CHAPTER
15

# AAGA in children

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## HEADLINE

15.1. Patients aged up to 16 years old were classed as children. There were eight cases of Certain/probable or Possible awareness in children reported to NAP5, and 13 cases that were judged unassessable. The incidence of reports of AAGA in children in NAP5 is significantly lower than the previously reported incidence in prospective studies which used a Brice-type questionnaire. Some cases were first reported decades after the event, and by patients who reported significant psychological distress as a consequence. A minority of cases were reported by patients aged ≤5 years old. Differences in patient experience, memory formation, childhood perceptions and parental attitudes may contribute to the apparent low rate of reporting of cases of AAGA in children.

## BACKGROUND

15.2 There are five recent publications investigating the incidence of recall of events during anaesthesia in children undergoing 'modern' anaesthesia. The incidences range from 0.2 to 1.2% (see Table 15.1). All of the studies gathered reports by direct questioning of a series of children using various modifications of the Brice questionnaire (Brice et al.,1970). Combining all the data, the overall incidence of awareness was 0.74% (~1:135; Davidson et al., 2011).

15.3 The contributing researchers had used different methods to determine recall, and there were other important possible differences in their patient samples, yet these data may be the best current estimate of AAGA incidence in children. It is clear and noteworthy that 0.74% (~1:135) is appreciably higher than the 0.1–0.2% incidence (~1–2:1,000) of AAGA found in adults (Avidan et al., 2008; Avidan et al., 2011; Myles et al., 2004; Sandin et al., 2000; Sebel et al., 2004; Wennervirta et al., 2002). Existing evidence therefore suggests that AAGA may be more common in children than in adults.

15.4 In addition to the raw incidence, the type and quality of experience is also relevant. In all these studies, children reported mainly tactile and auditory phenomenon (on average in 79% and 55% of children, respectively) and even though some had been scared (24%) or in pain (24%), children did not appear distressed afterwards. When seven of the cases from a previous study (Davidson et al., 2005) were followed-up, none needed psychological treatment (Phelan el al., 2009). Nevertheless, children can develop post-traumatic stress disorder (PTSD) following AAGA. Osterman et al. (2001) reported 16 children who came forward in response to a public advertisement and nine of these were assessed as having moderate to severe PTSD related to AAGA. However, these were by definition a self-selecting group.

15.5 There are reasons to make us suspect that AAGA is fundamentally different in children compared with adults. In the studies above, the youngest child was 6 years old (there were six 6–year olds, five 7–year olds and five 8–year olds). Anaesthesia technique,

**Table 15.1.** Recent publications of incidence of AAGA in children

| Authors | Incidence | Number | Age range (yrs) |
|---|---|---|---|
| Davidson et al., 2008<br>Blusse Van Oud-Albas et al., 2008<br>Davidson et al., 2005<br>Malviya et al., 2009<br>Lopez and Habre, 2009 | 0.2%<br>0.6%<br>0.8%<br>0.8%<br>1.2% | 1 of 500<br>6 of 928<br>7 of 864<br>14 of 1784<br>5 of 410 | 5–12<br>3–16<br>5–12<br>3–15<br>6–16 |
| Aggregate: from Davidson et al., 2011 (95% CI) | 0.74% (0.29-1.19%) | 33 out of 4486 | 3-16 |

dose requirement, use of neuromuscular blocking drugs, level of consciousness monitoring, types of surgery, patient appreciation of events (real or imagined), memory formation and communication ability are all different from adults, and these factors may explain the differences between adult and child incidences and experiences of AAGA.

15.6 In the 1970s, thiopental, halothane and suxamethonium were in everyday use, whereas today, propofol, isoflurane, sevoflurane and a variety of neuromuscular blocking agents are standard drugs. McKie & Thorpe (1973) found that ten of 202 (~5%) children experienced AAGA with these older regimens. Before, the 1990s, the popular 'Liverpool technique' involved profound neuromuscular blockade with high dose opioid and nitrous oxide with no volatile agent and four of the ten AAGA patients in the McKie & Thorpe study received this technique. Another study of 220 children undergoing the Liverpool technique reported that none of the children had recall, but 23 (~10%) experienced peri-operative dreaming (Hobbs et al., 1988), and that this was also associated with use of suxamethonium. A subsequent study of 144 children reported that the incidence of dreaming was reduced from 17% to 3% by the use of a small dose of tubocurarine before suxamethonium (O'Sullivan et al., 1988) and it was proposed that muscle-spindle activation caused by suxamethonium muscular fasciculation may provoke dreaming. Although the high incidence of dreaming implies some degree of cerebral functioning, none of these patients had recall of intra-operative events.

