, CHD, stiffness of joints and GU defects</td>
<td>Difficult intubation due to limited mouth opening, position, and pad carefully</td>
</tr>
<tr>
<td>Beare-Stevenson syndrome</td>
<td>Craniosynostosis, hydrocephalus, choanal atresia, midface hypoplasia, proptosis, hypertelorism, cutis gyratum, tracheal stenosis, and cervical spine defects</td>
<td>Difficult airway, beware of tracheal stenosis and caution with neck movements</td>
</tr>
<tr>
<td>Beckwith-Wiedemann syndrome</td>
<td>Exomphalos, macroglossia and gigantism</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tongue reduction required at time of palate repair</td>
</tr>
<tr>
<td>CATCH 22 (Velocardiofacial syndrome)</td>
<td>Most common syndrome associated with CLP</td>
<td>Difficult airway</td>
</tr>
<tr>
<td></td>
<td>Cardiac defect, abnormal face, thymic hypoplasia, cleft palate and hypocalcaemia (Di George syndrome)</td>
<td>Hypocalcaemia</td>
</tr>
<tr>
<td>Cornelia de Lange syndrome</td>
<td>Growth failure, micromelia, micrognathia, mental retardation, CHD in 15%</td>
<td>Airway obstruction, difficult intubation</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>Short stature, mental retardation (variable), macroglossia, unstable cervical spine, narrow subglottic space and CHD in 50%</td>
<td>Difficult intubation, airway obstruction and caution with neck movements</td>
</tr>
<tr>
<td>Foetal alcohol syndrome</td>
<td>Small palpebral fissures, smooth philtrim, thin upper lip, growth deficiency, CNS abnormalities, microphalaxy</td>
<td>Behavioural dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficult laryngoscopy and tracheal intubation</td>
</tr>
<tr>
<td>Goldenhar syndrome</td>
<td>Defect of the 1st and 2nd branchial arches</td>
<td>Difficult airway (intubation may become more difficult with increasing age), laryngeal anomaly, lung hypoplasia – ventilatory problems, cardiac and pulmonary complications</td>
</tr>
<tr>
<td>Kabuki syndrome</td>
<td>Craniofacial and skeletal defects, hypotonia, CHD, visceral and urogenital defects</td>
<td>Difficult airway</td>
</tr>
<tr>
<td>King syndrome</td>
<td>Congenital myopathy, MH trait Dysmorphic features</td>
<td>Malignant hyperthermia (MH)</td>
</tr>
<tr>
<td>Klippel-Feil syndrome</td>
<td>Limited neck movement, renal anomalies</td>
<td>Difficult airway</td>
</tr>
<tr>
<td>Miller syndrome</td>
<td>Mandibular defects, limb anomalies and renal defects</td>
<td>Difficult airway</td>
</tr>
<tr>
<td>Multiple Pterygium syndrome</td>
<td>Webbing of skin, syngnathia, ankyloglossia, and web neck</td>
<td>Difficult airway (more severe with age) and MH association</td>
</tr>
<tr>
<td>Nager syndrome</td>
<td>Malar hypoplasia, micrognathia, CHD, radial hypoplasia, absent thumbs, and vertebral anomalies</td>
<td>Difficult airway, limited mouth opening and cervical spine anomalies</td>
</tr>
<tr>
<td>Oto-palatal-digital syndrome</td>
<td>Skull deformity, hearing loss, cervical spine defect, limb defects and thoracic hypoplasia</td>
<td>Possible brain-stem compression causing postoperative respiratory depression</td>
</tr>
<tr>
<td>Patau’s syndrome (Trisomy 13)</td>
<td>Microcephaly, mental retardation, micrognathia, CHD and fatal in infancy</td>
<td>Difficult airway</td>
</tr>
<tr>
<td>Pierre-Robin sequence</td>
<td>Micrognathia and cleft palate in 80% of cases</td>
<td>Difficult airway, postoperative airway obstruction (Intubation becomes easier with age due to mandibular growth)</td>
</tr>
<tr>
<td>Seckel syndrome</td>
<td>Bird-like face, dwarfism, microcephaly, possible glottis narrowing</td>
<td>Difficult airway, Monitor ventilation postop (postoperative apnoea)</td>
</tr>
<tr>
<td>Smith-Lemli-Opitz syndrome</td>
<td>Growth failure, microcephaly, mental retardation, CHD, renal defects, hypotonia, GORD, and thymic hypoplasia</td>
<td>Possible difficult airway, intraoperative muscle rigidity and thermoregulatory problems</td>
</tr>
<tr>
<td>Stickler syndrome</td>
<td>Progressive connective tissue disorder (AD), midface hypoplasia, micrognathia, Pierre Robin sequence, retinal detachment and early cataracts, deafness, hypermobility of joints</td>
<td>Difficult airway</td>
</tr>
<tr>
<td>Spondylo-epiphyseal Dysplasia congenita</td>
<td>Dwarfism and C1–C2 instability</td>
<td>Caution with neck movements during intubation and positioning</td>
</tr>
<tr>
<td>Treacher Collins syndrome</td>
<td>Hypoplastic zygoma and mandible, macrostomia and cleft or high arched palate</td>
<td>Difficult airway (intubation may become more difficult with increasing age)</td>
</tr>
<tr>
<td>Walker-Warburg syndrome</td>
<td>Micrognathia, hypotonia, hydrocephalus, mental retardation and GU anomalies</td>
<td>Difficult intubation and postoperative hypventilation</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>Cleft palate, lung hypoplasia, macrognathia and CHD</td>
<td>Difficult airway</td>
</tr>
</tbody>
</table>
Associated syndromes

Most children have an isolated malformation but approximately 22–37% have an associated malformation. Isolated cleft palate has the highest incidence of associated malformations (28–47%), with cleft lip at around 8–13% and CLP from 28–37%. Over 200 syndromes/sequences (Table II) are associated with CLP and some have significant anaesthetic implications. Most syndromes are rare but some of the more common syndromes of interest to anaesthesia are:

1. Pierre Robin sequence
2. Treacher Collins syndrome
3. Goldenhar syndrome
4. Velocardiofacial syndrome
5. Foetal alcohol syndrome
6. Stickler syndrome
7. Down syndrome
8. Klippel-Feil

Summary of the associated problems:

1. Associated congenital abnormalities (the most prominent have been highlighted in Table II)
2. Congenital heart disease (5–10% of patients)
3. Chronic rhinorrhoea
4. Chronic airway obstruction or sleep apnoea
5. Right ventricular hypertrophy and cor-pulmonale because of chronic hypoxia secondary to airway obstruction
6. Anticipated difficult intubation and extubation

Timing of surgical repair

Classically CL is repaired between 3–6 months but there is an increasing trend to operate during the neonatal period. CP is repaired at a later age between 3–9 months sometimes even up to 18 months. Depending on the surgeon’s preference it may be a primary repair or a staged repair to promote normal speech development and reduce nasal regurgitation. Surgery may be delayed to optimise any associated malformations.

CLP patients are likely to require further surgery either related to the primary problem e.g. plastic improvements to a CL repair, or for associated abnormalities. Around 20% will require pharyngoplasty for velopharyngeal dysfunction at around 4–6 years. Primary palatoplasty disrupts normal palate growth and despite orthodontic treatment, some will require significant maxillofacial surgery in their teens to correct midface hypoplasia and maxillary retrusion.

Anaesthesia considerations

Preoperative assessment

A thorough preoperative evaluation is essential to reduce any risk of anaesthesia-related morbidity and mortality.

1. Is there a syndrome present?
   - Ensure a thorough examination being sure to evaluate for a cardiac defect which may require an Echo; especially if a murmur is noted.

2. Airway management: is the intubation potentially difficult?
   - Most non-syndromic infants are not difficult to intubate.
   - Some syndromes are associated with difficult intubation.
   - Factors associated with difficulty include: bilateral cleft lip, retrognathia, micrognathia, infants < 6 months of age and to a lesser extent left-sided cleft lip and alveolus.

3. Upper respiratory tract infection (URTI)?
   - Chronic rhinorrhoea is common with CLP due to reflux of food into the nasal passage with resultant overt and often recurrent URTI.
   - Postoperative respiratory complications increase with the severity of the defect.
   - At risk of reactive airways.

4. Chronic airway obstruction?
   - Look for signs of chronic airway obstruction: snoring, apnoea during feeds/protracted feeding time.
   - Older children may have chronic hypoxia, right ventricular hypertrophy and eventually cor-pulmonale requiring a preoperative Echo.
   - Beware of sedative drugs as these patients are more sensitive to their effects.

5. Nutrition and hydration
   - Feeding difficulties are common in CLP as it may be difficult to create a sufficient seal during suckling. This results in the infants being dehydrated and malnourished requiring surgery to be deferred until they can be optimised.
   - Nutritional or physiological anaemia may occur but routine haemoglobin testing is not advocated.

6. Premedication
   - Usually not necessary.
   - Sedatives may aggravate chronic airway obstruction and should be avoided.
   - Establishing a rapport with the infant and caregiver may prove to be helpful but not always possible with an anxious patient/caregiver.
   - Individualising each patient is essential and premedication may be considered in children > 1 year (relative) and no airway concerns (syndromes or signs of airway obstruction).
   - Medications that have been used include: oral paracetamol with/without midazolam, oral ketamine mixed with paracetamol and intra-nasal dexmedetomidine.
   - An anticholinergic (atropine or glycopyrrolate) may be considered to reduce secretions.

Intraoperative management

Generally an inhalational induction is performed but total intravenous anaesthesia (TIVA), using a remifentanil-propofol infusion, has compared favourably with a sevoflurane-fentanyl anaesthesia in a small group of patients. Upon obtaining intravenous access, the airway can be secured using a south-facing oral Rae endotracheal tube and positive pressure ventilation initiated. Maintain spontaneous ventilation until the ability to face mask ventilate has been confirmed and a muscle
relaxant (e.g. suxamethonium 1–2 mg/kg or a non-depolarising agent) can then be administered if no difficulties with intubation are anticipated. Ten percent of ASA 1 patients for CLP repair will have difficult laryngoscopy (Cormack and Lehane grade III-IV views) and the incidence in those with associated syndromes rises. 

Tricky intubation tips:
- Instead of using a curved laryngoscope blade, consider a straight blade.
- Large alveolar defects may hamper laryngoscopy – pack the defect with gauze to help prevent the blade from slipping into the cleft (especially left-side defects).
- In a patient with bilateral cleft lip, the central lip prominence can hinder midline laryngoscopy – consider using a Miller blade with a lateral approach.
- Always be prepared for a potential difficult intubation with difficult airway equipment readily available especially for any syndromic child (e.g. alternative laryngoscopes, a stylet or gum elastic bougie, and laryngeal masks (LMA)).

