

Avoiding adverse outcomes in anaesthesia. The relevant As: allergy, asthma airway and anaphylaxis

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Abstract

The perioperative preparation of children presenting for surgery aims to identify medical problems that might influence the outcome and to institute management strategies to reduce those risks. Adverse respiratory events remain a significant cause of morbidity and mortality in modern paediatric anaesthesia. This manuscript addresses some common medical problems that may impact on the anaesthetic. These include upper respiratory tract infections, and allergy and asthma; conditions whose optimal management should invoke daily discussions, and which can have significant implications if not managed correctly.

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Introduction

The perioperative preparation of children presenting for surgery aims to identify medical problems that might influence the outcome and to institute management strategies to reduce those risks. Respiratory and airway complications remain the most significant cause of morbidity and mortality in modern paediatric anaesthesia.¹ Common medical problems that are encountered in daily clinical practice include the child with an upper respiratory tract infection (URTI), allergies and asthma. The ideal management of these problems is discussion almost on a daily basis because the guidelines are not clear cut, and the risks may be significant and even potentially life-threatening, particularly when managed incorrectly. Comorbidity involving any combination of these problems significantly increases the risk.²⁻⁸

Upper respiratory tract infections

Most young children have frequent URITs. They present with a spectrum of signs and symptoms, depending on the acuity of the illness. It stands to reason that at some point, children will present for surgery with an acute infection, or soon after a recent URTI. The dilemma as to whether or not to cancel, proceed or postpone elective surgery has been a source of debate for many years.²⁻⁸ All too often, particularly in day-case surgery, this decision is left to the

anaesthesiologist, who is pressured to make last-minute decisions by the family, the surgeon, and even hospital management. Late cancellations can be very disruptive to the surgical schedule.

In reviewing the literature, there is little uniformity or a single definition of an URTI that can be universally applied. Many researchers select certain surgical procedures and times of the year to ensure maximal enrolment for their study. Severe cases are excluded. Most of the studies were carried out in the "halothane and thiopentone suxamethonium" era. It is impossible to extrapolate from these studies when using drugs that are available today (sevoflurane, propofol and remifentanyl). The clinical impression is that the risks are significantly reduced, but there is less evidence of that.

Definitions also vary from one publication to the next, but essentially, children fall into three categories.²⁻⁸ Firstly, there are those who present with a fever, malaise, rhinorrhoea (clear or purulent), a sore or scratchy throat, sneezing, nasal congestion, a productive cough and chest signs, and who are clearly unwell. It is easy to make a decision about this group. Cancellation is required, unless the procedure is an emergency. This group is excluded from most studies.

The second group develops symptoms a day or two before the elective procedure. The parents call the surgeon or anaesthesiologist the night before. Surgery is cancelled and rescheduled in two weeks' time, and the child returns

with minimal or no symptoms. Alternatively, a conversation with the parents clarifies the severity of the symptoms and a decision is made to re-evaluate the child on the morning of surgery.

But the majority of children fall into the third category, i.e. those who have had a URTI with symptoms for days or even weeks, and who are stable or improving. Most studies exclude the first and second group, and only include those with mild URTI symptoms.

Although URTI implies an upper airway problem, the upper and lower airways are always involved to a variable degree. Viral infection damages the ciliary apparatus and mucosal epithelium, exposing the underlying nerve endings. Consequently, the airway is sensitised to the irritant effect of the inhalational agents and secretions. Airway smooth muscle activity is enhanced. In addition, a ventilation perfusion mismatch occurs, the closing volume increases and there is a reduction in functional residual capacity. Although the clinical symptoms resolve, usually within two weeks, the airway irritability may persist for up to 6-8 weeks. It is the severity of these subclinical changes that ultimately influences the decision as to whether or not to defer surgery.³

Airway-related events, the most common adverse anaesthetic problem, include airway obstruction, bronchospasm, laryngospasm, breath holding, post-extubation croup, coughing, desaturation and bradycardia,³⁻⁵ and anecdotal reports of atelectasis, pneumonia, and even death.⁹⁻¹² Factors that have been shown to increase the risk of respiratory events include more symptomatic children with nasal congestion and copious secretions, airway instrumentation in children under five years of age, surgery involving the airway, a history of reactive airways or snoring, prematurity, parental confirmation of the presence of a URTI and passive smoking.^{3,5} Infants under six months of age are at greatest risk.

