Not all crystalloid solutions are equal

Editors,—I read with interest the article by Ruttmann, James and Aronson concerning haemodilution with hydroxethyl starch and normal saline. However, I disagree with their conclusion that they have shown that haemodilution per se exerted a procoagulant effect in both groups. Instead, I propose that their conclusion should be that they demonstrated that haemodilution with normal saline resulted in these changes. They did not state that the hydroxethyl starch was dissolved in 0.9% sodium chloride, although that is the usual formulation. If this were the case, one would expect the changes that were found in the normal saline group to be present also in the hydroxethyl starch group, just as they described.

Normal saline has a pH of 6.1, osmolality of 308 mosmol kg\(^{-1}\), sodium ion concentration of 154 mEq litre\(^{-1}\) and chloride ion concentration of 154 mEq litre\(^{-1}\). As would be expected, post-infusion serum values reflected those of i.v. fluids, especially when the latter were administered rapidly. Therefore, after normal saline has been infused, there is an increase in serum sodium, chloride and osmolality, and a decrease in serum pH. Administration of another crystalloid, such as Hartmann’s solution, results in different serum values because Hartmann’s solution has a higher pH (6.5), lower osmolality (273 mosmol kg\(^{-1}\) calculated and 284 mosmol kg\(^{-1}\) measured), and different electrolyte concentrations compared with normal saline.

The procoagulant changes reported in their article could have been caused by the changes in serum electrolyte concentration, osmolality or pH associated with infusion of normal saline, rather than by haemodilution. It would be interesting to know if the changes in coagulation reported in this article could have been avoided by the use of a different crystalloid such as Hartmann’s solution.

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Editor,—We thank Dr Williams for her interest in our article on haemodilution and are grateful for the opportunity to reply. First, we confirm the comment that the hydroxethyl starch is dissolved in 0.9% sodium chloride. Second, we ourselves considered the possibility that the haemodilution effect may have been a result of the nature of the crystalloid solution used, particularly the pH variability and perhaps the temperature. The original work on haemodilution published by Tocantins, Carroll and Holburn suggested that the nature of the diluent solution was unimportant. They investigated the effect on coagulation of buffered beef fibrinogen, 5% glucose, acacia, buffered 0.85% saline and imidazole buffer solution, and concluded that all crystalloid solutions appeared to exert a similar effect. We have recently completed a study in which a warmed (37°C), buffered solution with a pH of 7.4 and electrolyte content similar to that of human plasma, except for calcium (Plasmalyte B), produced identical effects on coagulation to those seen with normal saline. Other workers in this field have shown that the calcium content does not appear to alter the observation of hypercoaguability produced by haemodilution.

It would appear, therefore, that the answer to Williams’ very pertinent question is that the nature of the crystalloid solution is unlikely to alter the observed effects of haemodilution, although we ourselves have not examined the effects of a non-electrolyte solution such as 5% dextrose.

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Morbidity after day-case tonsillectomy in children

Editor,—Church, in his letter, comments on the high incidence of nausea and vomiting (40%) reported by Splinter and Rhine and compares this with his own experience of a less than 5% incidence of this unpleasant complication. Splinter and Rhine in their response ponder on this difference when a very similar technique was used by both parties.

One explanation not mentioned in these letters is the duration of surgery. I believe that it is quite likely that a British tonsillectomy is of significantly shorter duration than a North American tonsillectomy. We even have some surgeons who can stretch a tonsillectomy and adenoidectomy to 1.5 h!

Years ago, I noted that postoperative nausea and vomiting (PONV) in paediatric surgical outpatient was less common after operations of short duration. Decreased PONV associated with shorter anaesthesia has also been observed by Smith and by Fahy and Marshall. There are many factors which may influence the incidence of PONV, all of which must be considered when conducting studies, and especially when comparing the results from different centres. The influence of more prolonged anaesthesia on the incidence of PONV has not received the attention that it deserves.

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Inhaled nitric oxide and the longitudinal distribution of PVR in ARDS

Editor,—I should like to comment on the article by Benzing and colleagues who attempted to demonstrate the effects of inhaled nitric oxide on the longitudinal distribution of pulmonary vascular resistance (PVR) in ARDS. Their assertion is that nitric oxide affects pre- and post-capillary resistances with different dose responses, and their assumption is that both of these components of total PVR can be measured by analysis of the pressure–time curve after inflation of the balloon of a Swan–Ganz catheter. It is unfortunate, especially in view of their clear exposition of the argument as to the importance of the differential effects of pre- and post-capillary resistance in oedema formation in ARDS, that these assumptions cannot be supported because their measurement technique is flawed and their data are questionable.

