

probability of propulsion occurring after a postoperative episode of emesis can be predicted by the amount of preoperative exophthalmos. Nonetheless, in patients with significant exophthalmos, a careful history regarding eye problems related to Valsalva or episodes of vomiting may yield eye-opening results and increase the level of suspicion for this rare event that can be associated with PONV.

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Atrioventricular Dissociation

To the Editor:

Cardiac dysrhythmias can be accompanied by significant morbidity and mortality. The following report describes the occurrence of atrioventricular dissociation during the routine induction of general anesthesia.

A 60-yr-old, 75-kg woman with hypertension controlled with verapamil (240 mg) and metoprolol (100 mg) presented for total abdominal hysterectomy. Preoperative electrocardiogram (ECG) revealed sinus rhythm at 62 bpm, and echocardiogram showed left ventricular hypertrophy (LVH). Propofol 140 mg, lidocaine 100 mg, fentanyl 150 μ g, and vecuronium 7 mg were delivered IV. The blood pressure decreased from 140/78 to 89/53 mm Hg and the heart rate from 62 to 45 bpm. The ECG showed a bradycardia consistent with atrioventricular dissociation (Figure 1A) that persisted despite ephedrine 10 mg IV and then successive doses of atropine (0.3, 0.8, 1.0, and 2 mg IV). With isoproterenol 4 μ g IV, the bradycardia converted to sinus rhythm at 68 bpm (Figure 1B), and the blood pressure increased to 93/51 mm Hg.

Dysrhythmias occur after the administration of several medications. Severe bradycardia and asystole have been attributed to the lack of vagolytic activity of vecuronium in combination with sufentanil or their interaction with the patients' β -adrenergic and/or calcium channel blocker (1). Autonomic imbalance has also been attributed to epidural lidocaine in combination with atenolol and diltiazem (2).

Despite its history of being a hemodynamically neutral muscle relaxant, vecuronium is a possible source of the arrhythmia (3). Autonomic imbalance may have been created by the lidocaine and narcotic combination, particularly in the face of β -adrenergic blocker and calcium channel blocker use (2). The existing adrenergic blockade may have caused the ineffectiveness of the indirect-acting sympathomimetic ephedrine. The direct-acting β_1 agonist isoproterenol may have provided adequate β_1 stimulation to overcome this blockade. Another possible treatment is calcium chloride (4). Because of the LVH, the loss of coordinated atrial contraction may explain the hypotension. Because of the potential for arrhythmias during the administration of anesthetics, diligent ECG monitoring is essential for all patients undergoing anesthesia, especially those taking β and/or calcium channel blockers.

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Figure 1. A, After induction, ECG showed atrioventricular dissociation. B, After isoproterenol, ECG returned to sinus rhythm.

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Reported Data on Granisetron and Postoperative Nausea and Vomiting by Fujii et al. Are Incredibly Nice!

To the Editor:

We read with interest the recent article of Fujii et al. (1) about granisetron in the prevention of postoperative nausea and vomiting (PONV). With increasing amazement, we noticed that the results reported by Fujii et al. are incredibly nice and we became skeptical when we realized that side effects were almost always identical in all groups.

During 1994-1999, 47 articles have been published by Fujii et al. ([http://www.nlm.nih.gov/>search "Fujii-Y and granisetron"](http://www.nlm.nih.gov/>search/Fujii-Y+and+granisetron)) (1-47). In 21 articles, the most frequently reported side effect, headache, is given for the overall 24-h period of observation (Table 1). In 13 articles, the frequency of headache was reported to be identical in all groups (5,7-11,15,16,19,20,29,40,43), while this side effect differed, at most, by one patient per group in the remaining 8 papers (4,6,12-14,27,28,32). Surely, assuming that the study drug has no impact on a side effect, one would expect similar results between the groups. However, identical results are still relatively rare as binominal distribution causes a certain variability in reality. Thus, we tested the null hypothesis that the reported identical incidences could have occurred by chance with the alternative hypothesis that an underlying reason lead to such identical results.

First, the incidence of headache (p) was calculated by the total number of patients with headache ($n = 186$) divided by the total number of patients ($n = 2369$) in the 21 studies, resulting in an incidence (with lower to upper 95% confidence intervals) of $p = 0.0785$ (0.0681 to 0.09).

Second, the probability (P) that x out of n patients will experience headache will generally be calculated according to formula for the binominal distribution $P = (n!/(x!(n-x)!)) \times p^x \times (1-p)^{n-x}$ (48). Third, for each study, the probability that all (z) groups have identical results with x patients suffering from headache is calculated by $P = P^z$. These calculations were done for x between 0 and 10 as the probabilities for $x > 10$ were too small to have any impact on the calculation (Table 1).