Viral myocarditis, a particularly difficult clinical diagnosis, has been described in a number of sudden deaths that have occurred while under anaesthesia.⁹⁻¹² Although rare, unsuspected myocarditis remains a major concern in the child with symptoms of a "cold".

When making a preoperative assessment, it is important to exclude symptoms relating to an allergy, usually seasonal, or whether they are prodromal symptoms of an infectious disease, e.g. measles, mumps, chickenpox, rubella and meningococcal infection, which may put other patients or staff at risk. Some syndromic children may have persistent mucopurulent rhinitis (Down's, Hurler's and Hunter's syndromes, cleft palate and patent ductus arteriosus) that may influence the decision. Rhinitis is common in these children, and it is important to establish whether or not there has been a change in the character of the secretions that is suggestive of an acute or chronic infection. Unilateral

rhinorrhoea suggests unilateral nasal obstruction, e.g. a foreign body or polyp.

When is it safe to proceed? The ideal time to reschedule surgery is far from settled. Airway hypersensitivity and reactivity persists for up to six weeks, particularly if the lower airway is involved. Some authors suggest that the lower airways are always involved! Children may have between 3-8 URTIs per annum. It is conceivable that if surgery is delayed for 4-6 weeks after each episode, there may be only a small window of time in which the child is asymptomatic and "fit" for surgery if this guideline is applied.

Tait et al⁴ showed that the incidence of easily treatable airway complications was similar in the acutely symptomatic to that in subjects who had had symptoms for four weeks. In this study,⁴ which included 1 078 children aged one month to 18 years with mild URTI symptoms, children who presented for elective surgery with a recent URTI (within four weeks) fared as well as those with acute symptoms. It was concluded that with careful airway management, most of these children can undergo elective procedures without increased morbidity or long-term sequelae. There was no statistically significant difference in the incidence of laryngospasm or bronchospasm with regard to acute or recent URTIs with mild symptoms, compared to that in the asymptomatic children. Although these children have an increased risk of adverse respiratory events (coughing, breath holding and desaturation), these are easily treatable by experienced anaesthesiologists.

Schreiner et al showed that nearly 2 000 cases would have to be cancelled to prevent 15 cases of laryngospasm in experienced hands.⁶ Delaying or cancelling the procedure does not significantly alter the incidence of adverse respiratory events. Little is gained, except to create inconvenience for the family and all concerned in order to prevent an easily treatable problem that occurs in a minority of patients.

Predicting which child with a URTI is likely to have an adverse event has recently been studied.¹³ Adverse respiratory events occurred when the children were symptomatic less than two weeks before the procedure. Symptoms that were present 2-4 weeks prior lowered the risk. Other risk factors included a family history of atopy, asthma and passive smoking.

Management of adverse respiratory events should evolve according to the particular circumstances, the cause, the available drugs and equipment, and the child's underlying condition. Most events respond to simple manoeuvres, such as continuous positive airway pressure support; and simple therapeutic measures, such as bronchodilators which are best given intravenously, suxamethonium 1 mg/kg, lignocaine 1 mg/kg, and endotracheal intubation and short-term ventilation, which should all be considered and used as indicated. Deepening the anaesthesia without compromising the child may also bring resolution.