Benzing and colleagues cited the work of Copass and colleagues to support the technique. These investigators propose a model of the pulmonary vasculature based on an analogous electrical circuit (fig. 1a) comprising arterial and venous resistors in series (PVR\(_{art}\) and PVR\(_{ven}\)), a capacitor (pulmonary capillary capacitance, \(C\)) and a voltage source (pulmonary artery pressure, PAP). Disconnecting the voltage source (inflating the balloon) allows the capacitor to...
discharge through the resistor, and allows the voltage to decay from the polarizing voltage to zero, just as pressure decays from PAP to pulmonary arterial wedge pressure (PAWP). For reasons for which there is no physical basis, the authors claim that the point at which the pressure changes from its rapid downstroke to its more gentle decay, represents pulmonary capillary pressure (PCP). They call this point the "point of inflection" and attempt to identify it by fitting a ruler through the curve by eye.

The mathematical definition of a "point of inflection" is the point on a function where the first-order derivative is maximum, that is the second order derivative equals zero. If Cope and colleagues' model is adopted, no such point exists since the discharge of a capacitor through a resistance (as in fig. 1A) is a simple exponential function, with a time constant equal to the product of capacitance and PVR.

I have modified the model of Cope and colleagues in an attempt to produce a more complex exponential which might possibly underlie Benzing's attempt to dissect the function into component parts. I did this by adding another (pulmonary arterial) capacitor (C°) to represent the elastance of the pulmonary arterial tree, as shown in figure 1B, since it is reasonable to assume that the pulmonary vasculature can be represented by an array of RC units. From this model, the total current flow through PVR° after opening the switch is given by the sum of the currents discharged from C° and C°.

Hence:

\[
(\text{PCP}_0 - \text{PAWP})/\text{PVR}_\text{ven} = C_°d(\text{PCP})/dt + C_°d(\text{PAP})/dt
\]

where d(PAP)/dt = (PAP - PCP - C°)C°/PVR°.

The symbolic solution to this is complex and so has been solved gradatim using a simple MS Excel spreadsheet, to plot PAP after balloon inflation for different values of \(\text{PVR}_\text{ven} \), \(C_°\) and \(C°\) for any given starting values of PAP and PAWP. The starting PCP is given by: PCP = (PAP - PCP° - C°)C°/PVR°. The resultant time courses of PAP° and PCP° are shown in figure 2, where the starting pressures are set to values similar to those measured by Benzing and colleagues. In figure 2A, the values of \(C_°\), \(C°\), PVR° and PVR° are chosen to best resemble their published pressure-time curve and the ratio of \(C_°/C°\) is 50:1. It can be seen that the true starting PCP differs considerably from the pressure at the "point of inflection". Note also that the actual ratio of PVR° to PVR has been set to approximately 0.1 in this example whereas Benzing and colleagues' estimation would be approximately 0.5. Only by making arterial and venous compliances and resistances similar, does the estimated PCP "appear" to approach the true value (fig. 2B) and even this is unsatisfactory because as both functions have similar time constants and boundary conditions, identification of a "point of inflection" is even more dubious.

It can also be shown from examination of series of these curves, that the estimated PVR°/PVR is decreased simply by reduction of PVR° which of course obligatorily increases the actual value of PVR°/PVR (table 1). Therefore, it is possible that in the subset of patients identified by Benzing and colleagues, the apparent effect of nitric oxide in reducing estimated PVR°/PVR was in fact artefactual, and mediated by a continued reduction in PVR°.

In reality, the situation is probably much more complicated than either Cope's or my model can predict. Not only is the pulmonary circulation extremely heterogeneous (with an unknown distribution of parallel resistances), but compliance of the pulmonary capillaries no doubt changes in ARDS and may also be affected by nitric oxide. This affects the kinetics of PAP decay and alters the position of Benzing's "inflection point" independently of the longitudinal distribution of PVR. It is also probable that the kinetics of the measured PAP decay are influenced by the damping properties of the transducer system which were modified (possibly inconstantly) by addition of an air bubble.

In summary, while the possibility exists of a differential effect of nitric oxide on pre- and post-capillary resistances in ARDS which may be beneficial with regard to transcapillary fluid flux, the data of Benzing and colleagues are insufficient to support it.

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Editor,—We appreciate the interesting comments of Dr Farmery on our method used for estimation of pulmonary capillary pressure (PCP) in ARDS patients.1 Determination of PCP in critically ill patients remains a subject of debate. However, most of the methods for PCP measurement which are used in experimental preparations, such as double occlusion pressure, micropuncture and the isogravimetric method, are not applicable in critically ill patients. The most widely used method for estimation of PCP in patients is analysis of the pulmonary artery pressure decay after balloon inflation.

Visual analysis of the pressure decay curve and determination of the “inflection point” have been used for PCP estimation in the past.2 It is correct that in a mathematical sense, a point of inflection on a function is a point where the second derivative is zero. (The first derivative is not necessarily maximum, it also may be minimum.) That means a mathematical point of inflection is present in somewhat S-shaped curves or in trigonometric functions. On the contrary, the decay of pulmonary artery pressure after balloon inflation is not S-shaped but biexponential.3 A biexponential function does not have a point of inflection in the mathematical sense. Nevertheless, many of the authors using visual analysis of pulmonary artery pressure decay have named the point where the pulmonary artery pressure changes from a rapid to a more slow decay “inflection point”. Therefore, we have adhered to this nomenclature.