15.7 Dreaming was also investigated by (Huang et al., 2005) who found that 10% of 864 children receiving isoflurane and nitrous oxide anaesthesia experienced intra-operative dreaming. It is reasonable therefore to conclude that dreaming is common and possibly not influenced by anaesthetic technique. Huang et al. (2005) reported that children distinguished clearly between what they recalled and what they dreamed, with dreams featuring fantastical themes such as birds, tortoises, and chocolate far removed from the experiences featuring in the AAGA reports.

15.8 Halothane was gradually replaced by sevoflurane during the 1990s. The potency of these two agents is debated. The MAC of halothane (~0.8%) is lower than that of sevoflurane (~2.2%), suggesting it is more potent. However, at equi-MAC doses there is less EEG suppression with halothane (Schwab et al., 2004), which would indicate it is less potent. The simplest explanation is that these two agents have different effects on the EEG. A more complex explanation relies on MAC being a measure of spinal cord, not cortical action. Halothane has a greater effect at the spinal cord (and therefore lower MAC) than sevoflurane and therefore, paradoxically, there is less suppression of cortical activity with halothane than with sevoflurane (i.e. despite a lower MAC, halothane is in fact the less potent agent (Antognini et al., 2002; Antognini & Carstens, 1999; Jinks et al., 2003). There are however no data to suggest AAGA is more common with halothane.

15.9 NAP5 offers an important opportunity to explore reports for paediatric experiences, insights, common problems and themes.

## NAP5 CASE REVIEW AND NUMERICAL ANALYSIS

15.10 For the purposes of NAP5 we defined a child as aged <16 years old.

15.11 There were 24 reports relating to children under the age of 16 years, and nine of these were classified as Certain/probable or Possible. There were four reports of AAGA from children in the age group 1–5 years. Due to the nature of the reports, in this chapter (unlike others) we also consider Unassessable reports.

15.12 Thirteen reports were Unassessable (Class E) or Statement Only and this formed the largest group in children. These cases lacked supporting evidence on which to judge them, meaning we were unable to make strong conclusions regarding accuracy, causes, experiences and sequelae. Although the reports were interesting and often compelling, because adequate details were not available, they could not be assessed or categorised further.

15.13 Nevertheless some Unassessable reports had common themes and are worthy of comment. Twelve of the 13 patients in this Class did not report their experience until years later, and sometimes there had been other anaesthetics in the intervening period between the AAGA event and the patient or carer making the report. It is worth emphasising that NAP5 only accepted new reports of AAGA: i.e. only cases that had never been reported to a healthcare professional before. The longest interval between AAGA and the report in this unassessable category was 62 yrs. The youngest patient at the time of AAGA was reported as having been aged ~5 yrs. Five adults expressed general anxiety or specific fears as a result of their experience, and two seem to have been traumatised (complex anxiety, and nightmares). One patient had only told her mother that she had been aware, and another had not been believed by relatives or carers. Four Unassessable reports were of AAGA during tonsillectomy.

15.14 However, the details of many unassessable reports were very sparse such that it was often difficult or impossible to speculate on the sort of operation or when the incident might have occurred.

15.15 In the Unassessable reports, six patients had long-term anxiety states which varied in severity. One patient seemed to be untroubled, yet admitted to nightmares related to her AAGA experience. Another was 'fearful' of future anaesthesia.

*Gaseous induction was under-represented in reports of AAGA from children*

**Table 15.2.** Summary of classification of NAP5 reports in children and young people. ICU, intensive care unit; swaps refers to syringe swaps (see Chapter 5, Methods for classifications)

| Age range (years) | All classes | Class A or B (Certain/ probable) | Class C (Sedation) | Class D (ICU) | Class E (Unassessable) or Statement Only | Class F (Unlikely) | Class G (Swaps) |
|---|---|---|---|---|---|---|---|
| 1–5 | 5 | 1 | | | 1 | 2 | |
| 6–10 | 9 | 3 | | | 6 | | |
| 11–15 | 10 | 4 | | | 6 | | |
| All ages | 300 | 141 | 32 | 6 | 89 | 12 | 20 |

### Vignettes from reports classed Unassessable or Statement Only

A patient now in their 70s remembered "people doing things" in his mouth during a tonsillectomy at the age of ~12 yrs.