To prevent soiling of the airway and ingestion of blood; a throat pack should always be inserted. Remember to remove the pack before emergence. A head ring and roll are placed under the patient’s shoulders to extend the neck and tip the head down. A Boyle-Davis gag is used during palate repair and vigilance is needed to prevent inadvertent extubation, intubation of the right main bronchus and endotracheal tube-kinking or occlusion.

Administer antibiotics, corticosteroids (dexamethasone 0,25 mg/kg) to reduce upper airway oedema, and anti-emetics. Provide appropriate intraoperative fluid therapy and consider 1% dextrose supplementation in patients high risk for hypoglycaemia (prolonged preoperative fasting, underweight children, and children < 4 years/< 15 kg).

Surgery usually lasts 1–2 hours. Blood loss is uncommon but CP repairs have the potential for significant blood loss so cross matching facilities should be available. In patients who are oozing, 10 mg/kg tranexamic acid may be considered but may be controversial.

Surgery is painful and a multimodal analgesic approach is essential. Provide regular dosing of simple analgesics as a baseline
- Paracetamol:
  - As a premedication, orally (20 mg/kg).
  - After induction, intravenously (15 mg/kg) or rectally (40 mg/kg).
- NSAIDS:
  - Effective analgesics.
  - Generally, only prescribed in infants > 6 months.
  - Given in the setting of cleft lip repair but avoided in cleft palate repairs due to the risk of bleeding. May then be considered 12 hours postoperatively.
- Opiates:
  - Short-acting agents recommended for CL repairs e.g. fentanyl 1–2 mcg/kg.
  - Longer-acting agents may be more appropriate for CP repairs as these are more painful e.g. morphine 0,05–0,1 mg/kg.
  - Advantage: smoother emergence with less crying which may reduce swelling and bleeding from the surgical site.
  - The use of long-acting opiates should be titrated to effect due to the risk of postoperative airway complications (postoperative sedation and respiratory depression).
- Regional anaesthesia:
  - Infraorbital nerve blocks can provide effective postoperative analgesia for up to 19 hours without the risk of respiratory depression when performed with adrenaline-containing bupivacaine. Bilateral blocks can safely be performed.
  - Studies have shown they provide better analgesia for a longer duration than peri-incisional infiltration and are superior to fentanyl titrations.
  - The infraorbital nerve supplies sensation to the skin and mucous membranes of the upper lip, lower eyelid, cheek and the alae nasi.
  - The infraorbital nerve can be blocked either intra-orally or extra-orally. Using a small gauge needle in the extra-oral approach; is placed superficially to the infraorbital foramen bilaterally (0,5–1 ml 0,25%–0,5% bupivacaine with 1:200 000 adrenaline).
- Maxillary nerve blocks via three approaches: intra-orally by blocking the palatine nerves, using an infrazygomatic approach or a suprazygomatic approach.
  - The maxillary nerve innervates the lower eyelid, the upper lip, the skin between them, the roof of the mouth and the palate.
  - For detailed descriptions on the blocks refer to:
  - Since there is no single effective block for CLP surgeries, pain management should always be supplemented with other modalities keeping in mind that the blocks reduce the opioid requirements effectively.

**Extubation**

It is important to remain vigilant and ensure the throat pack is removed at the end of surgery and this should be included as part of the swab count according to the WHO Surgical Safety Checklist.
Ensure the oropharynx is inspected for any blood clots and that haemostasis has been achieved. Suctioning should be kept to a minimum especially with CP repairs to avoid disrupting the surgical repair and may cause bleeding. Non-depolarising muscle relaxants should be adequately antagonised if they were used during the procedure. Extubate the child fully awake once the protective reflexes have returned.

Postoperative management

It is estimated that 15–20% of CLP repairs are associated with postoperative morbidity and a reoperation risk of around 2% related to bleeding and airway obstruction complications. Airway complications range from episodes of mild stridor to complete airway loss requiring re-intubation.

All children should be monitored in the recovery room until they are fully awake, their pain has been well controlled and there are no signs of bleeding.

Factors to consider in the postoperative period:

1. Airway obstruction
   a. Most commonly seen in recovery in the immediate postoperative period but careful monitoring allows for early detection as it may occur within the first 12–24 hours but even up to 48 hours post-surgery. Massive tongue swelling cases usually present within 90 minutes of the end of surgery.
   b. Most likely to occur in children with a preoperative airway concern. Especially in children with congenital abnormalities, namely Pierre Robin sequence. Insert a nasopharyngeal airway (NPA) at the end of the procedure in micrognathic patients.
   c. Occurs due to:
      i. Congenital abnormalities associated with micrognathia.
      ii. Anaesthetic or surgical complications:
         1. Swelling of the tongue from gag pressure, usually because of prolonged surgical time related to a wider cleft. The mouth is held open by the gag which exerts pressure on the alveolar ridge and tongue. Mucosal oedema results if too much pressure is applied for a prolonged period or the incorrect size retractor blade is used. This is due to impaired venous and lymphatic drainage, and is worsened by neck overextension and if steep Trendelenburg is used. The Boyles-Davis gag should be released for 5–10 minutes every hour especially during prolonged surgery. Upon removal of the gag inspect the whole oropharynx and base of the tongue. Should the tongue appear swollen or dusky in colour, decide whether extubation is appropriate and consider placing a NPA. The child should be closely observed in a high care environment or placed in ICU ventilated until the swelling has resolved.
         2. A retained throat pack.
         3. Bleeding or blood clots.
   d. Management depends on the degree of the obstruction:
      i. Simple manoeuvres:
         1. Place the child in the left lateral or prone, pull the tongue forward to relieve the obstruction. Consider providing temporary continuous positive airway pressure until the child has fully recovered.
         2. Consider placing a tongue suture to relieve the obstruction.
      ii. Other airway devices:
         1. Place a NPA or LMA.
      iii. Re-intubation: required if simple manoeuvres cannot establish a safe airway.
         1. Should reintubation be necessary, consider using a fibre optic scope and as a last resort in severe airway obstruction, a surgical airway. It is imperative to be familiar with the paediatric difficult airway algorithms.
         2. If there are any concerns on emergence of airway compromise, keep the child intubated and ventilated until the swelling subsides.
         3. Anticipate a difficult intubation even if with the initial procedure it may have been straightforward, as postoperative swelling and bleeding may distort the view at laryngoscopy.
      iv. Postoperative monitoring:
         1. Ideally all patients should be monitored in a high-dependency unit but patients at particular risk as a result of an associated syndrome or any who complicate should be monitored in ICU.
         2. Postoperative analgesia:
            a. Multimodal analgesic strategies should be continued into the postoperative period. This should include regular dosing of paracetamol and NSAIDs (infants over six months) and oral (tilidine 1 mg/kg) or intravenous opioids in selected cases and older children (morphine 0.05–0.1 mg/kg) provided airway obstruction is not a problem. Alternatively, consider rectal analgesics.
            b. If a nerve block is performed intraoperatively, this analgesia will continue into the postoperative period.
c. Infants may be reluctant to swallow for 24 hours post-repair and intravenous fluids may be required until oral intake has been re-established.¹

**Conclusion**

Every three minutes, a child somewhere in the world is born with a CLP, who, as a result is often unable to eat, speak, socialise or smile.¹ In Africa, approximately one in every 1 000 babies is born with a cleft lip or cleft palate.¹ If they do not receive reconstructive surgery, they may have many healthcare issues.¹ Despite the anaesthetic challenges we may face, the benefits of surgical repair are life-changing to these children and very rewarding.³ This is not simple cosmetic surgery nor a simple anaesthetic.³

**References**

The discovery of anaesthesia, over 170 years ago, heralded the start of an era in which surgery could be performed with greater safety and in a more humane manner. Our discovery of a way to circumvent pain and temporarily extinguish consciousness made life-saving surgery possible. The discovery of anaesthesia is widely considered to be one of the greatest discoveries in history.

Soon after the first public demonstration of general anaesthesia at Massachusetts General Hospital in 1846, an unprecedented enquiry into the workings of the brain commenced and several scientists put forward theories of how they thought anaesthesia worked. In 1847, the German scientist Ernst Von Bibra suggested that anaesthetic vapours worked by dissolving the lipid components of brain cells.1

This theory persisted for more than 50 years and was developed further by Meyer and Overton who postulated a unitary hypothesis of anaesthetic action.1 Throughout the subsequent decades several theories of anaesthetic action would be formulated but none would completely explain how anaesthetic agents worked.

Despite all the activity aimed at determining how anaesthetic agents worked, surprisingly little attention was given to explaining how the brain recovered from anaesthesia, that is, how consciousness was reignited once the effects of the drugs wore off. In fact, up until very recently the process of emergence was considered to be a passive process, purely related to anaesthetic washout.

However, an examination of dose response curves of anaesthetic agents reveals hysteresis in the system, i.e. the reverse process (emergence) does not exactly mirror the forward process (induction). This results in the emergence curve displaying a left shift. This observed hysteresis raises some questions about the mechanism of emergence from anaesthesia.

The Orexinergic System

In 1998, two different groups of researchers, working separately and independently from each other, almost simultaneously discovered a new neuropeptide.2 One group would call this neuropeptide ‘hypocretin’ and the other group would call it ‘orexin’.

Orexinergic neurons center on the lateral hypothalamus and project widely throughout the brain. This system has been shown to play an important role in appetite, feeding and in the maintenance of the awake state (i.e. the orexinergic system is ‘wake-promoting’).3

In 2000, a link between the orexinergic system and narcolepsy, a chronic neurological condition, was made.4 Narcolepsy is characterized by excessive daytime sleepiness, sleep paralysis, cataplexy and hypnogogic hallucinations.5 Immune mediated loss of orexinergic neurons has been shown to be key in the development of this condition.

Case reports have suggested that patients with narcolepsy may be at risk of significantly delayed emergence from anaesthesia.6 This suggests that the orexinergic system may play an active role in emerging from anaesthesia.

Kelz et al. examined the association between the orexinergic system and anaesthetic emergence.7 Their experiments used orexin agonists and orexin receptor antagonists to show the effects of orexin blockade on general anaesthesia. Their findings support the idea that the orexinergic system does play an essential role in emergence from general anaesthesia since in those animals subjected to orexin blockade, the emergence times were significantly prolonged. Their work also suggests that emergence is a separate active process involving distinct neural substrates and not merely the passive reverse of induction.