Estimation of PCP by visual determination of the “inflection point” correlates well with other methods of PCP determination.4–10 Maarek, Hakim and Chang compared the double occlusion pressure technique (ΔPc) with PCP calculated by back extrapolation of the exponential pressure decay (ΔP0) and with visual determination of PCP from the pressure tracings (ΔP0+). In isolated canine lung lobes during pulsatile perfusion under various experimental conditions,2 they found that both ΔPc and ΔP0+ gave good estimates of ΔPc, although ΔP0 values were slightly higher (mean 1.28 mm Hg) and visually determined ΔP0+ values were slightly lower (mean 0.67 mm Hg) than ΔPc. In quasi-intact dog left lower lobes, Hakim, Maarek and Chang compared ΔPc with extrapolated ΔP0 derived from an inflated pulmonary artery catheter and with visual ΔP0+ determination.5 Double occlusion was performed manually. ΔP0+ was lower than ΔPc. Holloway and colleagues2 compared visual analysis of pressure decay curves by determining the “inflection point” of the pressure decay with computer-reconstructed curves. They found an excellent correlation between both methods of analysis.

In our study, the “inflection point” was determined visually by placing a ruler on the rapid component of the pressure decline adjusted for the best fit and marking the point at which the slow component of the pressure profile deviated from the rapid component. Mathematically, a straight line was drawn through two points: (1) the point where pulmonary artery pressure starts to decrease after balloon inflation (t = 0 of equation (1), see below); (2) one point of the fast component of pressure decay curve at time t1. Adjusting for the best fit means that t1 is varied in a manner that the slopes of the straight line and the rapid component of the pressure decay curves are quite similar. When t1 reaches a point on the pressure decay curve where the difference between the slope of the pressure decay curve and the slope of the straight line becomes maximum, the deviation of the pressure decay from the straight line becomes visually most apparent. This point is marked as the “inflection point”.

The time course of pulmonary artery pressure decay (Pap(t)) and of pulmonary capillary pressure decay (PCP(t)) are described by biexponential functions:6

\[ P_{ap}(t) = A e^{\alpha t} + B e^{\beta t} + P_e \]  
\[ PCP(t) = AK e^{\alpha t} + BK e^{\beta t} + P_e \]  

where \( P_e \) = left atrial pressure and \( A, B, \alpha, \beta, K, \) and \( K_e \) = complex expressions which may be derived from pre-capillary (R) and post-capillary (P) vascular resistances, from (PCc), capillary (C), and post-capillary (Cv) vascular compliances, and from the transpulmonary pressure gradient at time \( 0 \left( P_{ap}(0) - P_e \right) \).

A straight line which we have drawn for PCP estimation crosses the ordinate \( (t=0) \) at a \( y \)-value of:

\[ P_{CPC}(0) = A + B + P_e \]  

The second point of the straight line at \( t=t_1 \) has a \( y \)-value of:

\[ P_{PCP}(t_1) = A e^{\alpha t_1} + B e^{\beta t_1} + P_e \]  

The slope \( t_1 \) of the straight line is a function of \( t_1 \):

\[ t_1 = \frac{P_{PCP}(t_1) - P_{CPC}(0)}{t_1} \]  

Replacing \( P_{PCP}(t_1) \) and \( P_{CPC}(0) \) in equations (4) and (5) results in:

\[ t_1 = \frac{A e^{\alpha t_1} + B e^{\beta t_1} - A - B}{t_1} \]  

The slope of the pulmonary artery pressure decay at time \( t_1 \) is the first derivative of equation (1) at \( t_1 \):

\[ D_{PAP}(t_1) = A e^{\alpha t_1} + B e^{\beta t_1} - A - B \]  

The difference between the slopes \( D_{PAP}(t_1) \) is maximum when the first derivative of \( D_{PAP}(t_1) \) (eqn (8)) is zero:

\[ \frac{dD_{PAP}(t_1)}{dt} = 0 \]  

Determination of equation (8) and determination of \( t_1 \) from equation (9) is not trivial. Therefore, we have programmed equations (2), (6), (7) and (8) in a simple Excel 5.0 sheet according to the theoretical analysis of Bacconnier, Eberhard and Grimbert and have varied the values for \( R_c, R_{c0}, C_c, C_v \). We then determined the time point \( t_i \) where the difference of slopes was maximum. \( D_{PAP}(t_i) \) as an estimate of \( P_e \) was then compared with the true \( P_{ap}(0) \) according to equation (2) (fig. 1).

