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More on Problems with Removing the Arrow FlexTip Epidural Catheter: Smooth In—Hardly Out?

To the Editor:-We read with great interest the letter from Woehlck et al.<sup>1</sup> and the accompanying response from Arrow Inc.,<sup>2</sup> (Reading, PA) concerning problems with removing the Arrow FlexTip epidural catheter. We wish to underline the importance of this topic with our own experience.

In a woman (65 yr, American Society of Anesthesiologists physical status III, 167 cm, 72 kg) a thoracic epidural catheter (7/8 interspace, in place for 7 days) could not be removed despite multiple attempts, including replacing the patient in the position in which the catheter had been inserted. Unfortunately the plastic outer portion disrupted first and then the wire. After radiographic visualization, the remaining part of the disrupted catheter needed to be removed surgically. Both parts of the disrupted catheter were sent to Arrow Inc., for analysis, but no signs of failure of material could be detected.

In a 48-yr-old man (American Society of Anesthesiologists physical status I, 187 cm, 83 kg) lumbar epidural anesthesia, with use of a FlexTip catheter for arthroscopic surgery of the knee, was induced with the patient in the right lateral decubitus position. After the operation, multiple attempts to remove the catheter while the patient was in the left lateral decubitus position were unsuccessful. Therefore, we turned the patient in the right lateral decubitus position, in which position the catheter originally had been inserted. During this maneuver, we observed that the catheter shifted around 2.5 cm within the skin across the back of the patient. After replacing the patient in the right lateral decubitus position the catheter could be removed without any problems.

#### Anesthesiology 2000; 93:1362

In Reply:-We appreciate the correspondence from Drs. Hopf and Leischik elaborating on the difficulties of removing the Arrow (Reading, PA) FlexTip epidural catheter. In our patient,<sup>1</sup> as in the first patient described by Drs. Hopf and Leischik, the catheter could not be removed even when the patient was in the position in which the catheter was placed originally. For the other cases they described, it seems that placing the patient in the original position resulted in easier removal of the catheter than while the patient was in any other position. This may imply that compressive forces that exist when the catheter is in place between bony structures may be minimized when the patient is returned to the original insertion position. It also implies that greater friction forces exist with this catheter than with other types of catheters.

As Keim<sup>2</sup> noted, the FlexTip Plus is made from a very soft polyurethane material. When passed through the epidural needle, it is probable that little if any lateral force exists that would produce friction that could impair insertion, and the softness of the catheter may be a significant attribute. It is probable that considerable lateral force is applied to the catheter by tissue after the needle is withdrawn. One

Thereafter, we were aware of at least two other patients in whom an epidural catheter could only be removed with considerable (in our experience, unusual) resistance in the sitting and semirecumbent positions, respectively, and we were unable to explain this phenomenon. Both catheters could be removed easily after replacing the patients in the lateral decubitus position, in which position the catheter originally had been inserted.

We agree completely with Keim<sup>2</sup> that (1) occasionally a FlexTip is more difficult to remove and requires extra care and (2) that, in the case of problems of removal of the FlexTip catheter, it might b removed successfully with the patient in the position in which it had been inserted originally. Therefore, we propose incorporation of both statements in the manufacturer guidelines for use.

\*Hans-Bernd Hopf, M.D., Matthias Leischik, M.D. \*Abteilung für Anär thesie und Intensivmedizin, Langen, Germany. H-B.Hopf@t-online.de

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2. Keim DG: Uncoiling of wire in Arrow FlexTip epidural catheter on remova ANESTHESIOLOGY 2000; 92:908-9

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ې can speculate that the coefficient of friction may not correlate with the firmness of the catheter, and could potentially be greater with the Flex Tip catheter than with other types of catheters. This might be  $ar{\overline{s}}$ important factor in the difficulty of removal. This seems to be an are $\overline{z}$ that may prove to be a fruitful topic for further study. We agree with Drs. Hopf and Leischik that the difficulty of removal may be of cong siderable clinical importance and should result in appropriate labeling of the device.

Harvey J. Woehlck, M.D., Medical College of Wisconsin, Froeder Memorial Lutheran Hospital, Milwaukee, Wisconsin. hwoehlck@mcw.edu

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# Rapid Opioid Detoxification during General Anesthesia: Is Death Not a Significant Outcome?