Neural Inertia

The hysteresis noted in dose response curves implies that within a particular dose range, the sleep-wake state of a subject depends on whether the subject is undergoing induction or emergence, that is, the current sleep-wake state depends on the previous state. At the dose indicated by the arrow in Figure 1, patients may be either awake or anaesthetized depending on which pathway (i.e. emergence or induction) they are on. This lagging behind of
observed phenomenon as compared to blood anaesthetic levels was originally attributed to slow receptor kinetics.

Recent work however has suggested that this explanation may be incomplete. Friedman et al suggest that hysteresis may be attributed to a property of neural circuits called neural inertia i.e. the tendency of neural systems to resist a change in their state.\(^8\)

This inertia affords the brain some degree of stability. From an evolutionary perspective it appears to be a safety mechanism, since if the sleep-wake state lacks stability, one may easily transition between states at any time. This lack of stability is seen in patients who suffer from narcolepsy, in whom uncontrollable episodes of falling asleep occur during the day. The fact that the brain stabilises in either the sleep state or the awake state is described as bistability, i.e. the ability to stabilise in one of two states.

Animal studies have shown that by manipulating the function of neural ion channels, neural inertia can be manipulated.\(^8\) An interesting finding of these studies is that emergence can be manipulated without affecting induction pathways. This adds weight to the argument that different circuits are involved with induction and emergence.

**Facilitating Active Emergence from Anaesthesia**

After the link between the orexergic system and anaesthesia had been established, the next natural step would be to determine whether the orexergic system could be used to facilitate a faster emergence from general anaesthesia. Researchers have shown that the use of an orexin agonist could speed up emergence from ketamine and propofol induced anaesthesia.\(^9,10\)

Dopaminergic and adrenergic pathways in the brain have been thought to be involved in arousal of the brain. Solt et al. studied the effects of methylphenidate on emergence from anaesthesia.\(^11\) Methylphenidate (Ritalin) inhibits dopamine and noradrenaline reuptake in the brain and is used primarily to treat attention deficit hyperactivity disorder. Their study found that intravenous methylphenidate rapidly induced emergence from isoflurane anaesthesia. A follow-up study showed that this could be replicated with propofol anaesthesia.\(^12\) These studies show that it may be possible to accelerate emergence from anaesthesia.

In an attempt to determine whether this effect was due to a general dopaminergic effect or the action of a specific dopaminergic nucleus, further work was done involving selective electrical stimulation of dopaminergic nuclei. The two main dopaminergic nuclei in the brain are the substantia nigra and the ventral tegmentum. It has been found that stimulation of the ventral tegmentum but not the substantia nigra induces emergence from general anaesthesia, similar to the effects seen with methylphenidate.\(^13\) These findings narrow the arousal inducing effects to specific circuits, i.e. those emanating from the ventral tegmentum rather than a widespread dopamine-mediated effect.

Acetylcholine is well known to have stimulatory effects on the brain. The question of whether or not these effects could be put to use in actively inducing emergence was addressed by Kenny et al.\(^14\) They used physostigmine, an acetylcholinesterase inhibitor that crosses the blood-brain-barrier, to increase brain levels of acetylcholine. Their findings showed that increasing acetylcholine levels did not induce emergence from anaesthesia as was seen by the use of methylphenidate.

**Transitional Dynamics**

Until now, we have had little knowledge of how the brain transitions from the anaesthetised state to the awake state; however, more and more work is being done these days to answer some fundamental questions about how this happens. It is now known that the brain does not emerge from anaesthesia in a gradual linear fashion.

Electroencephalographic (EEG) studies have examined the transition of the brain through various states as it regains consciousness. Using analogies from protein synthesis and folding (i.e. Levinthal’s Paradox) it appears that the brain does not sample all of the states available to it on the way to consciousness, instead it ‘jumps’ through a distinct set of states referred to as ‘metastable states’ in that they are stable for a few minutes at a time.\(^15\)

**Connectomics**

The relatively new field of connectomics is described as “the production and study of connectomes: comprehensive maps of connections within an organism’s nervous system, typically its brain…”\(^16\)

The brain has been called a network of networks which is a testament to its astounding complexity. Each neuron may have connections with thousands of other neurons. Connectomics is therefore an attempt to understand how the brain functions by examining its connections.

Areas of the brain may be connected to each other through axonal tracts, that is, they are spatially connected. These connections can be visualised as white matter tracts on images produced by tractography which utilises diffusion weighted...
images from MRI scans to display the connections between different areas of the brain.

Different areas of the brain may also be linked temporally even though they lack a direct anatomical connection, that is, they are activated at the same time and are said to be temporally connected. This is also referred to as functional connectivity.

Functional Connectivity

Recently there has been increasing interest in using the idea of functional connectivity to explain various brain functions. EEG data, collected over different regions of the brain and over a period of time, is analysed for connections between areas. One of the proposed mechanisms of anesthesia is the disconnection of brain regions from each other thereby disabling the brain's ability to generate consciousness. Studies of emergence use the corollary of this idea, that is, on emergence from anesthesia different areas of the brain reconnect in order to generate consciousness.

In their study, Chander et al. describe the brain's trajectory from the anaesthetised state to the awake state using EEG data from 100 patients undergoing orthopaedic surgery under general anaesthesia.17 According to their nomenclature, Slow Wave Anaesthesia (SWA) is that state seen just prior to discontinuing the anaesthetic. This state is characterized by a significantly large delta wave contribution (0.5 – 4 Hz). Non-Slow Wave Anaesthesia (NSWA) is described as that state having a lower delta wave contribution, i.e. it is largely a lower amplitude higher frequency signal.

The majority of patients in this study were shown to transition from Slow Wave Anaesthesia to Non-Slow Wave Anaesthesia. From this state, patients then transitioned to consciousness.

This study also found that the change in EEG patterns from sleep to awake were not gradual transitions of decreasing delta activity. Instead the findings show rapid transitions from one state to the next, where the brain settles for a period of time before rapidly transitioning to the next state. These findings echo the discovery by Hudson et al. of the brain jumping from ‘metastable state’ to ‘metastable state’.15

Of particular interest is the fact that the order of state transition appeared to be important to the quality of the emergence as experienced by the patients. Those patients who did not cycle through the states in a conventional order but woke up directly from the Slow Wave Anaesthesia (SWA) state experienced more pain and agitation, described as an undesirable emergence.

Emergence Delirium and Functional Connectivity

In a study of pediatric patients undergoing minor surgical procedures, Martin et al. also examined EEG data collected during emergence from anaesthesia.18 In keeping with the findings of Chander et al., this study found a stepwise progression through brain states as the patients emerged from general anesthesia. Patients transitioned from a delta dominant state to what they described as an indeterminate state characterised by low voltage high frequency activity. From this state the majority of patients transitioned to a state that had striking similarity to a natural sleep-like state (theta activity and the presence of spindles). The children then woke up gently and without agitation from this stage.

A small group of children did not transition to the natural sleep-like state, instead they emerged directly from the indeterminate state. These children experienced significant delirium upon waking – reiterating the idea that the order of transition to wakefulness is important to prevent emergence delirium.

Current and Future Clinical Applications from the Science of Emergence

Suvorexant (Belsomra) is a new drug used to treat insomnia. It belongs to the newly developed class called orexin antagonists. Since orexins and the orexinergic system stabilise the wake state, the use of an orexin antagonist allows the wake state to give way to sleep. It is pharmacologically distinct from traditional sedatives since it has no action on the benzodiazepine binding site on the GABA\textsubscript{A} receptor.

Studies that demonstrate the effects of methylphenidate on general anaesthesia may explain the clinical observation that patients who are taking methylphenidate to treat ADHD may require higher doses of anaesthetic agents to achieve sufficient depth of anaesthesia.

Unraveling the mysteries of how the brain regains consciousness is likely to provide answers to important questions in the field of anaesthesia - like why some patients take longer to emerge than others. The field is lacking in sufficient studies on human subjects in clinical settings but this likely to change as the scientific community gains greater enthusiasm for exploring emergence.

Even more exciting is the idea that we may be able to control emergence in the same way that we control induction. Not only would this be invaluable to the patient with delayed emergence, but it would also allow a greater margin of extubation safety in the patient with a difficult airway or respiratory disease. A rapid, controlled, and clear wake up could ensure that the patient maintains his/her own airway and breathes adequately.

The economics of healthcare is a consideration the world over, in developing as well as in developed countries. In the perioperative environment, operating room time is a hefty contributor to medical costs. Expediting wake up and extubation would allow for a significant shortening of this time and could therefore drive down expenditure.

Some scientists in the field also point to the fact that increased knowledge about emergence may have beneficial effects in non-anaesthetic fields. The hope is that this science will shine a light on how to reanimate the comatose brain. Could there be a mechanism by which a brain, which has been stabilised in the comatose state, could be nudged towards transitioning to wakefulness? Perhaps the answer to this and other questions could be found in the science of emergence.

References


Three-stage oesophagectomy

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Oesophagectomy is performed worldwide for a variety of indications ranging from benign conditions like oesophageal stricture and achalasia to malignant tumours.1

Three-stage oesophagectomy, also known as Mckeown procedure, involves a laparotomy for freeing and mobilisation of the stomach, a right thoracotomy for the oesophageal resection and a left-sided neck incision for the anastomosis of either the gastric tube or oesophageal conduit which could either be the jejunum or large colon.

The stomach mobilisation and oesophageal resection parts of the three-stage oesophagectomy can be done through a laparoscopic and thorascopic route respectively with some authors suggesting that the laparo-thoracoscopic approach could be better than the classical open Mckeown procedure.

Oesophageal cancer is the eighth commonest cancer in the world with an increasing incidence;2,3 about 30% of these patients are suitable for curative oesophagectomy. There are two main histological types of oesophageal cancers these being squamous cell carcinoma and adenocarcinoma.4 Most oesophageal cancers are squamous cell carcinoma worldwide, but the incidence of adenocarcinoma is rising in the western world, accounting for up to nearly 50% of all oesophageal cancers.1 The remainder of this article will focus on oesophagectomy for oesophageal cancer.

Anatomy of the oesophagus

In an adult the oesophagus is an 18–26 cm muscular tube which serves as a conduit for fluids and food particles from the oropharynx to the stomach. It originates behind the cricoid cartilage at the sixth cervical vertebra and extends up to the tenth thoracic vertebra where it joins the stomach just below the diaphragm.5 It is in close association with the trachea, recurrent laryngeal nerve, left main bronchus, left atrium and aorta within the thorax.