In our patients, total pulmonary vascular resistance (PVR = R_{PVR}) varied from 90 to 350 dyn s cm⁻³ which is 0.068–0.263 mm Hg s ml⁻¹. We have assumed that the balloon of the pulmonary artery catheter occludes a lobar artery. Thus the vascular resistance of the occluded vascular bed is approximately five times total pulmonary vascular resistance (i.e. 0.34–1.32 mm Hg s ml⁻¹). Human data for pulmonary vascular compliances, especially in ARDS, are not available. Vascular compliance measurements in dog lung lobes have yielded values of 1.35 ml mm Hg⁻¹ and -0.065 ml mm Hg⁻¹ kg body wt⁻¹ with an arterio–capillary–venous

![Figure 1](image-url)

**Figure 1** Visual analysis of pulmonary artery pressure (PAP) decay for determination of pulmonary capillary pressure (PCP). A straight line is drawn through two points of the pressure decay curve \( P_{ap}(0) \): (1) the point where PAP starts to decrease after balloon inflation \( P_{ap}(0) \); and (2) one point of the fast component of pressure decay curve at time \( t_1 \), is varied in a manner that the slopes of the straight line and the rapid component of the pressure decay curves are quite similar. When \( t_1 \) reaches a point on the pressure decay curve \( P_{ap}(0) \) where the difference between the slope of the pressure decay curve and the slope of the straight line becomes maximum, the deviation of the pressure decay from the straight line becomes visually most apparent. This point is marked as the inflection point and is an estimate of PCP. Estimated PCP is comparable with true PCP \( P_{PCP}(t_1) \) at time \( 0 \) (see also text).
distribution of $\sim 30:49:21$. If vascular compliance in humans is similar, lobar vascular compliance would be 4–4.5 ml mm Hg$^{-1}$ for a 70-kg patient. In ARDS, vascular compliance must be lower as a result of vasoactive mediators, pulmonary oedema and/or fibrosis.

We have performed a series of calculations: $R_{COT}$ was set at 0.4, 0.6, 0.8 and 1 mm Hg s ml$^{-1}$, $C_{TOT}$ at 1, 2 and 3 ml mm Hg$^{-1}$, with a fixed arterial–apillary–enous distribution of 30:50:20, and $R_v/R_{COT}$ at 0.3, 0.4, 0.5, 0.6 and 0.7. $P_{a(0)}–v$ was fixed at 30 mm Hg, and $P_{a}$ at 10 mm Hg.

The results of these calculations are shown in figure 2. The regression line between true and estimated PCP is $y = 0.96x$ with a correlation coefficient of 0.95. Thus estimated PCP underestimates true PCP but the error is relatively small. The observation that PCP estimation by visual analysis underestimates true PCP is in agreement with other studies.$^8$ The 95% confidence interval for the visual PCP determination is $\pm 1$ mm Hg.$^5$

Therefore, we have classified patients as nitric oxide responders when PCP decreased by at least 2 mm Hg.$^3$

Reducing pulse pressure by a small container with 0.4 ml of air increases compliance but does not change vascular resistance or longitudinal distribution of pulmonary vascular resistance. More importantly, pressure decay between diastolic pulmonary artery pressure and pulmonary artery wedge pressure (PAWP) should not be analysed but the decay between mean pulmonary artery pressure and PAWP should.$^6$ Therefore, we believe that visual analysis of pulmonary artery pressure decay, used in human studies, has some limitations, but is a good estimate of pulmonary capillary pressure. Our data$^1$ are also supported by our study demonstrating a decrease in transvascular albumin flux during nitric oxide inhalation.$^8$

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Intrathecal diamorphine for postoperative analgesia after Caesarean section

Editor,—Hussain and Russell$^1$ found less postoperative itching and sedation in women who had intrathecal diamorphine 0.2 mg compared with morphine 0.2 mg mixed with bupivacaine for Caesarean section. They concluded that “there seems little reason to prefer morphine to diamorphine in the UK”. I would like to take issue with this conclusion.

Diamorphine is presented only as a powder for reconstitution. The smallest mass of drug supplied is 5 mg, which must be appropriately diluted, and the correct volume of solution added to the bupivacaine. In contrast, preservative-free morphine is commercially available in the useful concentration of 2 mg in 10 ml. This may be conveniently offered to the anaesthetist to draw up 1 ml (for 0.2 mg) or 0.5 ml (for 0.1 mg), to which the desired volume of bupivacaine can be added. In the interests of minimizing the potential for drug error, particularly at emergency Caesarean section, the opioid which is ready to use seems vastly preferable.

Furthermore, morphine 0.1 mg compared with morphine 0.2 mg affords similar quality and duration of analgesia, with a reduced incidence of nausea and vomiting.$^2$ It would be interesting to establish whether diamorphine 0.1 mg has a better side effect profile than morphine 0.1 mg. However, even if diamorphine at this lower dose were shown to confer minor reductions in pain and sedation, I argue that this would not outweigh the risks inherent in the swift, accurate and aseptic preparation of the drug for intrathecal injection.