To the Editor:-We found the article by Gold et al.<sup>1</sup> in the December 1999 issue of ANESTHESIOLOGY, which described results with anesthesiaassisted rapid opioid detoxification (AROD) interesting. During the past decade, the practice of opioid detoxification during general anesthesia has become increasingly popular. Despite this, there is scant literature to document the advantages and disadvantages of this procedure. Therefore, Gold et al.1 provide valuable information about patient selection, the anesthetic techniques used, and the degree of residual symptoms observed after the procedure. They also present preliminary information regarding abstinence rates after AROD. The authors should be commended for providing this clinically useful information.

Unfortunately, the authors do not include in the abstract that 1 of the 20 patients died between 34 and 41 h after the end of the procedure. Not until near the end of the Results section of the body of this article is the death mentioned. Obviously, death is a terrible complication and a significant finding, particularly because this is an experimental procedure. Moreover, the authors state in the Results section of the abstract: "all 20 patients were successfully detoxified with no adverse events." This is outrageously misleading; in the hands of these authors, AROD has a mortality rate of 5% within 48 h; however, it seemed that the death was not directly the result of the administration of general anesthesia. Because of the absence of illicit drugs in the patient's system at the time of death, death was in all likelihood related to effects of the precipitated withdrawal process.

We agree with the authors' recommendation to provide continuous cardiac monitoring of AROD patients during their hospital stays. In a previous issue of ANESTHESIOLOGY, Kienbaum et al.,<sup>2</sup> reported profound increases in plasma epinephrine concentrations and cardiovascular stimulation during naloxone-precipitated opioid withdrawal during anesthesia. Even more recently, Allhoff et al.3 concluded that ultrashort opiate detoxification is associated with a risk of QT-interval prolongation and bradycardia. Furthermore, these effects could be related to hypokalemia or the use of clonidine during the procedure. Because of the increase in circulating catecholamines and the likeli-

Anesthesiology 2000; 93:1363-4

In Reply:-Dr. Whittington raises a valid point. The death of one patient after anesthesia-assisted rapid opioid detoxification is a significant event, and we clearly recognized it as such. However, his concern is over the decision to omit this information from the abstract and instead, to describe the patient's death in the Results section of the manuscript. He also takes issue with our statement of "successful detoxification of 20 patients without adverse events.<sup>1</sup>"

We gave serious thought to the construction of the abstract. We looked very closely at all the information available to determine the cause of death, but were unable to do so. Dr. Whittington believes that, because no illicit drugs were found in the patient's blood, death was "in all likelihood" related to the effects of the procedure. Our conclusions were much less clear. We considered the patient's history of hypertension and smoking as contributory to a possible myocardial infarction, and other causes of sudden death, for example, aneurysm or pulmonary embolus. We believe the abstract is not the place to speculate when information is not available.

Dr. Whittington mentions some well-known physiologic changes that can occur during some less widely used protocols, *i.e.*, increased plasma catecholamine levels and prolonged QT intervals. The issue hood of fluid and electrolyte loss during precipitated withdrawal, there is certainly the potential for a significant arrhythmia after AROD. Therefore, we also advocate the use of continuous monitoring (telemetry and pulse oximetry) during a hospital stay for AROD. We are conducting the first National Institutes of Health-funded (Bethesda, Maryland) randomized trial that compares the safety and effectiveness of AROD with two alternative methods of opioid detoxification, and we incorporate this monitoring for all AROD patients. Again (although this omission is far less serious), in the Conclusion section of the abstract, the authors do not mention the potential need for increased monitoring

We recognize that editorial considerations limit the material that ca be included in an abstract; these omissions from the abstract, however are serious. Today, computerized literature searches often yield little more than the abstract of an article. As a result, the most significange findings from a study must be included in the abstract of the article. W₫ therefore respectfully ask the editors to publish a correction to the abstract of this article. In a study designed to evaluate a novel, experience imental procedure, such as AROD, can there be a more significan finding than death?