Risk factors

Advanced age, male gender, smoking and thoracic radiation are recognised risk factors for both histological types of oesophageal cancers. Alcohol use, achalasia, poor oral hygiene, low socioeconomic status and black race are associated with squamous cell carcinoma, whereas in Caucasians, gastroesophageal reflux, Barrett’s oesophagus and obesity are associated with adenocarcinoma.2,4,6

Preoperative assessment

Because of the increasing early detection of oesophageal cancers and reflux-associated adenocarcinomas, obesity might be encountered in patients presenting for oesophagectomy. Commonly, patients will be underweight as a consequence of the dysphagia, poor socioeconomic status and cachexia associated with malignancy. Nutritional support should be considered in the malnourished and a multidisciplinary approach, including dieticians, cannot be overemphasised. Parenteral or enteral feeding through a nasogastric or jejunostomy tube should be initiated preoperatively where it is deemed necessary. Nevertheless, delaying surgery for the treatment of nutritional deficiencies by feeding has not been shown to improve outcome.4 Haematinsics should also be given to treat preoperative anaemia. Dehydration should be corrected with fluid therapy which will also unmask the haemoconcentration.

Smoking cessation is advised to minimise respiratory complications perioperatively and also because of the poor wound healing that is associated with it. Chest imaging is useful in detecting hyperinflation which will suggest obstructive airway disease, and any pulmonary infiltrates from either an infective process or aspiration as a result of the oesophageal cancer. Some centres routinely do a lung function test to risk-stratify patients preoperatively and for comparisons at the postoperative period with the preoperative baseline.

Neoadjuvant chemotherapy, with or without radiation, is used increasingly to improve curative resection rate.1,7 There is a delay of four to six weeks before surgery after the chemoradiation to minimise complications like bleeding, poor wound healing and postoperative infection. Commonly used chemotherapeutic agents are cisplatin, and 5-fluorouracil at times as a combination therapy which can increase the associated complications.1
Effort tolerance needs to be established preoperatively. Anaerobic threshold of less than 11 mls/kg/min is associated with poor outcome. Cardiopulmonary exercise testing is ideal where available. Other means of assessing effort tolerance like shuttle walk test, stair test and six minutes’ walk test should be used where cardiopulmonary exercise testing cannot be done.

Intraoperative

As previously mentioned, the McKeown technique involves a laparotomy, right-sided thoracotomy and a left-sided neck incision. Common challenges faced by the anaesthetist include positioning, long duration of surgery, blood loss and one lung ventilation (OLV).

Oesophageal surgery is a relative indication for OLV, but because of the ease of surgical access, it is almost always done during the oesophageal resection. Any method or device could be used for lung isolation depending on familiarity. In our setting a left-sided double lumen tube is used because of availability and a preference of intubating the bronchus of the ventilated lung. Lung protective ventilation has to be adhered to in order to minimise respiratory complications postoperatively which account for the highest morbidity at quoted rates between 17.7–38%. The pulmonary morbidity could either be pneumonia or pulmonary insufficiency requiring ventilation including ARDS.

Fluid therapy is important with excess fluids leading to pulmonary morbidity and a high likelihood of anastomotic leak. Inadequate fluids will also compromise haemodynamics with hypotension and a need for vasopressors which both can lead to poor capillary perfusion, poor wound healing and anastomotic leaks. Goal-directed fluid therapy could help in striking a good balance.

Adequate pain control perioperatively reduces the incidence of pulmonary complications. Thoracic epidural is considered a gold standard in most centres. Some literature suggests that paravertebral blocks are as efficacious as an epidural with fewer side-effects.

Hypotension can occur as a consequence of blood loss or compression of major vessels and the heart during thoracic dissection and also as a result of dehydration from the preoperative period unmasked by the anaesthetic agents. Compression of the heart can also result in arrhythmias. Good communication between the surgical team and the anaesthetist is important to recognise and deal with the complication timeously and appropriately.

Postoperative

Patients are cared for in a high dependency unit. With the advent of fast-track surgery, minimally invasive oesophagectomy and adequate pain control with thoracic epidural analgesia, some authors suggest that patients can be cared for in the ward unless there is a need for ventilation postoperatively which is currently uncommon with most patients being extubated in theatre.

Conclusion

Success for oncological surgery should not only be limited to 30-day morbidity or mortality, but should also include recurrence of the cancer. Anaesthetists, as the perioperative physicians, can have an influence on morbidity, mortality and cancer recurrence, a concept called “onco-anaesthesia”.

References

Managing an acute pulmonary embolism on the table

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Pulmonary embolism (PE) occurs in less than 1 in 1 000 in the general population, but is one of the commonest causes of death during hospital admissions. The incidence of pulmonary embolism during an anaesthetic, while unknown and exceedingly uncommon, is a devastating event for all involved, having a mortality of over 80%, half of whom will demise within the first 15 minutes.

The pathophysiology is simple; a piece of clot – usually from a deep vein thrombosis (DVT) – passes through the heart and lodges in one of the pulmonary arteries or arterioles producing an ischaemic area of lung with a resultant ventilation:perfusion mismatch. The size of this shunt is directly related to the size of the clot and the vessel that it occludes. The result is an increase in the alveolar–arterial oxygen difference, the arterial–end tidal carbon dioxide difference, hypoxia, acidosis, acute right ventricular failure, hypotension and cardiogenic shock and death.

Massive PE is easy to recognise due to catastrophic cardiac collapse, but is very difficult to treat, while smaller non-fatal pulmonary emboli can prove a diagnostic challenge. Management after initial diagnosis and resuscitation requires a delicate balance of anticoagulation and thrombolysis whilst avoiding bleeding.

Patients at risk for having a pulmonary embolus

The risk increases exponentially with a greater number of risk factors.

- Deep vein thrombosis – having a current DVT or history of DVTs and/or pulmonary embolus.
- Inherited clotting abnormalities – Factor V Leyden and protein S and C deficiency.
- Advancing age – above the age of 60 the risk doubles every 10 years.
- Gender – there is no male or female predominance.
- Immobility – being bed-ridden or immobile for a period of time.
- Recent surgery, bone fractures, trauma or indwelling catheters (especially central venous lines which can be associated with upper limb DVT).
- Associated disease states – cerebrovascular accident, cardiac failure, malignancy.
- Pregnancy, hormone therapy and contraceptive pills.
- Smoking.
- Surgery where non-haematological material may enter the venous system – fat embolus, amniotic fluid embolus, tumour embolus (especially renal cell carcinoma), bone embolus, renal calculi, foreign body embolus, (cement, catheters) and air embolus.

Signs and symptoms

The classic signs and symptoms of dyspnoea, chest pain, cough, fever, haemoptysis and syncope will not be seen under anaesthesia, making a reliance on monitors and other investigations the mainstay of diagnosis. Around 30% of PEs are asymptomatic, making a history unreliable. The following should trigger alarm bells:

- Signs of a DVT – unilateral leg swelling is seen in up to 80% of patients with a PE.
- The classically described S1Q3T3 ECG pattern is only seen in 20% of pulmonary emboli.
- Sudden drop in end tidal CO2 (ETCO2).
- Tachycardia and hypotension.
- Hypoxia (especially of sudden onset).

Diagnostic tests

In the presence of cardiogenic shock (tachycardia, hypotension, poor perfusion, raised central venous pressure) due to a suspected pulmonary embolus, the following investigations can aid the diagnosis:

- Arterial blood gas (ABG) – classically shows a raised \( P_{CO_2} \), hypoxia and acidosis (predominantly respiratory acidosis but there may be a concomitant metabolic acidosis due to poor perfusion following cardiogenic shock).
The $P_{\text{aCO}_2}$–ETCO$_2$ difference will be raised due to the increased shunt, as part of the lung is no longer being perfused.

Alveolar–arterial $O_2$ gradient will be increased due to perfusion:ventilation mismatch.

The classic blood gas findings of a PE in an awake, non-ventilated patient can be different to those of the ventilated patient as hyperventilation accompanying a pulmonary embolus causes a respiratory alkalosis initially.

- ECHO – TEE or TTE depending on the availability, looking for right ventricular dysfunction.
- Spiral CT scan or CT angiogram of the chest is the gold standard for diagnosis but is impossible to do on an unstable patient in an operating theatre.
- D Dimers – these fibrin degradation products show that formed thrombus is being broken down, but are not available at the bedside and are also raised following trauma, surgery, as well as in DVT and PE.
- Ultrasound of the limbs may produce evidence of a DVT.
- Troponin assays – elevated troponin T or I indicate myocardial damage which is suggestive of an acute coronary syndrome rather than an acute PE.
  - Troponins elevated immediately after a suspected PE is suggestive of coronary syndromes as troponin levels take 3–6 hours to rise after myocardial damage.
  - Any cardiac condition associated with ischaemia can also raise troponins.
- V:Q scans – ventilation:perfusion scans’ role is in awake, stable patients, not under anaesthesia. The advantage is they require lower doses of radiation and no contrast media offering some benefit in pregnancy and renal failure. Positive scans have great predictive value for initiating treatment while negative scans do not rule out PE.

Differential diagnosis

While the diagnostic tests may help ascertain a more accurate diagnosis, the differential diagnosis of any cause of rapid onset cardiogenic shock must be considered:

- Anaphylaxis
- Aortic dissection
- Stroke
- Cardiac arrhythmias (tachyarrhythmias, bradyarrhythmias, heart blocks)
- Sepsis
- Hypertrophic obstructive cardiomyopathy (HOCM)

Management

With little time between the onset of symptoms and death following a pulmonary embolus, diagnosis, resuscitation and management of the condition need to be done simultaneously.7

1. Systemic function support
   - Resuscitating and restoration of cardiovascular function.
   - Early CPR is often needed.
   - Ventilation with 100% oxygen in an attempt to reverse hypoxia.
     - Hyperventilation will not decrease the $P_{\text{aCO}_2}$ due to the V:Q mismatch while high levels of PEEP and high ventilatory pressures may diminish pulmonary blood flow from the right ventricle.
   - Inotropic support.
   - Diagnosis with ABG and ECHO.
   - Eliminate other causes of haemodynamic instability (myocardial infarction, arrhythmias, anaphylaxis, cerebral bleed and aortic rupture).
   - Once stable, CT scan or CT angiogram.

Once the patient is stabilised and a definitive diagnosis is made, a variety of treatment options are available, depending on local expertise and availability of equipment. The optimal treatment path has not been decided upon yet. Reperfusion should be undertaken as soon as possible and is often needed as a part of resuscitation of a patient who remains haemodynamically unstable.8

2. Reperfusion of area affected by embolus
   - Thrombolyis – using urokinase, tPA (tissue plasminogen activator) is the first-line therapy to attempt to lyse the embolus. It should be administered as soon as a diagnosis has been made in patients who remain haemodynamically unstable.
     - Systemic – easy and quick to deliver and can be given via a peripheral line, but with a high risk of intercranial, wound and surgical-site bleeding.
     - Catheter-directed thrombolysis – smaller doses given into the occluded vessel or area with less risk of bleeding complications.9,10
     - Open sternotomy placement of catheter directly into right ventricle or pulmonary artery.