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Editor,—Dr Levy is correct when he suggests there is a small potential for a drug dose error because of the necessity to prepare the powdered diamorphine. But, in mitigation, this is a very straightforward dilution, even for a harassed anaesthetist. I am also
grateful to him for drawing my attention to the availability of preservative-free morphine (2 mg in 10 ml); our pharmacy is unaware of its existence. Dr Levy has to consider the relative risk potential for an adverse outcome between diamorphine and morphine. We have the greatest risk for an accident—a drug dilution error with diamorphine while under the supervision of the anaesthetist or delayed respiratory depression in an unobserved patient?

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Editor,—We read with interest the study of Husaini and Russell comparing intrathecal diamorphine and morphine for postoperative analgesia after Caesarean section under spinal anaesthesia. We recognize the value of this study in demonstrating the excellent postoperative analgesia that can be obtained using these drugs after such surgery and would encourage other obstetric anaesthetists to consider using the technique in their own practice.

Husaini and Russell suggest that intrathecal diamorphine may be superior to morphine for early postoperative analgesia after Caesarean section. Theoretically, this might be expected because of the higher lipid solubility of diamorphine providing a more rapid onset. However, their suggestions are based on the mean use of patient-controlled analgesia (PCA) morphine in the first 4 h after spinal anaesthetic; that is, an average morphine dose of 4.2 mg (median 2.5 mg) in those patients receiving intrathecal morphine compared with an average of 2.1 mg (median 1.5 mg) in those patients receiving intrathecal diamorphine. As stated by the authors, however, this result was not statistically significant. Furthermore, we do not believe these small amounts of morphine to be large enough to suggest a clinically important difference between the two groups. We would add our concerns that the initial set-up period of PCA use may involve administration of demonstration doses by carers and of “try it out” doses by the patient. Although these “inappropriate” doses are likely to be similar in the two groups we would recommend caution in interpretation of the amount of PCA opioid used in this initial period.

We would like to draw the authors’ attention to our developing clinical experience of using intrathecal morphine and diamorphine for postoperative analgesia after Caesarean section. We have introduced this technique into our unit following recent personal experience (J.H.) at the Women’s and Children’s Hospital in Adelaide, South Australia, where intrathecal morphine has been used successfully for a number of years (diamorphine is not available for clinical use in Australia). We, like Husaini and Russell, are interested in the relative merits of morphine and diamorphine when used in this way. We now have an audited series of 24 patients who underwent Caesarean section under regional anaesthesia and received intrathecal morphine 150 μg (12 patients) or diamorphine 200 μg (12 patients). Half of the morphine group also received intrathecal fentanyl 10–15 μg. Additional postoperative analgesia was provided with diclofenac sodium 100 mg per rectum at the end of surgery and 50 mg orally three times daily thereafter. Oral paracetamol and codeine combinations were prescribed as required. All patients underwent uneventful surgery and none required intraoperative supplementation to their anaesthetic. As in the author’s study, we found a higher incidence of pruritis in those given morphine compared with diamorphine although there was no difference in the incidence of nausea and sedation when assessed by nursing staff. Postoperative analgesia, however, appeared to be quite different between our two groups of patients. Our patients are regularly assessed by nursing staff in the first 24 h after operation using a verbal scale (none, mild, moderate or severe pain). In the morphine group, 11 of 12 patients had no pain or, at worst, mild pain. One patient developed moderate pain and no patient had severe pain. None of our patients who received intrathecal morphine required parenteral opioid after operation. In the diamorphine group, however, six of 12 patients had mild or no pain but six patients had moderate or severe pain. Two of these patients had severe pain, requiring rescue morphine i.v.

Why does our clinical experience of these techniques differ from the findings of Husaini and Russell? We suspect that the answer lies in the way postoperative analgesia is provided and the way patients are assessed. When using PCA morphine, patients tend to dose themselves until they find their own individual level of acceptable pain. There is no reason to expect that this acceptable level of pain differs between the two groups. Therefore, one would expect visual analogue scores (VAS) to be similar in each group irrespective of the intrathecal opioid used, although we accept that initially these scores may differ until PCA analgesia levels are established. Therefore, VAS levels are of limited value in comparing the two analgesic techniques in this situation but merely reflect similar access to analgesia in the two groups.

To compare the analgesic effects of the two techniques it is more pertinent, as in the study of Husaini and Russell, to examine the amount of postoperative opioid used. However, it is here where this study may be misleading. First is the provision of “as required” oral opioid. Although the number of patients using oral opioid was recorded in the study, the actual amount used was not documented. Thus there is uncertainty as to the total amounts of postoperative opioid received in several patients. Second, a large proportion of each group of patients failed to receive follow-up diclofenac on the prescribed regular basis, the reason often being that the patient felt comfortable. We feel that this is likely to reflect the amounts of PCA morphine administered in such a way as to mask any difference between the groups. Comfortable patients, declining diclofenac, may subsequently have become uncomfortable in the absence of the opioid sparing effects of non-steroidal analgesia resulting in increased PCA morphine use. The converse is that uncomfortable patients, accepting diclofenac, might then go on to use less morphine. Effectively, patients with good analgesia have been allowed to select themselves into becoming patients with poor analgesia and vice versa. This obviously has an unpredictable effect on PCA use and results in any differences between the two groups being more difficult to detect. We suggest future studies of this type should address these problems by limiting opioid availability to PCA with, if needed, titrated, documented i.v. rescue doses, and where not contraindicated, non-steroidal analgesia should be given to all patients irrespective of the level of pain at the time of dosing. This is more likely to be achieved by prescribing follow-up diclofenac by the oral route. We recognize the value of the study of Husaini and Russell in demonstrating the effectiveness of both intrathecal morphine and diamorphine for postoperative analgesia after Caesarean section. However, we remain sceptical that intrathecal diamorphine will prove as effective as intrathecal morphine and believe further studies are required to clarify this issue.