Fourth, the joint probability that a study results in any identical number of patients is calculated by the sum of the single probabilities for $x = 0, 1, 2, \dots, 10$, also given in Table 1.

Fifth, the joint probabilities of all 18 separate studies with more than two groups—all three studies with two groups had identical results anyway—was in the range of $P = 0.0002$ to 0.0548 . To make it safe and simple, the hypothesis that 10 of 18 studies will result in identical numbers was tested by applying again the above mentioned formula

Table 1. Incidence of Headache per Group in the Investigated Publications and Calculated Probabilities of Obtaining Identical Groups

Reference	Headache/all patients reported groups						Probability that in all groups the identical number of <i>n</i> patients will suffer from headache <i>n</i> patients:										Joint probability P	
	1	2	3	4	5	6	0	1	2	3	4	5	6	7	8	9		10
Acta Anaesthesiol Scand 1997;41:746-749	2/25	2/25					1.68E-02	7.61E-02	7.95E-02	3.39E-02	7.45E-03	9.53E-04	7.69E-05	4.11E-06	1.51E-07	3.91E-09	7.26E-11	0.2148
Acta Anaesthesiol Scand 1997;41:1167-1170	2/30	2/30	2/30	2/30			5.49E-05	2.34E-03	5.45E-03	2.18E-03	2.38E-04	9.17E-06	1.46E-07	1.06E-09	3.81E-12	7.16E-15	7.34E-18	0.0103
Acta Anaesthesiol Scand 1998;42:220-224	2/30	2/30	2/30	2/30			5.49E-05	2.34E-03	5.45E-03	2.18E-03	2.38E-04	9.17E-06	1.46E-07	1.06E-09	3.81E-12	7.16E-15	7.34E-18	0.0103
Acta Anaesthesiol Scand 1998;42:653-657	2/30	2/30	2/30	2/30			5.49E-05	2.34E-03	5.45E-03	2.18E-03	2.38E-04	9.17E-06	1.46E-07	1.06E-09	3.81E-12	7.16E-15	7.34E-18	0.0103
Anesth Analg 1997;85:913-917	3/45	3/45	3/45	3/45	3/45	3/45	2.59E-10	8.23E-07	3.56E-05	1.18E-04	6.05E-05	7.03E-06	2.36E-07	2.70E-09	1.18E-11	2.18E-14	1.82E-17	0.0002
Br J Anaesth 1998;81:387-389	4/50	4/50	4/50				4.72E-06	3.65E-04	3.32E-03	8.40E-03	8.43E-03	4.06E-03	1.06E-03	1.62E-04	1.56E-05	9.80E-07	4.17E-08	0.0258
Br J Anaesth 1998;81:390-392	2/40	2/40	2/40	2/40			2.09E-06	2.81E-04	2.14E-03	2.90E-03	1.12E-03	1.58E-04	9.66E-06	2.83E-07	4.32E-09	3.63E-11	1.77E-13	0.0066
Can J Anaesth 1995;42:387-390	1/22	1/22	1/22	1/22			7.51E-04	9.26E-03	5.93E-03	6.17E-04	1.65E-05	1.46E-07	4.96E-10	7.14E-13	4.64E-16	1.43E-19	2.15E-23	0.0166
Can J Anaesth 1995;42:852-856	1/25	2/25	1/25	1/25			2.82E-04	5.79E-03	6.32E-03	1.15E-03	5.54E-05	9.09E-07	5.91E-09	1.69E-11	2.28E-14	1.53E-17	5.27E-21	0.0136
Can J Anaesth 1996;43:35-38	2/25	2/25					1.68E-02	7.61E-02	7.95E-02	3.39E-02	7.45E-03	9.53E-04	7.69E-05	4.11E-06	1.51E-07	3.91E-09	7.26E-11	0.2148
Can J Anaesth 1996;43:110-114	2/25	2/25	2/30	2/30			2.82E-04	5.79E-03	6.32E-03	1.15E-03	5.54E-05	9.09E-07	5.91E-09	1.69E-11	2.28E-14	1.53E-17	5.27E-21	0.0136
Can J Anaesth 1996;43:660-664	2/20	2/20	2/20	2/20			1.44E-03	1.22E-02	5.22E-03	3.56E-04	6.12E-06	3.38E-08	6.95E-11	5.86E-14	2.15E-17	3.58E-21	2.76E-25	0.0192
Can J Anaesth 1996;43:1095-1099	2/24	2/23	2/23				2.78E-03	2.37E-02	2.23E-02	5.44E-03	4.87E-04	1.93E-05	3.78E-07	3.97E-09	2.36E-11	8.19E-14	1.71E-16	0.0548
Can J Anaesth 1996;43:1229-1232	2/30	2/30					7.41E-03	4.84E-02	7.38E-02	4.67E-02	1.54E-02	3.03E-03	3.81E-04	3.25E-05	1.95E-06	8.46E-08	2.71E-09	0.1952
Can J Anaesth 1997;44:273-277	2/20	2/20	2/26	2/25			1.44E-03	1.22E-02	5.22E-03	3.56E-04	6.12E-06	3.38E-08	6.95E-11	5.86E-14	2.15E-17	3.58E-21	2.76E-25	0.0192
Can J Anaesth 1997;44:489-493	2/25	2/25	3/35	3/35			2.82E-04	5.79E-03	6.32E-03	1.15E-03	5.54E-05	9.09E-07	5.91E-09	1.69E-11	2.28E-14	1.53E-17	5.27E-21	0.0136
Can J Anaesth 1997;44:820-824	3/30	3/30	2/30	3/30			5.49E-05	2.34E-03	5.45E-03	2.18E-03	2.38E-04	9.17E-06	1.46E-07	1.06E-09	3.81E-12	7.16E-15	7.34E-18	0.0103
Can J Anaesth 1998;45:153-156	3/30	2/30	2/30				6.38E-04	1.06E-02	2.01E-02	1.01E-02	1.92E-03	1.67E-04	7.45E-06	1.86E-07	2.73E-09	2.46E-11	1.41E-13	0.0435
Can J Anaesth 1998;45:541-544	4/50	3/50	4/50				4.72E-06	3.65E-04	3.32E-03	8.40E-03	8.43E-03	4.06E-03	1.06E-03	1.62E-04	1.56E-05	9.80E-07	4.17E-08	0.0258
Eur J Anaesthesiol 1999;16:62-65	3/30	3/30	3/30	3/30			5.49E-05	2.34E-03	5.45E-03	2.18E-03	2.38E-04	9.17E-06	1.46E-07	1.06E-09	3.81E-12	7.16E-15	7.34E-18	0.0103
Eur J Anaesthesiol 1999;16:376-379	4/50	4/50	4/50				4.72E-06	3.65E-04	3.32E-03	8.40E-03	8.43E-03	4.06E-03	1.06E-03	1.62E-04	1.56E-05	9.80E-07	4.17E-08	0.0258

