Abstract: PURPOSE OF REVIEW The term ‘safe use of anesthesia in children’ is ill-defined and requires definition of and focus on the ‘safe conduct of pediatric anesthesia’. RECENT FINDINGS The Safe Anesthesia For Every Tot initiative (www.safetots.org) has been set up during the last year to focus on the safe conduct of pediatric anesthesia. This initiative aims to provide guidance on markers of quality anesthesia care. The introduction and implementation of national regulations of ‘who, where, when and how’ are required and will result in an improved perioperative outcome in vulnerable children. The improvement of teaching, training, education and supervision of the safe conduct of pediatric anesthesia are the main goals of the safetots.org initiative. SUMMARY This initiative addresses the well known perioperative risks in young children, perioperative causes for cerebral morbidity as well as gaps in regulations, teaching and research. Defining the ‘who’, ‘where’, ‘when’ and ‘how’ in this context provides the framework for the safe conduct of pediatric anesthesia.

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Safe Anesthesia For Every Tot – The SAFETOTS initiative

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Summary
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Keywords
conduct, pediatric anesthesia, quality, safety

INTRODUCTION
An overwhelming angst of anesthesia-related neurotoxicity in small children has gripped the pediatric anesthetic community in the past decade leaving anesthesia providers with doubts if it is well tolerated to use anesthesia in young children. The term ‘safe use of anesthesia’, however, is ill-defined and also potentially misleading. It implies that specific combinations of anesthetic agents may cause harm in early childhood and are primarily responsible for poor long-term neurological outcomes following surgery in young children. In contrast, the ‘Safe Anesthesia For Every Tot’ initiative (www.safetots.org) aims to define the ‘safe conduct of anesthesia’ and addresses the need to raise the standard of perioperative anesthetic care in young children. The following sections illustrate the purpose of this initiative and provide the anesthesia caregiver guidance for ‘safe conduct of anesthesia’.

BACKGROUND
Retrospective cohort studies suggest a link between exposure to anesthesia/surgery in early childhood and subsequently altered neurobehavioral outcome. Assuming the existence of such a putative link, the underlying mechanisms remain undetermined. Based on overwhelming laboratory data showing general anesthetics-induced direct neurotoxicity, it has been suggested that general anesthetic agents may not be well tolerated in young children \[1,2\] [http://www.fda.gov/downloads/forconsumers/consumerupdates/ucm364244.pdf (March 2015)]. Considerable effort, led by the Food and Drug
Administration (FDA) and the SmartTots initiative, is currently devoted to evaluate this possibility. Initial results in humans are now available and continuously updated and summarized by the FDA endorsed SmartTots initiative (www.smarttots.org). A major difficulty these studies are struggling with is that it is virtually impossible to separate the pharmacodynamic effects of general anesthetics per se from a multitude of other factors that might also cause neurological damage, such as the stress of surgery or impairment of physiological parameters because of inadequate anesthesia management [3]. Therefore, to date, no definite causal link between certain anesthetic drugs or techniques and poor neurological outcome in children has been established [4–8].

An important, albeit less publicized, generally assumed fact in the pediatric anesthesia community is that poor conduct of anesthesia, independently of the kind of drug administered, can lead to significant neurological morbidity or even mortality in small children [9**,10]. In fact, the analysis of pediatric closed malpractice claims, regularly describes the causal relationship between anesthetic practice and morbidity; as well as mortality in even previously healthy children [11,12]. Partial brain damage, persistent vegetative state, brain death or even death represents only the most catastrophic outcomes. However, these closed malpractice claims merely represent the ‘tip of the iceberg’ as ‘near misses’ and other incidences, giving rise to more subtle neurological morbidity, are not included. It remains unclear whether these are always disclosed to parents, investigated or reported [10].

Defining the safe conduct of anesthesia and raising the standards of perioperative care in small children is, therefore, of utmost public health importance. Joint international efforts, including intense lobbying for education and raising widespread awareness on the importance of safe anesthesia conduct, are mandatory to achieve these goals.