A patient now in their 70s reported a period of wakefulness during surgery as a 12-year old child: he couldn't move but could hear. The patient had many anaesthetics since, yet this was the first time they had reported this incident.

A now ~50-year-old was fearful of anaesthesia because of being "awake and screaming throughout" during a tonsillectomy aged about 5 years.

A parent, bringing their child to a pre-op clinic, told of their own experience when they were 6 years old. They remembered having instruments put into their mouth and also a bright light overhead. The patient subsequently suffered with recurring nightmares and had some anxiety about future anaesthetics based on this experience.

During an operation on their leg in the 1970s, when aged 13 years, a patient remembered having had pain in their leg and being unable to say anything or move. There were no voices heard and the patient did not recall anyone operating. The patient had only ever told their mother.

A patient now in their 30s was anxious before their operation and admitted this was because they had been awake during an anaesthetic when aged 6. The patient had told their mother but she had replied that they were imagining it or not telling the truth.

A 45-year-old reported waking up with what the Panel felt was likely to be a mouth gag in place during tonsillectomy when aged 10 years.

15.16 There were eight Certain/probable and Possible cases and, because they are few and diverse in nature, all are presented below in order of the age at which the AAGA took place. Some reports are certainly very vague as to the timing, but the Panel consensus was that on balance of probabilities and given the details provided elsewhere relating to anaesthesia and surgery, they fitted the categories to which they were assigned.

### Vignettes from Certain/probable and Possible reports

A 15-year-old underwent an urgent operation. The anaesthetic involved a gaseous induction, paralysis and intubation, regional anaesthesia and then a change to TCI propofol. During surgery the patient moved in response to intra-operative blood sampling but there was no obvious response to surgery. The next day the patient remembered their leg being cut.

A child aged 11–15 years remembered being "put to sleep" but was unable to speak or move and remembered something was placed in their mouth. Before falling asleep the child described being pushed through doors into theatre. Intravenous induction including an opioid was followed by volatile anaesthesia and nitrous oxide.

At the end of surgery a child aged 11–15 years had residual weakness in recovery. Three days later the child remembered awakening with a tube in their mouth and in pain.

A patient aged 11–15 years underwent a prolonged cardiac catheterisation under general anaesthesia. A Hickman line was inserted towards the end of the anaesthetic and the patient remembered a pricking feeling. This was reported by the parents two years later.

15.17 There were two reports judged Unlikely or not AAGA (Class F). The reports illustrate that the sparseness and vagueness of the details sometimes led the NAP5 Panel to decide that, although AAGA was possible, the child's words did not necessarily mean that the experience was one that related to AAGA.

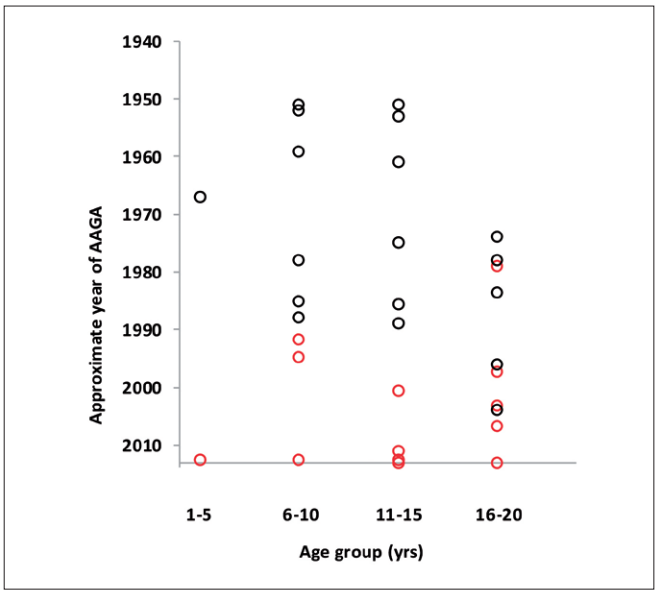
### Vignettes from reports judged unlikely or not AAGA

Before anaesthesia for removal of a leg plaster cast a 15-year-old said "this is when the saw goes buzz and my plaster is cracked". There had been several previous anaesthetics and all had seemed uneventful.