\*Robert A. Whittington, M.D., Eric D. Collins, M.D., Herber D. Kleber, M.D. \*Columbia University, New York, New York raw9@columbia.edu

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that is not well-known or perhaps not known at all is whether any of these changes persist into the postdetoxification period and, if so, for how long. The majority of patients undergoing the procedure ars discharged to home the day after the procedure; therefore, detailed collection of physiologic data has not been possible. This patient me all discharge criteria within 24 h of the procedure.

Our protocol specifically addressed the hemodynamic changes of withdrawal, and we did not see changes in heart rate, blood pressure, or the electrocardiogram. This is not to say that these types of events could not occur, but we did not see them in this patient. Furthermore, we clearly mention the potential need for postprocedure monitoring in the Discussion section; therefore, his comment concerning this "omission" is in error. We are pleased to see that Dr. Whittington has received support for a study that incorporates this type of monitoring. We look forward to his results and plan on proceeding the same way in our own program.

Finally, we used currently accepted clinical criteria in determining the end point for detoxification. These criteria were applied after the patient had emerged from anesthesia and before the patient's discharge from the postanesthesia care unit. We repeat our conclusion

from the study that all 20 patients were successfully detoxified without adverse events. We clearly describe adverse events that occurred, such as nausea or diarrhea and the death of a patient, but all were encountered in the postdetoxification period while the patients were with the rehabilitation service. We have treated 41 patients, and there have been no other deaths in our program.

Current efforts are under way to more fully explore the deaths associated with anesthesia-assisted rapid opioid detoxification worldwide. We join other practitioners and researchers in anticipating the results of those studies. There is no reason to publish a correction to our abstract

Anesthesiology 2000; 93:1364

\*Carl G. Gold, M.D., M.A., David J. Cullen, M.D., M.S., Scott Gonzales, M.D., Deirdre Houtmeyers, R.N., Mary Jo Dwyer, A.S. \*Gulf-Shore Anesthesia Associates, Corpus Christi, Texas. cgold@tiac.net

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## © 2000 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc. Which Parameter Measures the Effectiveness of Volume Preload in **Pregnant Patients?**

To the Editor:-- I congratulate Dr. Ueyama et al.1 for their work regarding the effects of crystalloid and colloid loading in parturients undergoing spinal anesthesia. However, the relevance of this workand many other studies concerning fluid loading-to fetal well-being is not entirely clear. Studies consistently have shown a beneficial effect of volume loading on maternal blood pressure or the response to the induction of spinal or epidural anesthesia. Moreover, the importance of maternal blood pressure on the fetus is unclear. For example, our work has shown that changes in cardiac output produced by volume loading may correlate better with uterine blood flow than does blood pressure.<sup>2</sup>

Profound hypotension clearly can compromise uterine perfusion, but the influence of lesser changes or of various interventions used to influence blood pressure is unknown. In our opinion, the issue of volume loading may be centered on the wrong parameters. A far better end point would be something such as uterine blood flow or perhaps umbilical blood flow. In the past, these could only be assessed in animals.<sup>3</sup> However, Doppler methods now permit such measurements. In fact, the current availability of color Doppler makes it possible to measure not only flow velocities, but also absolute flow in selected vessels. To measure the effectiveness of therapeutic interventions in

Anesthesiology 2000; 93:1364

In Reply:-We thank Dr. Marcus for the interest in our work and the comments. In parturients with normal uteroplacental circulation, uterine blood flow is the major determinant of oxygen transport to the fetus. The increase in uterine blood flow after colloid preload suggested by Dr. Marcus is interesting. Our results suggested that colloid preloading resulted in marked increases in maternal cardiac output without significant change in blood pressure. Therefore, the increase in uterine blood flow may be associated with an increase in maternal cardiac output.

Doppler ultrasonography is the most commonly used method to measure uterine blood flow in humans. The velocity of the blood flow is one of the representative parameters measured with Doppler ultrasonography. However, the reliability of the measurements is controversial because shape of the waveform is affected by many factors, such as maternal cardiac output, elasticity of the vessel wall, outflow impedance, and blood viscosity. Calculation of blood flow necessitates precise determination of mean velocity, angle of insonation, and vessel diameter. Although angle of the insonation and blood velocity are

Downloaded obstetric anesthesia practice, future studies should take advantage of this new technology, rather than being limited to parameters such as blood pressure, blood volume, and cardiac output.