3. Clot removal
   - Standard therapy is an embolectomy from the pulmonary artery and/or right ventricle.
   - Percutaneous venous thrombectomy – used if not fit for surgery. Fifty percent success rate.

4. ECMO

If instituted rapidly, bypassing the lungs, ECMO allows for oxygenation while thrombolysis takes place. Veno-arterial cannulation during initial resuscitation pre- or postthrombolysis has been described. High risk of bleeding.11
5. Prevention of further emboli

- Initial anticoagulation is started as soon as possible to prevent further clot propagation. The practice of combined thrombolysis and anticoagulation in the acute period after proven DVT and PE is increased. The choice of agent is determined by local practice, the type of surgery, in combination with the patient’s risk factors.
  - Vitamin K antagonists inhibit the synthesis of Factors II, VII, IX and X.
  - Heparins inhibit Factor Xa and thrombin indirectly through antithrombin III.
  - Fondaparinux indirectly inhibits Factor Xa only via antithrombin III.
  - Rivaroxaban, apixaban and edoxaban directly inhibit Factor Xa.
  - Dabigatran directly inhibits thrombin.
- Insertion of venocaval filters – though controversial – has been shown to decrease the incidence of pulmonary emboli from proven DVT in high risk patients but may have a risk of venocaval occlusion. New removable filters may have a role to play during a high-risk episode.7,12

Bleeding

A major complication of thrombolysis and anticoagulation is bleeding which is associated with marked morbidity and mortality. Patients who need thrombolysis and anticoagulation during or soon after surgery are obviously at high risk for developing a bleeding complication and should be managed by maintaining clotting factors and direct pressure where possible. Patients who have not had surgery, at increased risk of bleeding after anticoagulant therapy, in descending order, are13:
  - Active gastroduodenal ulcer
  - Bleeding during the three months before admission
  - Platelet count < 50/l
  - Advanced age ≥ 85 years
  - Severe renal failure GFR < 30 ml/min/m²
  - Hepatic failure (INR > 1.5)
  - Patients in intensive care unit/coronary care unit
  - Presence of central venous catheter
  - Rheumatic disease
  - Cancer at the time of hospital admission

Conclusion

The rare event of sudden hypotension, decreased end tidal carbon dioxide and hypoxia under anaesthesia has a potential fatal outcome and should be managed as a pulmonary embolus, requiring rapid resuscitation, early diagnosis with thrombolysis and anticoagulation. Persistent haemodynamic instability requires early intervention and clot removal if possible. In the perioperative period bleeding is an ever-present risk.

References

Clinical use of nerve stimulators

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Nerve stimulators are used in the following clinical roles:
1. Neuromuscular monitoring of muscle relaxant effects
2. Location of nerves for loco-regional anaesthesia
3. Surface nerve mapping

The physical properties of each of these monitors differ allowing for different detection techniques and strength of stimulation dependent on the site stimulated.

The physics behind how a nerve stimulator works 1,2

Maximal stimulus: A pulse duration and current large and long enough to stimulate all nerve fibres.

Supra maximal stimulus: A stimulus 10–20% greater than the stimulus required to stimulate all fibres ensuring all muscle fibres are stimulated to contract every time, producing the maximal force. This is 2.5 – 3 times greater than required to produce the initial response – what we use clinically.

The neural response depends on current density not voltage. To achieve a consistent, repeatable maximal response, the current density must be greater than what is needed to get a maximal response.

Using Ohm’s law where: \( V = IR \) [Potential difference (Voltage) = Current x resistance]

\[
\text{Current} = \frac{\text{Voltage}}{\text{Resistance}}
\]

To produce a constant current with changes in skin resistance (normal between 500 – 2000Ω) requires a change in voltage.

Old nerve stimulators required a change in voltage to be dialled in, to deliver the required current. (The stimulator showed you what current was given and you had to make the adjustments).

All current nerve stimulators are constant current stimulators which through feedback detect changes in the current delivered and alter the voltage accordingly, so the desired current is always given.

Determinants of neural stimulation

The following factors will determine if a nerve will respond to a stimulus:
1. Rheobase of the nerve – the inherent minimum current needed to stimulate that nerve.
2. Chronaxy of the nerve – the inherent length of time the nerve needs to be stimulated to produce a response.
3. Polarity of the electrodes – negative (black) electrodes are more efficient at causing a nerve to depolarise.
4. Distance of the nerve from the electrode – the further the nerve is from the electrode the more current is needed to stimulate it.
   a. Coulombs law: Current required = Minimal current/distance
4. Area of the electrode – smaller electrodes will produce a greater current density.

Measurement of response

1. Visual
   - Inaccurate; unable to see fade.
2. **Tactile**
   - Better than visual; may detect fade especially with DBS.

3. **Clinical**
   - Patients may be able to breathe, lift their head and squeeze a hand while still having 75% of their NMJ receptors blocked.

4. **Acceleromyography**
   - The commonest method of monitoring a block.
   - A pizo-electric crystal is usually attached to the thumb and its acceleration measured after having the ulnar nerve stimulated.
   - Applying Newton’s second law:
     \[
     \text{Force} = \text{Mass} \times \text{acceleration}
     \]
   - The thumb provides a constant mass therefore the force of contraction = acceleration.

5. **Mechanomyography**
   - A cumbersome time consuming method that involves fixing the limb and applying a preload to the thumb to ensure contraction is detected from zero.
   - A transducer measures the force of contraction, which is then amplified to produce a value.

6. **Electromyography**
   - An ECG for muscles that can be used for muscles that are not available for the mechanical stimulation.
   - 5 Electrodes are attached as follows
     1. 2 stimulating electrodes over the nerve
     2. 1 receiving electrode over the muscle
     3. 1 reference electrode on the tendon
     4. 1 ground electrode to diminish artefact (between the stimulating and receiving electrodes).
   - Artefacts are common especially with electrical interference
   - Electrodes need to be placed at least 15 minutes prior to stimulation to diminish early detection.
   - Incorrect electrode placement is easy.

**Site of measurement**
The effect of neuromuscular blocking drugs on different muscle groups is not uniform. The adductor pollicis, which is the easiest muscle to monitor, is much more sensitive to the effects of neuromuscular blocking drugs than the laryngeal muscles and diaphragm, displaying faster onset time, slower recovery and requiring lower doses to produce complete blockade. Recovery of the adductor pollicis therefore ensures recovery of the airway muscles. Other easy-to-use sites are the facial nerve with detection of orbicularis oculi (there is even an acceleromyograph connection made for the upper eyelid), the peroneal and the posterior tibial nerve in the leg.

**Clinical modes of neuromuscular monitoring**

**Single Twitch**
A single twitch of 0.2msec duration is of very little clinical use as it occurs in isolation and demonstrates little other than that the muscle is stimulated.

**Train-of-four (TOF)**
Four twitches of 0.2msec duration at 2Hz (a twitch every 0.5 sec); 4 twitches allow comparison between each other and are used in assessing recovery from blockade.

Blockade with a DMR produces a TOF pattern that has a constant diminution in twitch height over time. NDMRs produce a pattern where each twitch is smaller than the preceding, twitch while the number of twitches increases with progressive recovery.

Two different patterns can be utilised clinically with a TOF.
**TOF count:** is the number of twitches present and are referred to as T1, T2, T3, T4.
**TOF ratio:** Once all four twitches in TOF are present the ratio between the first (T1) and fourth twitch (T4) is calculated which represents the amount of recovery present. This needs to be objectively measured using an acceleromyograph or a mechanomyograph.

**Train-of-four in depolarising and non-depolarising muscle relaxants**

**Train-of-four ratio**

A single twitch of 0.2msec duration is of very little clinical use as it occurs in isolation and demonstrates little other than that the muscle is stimulated.
Double burst stimulus (DBS):
A burst of 2 or 3 impulses separated by 0.75 seconds. Two patterns are used, 3:2 or 3:3, representing the number of twitches in each burst. Each burst occurs at a rate of 50Hz, (3 twitches take 0.06sec and 2 twitches 0.04 seconds). It is used in place of a TOF when no objective detector of muscle contraction is available as the larger contraction produced is easier to assess manually than a single twitch from a TOF.

Tetanic stimulation:
50Hz burst of stimulation lasting for 5 seconds. The prolonged tetanic stimulus mobilises all stores of ACh and stimulates excess production of ACh to repopulate ACh stores. Clinically, it is combined with a post tetanic count.

Post tetanic count (PTC):
Uses the mobilised ACh from a tetanic stimulation to evaluate intense blockade, when no twitch is present on a TOF. 3 seconds after a tetanic stimulus, a single twitch at 1 second intervals is delivered. The number of twitches present allows an estimation of how long it will take until T1 appears on a TOF. This varies for each agent. (As a rough guide 10 twitches on a PTC means that a single twitch on a TOF will occur in about 10 minutes.)

Fade
Is a reduction of muscle response from the first to last twitch in a TOF in NDMR. The mechanism of this is twofold:

NDMR block the pre-synaptic cholinergic receptors (along with post-synaptic nicotinic receptors) and this inhibits the reuptake of choline. This results in less ACh being produced.

ACh competes with the NDMR for binding sites. Following a stimulus, a large excess of ACh is released into the neuromuscular junction. ACh is metabolised faster than the NDMR is removed. With each subsequent stimulus, fewer receptors are available as they are bound by the NDMR, producing progressively weaker muscle contraction.

Phase II block
Fade occurring on a TOF when using a DMR. The reason is poorly understood, but revolves around continual binding and activation of the ACh receptor by the DMR, producing an ionic imbalance in the neuromuscular junction as Na⁺ is continually moving into the cell. AChE inhibitors such as neostigmine will not reverse this phenomenon.

Clinical use of nerve stimulating modalities

<table>
<thead>
<tr>
<th>MODE</th>
<th>CLINICAL USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single twitch</td>
<td>Little use</td>
</tr>
<tr>
<td>Train-of-four</td>
<td>Once T2 is present reversal with neostigmine is probable. Recovery of blockade back to normal. Complete reversal.</td>
</tr>
<tr>
<td>Double burst stimulus</td>
<td>Recovery from blockade where no objective monitor is available.</td>
</tr>
<tr>
<td>Post tetanic count</td>
<td>Depth of block Recovery from intense blockade to a single twitch on TOF</td>
</tr>
</tbody>
</table>

Clinical end points of neuromuscular blocking drugs

<table>
<thead>
<tr>
<th>CLINICAL PARAMETER</th>
<th>NERVE STIMULATOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep block - no movement possible</td>
<td>PTC 0 or 1</td>
</tr>
<tr>
<td>Surgical block - movement may occur</td>
<td>TOF T1–T2</td>
</tr>
<tr>
<td>Reversal with neostigmine possible</td>
<td>TOF &gt; T2</td>
</tr>
<tr>
<td>Airway reflexes returned</td>
<td>TOF ratio &gt; 90%</td>
</tr>
</tbody>
</table>

Should all patients receiving NDMR be monitored with a nerve stimulator?