The ideal anaesthetic is also a matter of debate. Differences in study design and a lack of uniformity regarding the types and surgical procedures and the duration thereof, the types of airway instrumentation and the choice of anaesthetic for the child with a URTI have provided no answers. Anaesthetic management should aim to reduce stimulation of a potentially irritable airway. Propofol has major advantages over other agents. Isoflurane and desflurane both cause significant airway irritability and should be avoided. Any airway instrumentation is associated with more adverse respiratory events.^{6,13,14} A face mask is considered to be the method of choice, whenever possible.^{3,5,14} Laryngeal mask airway (LMA) intubation has fewer complications^{3,14} than endotracheal intubation, which in some studies has been associated with an 11-fold increase in adverse events.⁶ The risk of deep extubation is no different to that of awake extubation.

In today's economic climate and managed healthcare environment, other factors come into the equation. These include the distance travelled to the hospital, whether or not the parents have taken special leave, the attitude of the family, the number of previous cancellations and the experience of the anaesthesiologist. The impact of cancellation on the family can be substantial. Disruption of the operating schedule and the cost of staffing an operating room that has not been used are further considerations. These should not directly influence the decision, but realistically they often do! Ultimately, the child's safety should be the primary consideration.

Allergy

Parents frequently indicate that their children have multiple drug allergies which have often not been validated. Parents confuse side-effects with true allergy. Potential allergic cross-reactivity between drugs and food is frequently considered to be a perioperative risk factor that needs to be addressed. Allergenic cross-reactivity is defined by the response of individual antibodies to other allergens with structural similarity, and can be seen in families of drugs or agents used during the perioperative period. "Multiple drug allergy syndrome" or "multiple drug hypersensitivity" is a clinical condition that is characterised by the propensity to react to chemically unrelated drugs, mainly antibiotics.¹⁵ In most cases, the syndrome presents as acute urticaria, angioedema, or both, after administration of the allergenic compounds.¹⁵

Immediate allergic hypersensitivity reactions are triggered by specific immunological mechanisms mediated by antibodies, usually the immunoglobulin E isotype, and can lead to life-threatening symptoms.¹⁶ The main risk factor for anaphylaxis is a previous, uninvestigated severe immediate hypersensitivity reaction during the perioperative period. Neuromuscular blocking agents and antibiotics are the most common triggers. If possible, a history of drug-

induced anaphylaxis should be confirmed by appropriate evaluation.¹⁶⁻²⁰

Many food allergies, e.g. egg, soy, peanuts, seafood and shellfish, are often mistakenly considered to be a contraindication to some medications, although the evidence for this is lacking. Many false assumptions about drug allergies are based on anecdotal case reports. The evidence suggests that egg-, soy-, or peanut-allergic patients are not more likely to develop anaphylaxis when exposed to propofol. Egg allergy is most common during childhood, and is usually outgrown by adulthood.²¹ Generally, egg-allergic patients demonstrate immediate hypersensitivity to the protein in egg whites (ovomucoid and ovalbumin), whereas lecithin, which is not the allergenic determinant, is found in the egg yolk. Propofol is marketed in an oil-water emulsion using soybean oil (10%), and egg lecithin (1.2%) as the emulsifying agent. The documented anaphylactic reactions are caused by the isopropyl or phenol groups in propofol, rather than the lipid vehicle.^{22,23} Therefore, there is little or no reason to contraindicate propofol in egg-allergic patients.

There is also little or no reason to contraindicate propofol in children with a soy or peanut allergy either. Soy allergy is an early-onset food allergy that affects approximately 0.4% of children. Most children develop tolerance by late childhood.²⁴ Refined soy oil, such as that that is present in propofol, is safe for people with a soy allergy because the allergenic proteins are removed during the refining process. Soy and peanuts are both leguminous plants, and thus any cross-reactivity should not necessitate the avoidance of propofol. Shellfish (crustaceans and molluscs) or fish are one of the most common foods that provoke severe anaphylaxis.²⁵ The major allergen in fish is the muscle protein, parvalbumin, and tropomyosin in crustaceans. Shellfish allergens do not cross-react with fish allergens. Because the allergenic determinants for shellfish and fish are muscle proteins, and not other components, such as iodine, there is no reason to modify the anaesthetic protocol in cases of shellfish- or fish-allergic patients. There is no cross-reactivity between iodinated contrast agents, povidone iodine or seafood as the allergenic determinant is not iodine for any of them. The only contraindication to povidone iodine is a previous documented hypersensitivity reaction. Although the precise allergenic agent in povidone iodine has not been elucidated, it is not the iodine atom.²⁶