The ‘Safe Anesthesia For Every Tot’ initiative (www.safetots.org), presented herein, is a recently created international venture that is primarily devoted to this issue. Particularly, this initiative addresses the well known perioperative risks in young children, important intraoperative factors for cerebral morbidity as well as gaps in regulations, teaching and research. Defining the ‘who’, ‘when’, ‘where and how’ in this context provides the framework for the safe conduct of pediatric anesthesia [1,13,14].

THE GAP BETWEEN ‘STATE OF THE ART’ AND DAILY PEDIATRIC ANESTHESIA CARE

‘State of the art’ in pediatric anesthesia is frequently defined and propagated at scientific meetings, congresses and in the literature in the form of expert lectures, opinions and reviews. However, economic pressures and sometimes lack of even basic staffing and logistic resources may lead to situations in which supposedly low-risk anesthesia is conducted by insufficiently trained and inexperienced personnel and thus rapidly turns into high-risk anesthesia.

Regulations are required

Healthcare payments for pediatric anesthesia are very unattractive in some countries resulting in cost cutting exercises by some (independent) anesthesia practitioners. These ‘cost-savings’ affect, but are not limited to, the provision of anesthetic assistants, equipment and medications.

Children are often also scheduled together with adults on operating lists in larger hospitals and university centers, in which professors and heads of surgical subspecialties often dictate the scheduling. The principle of a dedicated pediatric unit/center is that the surgeon follows the child and not vice versa. This mixed scheduling also leads to dilution of clinical experience for everybody involved. However, expertise and caseload of the anesthesiologist are accepted to be one of the most critical factors in outcome.

Unfortunately, there is no widespread and supported research activity on caseload and experience of anesthesiologists and related complications and outcomes. A previously recommended minimum yearly caseload for a pediatric anesthesiologist consists of 300 children up to 10 years and 12 infants up to 6 months of age [15] has not been widely implemented. It is, therefore, not surprising that anesthesia departments with less than 100–200 anesthetics in children per year ‘provide’ anesthesia in even critically ill preterm neonates and extensive surgical procedures driven by secondary motives. Clear strategies and recommendations followed by strict regulations for a best standard of clinical care are required. The ‘who’, ‘where’, ‘when’ and ‘how’ need
to be identified to achieve an optimal outcome for these vulnerable children [16,17].

Teaching and standards
Assurance of high quality clinical care requires relentless vigilance and a sustained commitment to proper training, education and supervision in pediatric anesthesia. This requires maintenance of knowledge and focused clinical expertise in the care of infants and children.

It is of note that some European countries (Denmark, Netherlands and Switzerland) necessitate two adequately qualified persons for induction and emergence of general anesthesia in young children. This is in stark contrast to daily clinical practice in many other countries.

Anesthesia residents and fellows are required to be supervised on a one-to-one basis and receive structured training and education. Anything less results in ‘survival’ medicine rather than quality-focused perioperative pediatric anesthesia care. Exemplary programs are available: http://www.ssai.info/education/training-programs/perioperative-anesthesia.html

Although it is now common knowledge that children in inexperienced hands have a higher perioperative anesthetic morbidity, several national anesthesia societies are not willing to accept and pursue a certification of specialized pediatric anesthesia as recently developed by the American Board of Anesthesiology (www.theaba.org/Home/examinations_certifications). The concept that a general anesthesiologist is able to provide anesthetic care for all patients from birth to any old age is outdated. In Denmark, anesthesia in children younger than 2 years of age is no longer part of the anesthesiological curriculum. In France, children less than 3 years of age have to be anesthetized by specialized pediatric anesthesiologists [18,19].

The ‘WHO’, ‘WHERE’, ‘WHEN’ AND ‘HOW’
The following section describes the ‘who’, ‘where’, ‘when’ and ‘how’ to anesthetize (young) children.

The ‘WHO’
Children undergoing anesthesia have an increased perioperative risk for morbidity and mortality compared with adults [20]. A minimum annual caseload of 200–300 children up to 10 years of age including 1 infant/per month/per anesthesiologist is recommended to keep complications low [15,21]. Occasional pediatric anesthetic practice (<100 per annum per anesthesiologist) carries a five times increased risk for complications when compared with regular operators (>200 p.a.) and severe complications of almost one in five in infants [21,22].