A mother reported that her toddler was distressed and had nightmares after sedation for a procedure. There were no further details provided.

15.18 There were often long intervals between the AAGA and reporting. Figure 15.1 shows the interval between AAGA and reporting according to the age group of the patient at the time of AAGA. Of all the reports about children (<16–year–old), only five were made by children or parents within a year of the event. Most reports were made many years later.

**Figure 15.1**. Year of AAGA, demonstrating interval between AAGA and first report. All reports were made in 2013; the y-axis relates to the approximate year of event. Red circles are Certain/probable and Possible reports; black circles are /unassessable reports. Note that the reports judged most likely to be valid are made more promptly; the longer the time interval the more likely they are to be judged Unassessable




15.19 There were five Certain/probable and three Possible reports in children. Of these reports two involved pain or paralysis, and four experienced perioperative distress. Over a longer timescale, three patients reported increased anxiety about subsequent anaesthesia. None were said to have psychological problems at the time of reporting.

15.20 Of Class A&B patients one was aged 1–5 years, three 6–10 years and four 11–15 years. ASA classes were three ASA 1 , one ASA 2, three ASA 3 and one unknown. All underwent intravenous induction (one unknown) though drugs varied (thiopental, propofol and ketamine). Half of the patients received sevoflurane, two isoflurane and one halothane. Five received nitrous oxide and three did not, four received neuromuscular blockade, two did not and in two it was not recorded. The phase of AAGA was induction in five, maintenance in two and emergence in one. Comparisons with the Activity Survey should be cautious as some reports were delayed but the absence of gas inductions is perhaps notable.

15.21 Inadequate analgesia was judged a contributory factor in three out of eight cases. One cause was a delay in continuing the anaesthetic after induction. Another factor was inadequate reversal of neuromuscular blockade. In four cases, no cause could be determined. The small number of reports prevents statistical analysis or investigation of associations between AAGA and anaesthetic technique. The reports did not give sufficient detail to make observations on the doses of anaesthetic drugs and the timings of AAGA in relation to the doses given. Depth of anaesthesia monitors were not used in any of these cases.

## DISCUSSION

15.22 There are two major findings of this chapter. The first is that very few children themselves reported AAGA. The second finding is that patients can delay reporting an AAGA event that occurred as a child for many years.

15.23 That only eight children reported AAGA that was classed Certain/probable or Possible suggests a surprisingly low incidence compared with the data published by Davidson et al. (2011) of an incidence 0.74% (~1:135). The NAP5 Activity Survey estimates that 488,500 general anaesthetics are administered to patients aged <16 years in the UK annually. This yields an incidence of just ~0.002% (or ~1: 60,000).

**Table 15.3.** Number of children (<16 yrs ) having sensations and experiences during AAGA; comparison with Class E (Unassessable) cases

| Class | pain | paralysis | tactile | auditory | visual | dreaming | distress |
|---|---|---|---|---|---|---|---|
| Certain/probable or Possible (Class A&B; (n=8) | 2 | 2 | 2 | 1 | 0 | 0 | 4 |
| Unassessable (Class E; n=13) | 2 | 2 | 6 | 2 | 2 | 0 | 7 |

15.24 If 0.74% is the true rate of AAGA, there should be approximately 3,700 children per year in the UK with recall of events during general anaesthesia. The explanation for the disparity in figures is possibly that these two incidences are of different events. NAP5 is a study of spontaneous reporting and did not involve direct questioning. It appears that, if the data of Davidson et al. (2011) are correct, the vast majority of children who experience some form of AAGA simply do not report it.

15.25 If children have AAGA but do not report it, they may delay their reporting until they are adults and our set of 13 Class E (Unassessable) and Statement Only reports support the presumption that many children do not report their AAGA until they are much older. Unfortunately, because of the delay, these reports were frequently Unassessable because hospital records and other supporting evidence are no longer available. Nevertheless, these delayed reports were plausible as stories, and it is reasonable to consider them to have some relevance.

15.26 This group who delayed reporting is also interesting because approximately half of them had long term psychological effects which raises the possibility that at least part of the reason for non-reporting at the time is that the experience was too traumatic to report. However, because these cases were Unassessable, we simply cannot be sure the distress was specifically caused by AAGA and not related to other distressing experiences of undergoing surgery, or adverse experiences suffered in the course of life. Research is needed to establish if adverse memories are related to AAGA, or to the experience of hospitalisation, etc (Lerwick, 2013).