Asthma

Asthma is a disorder that presents with a spectrum of airway obstruction, inflammation and hyper-responsiveness. It is a chronic inflammatory disorder of the airways that may cause recurrent episodes of coughing (particularly at night or in the early morning), wheezing, shortness of breath and chest tightness in susceptible individuals. Usually, these episodes are associated with widespread but variable airflow

obstruction that is often reversible, either spontaneously or with treatment.

Worldwide, asthma seems to be on the increase, particularly in industrialised countries. It is estimated that up to 300-million people are affected, and it is implicated in one of every 250 deaths. The prevalence of asthma in children, based on a previous diagnosis of asthma and more than one asthma attack in the previous year, is 5.5%. Contributing factors that predispose to the development and severity of asthma include a genetic predisposition, a history of atopy, exposure to airborne allergens (sensitivity to the house dust mite), and a history of viral respiratory infections, which are commonly respiratory syncytial viral or rhinovirus.²⁷ Asthma-triggering agents include respiratory infections, inhalants (animal fur, house dust mites, mould or pollen), irritants (cigarette smoke), temperature changes (cold air), exercise and anxiety. The National Asthma Education and Prevention Program Expert Panel Report 3 categorises asthmatics into groups based on the severity of their disease.²⁷

Ultimately, asthma represents a dynamic interaction between the host and environmental factors. The immunological-inflammatory pathways involved in the pathogenesis of asthma are complex and include lymphocytes, immunoglobulin E, eosinophils, neutrophils, mast cells, leukotrienes and cytokines. These pathways are triggered and modified by extrinsic and environmental factors.

The asthmatic child, even when asymptomatic, is at risk of perioperative morbidity (bronchospasm and anaphylaxis) which may progress to mortality if not recognised or poorly managed. This is particularly true if the child is exposed to allergens or other triggering agents during anaesthesia.

Especially important in the preoperative evaluation is assessment of disease severity, and how well the asthma symptoms are currently being controlled. The mainstay of treatment is inhaled β_2 agonists (quick or long acting) by metered dose inhalers.²⁸ The long-acting agents do not suppress inflammation and should not be used without anti-inflammatory treatment for the control of asthma. Inhaled and parenteral corticosteroids are the cornerstone of therapy to stabilise and improve persistent asthma. Leucotriene modifiers inhibit the leucotriene pathway, a mediator of bronchoconstriction. Evidence of their beneficial effect on inflammation is conflicting and they are not useful in acute treatment.²⁸

Information regarding medication, including oral steroid use, emergency visits or admissions to the hospital which included intravenous infusions or intubation should be obtained. They all provide an indication as to the severity of the disease. Previous anaesthetic history, presence of known allergies, coughing or sputum production, and level of activity, should also be assessed. Asthmatics with "atopy" are particularly predisposed to have allergic reactions. The anaesthesiologist should be prepared for

the possibility of an anaphylactic reaction to allergens in the operating room, such as antibiotics, muscle relaxants or latex. When asthma is well controlled, it probably confers no additional risk for perioperative complications. When it is poorly controlled, it almost always does.²⁸ Prior to elective procedures, optimal control of symptoms should be achieved. If not well controlled, the child should be deferred for additional therapy, which may need to include a short course of oral steroids. Oral prednisone dexamethasone may be needed.^{29,30} Patients with asthma should not have elective surgery during an acute viral respiratory infection since the risk of laryngospasm and bronchospasm is high.