for the binomial distribution with the highest probability of 0.0548. This resulted in a final probability (P_{final}) that 10 of those 18 studies will have identical results by chance of $P_{\text{final}} = 6.78 \times 10^{-9}$!

Thus, we have to reject the null hypothesis that the frequency of identical results simply occurred because of the assumption that the incidence of headache is not affected by the intervention, and we have to conclude that there must be an underlying influence causing such incredibly nice data reported by Fujii et al.

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In Response:

Thank you for the opportunity to answer the questions by a reader of *Anesthesia & Analgesia*. As previously described in the first report by us (1), we evaluated the efficacy and safety of granisetron, a selective 5-hydroxytryptamine Type 3 (5-HT₃) receptor antagonist, for preventing postoperative nausea and vomiting (PONV) in women undergoing major gynecologic surgery. Consequently, granisetron was effective for the control of PONV after major gynecologic surgery, with little adverse event. Since then, we have investigated to assess the prophylactic antiemetic therapy with granisetron for preventing PONV after various types of surgery, such as pediatric tonsillectomy, breast surgery, middle ear surgery, and thyroidectomy, with a relatively high incidence of PONV when no prophylactic antiemetic is given.

Granisetron lacks the sedative, dyspholic, and extrapyramidal symptoms associated with non-5-HT₃ receptor antagonist (e.g., droperidol, metoclopramide) (2,3). Mild headache occurs in patients receiving granisetron for preventing chemotherapy-induced emesis (4). Similarly, in a number of our studies regarding granisetron and PONV, we found that several patients who had received granisetron experienced mild headache and that an incidence of headache was approximately 10%. Consequently, an incidence of headache seems to be identical, but it was true. How much evidence is required to provide adequate proof about

antiemetics' adverse events introduced recently by several investigators?