Viby-Morgensen’s ground breaking study in 1979 alerted one to the unpredictability of NDMR despite monitoring with nerve stimulators. Studies since have shown that nothing much has changed in the ensuing years.6,5 Neuromuscular monitoring has not decreased this unpredictability and the quest for a short acting, predictable agent continues. Residual paralysis has associated morbidity and mortality. Why do NDMRs present such a problem with the predictability of termination of effects?

1. No ideal neuromuscular blocking agent exists.
   - All agents have an onset time that is inversely related to the agent’s potency (potent agents take longer to work and last longer).
   - All agents require some degree of organ dependent metabolism for their spontaneous elimination.

2. There is vast inter-patient and drug variability.
   - Renal and hepatic function vary between patients and age groups.
   - Adjuvant agents such as magnesium, propofol, sevoflurane and opiates may alter pharmacokinetics and dynamics.

3. Top up doses increase the unpredictability of duration of action further.
   - Doses of 10% of the intubation dose have up to 2-fold difference in duration of action.
4. Reversal by competitive antagonism is not completely effective.
   ▫ The balance of amount of NDMR to ACh is constantly changing and until the agent is fully metabolised this can revert to paralysis.
5. Reversal agents have significant adverse effects.
   ▫ Neostigmine (bradycardia, peristalsis, abdominal cramps, bronchospasm, nausea and vomiting, muscle paralysis)
   ▫ Glycopyrrolate (tachycardia, dry mouth, cardiac arrhythmia, urinary retention, blurred vision, disorientation)
6. Monitoring provides little improved predictability.
   ▫ Due to constant competition between ACh and the NDMR, which is compounded by drug and patient variability.

Neuromuscular monitoring in the era of sugammadex

The introduction of the novel reversal agent sugammadex has provided a solution to the unpredictability of NDMR. Due to its irreversible binding and neutralising of rocuronium, vecuronium and to a lesser degree pancuronium, the effect of even large doses of amino steroidal muscle relaxants can be rapidly terminated. Logically, one expects that neuromuscular monitoring is no longer needed as complete reversal can now occur.

Unfortunately, the binding of rocuronium and sugammadex is a 1 to 1 interaction, so dosing must be adequate to allow encapsulation of all rocuronium molecules. If under-dosing occurs, residual curarisation is possible while overdosing results in wastage of a rather expensive drug. Neuromuscular monitoring has become imperative when using sugammadex as it determines the dose of sugammadex needed.

Dosing of sugammadex according to nerve stimulation

<table>
<thead>
<tr>
<th>Block</th>
<th>Nerve stimulator tracing</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete: straight after intubating dose</td>
<td>Initial fade may still be present</td>
<td>16 mg/kg</td>
</tr>
<tr>
<td>Deep blockade</td>
<td>TOF of 0 and a PTC of 0–10</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>Moderate</td>
<td>PTC &gt; 10 or twitch on TOF</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>“Neostigmine reversible” block</td>
<td>TOF of &gt; 2 twitches</td>
<td>2 mg/kg</td>
</tr>
</tbody>
</table>

This tracing of a TOF ratio shows the danger of inadequate dosing of sugammadex. Its recognition and correction was possible due to continuous neuromuscular monitoring.

- Sugammadex at 0.5 mg/kg was given to an elderly female with a TOF ratio of 25%
- Initial recovery to a TOF ratio of 80% occurred within 2 minutes.
- The TOF ratio then reverted to a constant 60–70%
- A second dose of 1 mg/kg of sugammadex was given resulting in a sustained TOF of > 95%.

Conclusion

The use of neuromuscular monitoring has provided a snap shot of an everchanging balance between paralysis (amount of muscle relaxant present in the body) and reversal (amount of acetylcholine present). Due to the unpredicatable nature of this balance, the use of neuromuscular monitoring has not changed the incidence of postoperative residual curarisation even when reversed competitively with neostigmine. The advent of the neuromuscular blocking agent binding reversal agent sugammadex has produced the need for better understanding and greater use of neuromuscular monitoring as recovery from different depths of blockade can now be predictably controlled and managed.

References and further reading

Anaesthesia for a patient with Achondroplasia presenting for Caesarean section

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Introduction

Achondroplasia is the commonest form of dwarfism and occurs in approximately 1.5 per 10 000 live births.1 Achondroplasia is caused by mutations in the Fibroblast Growth Factor Receptor 3 Gene (FGFR 3) and occurs as a result of sporadic mutations in 90% of cases, but may also be inherited as an autosomal dominant trait.2 Due to the relatively small maternal pelvis but normal size of the foetal head cephalo-pelvic disproportion is common in pregnant achondroplastic patients3 and the majority of them present for Caesarean delivery. Both general and regional anaesthesia may be complicated in achondroplastic patients especially when performed during the third trimester of pregnancy.

Anatomical and pathophysiological abnormalities

A reduced rate of endochondreal ossification in association with normal periosteal bone formation4 results in the characteristic appearance of achondroplastic dwarfs: short stature with proximal limb shortening; large head with frontal bossing, flattened nasal bridge and maxillary hypoplasia as well as spinal deformities in the form of lumbar hyperlordosis and thoracolumbar kyphosis.1

The brachycephalic large head, facial features, large tongue and narrow upper airway predispose these patients to upper airway obstruction and obstructive sleep apnoea.5-7 There are also several case reports of difficult laryngoscopy and tracheal intubation5-7 but Mayhew, Katz, Miner et al. encountered no difficulty in the airway management of 26 achondroplastic patients presenting for 37 general anaesthetics.4 It is however important to note that none of the 26 patients were pregnant.

Proximal spinal cord compression caused by foramen magnum stenosis may result in central apnoea in patients with achondroplasia and hyperextension of the neck should always be avoided.8 This limitation of neck extension may contribute to the difficulties encountered in tracheal intubation.5,7 It has also been postulated that the increased incidence of hydrocephalus in achondroplastic patients may be due to reduced cerebrospinal fluid flow at the level of the foramen magnum stenosis.1

Numerous other spinal abnormalities in patients with achondroplasia may result in neuraxial anaesthesia being very difficult to perform. Bony landmarks are often difficult to identify due to the lumbar hyperlordosis and thoracic kyphoscoliosis.9 Abnormally shaped vertebrae and hyperplastic discs result in smaller than usual epidural and subarachnoid spaces.1 This may result in difficulties in identifying the epidural space as well as difficulties in feeding epidural catheters. Accidental dural puncture is also more common and more difficult to identify.6 Engorged epidural veins increase the risk of venous puncture and contribute to the unpredictable spread of local anaesthetic.10

The kyphoscoliosis and lumbar hyperlordosis commonly seen in patients with achondroplasia may lead to restrictive pulmonary dysfunction characterized by reduced vital capacity and reduced functional residual capacity.1 The restrictive lung disease as well as the upper airway obstruction and sleep apnoea may contribute to the development of pulmonary hypertension and cor pulmonale.1 In pregnant achondroplastic patients the foetal head often cannot engage in the narrow pelvis. As a result the uterus remains entirely intra-abdominal and splints the diaphragm, further reducing the functional residual capacity.9 The haemodynamic effects of aorto-caval compression by the intra-abdominal uterus are also likely to be more pronounced especially with neuraxial anaesthesia.1,10

Anaesthetic technique

The anaesthetic management of a patient with achondroplasia presents unique challenges to the anaesthetist. The addition of the anaesthetic risks associated with the third trimester of pregnancy mandates meticulous planning by a multidisciplinary team consisting of anaesthetists, obstetricians, neonatologists and midwives. A thorough preoperative workup of the patient is essential.

Historically, despite the potential difficulties associated with the airway management of achondroplastic patients, general anaesthesia has been favoured over regional anaesthesia.7 There are however numerous case reports of Caesarean sections

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being performed under regional anaesthesia in patients with achondroplasia.3,9,11,12

Due to the proximal limb shortening, non-invasive blood pressure monitoring may be difficult.1 Peripheral intra-arterial blood pressure monitoring should be considered in anticipation of the more pronounced haemodynamic effects of aorto-caval compression. The placement of peripheral lines may be more difficult due to the presence of excess skin and soft tissue, and the landmarks for the placement of central venous catheters may be more difficult to identify.4 The main concern with providing general anaesthesia to pregnant patients with achondroplasia is the potential difficulty of the airway management. Aspiration prophylaxis should always be administered but sedative premedication is contraindicated in patients with central or obstructive sleep apnoea. A meticulous airway management plan should be in place and excessive extension of the neck should always be avoided.5 The endotracheal tube size should be reduced and should be based on the patient’s weight.4 If significant thoracolumbar kyphosis is present, cardio-respiratory function may be compromised2 and ventilation may be problematic.

All anaesthetic drugs should be dosed according to the patient’s weight as the use of average adult dosages will possibly result in overdosing.13 The anatomical abnormalities present in the thoracolumbar spine may make regional anaesthesia technically more difficult in patients with achondroplasia and the risk of complications is increased due to the smaller than usual epidural and subarachnoid spaces.6,11 Due to the unpredictable spread of local anaesthesia, there are no epidural dosage guidelines. The volume of the test dose should be reduced and local anaesthesia should be titrated against the block height in small incremental doses.9 Wardall and Frame reported that a dose of only 5 ml of 0.5%plain bupivacaine produced a block to T4 in a pregnant patient with achondroplasia.10 The slow onset of bupivacaine makes it difficult to titrate precisely and it has been suggested that the use of a local anaesthetic with shorter onset time may be more appropriate.1 Carstoniu, Yee and Halpern gave a test dose of 1 ml lidocaine 2% with epinephrine 1:200 000 as a test dose. 5 minutes later they administered 3 2 ml doses of the same solution at 3 minute intervals followed by a 1 ml bolus together with 50 µg fentanyl prior to skin incision. A T5 level was established.11

As epidural anaesthesia allows for titration of the local anaesthetic, it is preferred to spinal anaesthesia. However, the titration of dose to block height is time consuming and epidural anaesthesia may not be ideal in patients presenting for emergency Caesarean section. There are only a few case reports of the successful use of spinal anaesthesia for Caesarean section in patients with achondroplasia. Ravenscroft, Govender and Rout reduced their standard subarachnoid dosage regime for emergency Caesarean section by 30% and produced a block to T3.12 Osorio Rudas, Socha García, Upegui et al. administered 5 mg of hyperbaric bupivacaime together with 64 µg of morphine and 16 µg of fentanyl into the subarachnoid space as part of a combined spinal epidural technique and produced a sensory block up to T4.14 Crawford and Dutton recommend the use of microspinal catheters and the administration of incremental doses of local anaesthetic, if spinal anaesthesia is to be considered.15

Irrespective of which neuraxial technique is used, the haemodynamic effects of aorto-caval compression may be more severe than in patients who do not have achondroplasia and should be aggressively managed.