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Editor,—I am very pleased that Drs Cutts and Hopkinson have shown so much interest in our article and in their encouragement of others to use intrathecal morphine or diamorphine for pain relief after Caesarean section. They point out potential problems which may have influenced patient PCA use in the early postoperative period and suggest that these problems could account for the small difference and trend in PCA morphine use which we observed.1 They go on to suggest that even if the trend towards more PCA use in the morphine group is true, it is not clinically significant. To answer these points, demonstration PCA doses were not given by staff but the possibility of “try out” doses by patients cannot be ruled out. If such “inappropriate doses” were used, our data suggest no difference in behaviour between the groups; seven diamorphine and six morphine patients used no PCA morphine in the first 4 h and another three patients in each group used only one dose. I would not dispute the fact that the small difference between the group average doses of PCA morphine used in the first 4-h period is of little clinical significance but my anxiety is directed more towards those patients who may be more demanding in their PCA demands (e.g. 3 or more in the first 4 h): only two women in the diamorphine group but seven in the morphine group fell into this category. This difference between the groups in the numbers using larger amounts of PCA morphine just fails to achieve the usually accepted level of statistical significance of 5%. However, there is a clinically relevant difference in the early postoperative period.

Contrary to our findings, the audit being undertaken by Drs Cutts and Hopkinson suggests that morphine is superior to diamorphine and they wonder why their clinical experience is at odds with our study. I feel that the principal reason has been discussed already in our original article:1 the use of a PCA is the only

valid way of making a true comparison between different analgesia regimens. In their audit, pain is assessed on a verbal score by the midwives. Would different midwives at different times obtain similar pain assessments and, if they did, would they then set in motion the same response? How does the ward workload affect the response? It would also appear that parental opioids are not available routinely and rescue analgesia has to be provided by medical staff. Additionally, half of the morphine patients had intrathecal diamorphine and this is known to provide significant early postoperative analgesia but we are not told whether it was early or late when the difference between their morphine and diamorphine groups occurred. All of these individual points can introduce unknown confounding biases. In our study, although the doses of oral opioid used were not recorded it can be seen that compared with the diamorphine group, twice as many morphine patients used oral opioid but the VAS scores and PCA morphine demands were the same. In addition, almost identical numbers of patients in each group did not receive their full dose of diclofenac.

The importance of VAS scores is to ensure that patients in both groups attain a similar level of comfort because only then can there be a true comparison between the PCA requirements be made. If one group has higher VAS scores for pain and lower PCA demands than another group, then no reliable comparison of the PCA doses can be made. If one group has higher VAS scores and higher PCA demands, then again it is difficult to compare the groups but at least both differences are in the same direction and the real difference between the groups will be greater than a simple comparison of the PCA demands would suggest. The fact that, compared with the diamorphine group, the same, or more, morphine group patients used ancillary drugs does not support the suggestion that patients in the intrathecal diamorphine group are being “helped” so that their PCA demands are reduced to equal the demands in the morphine group. If anything, the contrary effect may be occurring.

The problem with administration of non-steroidal drugs is highlighted by Cutts and Hopkins and I would agree that ideally these drugs should be given to all patients in the immediate postoperative period, irrespective of the presence or absence of pain. This was our intention but events conspired against us. We recognized the potential difficulties of ensuring regular administration of non-steroidal agents in the planning stages and diclofenac was not our first choice. Our first choice was to use oral piroxicam 40 mg at the end of surgery (given as Feldene melt). However, we were prevented from using piroxicam by the Ethics Committee on the basis of information present in the data sheets for the two drugs; the data sheet for piroxicam specifically stipulates “Feldene is not recommended for use in nursing mothers”. The data sheet for diclofenac merely states that “traces of active substance have been detected in breast milk, but in quantities so small that no undesirable effects on the infant are to be expected”. We chose the rectal route for diclofenac to circumvent potential problems with nausea and/or vomiting but the reluctance of British women for the rectal route was just as troublesome a problem.