\*Marco A. E. Marcus, M.D., Ph.D., Thomas Möllhoff, M.D., Ph.D. Harthmut Buerkle, M.D., Ph.D., Gerd Brodner, M.D., Hugo van Aken, M.D., F.R.C.A., F.A.N.Z.C.A., Ph.D. \*Westfälische Wilhelms Universität, Münster, Germany. marcus@anit.uni-muenster.de a

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determined correctly, accurate measurement of small-vessel diameters such as the diameter of a uterine artery, is difficult. It is also not clear whether the blood flow reflects the functional placental perfusion because some portion of blood flow is shunted to the myometriumg Therefore, extrapolation of measurements from the Doppler ultrasono graphic method must be done with caution.

As Dr. Marcus pointed out, an understanding of the uteroplacenta blood flow is essential in obstetric anesthesia practice. However, the goal of our anesthetic management is to maintain fetal oxygenation, not uterine artery blood flow. We think that, in the future, fetal oxygenation monitoring would show the effect of preloading on fetal oxygenation.

Hiroshi Ueyama, M.D., Osaka University Medical School, Suita, Osaka, Japan. ueyama@hp-op.med.osaka-u.ac.jp

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# Ten Milligrams Intrathecal Bupivacaine Is Too High for Spinal Anesthesia for Hip Surgery in the Geriatric Population

To the Editor:-Ben-David et al.1 have shown the advantages of combined low-dose bupivacaine and fentanyl spinal anesthesia versus a "conventional" dose of 10 mg bupivacaine. The 90% incidence of hypotension in the 10-mg bupivacaine group is very high (one of the disadvantages of including a small number of patients). This could have been minimized if the authors had chosen a smaller dose for the control group. Biboulet et al.2 considered a dose of 5 mg intrathecal bupivacaine to be "too high" to limit the block to T10 in geriatric patients because of a 40% incidence of hypotension. Moreover, Bendavid et al.3 have shown that a dose of 7.5 mg bupivacaine can produce an acceptable block up to T8. Choosing a 10-mg dose as a control in this study that involved geriatric patients exacerbated the differences among the two groups.

The authors did not mention anything about the quality of motor block in the minidose bupivacaine group. A previous study with 5 mg bupivacaine showed that in nearly 80% of the patients a Bromage scale score of 2 or 3 was not achieved.<sup>3</sup>

I wonder whether the incidence of hypotension could be further lowered if "unilateral" spinal were attempted. It has been shown that glucose-free bupivacaine is hypobaric<sup>4</sup> and, in low doses, can be used to provide satisfactory unilateral block and hemodynamic stability.<sup>5</sup>

Anesthesiology 2000; 93:1365

In Reply:-Our finding of a 90% incidence of hypotension after single-dose ("conventional") spinal anesthesia in elderly patients is consistent with the high incidence of hypotension reported in the literature.1 Others have reported a 100% incidence of hypotension necessitating vasopressor treatment.<sup>2</sup> Buggy et al.<sup>3</sup> found a 75% incidence of systolic hypotension even with a volume loading of 500 ml hetastarch, 6%, plus 500 ml Hartmann's solution. The strong association of spinal hypotension with ST depression in this patient population is cause for concern.4

Our choice of a 10-mg dose of spinal bupivacaine was intended to represent conventional practice and not necessarily the lowest dose of bupivacaine. This choice was arbitrary and, I suspect, underestimates the dosing used by many of our colleagues. The important point, however, is that, rather than treat hypotension, one can avoid it by using a low-dose local anesthetic plus an opiate spinal technique.

It is true that this technique provides a "nociceptive block" and does not provide a profound motor block. Certainly, there are surgeries in which the need for an intense motor block would necessitate higher doses of local anesthetic if one is to use spinal anesthesia. Likewise, there are surgeries (e.g., ambulatory) in which the absence of a profound motor block may be advantageous.