On the day of surgery, patients with asthma should continue their medications as usual. Inhaled β_2 agonists should be given 1-2 hours prior to surgery. Premedication is usually indicated (oral midazolam (0.5-1 mg/kg) since anxiety may precipitate an acute episode. Systemic corticosteroids use in the previous six months is an indication that stress dose coverage is needed to avoid an adrenal crisis. High-dose inhaled corticosteroids use may also indicate perioperative stress dose coverage in certain patients.

The anaesthetic plan should provide a balance between suppression and avoidance of bronchospasm, with the usual goals of patient safety, comfort and a quiet surgical field. Drugs that release histamine from mast cells should be avoided. These include thiopentone, many muscle relaxants (atracurium, d-tubocurarine and mivacurium), and analgesics (morphine). Ketamine is ideal since it produces smooth muscle relaxation and bronchodilatation, both directly and via release of catecholamines. Propofol causes profound depression of airway reflexes, and when compared to thiopentone, there is a significantly lower incidence of wheezing following intubation.³¹ The alpha 2 agonist, dexmedetomidine, has a favourable profile, including anxiolysis, sympatholysis and drying of secretions without respiratory depression,²⁶ but is still "off label".

Airway instrumentation under a light level of anaesthesia should be avoided. Avoiding intubation by using a mask or LMA for appropriate cases is optimal. An inhaled β_2 agonist immediately prior to induction may decrease the risk of bronchospasm that can occur with intubation.³² Topical local anaesthesia (lignocaine 5 mg/kg maximum) is also useful as it obtunds the sensory loop of the reflex arc, thus preventing reflex bronchoconstriction. However, an aerosol spray containing a propellant in addition to lignocaine, may trigger airway reactivity. A squirt of lignocaine directed onto the upper airway from a syringe, or intravenous lignocaine, is preferable.

Sevoflurane is the agent of choice for inhalational induction for a variety of reasons. It has a positive bronchodilating effect, and a lower incidence of laryngospasm and cardiac dysrhythmias than that of halothane, isoflurane or other volatile anaesthetics. Propofol infusion can also be used for the maintenance of anaesthesia. Desflurane, an airway

irritant, may cause an elevation in airway resistance in children with airway susceptibility, and should not be used.

Intraoperatively, bronchospasm can be provoked by laryngoscopy, tracheal intubation, airway suctioning, cold-inspired gases and tracheal extubation. Airway tone is increased by vagal stimulation caused by endoscopy, peritoneal or visceral stretch.²⁶ Inhalation agents and gases should be humidified to prevent inspissation of the already-thick secretions. Tracheal suctioning should be performed only when the child is deeply anaesthetised, or when there is topical anaesthesia. The mode of ventilation should be low-inflating pressure, with prolonged expiratory time. Potentially, deep extubation avoids the risk of bronchospasm from coughing on the endotracheal tube. The reversal of neuromuscular blockade with neostigmine does not cause bronchospasm if atropine or glycopyrrolate are administered concurrently.

Regional anaesthetic techniques are useful for postoperative analgesia. There are concerns about the use of nonsteroidal anti-inflammatory drugs (NSAIDs). Despite the fact that many asthmatics have used ibuprofen without a problem, a recent meta-analysis suggests that NSAIDs should be avoided in those with a history of an adverse response to a NSAID, and in those who have not been previously exposed to one.³³

Conclusion

The anaesthesiologist should focus on signs and symptoms that quantify respiratory status when conducting a preoperative assessment of a child with a URTI or asthma. Parents are useful barometers of their child's condition and any day-to-day changes from baseline. Children with coexisting pulmonary disease, particularly reactive airway disease, and infants under six months of age with an active URTI, are at greater risk. Food or drug allergies may be additional confounders. As the world becomes increasingly polluted and industrialised, it can be expected that more allergens will impact on the daily lives of patients.

The final decision to proceed with surgery should rest with the individual anaesthesiologist and will be influenced by his or her ability, experience and comfort level in managing predictable complications in a child with URTI or asthma. Clearly, those with more experience may be prepared to proceed with younger patients with or without additional pathology, while others with less experience may not. Whatever the decision, the child's safety remains paramount!

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