We were most unhappy when we discovered that diclofenac had not been given as prescribed but the midwives countered by pointing out that the women who refused rectal diclofenac were comfortable. I can reassure Drs Cutts and Hopkinson that those women who did make the very high morphine demands all received prescribed diclofenac. Thus these women did not self-select and become uncomfortable because of the absence of an opioid sparing effect of diclofenac.

As pointed out in our article, the doses of PCA morphine used in both our study groups were identical to the PCA morphine used in the diamorphine group in a previous study comparing intrathecal diamorphine with placebo after elective Caesarean section. Apart from the slight doubts about the early postoperative period, I believe that our results, taken over these two studies, indicate little difference in the analgesic properties between intrathecal morphine and diamorphine.

### Induction of anaesthesia with sevoflurane and low-dose remifentanil: asystole following laryngoscopy

**Editor,—**We wish to describe the first reported case in an adult of asystole during intubation after inhalation induction with sevoflurane and remifentanil 0.5 μg kg⁻¹. A 65-year-old man with stable angina pectoris was admitted to hospital for routine coronary artery bypass surgery. He had two vessel disease, with mildly impaired left ventricular function. His admission heart rate (HR) and mean arterial pressure (MAP) were 51 beat min⁻¹ and 100 mm Hg, respectively. He gave no history of pre-syncpe, syncope, vasovagal reactions or hypothyroidism. His angina symptoms were controlled medically with atenolol 50 mg daily, diltiazem 60 mg tid and isosorbide dinitrate 30 mg tid. These medications were continued up to and including the day of surgery. The patient was premedicated with lorazepam 3 mg. Anaesthesia was induced with vital capacity breaths of 5% inspired sevoflurane in oxygen. Loss of consciousness occurred uneventfully within 45 s, following which the inspired sevoflurane concentration was reduced to 3%. Heart rates before and after induction were 48 and 52 beat min⁻¹, respectively, and MAP values were 104 and 96 mm Hg, respectively. After loss of consciousness, rocuronium 0.6 mg kg⁻¹ was given, and remifentanil 0.5 μg kg⁻¹ was administered over 90 s, followed by infusion of 0.025 μg kg⁻¹ min⁻¹. Over the next 2 min, HR and MAP decreased to 40 beat min⁻¹ and 78 mm Hg. End-tidal sevoflurane concentration at this time was 2.2%. Immediately after laryngoscopy, the ECG changed abruptly from sinus rhythm to asystole. This was confirmed by the absence of a radial arterial pressure trace. One precordial thump was delivered, which resulted in a single ventricular complex. Atropine 0.6 mg was administered and followed by a second precordial thump, which successfully restored sinus rhythm, at a rate of 50 beat min⁻¹, with an MAP 86 mm Hg. The duration of asystole was 24 s. There were no acute ST-segment changes. The remainder of the anaesthetic was uneventful.

Vital capacity induction with sevoflurane in adults has been shown to be smooth and to maintain good cardiovascular stability with either no change, or an increase, in heart rate. Bradycardia after gaseous induction in children with 8% sevoflurane has been reported, possibly reflecting relative over-dosage. In our patient, HR increased from 48 beat min⁻¹ before induction to 52 beat min⁻¹ after induction. The end-tidal sevoflurane concentration before intubation was 2.2%. Sevoflurane is therefore unlikely to have contributed to the subsequent asystole.
Potent opioids are used frequently to reduce the pressor response to intubation, particularly in patients with ischaemic heart disease. However, potent mu agonists, fentanyl, alfentanil and sufentanil, can cause bradycardia and even asystole.6 8 The mechanism is likely a result of stimulation of the central vagal nucleus.7 There is mounting evidence of the potential of remifentanil to cause severe bradycardia.8 9 The timing of bradycardia and asystole in the case described coincided with the bolus dose of remifentanil, implicating this as the causative agent. A major predisposing factor in the patient was combined beta-adrenergic antagonist and calcium channel block therapy. Both classes of drugs have negative chronotropic effects which can be additive.10 Asystole occurred after potentiation of the vagotonic effects of laryngoscopy by remifentanil, in a patient whose sinoatrial activity was already severely depressed and who was unable to mount a balanced sympathetic response.

This case is reported to highlight the potential of remifentanil to cause severe bradycardia. When given in combination with beta-adrenergic and calcium channel block, even a relatively low dose of remifentanil, as used in this case, can result in asystole.

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Aprotinin therapy and disseminated intravascular coagulation after hip replacement

Editor,—We read the case report by Logan regarding a patient who developed disseminated intravascular coagulation after the use of polymethylacrylate bone cement during a revision hip replacement and died shortly after.1 We wish to report an almost identical case in which the use of aprotinin resulted in correction of haemostatic failure.