Our article did not intend to suggest that there is no other way to reduce the hypotension of spinal anesthesia. Titrated dosing with

This may be particularly useful in geriatric patients who are likely to be more sensitive to the sympathetic blockade induced by intrathecal local anesthetics.

Santhanagopalan Kannan, M.D., Queen Elizabeth Hospital, Birmingham B15 2TH, United Kingdom. achalu@btinternet.com

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continuous spinal anesthesia is fairly effective in this regard,<sup>2</sup> but it is my impression that many practitioners prefer the speed and simplicity of a single-shot technique. Although unilateral spinal anesthesia migh offer greater hemodynamic stability than bilateral blockade, at best it is impractical (time-consuming) when surgery is to be performed with the patient in the supine position.

Bruce Ben-David, M.D., Allegheny General Hospital, Pittsburgh Pennsylvania. bbendavid@mindspring.com

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Anesthesiology 2000; 93:1365-6

© 2000 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc. Patient in "Sniffing Position"

To the Editor:-Contrary to the statement in the letter by Adnet et al.,<sup>1</sup> figure 1 does not show a patient in the sniffing position. The sniffing position necessitates approximately 30-35° of flexion of the neck axis on the chest axis. Placing a patient's head on a pillow is irrelevant if it does not achieve this end point. In figure 1 of the letter by Adnet et

al.<sup>1</sup> the neck seems to be flexed on the chest by only 5°. If the neck had been flexed on the chest by approximately 30-35°, the laryngeal axis would be almost identical to the pharyngeal axis, and the laryngeal and pharyngeal axes would be much closer to the oral axis. In addition, flexion of the neck on the chest might have permitted a slightly greater

degree of extension of the head axis on the neck axis, thereby further bringing the laryngeal, pharyngeal, and oral axes into alignment. I do not believe that figure 1 of the letter by Adnet et al.<sup>1</sup> shows the patient in sniffing position.

Jonathan L. Benumof, M.D., University of California San Diego Medical Center, San Diego, California. jbenumof@ucsd.edu

Anesthesiology 2000; 93:1366

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position adopted for autoscopy (laryngoscopy) must therefore be

@ 2000 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc. Historical Perspective of the "Sniffing Position"

To the Editor:-Sir, may we contribute a small historical addendum to the correspondence from Adnet et al.1 concerning the correct positioning for laryngoscopy and tracheal intubation? The authors state that it is Chevalier Jackson who is credited with observing that alignment of oral, pharyngeal, and laryngeal axes is necessary for successful visualisation of the larynx and subsequent tracheal intubation; a description of his technique was published in the literature in 1913 and helped to popularize routine laryngoscopy. However, the principles of laryngoscopy had been laid some 18 yr before by Alfred Kirstein, a Berlin physician who invented the laryngoscope.<sup>2</sup> In his publication about direct laryngoscopy,3 Kirstein reported that

... the body must be placed in such a position that an imaginary continuation of the laryngotracheal tube would fall within the opening of the mouth .... When the military position is assumed, the continuation of the windpipe would strike somewhere in the neighbourhood of the root of the nose; when the head is bent comfortably backward, as in looking aloft, it would about strike the chin . . . . The

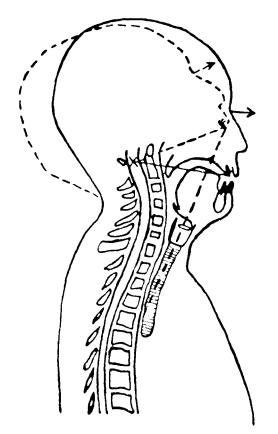


Fig. 1. Kirstein's suggested position (dotted lines) for laryngoscopy. Reprinted with permission.<sup>2</sup>

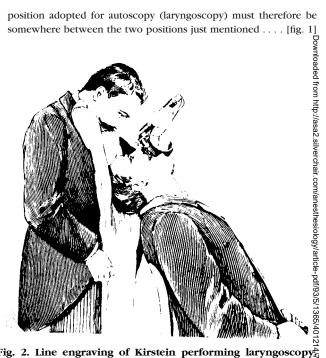


Fig. 2. Line engraving of Kirstein performing laryngoscopy Reprinted with permission.<sup>2</sup>

Kirstein was therefore almost certainly the first to describe what subsequently became called the "sniffing the morning air" position. His practical conduct of laryngoscopy (fig. 2) clearly shows that he was

also aware of the importance of rotation at the atlantooccipital joint.