The pediatric population undergoing anesthesia is too small in order to maintain sufficient skills for every anesthesiologist. Ideally, all children undergoing anesthesia should be regionally concentrated in specialized centers by pediatric anesthesiologists [17]. Large university centers have to pool these patients in pediatric operating theatres staffed by adequately trained pediatric anesthesiologists and pediatric nurses. Children treated/investigated in specialized areas (radiotherapy, cardiac catheter labs, X-ray, Proton, MRI and other special labs) requiring deep sedation or general anesthesia also necessitate a specialized pediatric anesthesia team. Residents/fellows in pediatric anesthesia departments must be supervised in 1:1 manner by an experienced consultant pediatric anesthesiologist at least during induction and preparation, during emergence and extubation as well as at any time during surgery if needed. General anesthesiologists should be able to provide emergency support anesthesia for limb and life-saving interventions and transportation to a specialized center. Education and regular training and update in pediatric centers are required to ensure that general anesthesiologists maintain their essential skills throughout their careers.

The ‘WHERE’
Neonates, infants and small children must be anesthetized in specialized pediatric centers with a 24/7 pediatric anesthesia service, educated pediatric anesthesia nurses and postoperative recovery facilities for neonates and children [23,24]. Hospitals with day cases and in-patients must have a minimum volume of 1000–1500 children aged less than 10 years per annum. This minimum volume will be required to cover a 24/7 anesthesia service with five consultants performing 200–300 pediatric anesthetics each per annum. It also allows the establishment of a structured pediatric anesthesia service with departmental teaching, workshops, regulations, standard operating protocols (SOPs) for acute crisis situations, pain service, specialized nursing staff and appropriate equipment. Hospitals responsible for elective locoregional pediatric surgical service should rely on an external sufficiently trained pediatric anesthesia team, providing service for different hospitals or facilities. The same principle applies to private dental suites, specialized areas or private hospitals and units.

The ‘WHEN’
The optimal timing of elective operative procedures is crucial. Careful considerations should be given to
balance impact of delaying such procedures electively on the surgical/diagnostic result, general anesthesia risk in newborn and infants and avoiding emergency procedures which do carry a higher perioperative risk [25]. An open discussion and decision is required if postponing surgery may risk the future well-being of the child.

The ‘HOW’
General practice points of good perioperative pediatric care are required. The main principle is to consider the perioperative anesthesia risk and the perceived need for surgery or intervention. This necessitates a working partnership of all parties involved in the perioperative care. Surgical interventions should be coordinated and profit-generating cost-cutting care be avoided. A supplementation of general anesthesia with regional techniques whenever possible is to be achieved. However, regional anesthesia misuse must be avoided [14,26].

One of the greatest challenges will be the development of generalized SOPs for common pediatric scenarios.

What to tell the parents, surgeons and referring practitioners
There is no proven causal link between anesthetic agents and cerebral damage in neonates, infants and small children. However, there is a definite causal relationship between poor perioperative anesthetic care and persistent poor neurological outcome and mortality in neonates, infants and small children. Perioperative complications during pediatric anesthesia are dependent on the age, preoperative morbidity as well as the experience of the anesthesiologist [27].

Neonates, infants and small children should be treated in pediatric centers and all children treated by experienced pediatric anesthesiologists. Pediatric anesthesiologist have been trained for a minimum of 1 year at a large pediatric center and provide anesthesia for a minimum of 200–300 children per annum.

Children require to be operated in a pediatric operating theatre and not being scheduled on adult lists.

Good pediatric anesthesia care also requires pediatric nurses, postanesthesia recovery facilities, established SOPs, continuous education and training.

POOR CONDUCT OF ANESTHESIA – THE KNOWN DANGERS AND CONSEQUENCES
Subclinical cerebral damage caused by perioperative adverse events including perioperative cardiac arrest, prolonged cardio-respiratory depression or cerebral edema are frequently results of a poor conduct of anesthesia. Complications in pediatric anesthesia are directly related to the (in-)experience of the anesthesiologist in charge.