A 90-yr-old female known to have aortic stenosis (gradient 50 mm Hg) and left ventricular hypertrophy underwent a left revision hip replacement under general anaesthesia with continuous central venous pressure and arterial pressure measurement. The intra-operative course was unremarkable apart from episodes of hypotension after induction and after cement insertion which required treatment with metaraminol. Approximately 90 min after cement insertion and while the patient was in the postoperative recovery area, another episode of hypotension occurred (68/43 mm Hg) and this was associated with a decrease in central venous pressure from 8 to 1 mm Hg. Inspection of the wound revealed blood seeping through the dressing; the wound drain had rapidly filled with another 450 ml of blood. A clotting screen at that time revealed a prothrombin time four times normal, activated partial thromboplastin time 98 s, platelet count 56 x 10^9 litre^-1 and haemoglobin concentration 8 g dl^-1. Over the next 45 min, despite 4 units of FFP, 2 units of platelets and 6 units of blood, the bleeding continued and repeat studies confirmed ongoing consumption coagulopathy. A test dose of aprotinin 50 ml was administered and this was followed by continuous infusion at 50 ml h^-1 for the next 1 h. Within 40 min of commencing this therapy, clot formation was noted for the first time and the requirement for blood/colloid replacement was reduced. In total, 17 units of blood were transfused. The rest of the recovery period was uneventful and further FFP and platelets were not required.

Aprotinin is an inhibitor of proteolytic enzymes, including plasmin. Clinical studies have demonstrated or suggested a protective effect against haemorrhage in surgical situations which have included liver transplantation and vascular surgery.1 2 In this case, where a severe coagulopathy was associated with polymethylacrylate bone cement and hip surgery, we observed rapid reversal of haemostatic failure and would advocate its use in similar circumstances.

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References


**Laryngeal mask and tonsillectomy**

Editor,—We read with interest the letter from Dr Venn1 which highlighted a complication of the use of the laryngeal mask airway (LMA) during tonsillectomy in an adult male. He described snaring of the pilot balloon tubing by the surgeon which caused it to be severed and the LMA cuff to deflate during the surgical procedure. The consequences of such an event in the presence of intra-operative tonsillar haemorrhage, we agree, can be serious.

It is essential, therefore, that the anaesthetist is fastidious when inserting the LMA after induction, ensuring that it is the correct size for the patient, does not rotate on insertion, remains seated in the midline and is adequately secured. Once inserted, it is then our practice to align the flexible LMA tubing together with the pilot tubing in the midline over the lower incisors and lip, and secure them firmly, taking care to avoid any slack which would allow either of the tubes to drift and potentially become trapped by the Boyle–Davis gag or, in this case, the snare. If this technique is adhered to, we see no reason to resort to taping the pilot tubing to the main tubing of the mask.

Indeed, this method of taping may alter the unique characteristics of the reinforced LMA that make it so adaptable in its use. During the manufacture of the LMA, the main tubing, which is composed of silicone, is formed separately from the pilot tubing and unlike a tracheal tube, the pilot tubing is not incorporated into the main construction, as this would lead to a reduction in the flexibility of the LMA, the very nature of which makes it ideal for intra-oral surgery. It has also been reported that the mask may become obstructed by the Boyle–Davis gag; this is usually a result of the LMA being too large or too large a blade on the gag being selected.2

We cannot stress enough, therefore, that when the airway is shared between anaesthetist and surgeon, both need to be extra vigilant to ensure airway patency.

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Editor,—I was interested to read the report of surgical damage to the pilot tube while using a laryngeal mask for airway maintenance during tonsillectomy.3 Dr Venn is incorrect in asserting that this complication has not been reported previously, however.

My colleague and I encountered an almost identical situation during tonsillectomy on a 15-yr-old girl. In our case, the problem came to light when the surgeon handed the severed end of the pilot tube to the scrub nurse along with the first tonsil. Fortunately, the laryngeal mask continued to perform its function with atmospheric pressure only in the cuff, the larynx was not soiled and there was no evidence of airway obstruction. Therefore, we were able to complete the case without replacement of the laryngeal mask.

An awareness of the recommendation to secure the pilot tube alongside the stem of the laryngeal mask, made in our report,4 may have prevented the further incidence of this unfortunate complication.

J. A. SHORT
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Editor,—Thank you for the opportunity to reply to Drs Porter and Bailey and Dr Short on my correspondence about a complication while using a flexible laryngeal mask airway for tonsillectomy.

I note that a similar complication was reported by Short and Melillo in 1997. I presume that in their case the pilot tube had sealed while being transected, thus maintaining pressure in the cuff with no change in the patency of the airway. This does sometimes occur and is a good reason to use a syringe to deflate the cuffs of tracheal tubes rather than cutting the pilot tube before extubation. The case I reported demonstrates that this will not always happen.

While I welcome the comment made by Porter and Bailey regarding vigilance when inserting the laryngeal mask for shared airway cases, I do not fully understand their reservations about taping the pilot tube to the main tube. I presume the altered characteristics to which they refer relate to possible tension on the pilot tube while using a laryngeal mask for airway maintenance during tonsillectomy. I was interested to read the report of surgical damage to the pilot tube while using a laryngeal mask for airway maintenance during tonsillectomy. Dr Venn is incorrect in asserting that this complication has not been reported previously, however.

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