\*Nicholas P. Hirsch, M.B., B.S., F.R.C.A., Gary B. Smith, B.M.g F.R.C.A., F.R.C.P. \*The National Hospital for Neurology and Neurosurgery, Queen Square, London WCIN 3BG, United Kingdomg hirsch@btinternet.com 2024

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(Accepted for publication June 1, 2000.)

In Reply:-We agree with Professor Benumof that the angle of flexion of the neck shown on the radiograph was not exactly 30-35° from the horizontal axis. This radiograph was obtained while the patient was in standard position for intubation, with a cushion under the head as routinely performed in our operating room. However, we are not sure that the angle was  $5^{\circ}$ , as stipulated by Professor Benumof. Professor Benumof stated that the sniffing position necessitates 30-35° of flexion of the neck axis on the chest. This was established by Horton et al.1 These angles were defined between (1) the neck axis (defined by two landmarks: anterior portion of the cricoid and the lowermost depth palpable in the sternal notch) and (2) the horizontal axis.<sup>1</sup> Our radiography was performed with use of a portable X-ray machine; therefore, it is uncertain that the bottom of the radiograph corresponds to the horizontal axis. Moreover, because the two landmarks described by Horton et al.1 are not visible in the radiograph, it is difficult to measure the angle of the neck flexion. We also disagree with Professor Benumof in establishing a relation between the degree of neck flexion (or extension of the head) and the alignment of the oral, pharyngeal, and laryngeal axes. This relation has never been shown. The relation between angle of neck flexion (or head extension) and alignment of the three axes (oral, pharyngeal, and laryngeal) has never been investigated scientifically to our knowledge. The figure reproduced in the textbook by Benumof<sup>2</sup> shows a patient in the sniffing position with the hard palate (i.e., oral axis) in line with the trachea; this alignment is almost impossible to attain in a anatomically normal patient, whatever the angle of neck flexion. The most important point is that, in the classic article by Bannister et al.,2 this anatomic error was described because the figure is not true to the radiograph. Nevertheless, this figure has found its way into the anesthesiology literature.

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We thank Dr. Hirsch and Dr. Smith for their interesting historical contribution. We can credit Dr. Kirstein as the first author who described atlantooccipal extension for direct laryngoscopy. However, Chevalier Jackson, in 1914, was the first who described clearly this maneuver for laryngoscopy to intubate a patient during anesthesia. The three-axis alignment theory was described not by Chevalier Jackson, but by Bannister in 1944.3 For the sake of completeness, the name "sniffing position" comes from the Magill<sup>4</sup> article (in 1936) in which he described the optimal head position for laryngoscopy:

... The head itself is slightly extended on the atlas, so that the mandible is approximately at right angles to the table. When he wishes to sniff the air, a man in the normal erect posture insting tively and unconsciously takes this attitude ....

Frederic Adnet, M.D., Ph.D., Hopital Avicenne, Bobigny, France frederic.adnet@avc.ap-hop-paris.fr from http://asa2.

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To the Editor:—We read with interest the study by MacGregor et al.,<sup>1</sup> which showed that markedly different dopamine plasma levels may result from similar infusion rates in a homogenous population. Their results bear considerable similarity to a study we performed with epinephrine infusions at a time when arrhythmogenicity of anesthetics was a major concern. We identified that clearance of epinephrine and cardiac output were markedly and variably enhanced as much as 45 min after a large but brief epinephrine infusion in a canine model<sup>2</sup>; however, arrhythmias tended to occur at similar plasma levels. Presumably because of this difference in cardiac output and clearance of epinephrine, different infusion rates were necessary to produce similar plasma levels of epinephrine; however, the range was not as dramatic as those determined by MacGregor et al.<sup>1</sup> with dopamine. Because dopamine and epinephrine both stimulate a multitude of catecholamine receptors, some of which have opposing hemodynamic effects, one should not find these results surprising. The phenomenon of attaining markedly different plasma levels for a particular infusion rate

adrenoceptors. The results may be even more variable when subjecte  $\mathbf{\hat{a}}$ to interactions with  $\alpha$ - and  $\beta$ -adrenoceptor blocking drugs, which mag alter the effects of these catecholamines on circulation and ultimately

on their own clearance. Harvey J. Woehlck, M.D., Froedtert Memorial Lutheran Hospital Milwaukee, Wisconsin. hwoehlck@mcw.edu References