15.27 Previous studies suggest that appreciable long-term distress is uncommon in children after AAGA (i.e. that established by Brice-type questioning), and that few need psychological treatment (Phelan et al., 2009). Intuitively, parents would normally be expected to be very sensitive to behavioural changes in their children after anaesthesia, especially where this was causing adverse reactions out of proportion to what they would regard as normal stresses of needing surgery. Regardless of whether children experience AAGA more frequently than adults, the current consensus appears to be that the consequences are less likely to be severe. However, our NAP5 reports (especially the unassessable, Class E, cases) may represent a different cohort, being spontaneous reports perhaps more likely, therefore, to exhibit long term sequelae.

*Reports of AAGA from children may be delayed. Reports should be listened to carefully and children believed*

15.28 The reasons why children do not report their AAGA experiences are worth examining – and ripe for future research. We can speculate that reasons might include the nature of the experience not being sufficiently compelling or interpretable. Or, children may lack the language or vocabulary to explain what happened. Distress, fear and confusion may inhibit communication. Their awareness may be difficult to separate from dreaming or nightmares. Children are likely to tell their parents first, and therefore the report often depends on the parents. Their parents may have a reassuring influence and may suppress reporting. In the NAP5 cohort, one patient had only told their mother, and another said that they were disbelieved by their parents. Perhaps the parent's perception of what has happened is a dominant factor. All these possibilities may limit or prevent the communication of the child's experience. A child might find it difficult for social reasons to report AAGA but, with the passage of time, they may consolidate memories and feel able to report their childhood experiences later, particularly when anxious about a further operation. Even adults may decline to report AAGA without obvious reason (Villafrance et al., 2013).

15.29 It is plausible that children are less likely to form memories of AAGA because they lack understanding or information about what happens during surgery. Nevertheless there is good evidence to suggest that by the time children have sufficient language ability to report their experiences, they also have sufficient memory ability to recall AAGA.

*AAGA was rarely reported by younger children*

15.30 Recall can be demonstrated in infants of 7 to 8 months old, who are able to find hidden objects, with retention increasing with age (Bauer, 1996). By age 9 months, information can be retained for four weeks, by 10 months for up to 6 months, (Carver & Bauer, 2001) and at age 11 months up to 12 months (Bauer, 1996; McDonough & Mandler,1994). At age 2 to 3 years language and a sense of self develop, and both of these are important in the formation of explicit memory (Howe et al., 1994). Adults generally do not remember their childhood events before the age of 3 to 4 years (this is termed infantile amnesia), although very emotional events are recalled from a younger age so there are reports of young adults who can remember their hospital admission when they were aged 2 years (Usher & Neiseer, 1993). Infantile amnesia develops gradually though, so 5–7-year-olds in Bauer's recent study were able to recall 60% of events they discussed with their mothers in a recorded conversation at age 3 (Bauer and Larkina, 2013). Source memory – the ability to recall where or when a remembered event occurred – improves dramatically at this age (Drummey & Newcombe, 2002), making it more likely that children who experience AAGA from around 6 years onwards will be able to recall it as something that happened during anaesthesia.

15.31 Adult memories of childhood AAGA may be somewhat immune to the passage of time for several reasons: emotional events tend to be well encoded in memory (Cahill & Mcgaugh, 1996), memories of AAGA are perhaps unlikely to have been discussed and shared with others, which is a potential cause of memory distortion (Pryor & Root, 2013), and such memories are less likely to have been overwritten by other similar experiences than memories of more common events.

15.32 There are pharmacological factors that could affect AAGA. The concentration of inhalational anaesthesia required to maintain immobility in small children is higher than in adults (Mapleson 1996) and if dosing is titrated to adult values this could expose children to greater risk of AAGA. However, MAC is related to the dose required to cause suppression of the spinal cord rather than the cerebral cortex (Antognini & Carstens 2002), and if the inhalational dose is adjusted to MAC then it is likely that the cerebral cortex is anaesthetized more deeply in small children than in adults. This would be consistent with the NAP5 finding that AAGA in children is, if anything, rarer than in adults.

15.33 The number of Certain/probable or Possible reports was fewer in children (8) than in adults (133). Using the NAP5 Activity Survey data for denominators, we estimate the incidence of these reports to be ~0.002% (1 in 60,000) in children (denominator of 488,500), and ~0.005% (1 in 17,000) in adults (denominator of ~2,300,000).

