12. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; **282**: 1458–65
13. Morrison CE, Ritchie-McLean S, Jha A, et al. Two hours too long: time to review fasting guidelines for clear fluids? *Br J Anaesth* 2020; **124**: 363–6
14. Brener W, Hendrix TR, McHugh PR. Regulation of the gastric emptying of glucose. *Gastroenterology* 1983; **85**: 76–82
15. Søreide E, Eriksson LI, Hirlekar G, et al. Pre-operative fasting guidelines: an update. *Acta Anaesthesiol Scand* 2005; **49**: 1041–7
16. Charlesworth M, Wiles MD. Pre-operative gastric ultrasound – should we look inside Schrödinger's gut? *Anaesthesia* 2019; **74**: 109–12
17. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003; **362**: 1225–30
18. Dixon-Woods M, McNicol S, Martin G. Ten challenges in improving quality in healthcare: lessons from the Health Foundation's programme evaluations and relevant literature. *BMJ Qual Saf* 2012; **21**: 876–84
19. Yentis SM. Research not research. *Anaesthesia* 2016; **71**: 871–4
20. NHS Improvement. *Quality, service improvement and redesign (QSIR) tools*. Available from: https://improvement.nhs.uk/resources/quality-service-improvement-and-redesign-qsir-tools/. [Accessed 31 October 2019]

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Two hours too long: time to review fasting guidelines for clear fluids

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Making multiple, small, incremental improvements across the whole of the perioperative pathway is likely to be the best way of improving outcomes from elective surgery in the developed world. Reducing the duration of the preoperative fast for clear fluids may be one way to cheaply and easily improve postoperative outcomes, particularly for the older and multimorbid patients who make up an increasing proportion of patients presenting for elective surgery. Reducing the duration of the preoperative fast may also improve patient satisfaction.

The international consensus for clear fluid fasting for children has recently changed, allowing children to drink up until 1 h before induction of anaesthesia.[1] The rationale for the change was fourfold: firstly, a 2-h fasting rule actually translates into a much longer fasting time; patients fast not for 2 h, but for much longer before operation.[2] Secondly, prolonged fasting of clear fluids is unnecessary, and results in considerable patient dissatisfaction and discomfort, and potentially causes harm. Thirdly, prolonged fasting does not reliably result in an empty stomach; having a drink of water may paradoxically reduce residual gastric volumes and increase pH a short time later. Finally, even if regurgitation and aspiration of clear fluid occurs, it is unlikely to result in morbidity. Here we discuss the current evidence with regard to gastric emptying, aspiration risks, and negative sequelae of prolonged fasting in adult patients, and suggest that it is time to align adult and paediatric guidelines for clear fluid fasting.

History of preoperative fasting

In the early days of anaesthesia in the 19th century, drinking fluids was actively encouraged until 3 h before surgery. Patients were specifically advised to drink glucose water, beef tea, or China tea.[3] Interestingly, the rationale for this 3-h fast was the prevention of postoperative vomiting rather than a reduction in risk of aspiration during anaesthesia.[3] It was only after Mendelson highlighted the risks associated with aspiration of solid gastric contents in obstetric patients that 'nil by mouth after midnight' became the standard recommendation.[3,4] This recommendation persisted for several decades

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because of the mistaken belief that the longer the fasting time the lower the risk of aspiration. Current international guidelines now recommend allowing intake of clear fluids up until 2 h before elective anaesthesia.

What is the problem with 2-h fasting time for clear fluids?

Despite the current 2-h rule, in reality patients are often fasted for much longer. Mean clear fluid fasting times for adult patients are 9–12 h.[2,5] Theatre work is unpredictable and start times (other than for the first patient) are uncertain and change at short notice. With a 2-h fast requirement, patients and hospital staff do not know when intake of clear fluid should stop. As a result, patients are often kept nil-by-mouth for much longer 'to be on the safe side' for fear of cancellation or postponement if patients are called to theatre sooner than expected. The problem is not so much that patients cannot tolerate a fasting for 2 h, but more the reality of what the 2-h fast means in the real world.

Would changing guidelines make any difference?

Patients often arrive in hospital having not had anything to drink since the previous evening. With the current 2-h policy, they then cannot drink after they arrive because of uncertainty about their theatre time. However, a 1-h policy means that patients could drink up to arrival at hospital and then could be given a drink when they are admitted, regardless of their expected theatre time. A drink of water on arrival has become standard practice in many paediatric surgical units, and this change has resulted in a significant reduction in actual fasting duration to 1.7–3.1 h.[6,7] Although most children are fasted for clear fluids for longer than the recommended 1 h, the reality of a 2–3 h fast is much more acceptable, and physiologically more normal, for most patients.