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Nonpharmacologic Sedation in a Deaf Child

To the Editor:

A 3-yr-old child was referred to our institution for a magnetic resonance imaging (MRI) examination of the ears. He had a partial deafness. Previously, he underwent an unilateral cochlear implant, which had failed. The MRI examination was performed to find the cause of the failure.

When asked about fasting hours, his father admitted that the child had eaten 30 min before the time set for the examination. Because of a very busy schedule, it was not possible to postpone his examination. It was decided after consulting with his father to try to put him to sleep "naturally." His father took him in his arms and, indeed, he fell asleep. We were able to proceed with the MRI scan for 45 min uneventfully. It was a good alternative because in this particular case, we did not need to inject gadolinium contrast (so no need for an IV line). In addition, because of his deafness, the noise of the MRI machine did not wake the child, and he remained motionless.

For ambulatory pediatric sedation, a natural sleep is, in certain conditions, an alternative that should be kept in mind.

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Fiberoptic Endotracheal Intubation Through an Ultra-Thin Bronchoscope with Suction Channel in a Newborn with Difficult Airway

To the Editor:

Management of the airway may be difficult in newborns with craniofacial and neck malformations (1). Previous experiences with flexible endoscopic intubation in neonates have shown encouraging results, but a number of limitations, such as no directional control at the tip or lack of an operative channel, were also reported (2,3). We describe a successful intubation by a new 2.5-mm fiberoptic bronchoscope with a 1.2-mm suction channel in a newborn with difficult airway.

A 2300-g infant, born at 35 wk of gestation after an urgent cesarean delivery for fetal distress, needed cardiopulmonary resuscitation at birth. Endotracheal intubation was achieved only after several attempts with a 3.0-mm tube inserted nasotracheally. On arrival to our unit, physical examination showed dysmorphic face, micrognathia, and arthrogyposis. A gross air leak around the endotracheal tube (ETT) prevented an adequate ventilation of the patient. We decided to explore the patient's larynx before exchanging the ETT with a larger one, but micrognathia did not allow

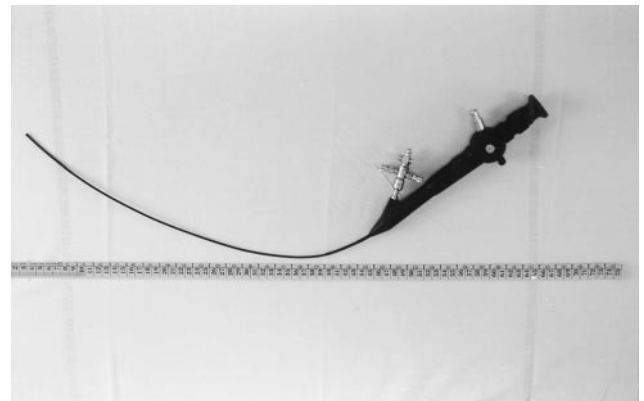


Figure 1. Fiberoptic flexible bronchoscope.

proper visualization by conventional laryngoscopy. Thus, we inserted a 3.5-mm ETT using a fiberoptic flexible bronchoscope (Richard Wolf-GmbH, Knittlingen, Germany). This endoscope has a 2.5-mm outer diameter, a 1.2-mm instrument channel, an angle of deflection at the tip of 160° up and 130° down, and a working length of 450 mm (Figure 1). During the procedure, we could remove secretions and provide topical anesthesia via the suction channel of the endoscope. No complications were noted.

We believe this new ultra-thin bronchoscope may be useful in newborns and small infants when a difficult intubation is anticipated or, alternatively, when lower airway evaluation, suctioning, bronchoalveolar lavage, or supplemental oxygen delivery during intubation is required.

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Which Intravenous Sodium Channel Blocker for Neuropathic Pain?

To the Editor:

McCleane's (1) comparison of IV phenytoin with placebo to relieve neuropathic pain is of interest in an area in which the only two previously controlled trials with oral phenytoin produced conflicting results (2,3).

However, McCleane's study statistically analyzes mean pain scores rather than determining from individual patient scores clinical significance, i.e., >50% pain relief and >75% relief. The decrease in overall pain score (0-10 linear visual analog score) in the phenytoin group from a mean (\pm SD) of 4.62 (\pm 3.46) to 3.25 (\pm 2.95) does not quantify the "significant benefit" judged by 8 of 20 patients, making comparison with other analgesics difficult. Furthermore, although both groups included the same patients, the mean overall pain score in the placebo group preinfusion was much higher 7.18 (\pm 1.47) than the phenytoin group 4.62 (\pm 3.46), suggesting a significant change in pain severity during the week between infusions, which would affect outcome.