15.34 In the NAP5 Activity Survey data sample, neuromuscular blockade was used less frequently in children than in adults (25% v 50%). The increased need for neuromuscular blockade in adults may be because the spectrum of surgical interventions is different, or perhaps because adults have degenerative or ischaemic cardiovascular diseases that prevent them receiving high doses of anaesthetic to achieve immobility. Since AAGA is so intimately linked with use of neuromuscular blockade, these factors may partially explain why reports of AAGA were more common in adults.

15.35 The historical timing of AAGA might be linked with types of drugs used at that time. There was only one report of AAGA 40–50 years ago but seven reports from 20–40 years ago. The 'Liverpool technique' was in use throughout these years but probably ceased being used around 20 years ago. Halothane is no longer used for induction of anaesthesia and probably stopped being used in most UK hospitals around ten years ago. Nevertheless, no obvious cluster can be seen in Figure 15.1.

15.36 Depth of anaesthesia (DOA) monitoring has not been used commonly in children (Myles et al., 2003), but this may be changing. A survey of paediatric anaesthetists in the UK and abroad has shown that there is a general recognition that AAGA is a problem in children, and 10% of those questioned said that they used DOA monitoring (Engelhardt et al., 2007). The NAP5 Activity Survey found that very few (~0.5%) children had processed

EEG or related monitors during anaesthesia. The EEG of awake and naturally sleeping infants is different from adults, and commercial monitors of processed EEG have not been validated in small children.(Murat & Constant, 2005; Shander & Lobel, 2005), which may explain a reluctance to use them.

15.37 The detection of awareness during muscle relaxation can be achieved with the isolated forearm technique (Russell & Wang, 1996; Tunstall, 1977), and the method has been used successfully in children over the age of 5 years. Byers & Muir (1997) found that eight of 41 children (~20%) responded to command during halothane anesthesia and more recently Andrade et al. (2008) found that two of 184 children (~1%) responded during isoflurane anaesthesia. Interestingly, no child, in either study, could recall any intra-operative event.

15.38 The paucity of AAGA cases involving children reported to NAP5 means it is unjustified to make specific recommendations about prevention and management of AAGA in this group. Nevertheless we offer some learning points:

(a) Spontaneous reporting of AAGA by children after their anaesthesia is very rare. When it is reported this may be delayed until adulthood (when inevitably confirmation of its veracity and interpretation becomes very difficult if not impossible).

(b) However, when made, children's reports of AAGA can be as reliable as those from adults.

(c) Reports of AAGA may be received by parents but not transmitted further, though the reasons for this are unclear. Children should be believed and treated sympathetically.

(d) Serious long term psychological harm and anxiety states are rare, but do occur after AAGA in children.

## IMPLICATIONS FOR RESEARCH

**Research Implication 15.1**
The finding that many children wait for years before reporting AAGA, and that about half of these appear to suffer adverse psychological symptoms or new anxiety states warrants further research to establish if AAGA is a specific cause, or if memories are conflated with the trauma of surgery or hospitalisation.

**Research Implication 15.2**
Long-term follow up of children who spontaneously report AAGA vs those who admit it on direct (Brice) questioning will help establish if there is a difference between the two cohorts in the type of experience of AAGA.

**Research Implication 15.3**
Research into memory formation in children is highly relevant for paediatric anaesthesia and the study of AAGA in children. It would be important to ascertain how anaesthetic drugs interact with memory formation in children.

**Research Implication 15.4**
There is considerable scope for assessing the utility of depth of anaesthesia monitoring (including both EEG-based methods and the isolated forearm technique) in children.

**Research Implication 15.5**
There is a need to define more clearly the explicit psychological support needed by a child (as compared with an adult) distressed by an experience of AAGA who reports it soon after the event.

**Research Implication 15.6**
The psychological impact (and hence support needs) of an adult reporting AAGA experienced as a child are important to define. It is unknown if these are different from the needs of an adult who delays reporting of AAGA that occurred originally in adulthood.

**Research Implication 15.7**
There appears sparse basic pharmacokinetic or pharmacodynamic data for common anaesthetic agents in children. Without this important information, it will be difficult or impossible to understand anaesthetic action, and hence solve the problem of AAGA in children.

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