Negative effects of prolonged fasting

The negative effects of prolonged fasting have historically been viewed as an unavoidable inconvenience associated with anaesthesia and surgery. Prolonged fasting results in unpleasant symptoms of thirst, hunger, anxiety, and malaise,[8,9] increased incidence of postoperative nausea and vomiting, and may be the cause of significant patient dissatisfaction.[9,10] Administration of a carbohydrate-rich drink has been shown to reduce many of these unpleasant symptoms more effectively than a placebo of flavoured water,[8] and may be a means of further ameliorating untoward effects of prolonged fasting.

Metabolic derangements caused by the stress response, such as hyperglycaemia, insulin resistance, lipolysis, and nitrogen loss, are associated with poorer outcomes in elective surgery. Prolonged fasting in healthy volunteers is itself associated with increased insulin resistance.[11,12] Preoperative loading with clear glucose-containing drinks has been shown to attenuate these harmful metabolic responses to surgery and fasting,[11] and these are embedded in many enhanced recovery protocols.

Preoperative dehydration caused by excessive fasting may contribute to hypovolaemia and haemodynamic instability during anaesthesia. Hypovolaemia has negative effects on cardiac output and oxygen delivery. Although an association between fasting and haemodynamic instability is not demonstrated in most studies (as measured by changes in vital signs, and echocardiographic measures of volume status), most of these studies were performed in healthy ASA physical status 1–2 volunteers. The findings from these studies therefore may not be extrapolated to the increasingly older and multi-morbid population that present for elective anaesthesia. The detrimental effects of a prolonged fast may be greater in high-risk populations, such as those at the extremes of age or those with cardiovascular disease. Indeed, a study in young children showed that reducing the duration of the preoperative fast reduced haemodynamic instability during induction of anaesthesia.[9]

There is limited evidence that prolonged fasting is associated with increased postoperative delirium. In an observational cohort study, 910 patients were screened for postoperative delirium: 89.0% of patients in the delirious group had been fasted for fluids for more than 6 h compared with 74.2% of the non-delirious group ($P<0.001$).[13] It is plausible that prolonged fasting may exacerbate the complex syndrome that is postoperative delirium; it is thus likely that the negative sequelae resulting from a prolonged fast may be a modifiable precipitating factor.

Prolonged fasting, gastric volumes, and acidity of gastric contents

Although fasting is associated with adverse effects, a stomach as empty as possible is desirable before anaesthesia to reduce the risk of passive regurgitation and pulmonary aspiration of stomach contents. A residual gastric volume of less than 1.5 ml kg^{-1} has been deemed an acceptable volume for baseline risk of aspiration.[14]

It is often assumed that fasting results in low gastric residual stomach volume, and also that after a fast, with no stimulus for gastric acid production, the pH of any stomach fluid will be higher and therefore less irritating to the lungs in the event of aspiration. However, there is substantial evidence that fasting does not reliably result in an empty stomach or fluid with higher pH. Multiple studies have shown either no significant difference in gastric fluid volume or pH in patients given oral fluids around 2 h before operation, and some have even shown a reduction in gastric volume in those given a drink.[14–16] Furthermore, an ultrasound study of ASA physical status 1–3 patients presenting for elective anaesthesia apparently without risk factors for delayed gastric emptying showed that despite fasting, around 6% of patients had a significant volume of residual gastric fluid, and 1.7% had solid contents identified.[14]

Ultrasound studies of gastric emptying of fluids in healthy adults show that water is rapidly emptied from the stomach, with the volume of gastric contents returning to baseline within 30 min of ingestion of even large volumes of water.[17] Increasing the calorie concentration of fluids tends to slow gastric emptying. For example, milk drinks are emptied at the same rate as clear juice if the calorie content is similar.[16]

Proponents of gastric ultrasonography have suggested that measurement of gastric contents would be a more reliable means of ensuring an empty stomach before induction of anaesthesia than fasting instructions alone.[14] If unacceptable gastric content is identified (particularly solid content), then anaesthesia should be delayed, or appropriate precautions used to prevent aspiration.