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Anesthesiology 2000; 93:1368

In Reply:-Information concerning the use of catecholamines continues to be confusing and conflicting. A recent study by Ichai et al.1 showed that dopamine, in doses of 3-, 7-, and  $12-\mu g \cdot kg^{-1} \cdot min^{-1}$ , increased creatinine clearance in a group of critically ill patients, whereas similar doses of dobutamine had no effect on this parameter of renal function. These data directly contradict a previous study performed by Duke et al.<sup>2</sup> 5 yr previously. These conflicting results, combined with information such as the data by Woehlck et al. further substantiate the fact that plasma concentrations, clinical effects, and outcomes are very unpredictable with catecholamines. It is my hope that we are developing a standard of care concerning the use of catecholamines in the intensive care unit: these medications should be titrated to a specific desired effect rather than being used in "standard" doses for unclear therapeutic endpoints.

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Drew A. MacGregor, M.D., Wake Forest University School of Medicine, Winston-Salem, North Carolina. dmacg@wfubmc.edu

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# Preemptive Analgesia: What Does It Really Mean?

To the Editor:--I read with interest the article by Motamed et al.<sup>1</sup> in the February issue of ANESTHESIOLOGY, and agree with their finding that intravenously administered morphine-6-glucuronide (M-6-G) lacks analgesic effect. However, I am troubled by their conclusion (reflected in the title) that preemptive M-6-G is not an effective analgesic. Their methods indicate that at the beginning of skin closure, patients received intravenous morphine sulfate, M-6-G, or saline. The use of the word "preemptive" in this regard is wrong because the analgesics were administered after the surgical incision and because they were not maintained postoperatively.

The goal of preemptive analgesia is to prevent the establishment of central sensitization, which then amplifies postoperative pain.<sup>2,3</sup> Postinjury analgesia usually has a reduced effect because central sensitization already has been established. Carr<sup>4</sup> cautions against the routine use of the word preemptive. He states that preemptive refers to measures that prevent sensitization of cells within the spinal cord dorsal horn and that preemptive anesthesia by definition must be accomplished before the onset of nociception. Central hypersensitivity may develop despite the use of analgesia before a noxious stimulus. This may happen if the analgesia is inadequate to prevent central sensitization or if the analgesia is only provided before the stimulus. Postinjury hypersensitivity develops

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In Reply:-Dr. Hepner rightly calls attention to the misuse of the word "preemptive." In our study,<sup>1</sup> we suggested in the title that morphine-6-glucuronide (M-6-G) lacks preemptive analgesic effect. From a semantic point of view, we agree with Dr. Hepner's comment because M-6-G was administered after the start of surgery. Nevertheless, we stress that most anesthesiologists use central analgesics in combination with intravenous general anesthetics at induction of anesthesia. Thus, in our routine practice, preemptive analgesia is commonly used without deliberate intention.

secondary to inflammatory changes that occur as a result of an injury and can also lead to central sensitization.

In summary, preemptive analgesia must occur before the injury must be adequate to prevent central sensitization, and must be main tained postoperatively to prevent the inflammatory changes associate with postinjury hypersensitivity.

David L. Hepner, M.D., Brigham and Women's Hospital, Harvare Medical School, Boston, Massachusetts. dhepner@zeus.bwh.harvard.edu

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\*Philippe Duvaldestin, M.D., Cyrus Motamed, M.D., Xaviek Mazoit, M.D., Khaldoun Ghanouchi, M.D., Frederic Guirimand, M.D., Kou Abhay, M.D., Thomas Lieutaud, M.D., Said Bensaid, M.D., Christine Fernandez, Ph.D. \*Hôpital Henri Mondor, Creteil, France. philippe.duvaldestin@hmn.ap-hop-paris.fr

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