Summary

The management of a pregnant patient with achondroplasia requires a multidisciplinary team approach. After a thorough preoperative assessment of the patient a meticulous anaesthesia plan needs to be devised. Both general and regional anaesthesia pose significant risk to patients with achondroplasia, especially during the third trimester of pregnancy, and management plans need to be individualized.

References

Anaesthetic management in paediatric burns

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Introduction

Children are typically prone to burns due to the inability to recognise danger (in younger age groups) and the risk-taking behaviours of the older, mobile child. They also have thinner skin, lose proportionally more fluid, are more prone to hypothermia and mount a greater systemic inflammatory response. Most burns are caused by thermal injury (scalds, flame or cold) and less frequently by electrical, radiation or chemical injury. The severity of a burn injury is dependent on age, the depth of burn, the total body surface area (TBSA) involved, the location of the burn injury, and the presence of inhalation injury. Surgical procedures in burns can be broadly divided into four groups: supportive (resuscitation, airway and pain management, colostomy); decompressive (fasciotomy, laparotomy for abdominal compartment syndrome); ablative (sloughectomy, debridement, amputations) and reconstructive (split skin grafts, flaps). Nowadays we appreciate that burn anaesthesia has a high complication rate. Contributing to this is sepsis; multiple organ failure; bleeding; difficulties in thermoregulation; the hypermetabolic state; nutritional and electrolyte imbalances; and the rapid rate at which decompensation can take place.

Improvement in patient outcomes has been attributed to advances in the understanding of burn injury pathophysiology, improved burn shock management, early aggressive surgical intervention and the development of specialised burn treatment centres where there is the early protocolised care of a multidisciplinary team which appreciates the essential need for meticulous attention to detail to ensure good outcomes.

Classification

Burn wound severity is quantified according to the TBSA burned and the wound depth. The TBSA burned is typically estimated by a head-to-toe visualisation of the wounds and subsequently calculated according to the ‘Rule of nines’ in adults, and the Lund-Browder age/growth-adjusted chart for children (Figure 1). This is essential as it affects many aspects of care, e.g. fluid resuscitation, drug dosing, surgical intervention, and outcome. Wound depth is based on the anatomical layers of the skin (Table 1). Reassessment of burn depth should be repeated 72 hours post injury as this may change as a result of management and interventions.

Table I. Classification of burns based on depth

<table>
<thead>
<tr>
<th>New classification (old classification)</th>
<th>Depth</th>
<th>Etiology</th>
<th>Appearance</th>
<th>Sensation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superficial</strong> (1st degree)</td>
<td>Confined to epidermis</td>
<td>Sunburn</td>
<td>Dry, red blanches oedematous soft, peeling</td>
<td>Sharp, uniform pain</td>
<td>Heals spontaneously ± 7 days</td>
</tr>
<tr>
<td><strong>Partial thickness</strong> (2nd degree)</td>
<td></td>
<td>Sunburn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Superficial</td>
<td>- Epidermis &amp; upper dermis</td>
<td>Scalds</td>
<td>Mottled &amp; red blanches</td>
<td>Dull or hyperactive pain</td>
<td>Heals spontaneously 14 – 21 days Requires excision &amp; grafting</td>
</tr>
<tr>
<td>- Deep</td>
<td>- Epidermis &amp; deep dermis</td>
<td>Flash burns Weak chemicals</td>
<td>Red or pink blisters</td>
<td>Sensitivity to air or temperature</td>
<td></td>
</tr>
<tr>
<td><strong>Full thickness</strong> (3rd degree)</td>
<td>Destruction of epidermis &amp; dermis</td>
<td>Immersion</td>
<td>No blanching</td>
<td>Painless to touch &amp; pin prick</td>
<td>Granulates and requires grafting: limited function</td>
</tr>
<tr>
<td>(4th degree)</td>
<td>Muscle, fascia, bone</td>
<td>Flame Electrical Chemical</td>
<td>Pale white or tan Charred, hard, dry, leathery</td>
<td>May hurt at deep pressure</td>
<td>Requires extensive debridement</td>
</tr>
</tbody>
</table>
Pathophysiology

Skin protects the host from bacterial invasion, and prevents heat, fluid and electrolyte losses. Its elasticity allows movement and growth; it has excretory (e.g., urea, water, ammonia) and endocrine (vitamin D) functions; and is the sensory and psychosocial interface. Major burns can thus cause massive heat, fluid and electrolyte losses. Its elasticity allows movement affecting virtually all organ systems. Burn injury pathophysiology evolves in two distinctive phases; an acute phase typified by burn shock which usually resolves within 24–48 hours, followed by a hypermetabolic phase which has been known to last up to 18 months after the burn.1,9

The initial phase occurs due to the release of circulating mediators such as tumour necrosis factor and interleukins that result in a systemic inflammatory response syndrome. Within six to eight hours of injury, increased microvascular permeability, vasodilatation, vascular stasis, decreased cardiac contractility and cardiac output cause significant oedema. The fluid and electrolyte leak from intravascular to interstitial space combined with evaporative fluid losses further impairs perfusion resulting in burn shock, a combination of distributive, hypovolemic and cardiogenic shock. Fluid requirements in the acute resuscitative phase (first 24 hours) are traditionally calculated using the Parklands formula: 2-4 ml x body weight x TBSA burned. Half of this is given in the first eight hours post injury and the rest over the following 16 hours.1,10

The hypermetabolic response occurs due to a surge in catecholamines and corticosteroids. The severity of this hyperdynamic, hypercatabolic response is related to the TBSA burned and the duration of exposure. Left untreated this can lead to physiologic exhaustion and death. Strategies to ameliorate this response include early surgical intervention, maintenance of a warm environment, constant nutritional support to replace

<table>
<thead>
<tr>
<th>System</th>
<th>Early / resuscitative phase (&lt; 48 hrs)</th>
<th>Late / hypermetabolic phase (&gt; 48 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Upper: laryngospasm, obstruction, oedema, hoarseness, stridor Lower: inhalation injury, chemical pneumonia, bronchospasm, respiratory distress syndrome, pneumonia, pulm oedema, V/Q mismatch</td>
<td>Circumferential chest wall restriction, tracheal stenosis, infection</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>“Fluid creep” oedema after over-resus ↓ CO, ↑ SVR, hypovolaemia, ischaemic reperfusion injury</td>
<td>↑ CO, ↑ myocardial oxygen consumption, tachycardia, ↓ SVR, systemic hypertension</td>
</tr>
<tr>
<td>Renal</td>
<td>↓ GFR, myoglobinuria, early AKI</td>
<td>↑ GFR, tubular dysfunction, late AKI</td>
</tr>
<tr>
<td>Endocrine &amp; Metabolic</td>
<td>Release of stress hormones, ↓ T₃ and T₄ Hypoparathyroidism → hypoCa, hypoMg, hypoPO₄, hypoNa and hyperNa</td>
<td>↑ metabolic rate, ↑ core body temp, ↑ muscle catabolism, ↑ lipolysis, ↑ glucolysis, ↑ futile substrate cycling, ↑ insulin resistance, ↓ thyroid hormones, ↓ Vit D, ↓ parathyroid hormone, all electrolytes may be affected</td>
</tr>
<tr>
<td>Hepatic</td>
<td>↓ perfusion, hepatic apoptosis with ↑ AST, ALT, bilirubin ↑ Intrahepatic fat and oedema</td>
<td>↑ metabolism, ↓ albumin and transferrin, ↑ acute phase proteins</td>
</tr>
<tr>
<td>Haematologic</td>
<td>Haemoconcentration initially followed by haemodilution with resus, blood loss and erythrocyte damage from heat. Haemolysis, thrombocytopena</td>
<td>Anaemia, hypercoagulable state, infection → sepsis, DIC</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>↓ perfusion with mucosal damage (early enteral feed encouraged), stasis, ischaemia Endotoxaemia</td>
<td>Stress ulcers, adynamic ileus, acalculous cholecystitis Bowel ischaemia, endotoxaemia, abdominal compartment syndrome</td>
</tr>
<tr>
<td>Neurologic</td>
<td>↑ cerebral oedema, ↑ ICP, confusion</td>
<td>Burn encephalopathy: seizures, hallucinations, personality disorders, delirium, coma; Hypertensive encephalopathy Pain: acute, chronic and neuropathic</td>
</tr>
<tr>
<td>Psychologic</td>
<td>Fear, anxiety, pain</td>
<td>Post-traumatic stress disorder, depression</td>
</tr>
<tr>
<td>Pharmacologic</td>
<td>Suxamethonium: hyperK after 12-24 hrs after injury</td>
<td>Non-depolarising muscle relaxant resistance, opioid resistance</td>
</tr>
</tbody>
</table>
the catabolic losses and pharmacological agents such as non-specific B-blockers and insulin. Systemic manifestations of these two phases are listed below (Table 2).

**Perioperative consideration**

1. **Trauma**

Despite the temptation to address the burn injury immediately, the child with a burn injury should be managed as any paediatric trauma case with a primary and secondary survey. The standard A,B,C method of assessment can be extended in the burns patient: A = airway; B = breathing; C = circulation; D = disability or drugs; E = exposure and environment (consider high risk of hypothermia); F = fluids and consideration of Foley’s catheter (initial fluid resuscitation + maintenance fluid calculated, assessment of adequacy of urinary output, ideal is 0.5 – 1.5 ml/kg/hr especially if rhabdomyolysis is suspected); and G = glucose and gastric tube (gastric decompression, consideration of early enteral feeding in major burns provided there is no contra-indication). The secondary survey involves an extensive history and examination which substantiates the events leading to the injury, e.g. time and type of burn, associated injury, management thus far, the existence of inhalational injury, tetanus immunisation and non-accidental injury, should be excluded. A recent haemoglobin, platelet count, coagulation screen, urea and electrolytes, blood gas and chest x-ray may be considered depending on which aspects of the burn injury the child displays and what surgical intervention is intended.