Hypotension and/or hypocapnia both lead to cerebral hypoperfusion and may be associated with subsequent brain injury [28**,29**]. However, hypotension in neonates and small children during anesthesia is frequently tolerated and even accepted. Treatment threshold for neonatal systolic hypotension is significantly different, for example, between North America at 45.5 mmHg and the internationally recommended 60 mmHg, respectively [30*,31]. Whether this difference alone explains the discrepancies in reported retrospective outcome studies is speculative [32–37].

The impact of the traditional and now largely abandoned perioperative use of hypotonic fluids on perioperative cerebral damage is not considered in retrospective human outcome studies. Profound hyponatremia results in seizure activity, coma and death. Only the most severe cases and clinical series with seizures, brain damage and deaths are reported [38–41]. Moderate perioperative hyponatremia can be suspected to cause subclinical neuronal damage detectable only years after surgery with special neuropsychometric testing hampering the establishment of the correct causality.

Younger and smaller children are at high risk of perioperative hypoxemia because of the relatively higher oxygen demand, lower oxygen reserves and for example a higher incidence of laryngospasm. Prolonged hypoxic episodes frequently occur in the perioperative period and are common at induction and emergence of anesthesia for emergency procedures [42–44].

Maintenance of body homeostasis (temperature, normovolemia and normoglycemia) as well as appropriate analgesia and anxiolysis are critical in reducing perioperative morbidity and improve the well-being of the child [28**,45–47].

A number of quality criteria of appropriately performed pediatric anesthesia must be introduced into pediatric anesthesia care and represent the concept of 10-N anesthesia (Fig. 1). They include avoidance of fear and pain as well as maintenance of homeostasis normotension, normal heart rate, normovolemia, normoxemia, normocarbia, normal electrolytes, normoglycemia and normothermia. These factors must be met before other factors potentially contributing to cognitive deficits and learning disabilities following surgery in early childhood can be considered in clinical studies.
Research activity on ‘safe conduct’ of anesthesia is currently sporadic and not coordinated. Progress, however, is made through a recently completed European Society of Anaesthesiology project (www.esahq.org/apricot). This study will provide further information regarding the relationship between caseload, organizational setup and outcome in pediatric anesthesia.

‘Safe pediatric anesthesia’ research is still concentrating on the effects of neurotoxicity instead on safe conduct of general anesthesia (blood pressures, PaCO$_2$, PaO$_2$, electrolytes, temperature, blood glucose, preoperative anxiety and postoperative pain) in the vulnerable child. The latter require combined international efforts and focus on the safe conduct of anesthesia.

There is a definite need to initiate coordinated international research agenda with the primary focus on how conduct of (in)appropriate anesthesia management impacts on neurodevelopment in pediatric populations. Future research on cognitive deficits and learning disabilities following general anesthesia in early childhood must investigate the impact of perioperative hypotension, low cardiac output, hypocarbia, hyponatremia and hypoxemia on brain injury and neurodevelopment. Several important and as yet unanswered issues also need to be addressed. For example, it is still unknown what can be considered as normal/acceptable well tolerated perioperative blood pressure in pediatric populations. Future prospective clinical studies investigating potential neurotoxic effects of anesthetic agents on the vulnerable brain have to outline and report perioperative anesthetic care data by means of electronic patient data management systems.

**CONCLUSION**

The aim of the Safe Anesthesia For Every Tot initiative (www.safetots.org) is to address the well known risk factors and causes for anesthetic morbidity, to focus on the safe conduct of anesthesia in young children and to provide guidance on markers of quality pediatric anesthesia care. The introduction and implementation of national regulations of ‘who, where, when and how’ will result in an improved perioperative outcome in vulnerable children. Therefore, addressing the teaching, training, education and supervision of the safe conduct of pediatric anesthesia are the main goals of the safetots.org initiative.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

■ of special interest

■■ of outstanding interest