Pulmonary aspiration of gastric contents

The Royal College of Anaesthetists 4th National Audit Project highlighted that although rare, aspiration is the most common reported cause of death under anaesthesia, and accounted for 23% of all cases reported as the 'primary' or 'secondary' major airway event.[18] The majority of cases reported were for urgent or emergency procedures. Death is most frequently caused by complete airway obstruction by particulate matter, with an estimated incidence of one in 350 000 anaesthetics.[18] The second large national review from Australia found 133 events of pulmonary aspiration with five deaths.[19] Overall rates of pulmonary aspiration under general anaesthesia including clear fluid has an incidence of between one in 900 to one in 10 000 cases,[20] fatal in one in 350 000.[18] In children, the aspiration rate is higher than adults (2–9.3 in 10 000).[10,21–23]

Aspiration of particulate matter or acidic material leads to leakage at the alveolar capillary bed, potentially causing cardiopulmonary failure, resulting in significant morbidity and mortality.[4] However, aspiration of clear fluid with a more neutral pH is usually not associated with severe harm; Mendelson[4] demonstrated that instilling liquid of neutral pH into the rabbit lung resulted in short-term respiratory distress that resolved within a few hours. There appear to be no significant long-term effects in adults who aspirate clear fluids under anaesthesia.[19,23]

Liberalising clear fluid fasting times in children does not increase the incidence of pulmonary aspiration, and does not increase morbidity and mortality.[6,7,21,22,24] Over a decade ago, the Scandinavian guidelines changed to encourage 150 ml of water to be taken with a premedication up to 1 h before general anaesthesia. There has been no increased incidence of adverse events.[25]

There is no evidence to suggest that increasing fasting times in high-risk patients reduces aspiration risk, and current guidelines are standardised across all patients. However, in children the contraindications listed by the adopted consensus statement include: gastro-oesophageal reflux (either being treated or investigated), renal failure, some enteropathies, oesophageal strictures, achalasia, diabetes mellitus with gastroparesis, or surgical contraindications. Patients at higher risk of pulmonary aspiration should be identified before general anaesthesia and appropriately managed to reduce this risk.

Conclusions

Current preoperative clear fluid fasting guidelines for adult patients need to be reviewed with serious consideration given to updating them in line with current paediatric guidelines, which more closely reflect current evidence and real-world practice. The reality is that a 2-h minimum fast often translates into a fast of 12 h or more, resulting in considerable patient discomfort, dissatisfaction, and potential for physiological harm. Neither does a prolonged fast guarantee an empty stomach, and clear fluid, particularly water, is emptied rapidly from the stomach; even relatively large volumes will be cleared from the stomach within 30 min of ingestion. Pulmonary aspiration in adults is rare, and generally only associated with significant morbidity and mortality if there is aspiration of solid matter. The guidance for children undergoing anaesthesia has changed for all age groups, many of who have a similar physiology to adults. We suggest that national governing bodies consider adopting a 1-h clear fluid fasting guideline for all age groups.

Author's contributions

Drafted this paper: CM, SR-M, AJ
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Reviewed and corrected the manuscript: MM

Declarations of interest

The authors declare that they have no conflicts of interest.

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References

1. Thomas M, Morrison C, Newton R, Schindler E. Consensus statement on clear fluids fasting for elective pediatric general anesthesia. *Paediatr Anaesth* 2018; **28**: 411–4
2. Brunet-Wood K, Simons M, Evasiuk A, et al. Surgical fasting guidelines in children: are we putting the evidence into practice? *J Pediatr Surg* 2016; **5**: 1289–302
3. Maltby RJ. Fasting from midnight - the history behind the dogma. *Best Pract Res Clin Anaesthesiol* 2006; **20**: 363–78
4. Mendelson C. The aspiration of stomach contents into the lungs during obstetric anaesthesia. *Am J Obstet Gynecol* 1946; **52**: 191–205
5. Tosun B, Yava A, Acikel C. Evaluating the effects of preoperative fasting and fluid limitation. *Int J Nurs Pract* 2015; **21**: 156–65
6. Newton R, Stuart G, Wildridge D, Thomas M. Using quality improvement methods to reduce clear fluid fasting times in children on the preoperative ward. *Paediatr Anaesth* 2017; **27**: 793–800
7. Andersson H, Zaren B, Frykholm P. Low incidence of pulmonary aspiration in children allowed intake of clear fluids until called to the operating suite. *Pediatr Anesth* 2015; **25**: 770–7
8. Hausel J, Nygren J, Lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. *Anesth Anal* 2001; **93**: 1344–50
9. Denhardt N, Beck C, Huber D, et al. Optimized preoperative fasting times decrease ketone body concentration and stabilize mean arterial blood pressure during induction of anaesthesia in children younger than 36 months: a prospective observational cohort study. *Pediatr Anesth* 2016; **26**: 838–43
10. Frykholm P, Schindler E, Sumpelmann R, Walker R, Weiss M. Pre-operative fasting in children. A review of the existing guidelines and recent developments. *Br J Anaesth* 2018; **120**: 469–74
11. Fawcett WJ, Thomas M. Pre-operative fasting in adults and children: clinical practice and guidelines. *Anaesthesia* 2018; **74**: 83–8
12. Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2008; **85**: 109–17
13. Radtke F, Franck M, MacGuill M, et al. Duration of fluid fasting and choice of analgesic are modifiable factors for early postoperative delirium. *Eur J Anaesth* 2010; **27**: 411–6
14. Van de Putte P, Vernieuwe L, Jerjir A, Verschueren L, Tacken M, Perlas A. When fasted is not empty: a