2. **Airway**

Securing the airway in the burns patient may be challenging. In the acute phase, patients may have thermal injury periorally making bag mask ventilation and securing of the endotracheal tube (ETT) difficult. Various techniques have been suggested including the “Gray-Rode technique” whereby an ETT is firmly secured by looping a nasogastric tube around the hard palate and securing it to the tube. In addition, the airway may be distorted due to oedema or dressings, narrowed due to healing with strictureing, there may be limited neck mobility and mouth opening due to fibrosis and contractures and the possibility of a difficult airway should always be considered. Depending on the injuries sustained, patient condition and surgical intervention, airway control can be through nasal cannulae with a capnography port (e.g. when using ketamine infusion), laryngeal mask airway or endotracheal tube. Recent evidence suggests that low pressure high volume cuffed endotracheal tubes should be used since patients may have decreased compliance and may require high ventilatory pressures that may leak around uncuffed tubes.

3. **Inhalational burns**

Inhalational injury is defined as the aspiration of superheated gases, steam, hot liquids, or noxious products of incomplete combustion. It has been found to be an independent predictor of mortality in burn patients and worsens survival. Smoke inhalation is likely to be present if the burn occurred in an enclosed space; clinically patient has burns to the face, neck, eyes, nose, upper trunk; or singed facial hair and soot in their sputum. One must be cognisant of the fact that symptoms may be delayed for up to 48 hours after the injury. Three clinical entities are possible. **Upper airway thermal injury** (above larynx) where there is direct damage due to heat energy, this may result in significant swelling of the pharynx and epiglottis and typically presents with inspiratory stridor, hoarseness/change in voice and a swollen uvula. **Lower airway thermal injury** (below larynx) where there is damage due to the toxic products of combustion. This causes sloughing, mucous secretion, inflammation, atelectasis, airway obstruction, subglottic stenosis and a predisposition to pneumonia. Typical signs are dyspnoea, coughing, wheezing, and production of copious secretions. These solidify to form casts which obstruct various sized airways, potentially creating areas of increased shunt and barotrauma. These patients may present for direct laryngoscopy or bronchoscopy to confirm the clinical findings. **Injury due to noxious gases** is the third entity. Carbon monoxide poisoning should be suspected in a patient who presents with nausea, vomiting, headache, hypotension, convulsions and coma. Pulse oximetry cannot differentiate between HbO₂ and HbCO and will overestimate the true oxygen saturation. Blood gas analysis using co-oximetry is required. Cyanide poisoning should be suspected in burn patients with unexplained and persistent lactic acidosis despite adequate fluid resuscitation.

4. **Intravenous access and monitoring**

Both vascular access and monitoring may be difficult in the burned patient. Considerations for vascular access are:

- Place vascular access at intact skin where possible.
- Large bore access is necessary if large fluid shifts and rapid volume replacement are anticipated.
- Intraosseous access may be necessary if intravenous vascular access is impossible.
- Central venous access may be necessary for rapid resuscitation, delivering of vasoactive agents and monitoring of blood gases.
- Invasive blood pressure monitoring may be needed for waveform analysis and continuous measurements.
- Invasive monitors are a potential infection risk.

The ASA standard monitors should be used where possible, however monitor placement may be difficult due to the lack of available sites because of burn wounds and operative field issues. It may be necessary to change position of monitors as the surgery progresses. Pulse oximetry may be unreliable due to extremity perfusion and hypothermia and may need to be placed on the ear lobe, buccal mucosa or tongue. Electrocardiogram electrodes can be placed in alternative areas to the chest or skin staples used with crocodile clips. Useful indicators in assessing the adequacy of resuscitation and perfusion include urine output (keep > 0.5 ml/kg/hr), lactates, base excess, central venous oxygen saturations, respiratory variations in the arterial waveform and capillary refill. Where possible, echocardiography can guide haemodynamic monitoring.
5. Fluid management

Despite advances in haemodynamic monitoring and the establishment of “goal-directed fluid therapy” concept, intravenous fluid management in the burns patient is still troublesome. In the acute phase the main aim is to preserve and restore tissue perfusion, and prevent ischaemia without causing excessive oedema and extravascular displacement of fluids. Balanced crystalloids should be used in the initial resuscitation, although it has been shown that these solutions have smaller volume expansion in comparison to colloids. This is because during the first 24 hours there is increased capillary permeability, colloids will pass to the extravascular space, exert an onnic effect and cause a paradoxical increase in what is commonly called the third space. The use of colloids in burn patients still remains controversial. Gelatins have not shown superiority over crystalloids. The small number of studies investigating colloids in burns do not show an increase in mortality or renal injury especially when using balanced HES. Hypertonic solutions, albumin and plasma have been associated with lower volume requirements, lower intra-abdominal pressure, and a lower incidence of compartment syndrome; hence, they have a role when appropriately used in burn patients. Intraoperatively a preload of 10–20 ml crystalloid should be considered. This may need to be followed by a blood transfusion.

6. Blood loss

For every 1% of burn wound excised, it is estimated potentially 3.4 % of a child’s blood volume is lost. Most severe burns will require blood transfusion at some point, but one must bear in mind the associated risks, e.g. transmission of infectious diseases, immune suppression or transfusion related lung injury (TRALI) and apply restrictive strategies to blood products where possible. Due to these risks a single universal transfusion trigger is being replaced by a physiological trigger. Factors that may guide transfusion are the preoperative haemoglobin measurements, blood volume status, acuity of blood loss, development of hypoxemia and clinical assessment of perfusion. Effective blood-conserving techniques include:

- Subdermal infiltration with tumescent solutions containing vasoconstrictors ± local anaesthetic, e.g. clysis (suggested mix: 100 mg bupivacaine without adrenaline + 2 mg adrenaline into a litre of Ringers lactate or if unavailable normal saline; maximum dose of 20 ml/kg).
- Applying adrenaline soaked swabs to excised areas
- Using compressive dressings or tourniquets
- Electrocautery
- Maintaining eutermia
- Major excision as early as possible after injury (septic tissue has been noted to bleed more)
- Staged procedures
- Fast, competent surgeon.

7. Temperature regulation

Hypothermia can easily occur in the burns paediatric patient due to the loss of cutaneous vasoconstriction, evaporative losses from skin, and high surface area to volume ratio. This is compounded by exposing various degrees of the anaesthetised patient resulting in potential temperature losses of up to 1˚C every 15 minutes when at ambient temperature. Due to the hypermetabolic state and inflammatory mediators, severe burn injury causes the hypothalamus to increase the threshold set-point by 0.03˚ C per % TBSA. It is thus important to maintain eutermia to avoid catecholamine release tissue catabolism and a further up-regulation of the hypermetabolic state. Hypothermia is best prevented by maintaining ambient temperatures of 28–32˚ C, warming all fluids (intravenous, clysis, and cleaning solutions), minimising body surface area exposed and providing effective convective or conductive warming devices. Core temperature must be continuously monitored.

8. Pharmacology

Pharmacodynamics and pharmacokinetics of drugs may be different in the paediatric burns patient. This is due to:

- Fluid compartment alterations with increased volume of distribution
- Changes in cardiac output
- Variability in organ perfusion
- Decreased renal and hepatic function
- Changes in serum protein levels (e.g. reduction in plasma albumin resulting in more free fraction of drugs that bind to albumin; alpha-acid glycoprotein levels may double as it is an acute phase protein)
- Hypermetabolism
- Alterations in specific drug receptors

It is important to titrate all medications to effect. Twenty-four hours after the burn the number of extra junctional acetylcholine receptors are increased and severe hyperkalaemia may occur if depolarising muscle relaxants are used. This is maximal at days 10–50, with the potassium rising by 3–5 mmol or more. This persists for years after the injury. In additional, burn patients (especially those with > 20 % TBSA) will have a marked resistance to non-depolarising muscle relaxants. A dose will have a longer onset of action and shorter recovery time. There may also be decreased cholinesterase activity with drugs metabolised by these enzymes having a longer duration of action.

9. Nutrition

Optimal nutritional support of the burned patient is best accomplished by early initiation of enteral nutrition, as this can modulate the hypermetabolic response and lessen catabolism. Patients with major burns will undergo multiple surgical interventions with cumulative loss of nutrition which is unacceptably high if feeds are stopped preoperatively for each procedure. The suggestion is that if a patient is going to have any airway manipulation in the operating theatre, strict fasting guidelines must be adhered to; if there will be no airway manipulation (e.g. child is intubated and ventilated in ICU) cases should be individualised, and feeds can be continued until time of surgery; if there is a confirmed nasojejunal tube in-situ, feeds may be continued until two hours preoperatively. Intraoperative post pyloric feeding remains controversial.
10. Pain

Burn pain is a combination of: background pain (proportional to the thermal injury); procedural pain (brief and intense pain generated by, e.g. debridement, change of dressings, rehabilitation); breakthrough pain (increase in pain levels at rest, with procedures or due to anxiety); postoperative pain (predictable and temporary, due to the creation of new and painful wounds); and chronic pain (most frequently neuropathic pain which can exist long after the wounds have healed). The challenge in managing burn pain is due to the multiple components that need to be addressed and the changing nature of the pain with time. Furthermore, pain assessment is often confounded by physiological manifestation of the burn injury.

A pre-emptive, multimodal and possibly multidisciplinary approach may be necessary especially in patients who present for multiple procedures who develop anxiety, post-traumatic disorders and chronic pain. Beyond simple analgesics, opioids are the cornerstone of pain control. However, one must be aware of how the abovementioned changes in pharmacology affect opioid therapy. Furthermore, there is the possibility of tolerance (resulting in a higher dose of drug to achieve same effects) and development of hyperalgesia where pain may be opioid resistant and require adjuvants such as ketamine, α₂ antagonists (clonidine or dexametomidine), gabapentin, benzodiazepines, amitriptyline, lignocaine infusion and Entonox. While regional and peripheral nerve blocks may offer benefit, it may be difficult to find appropriate sites. The addition of non-pharmacological methods of pain control ensures a comprehensive plan.

### Anaesthetic management

The knowledge of the pathophysiological process involved and the abovementioned perioperative considerations need to be taken into account when managing the burnt child. Other factors that must be contemplated are briefly summarised in Table 3.

### Conclusion

The management of a paediatric patient is unique in many ways, and much more so when they have sustained significant burns. It is important to understand the multiple physiologic disruptions and the alterations in pharmacokinetics and pharmacodynamics of commonly used anaesthetic agents. Thought must be given to the surgery intended, fluid resuscitation and potential airway and ventilatory challenges that the patient may present. The central role of adequacy of perfusion and pain management should be a constant concern through all the phases. Providing anaesthesia for burn surgery is challenging yet rewarding, as it facilitates recovery from some of the most devastating yet preventable injuries seen in paediatric anaesthesia.

### References