retrospective cohort study of gastric content in fasted surgical patients. *Br J Anaesth* 2017; **118**: 363–71
15. Maltby JR, Sutherland AD, Sale JP, Shaffer EA. Preoperative oral fluids: is a five-hour fasting justified prior to elective surgery? *Anesth Anal* 1986; **65**: 1112–6
16. Okabe T, Terashima H, Sakamoto A. A comparison of gastric emptying of soluble solid meals and clear fluids matched for volume and energy content: a pilot crossover study. *Anaesthesia* 2017; **72**: 1344–50
17. Okabe T, Terashima H, Sakamoto A. Determinants of liquid gastric emptying: comparisons between milk and isocalorically adjusted clear fluids. *Br J Anaesth* 2014; **114**: 77–82
18. Cook TM, Woodall N, Frerk C. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: anaesthesia. *Br J Anaesth* 2011; **106**: 617–31
19. Kluger MT, Short TG. Aspiration during anaesthesia: a review of 133 cases from the Australian Anaesthetic Incident Monitoring Study (AIMS). *Anaesthesia* 1999; **54**: 19–26
20. Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology* 1993; **78**: 56–62
21. Warner M, Warner M, Warner D, Warner L, Warner E. Perioperative pulmonary aspiration in infants and children. *Anaesthesia* 1999; **90**: 66–71
22. Borland L, Sereika S, Woelfel S, et al. Pulmonary aspiration in pediatric patients during general anaesthesia: incidence and outcome. *J Clin Anesth* 1998; **10**: 95–102
23. Walker R. Pulmonary aspiration in pediatric anesthetic practice in the UK: a prospective survey of specialist centers over a one-year period. *Paediatr Anaesth* 2013; **23**: 702–11
24. Tan Z, Lee S. Pulmonary aspiration under GA: a 13-year audit in a tertiary pediatric unit. *Paediatr Anaesth* 2016; **26**: 547–52
25. Soreide E, Eriksson LI, Hirekar G, et al. Pre-operative fasting guidelines: an update. *Acta Anaesthesiol Scand* 2005; **49**: 1041–7

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Achieving balance with power: lessons from the Balanced Anaesthesia Study

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The Balanced Anaesthesia Study was a large, multicentre, international randomised controlled trial (RCT) that posed the question: does light general anaesthesia (defined as a bispectral index [BIS] target of 50) improve survival at 1 yr after surgery in patients over 60 yr of age having major surgery when compared with deep general anaesthesia (defined as a BIS target of 35)? Median volatile anaesthetic administration was decreased by 30% from 1.10 age-adjusted minimum alveolar concentration (MAC) in the deep anaesthesia group to 0.78 age-adjusted MAC in the light anaesthesia group.[1] One year mortality rate was 6.5% in the light anaesthesia group and 7.2% in the deep anaesthesia group (absolute difference=0.8%; 95% confidence interval −0.5% to 2.0%), and the incidence of major perioperative adverse events was similar in the two groups. The investigators concluded that light general anaesthesia was not associated with lower 1 yr postoperative mortality than deep general anaesthesia.[1]

The Balanced Anaesthesia Study was by far the largest and most robust trial examining the impact of anaesthetic depth on intermediate-term postoperative mortality, enrolling 6644 patients from 73 centres in seven countries, and collecting multiple blinded endpoint assessments up to 1 yr after surgery. The investigators are to be lauded for the colossal effort involved in undertaking a trial of this magnitude and rigour. However, a key methodological consideration that limits interpretation and application of the trial's results is a lack of sufficient statistical power to detect differences in the primary