

Risk Assessment and Control Require Analysis of Both Outcomes and Process of Care

ALTHOUGH one may be tempted to neglect rare complications because they are infrequent and therefore difficult to study, they require our attention for several reasons. They are often severe. They are often thought by our patients and their families to be unacceptable. They occur in young and otherwise healthy patients. These comments are valid for most severe complications of regional anesthesia and particularly for spinal hematoma or meningitis associated with central neuraxial blocks. In this issue of ANESTHESIOLOGY, Moen *et al.*¹ report the results of a large investigation of severe neurologic complications after central neuraxial block. This study represents an enormous piece of work, and the authors should be commended for their efforts to gather data as completely as possible. The study also allows us to consider several features related to patient safety and to discuss emerging thinking in the study of rare events. General lessons can be made in three areas: how to collect data for rare events, how to analyze these data, and how to select and implement strategies to improve patient safety.

The reporting systems to study a rare event must cover a large number of institutions and must usually be implemented at a nationwide level (or even at a multinational level, as already done in studies related to aviation safety§). A system may rely on mandatory reporting; this is the case with regional blocks performed in Sweden during a 10-yr period thanks to the unique national registry to which all severe complications should be reported. However, even such a mandatory system does not guarantee that all existing cases will be reported, which may result in too few cases to identify causal factors to develop an effective safety strategy. This explains why Moen *et al.* judiciously searched for other

sources of information. Voluntary reporting systems offer a useful alternative (or addition) despite a significant risk of underreporting.² Because results are often debated locally, even more potential exists to improve the behavior of those acting in the cases, conduct in-depth causal analysis of cases, and identify precursory events.^{3,4} When precursors are identified, the usual strategy consists of expanding the scope of the reporting system to include near misses (fig. 1).⁵ When safety has been improved to such a high level that events occur very infrequently or even have not yet occurred (such as in the nuclear power industry), reporting systems are no longer efficient. Modeling risk becomes necessary and is a preemptive strategy based on prediction of what *could* happen.⁶ Unfortunately, risk control in anesthesiology has not yet reached such a high reliability level.

Regarding causal analysis, the authors rightly point out that, during the study period, Swedish anesthesiologists perceived thromboprophylaxis as a limited risk factor for spinal hematoma and that the first Swedish guidelines describing the management of regional anesthesia in patients receiving low-molecular-weight heparin were published after the end of the study period. However, the methodology does not allow us to establish any causal relation between factors and outcome. Behind the outcome is the process of care, and we must move from the question "What happened?" to "Why did it happen?" Moen *et al.* report 11 cases of hematoma that occurred in patients with coagulopathy or thromboprophylaxis administered in close relation with central neuraxial block. In some of these cases, failures would certainly have been identified, had the method been designed to address the process of care. These failures (*e.g.*, low-molecular-weight heparin overdose in elderly patients) are also contributing factors. However, shifting from "What happened?" to "Why did this happen?" also requires one to change investigation tools. According to James Reason, patent failures are those committed by clinicians working in direct contact with patients, whereas latent failures represent the consequences of structural, technical, or organizational characteristics often related to management decisions.⁷ Patent failures include human errors and have already been studied in anesthesia.⁸ Root cause analysis used by the Joint Commission of the United States|| or the systems analysis used by Vincent *et al.* in London# are typical examples of innovative methods to study system errors. However,

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§ Aviation Safety Reporting System. Available at: <http://asrs.arc.nasa.gov>. Accessed July 14, 2004.

|| Agency for Health Care Research and Quality. Available at: www.ahrq.gov. Accessed July 14, 2004.

National Patient Safety Agency. Available at: www.npsa.nhs.uk. Accessed July 14, 2004.

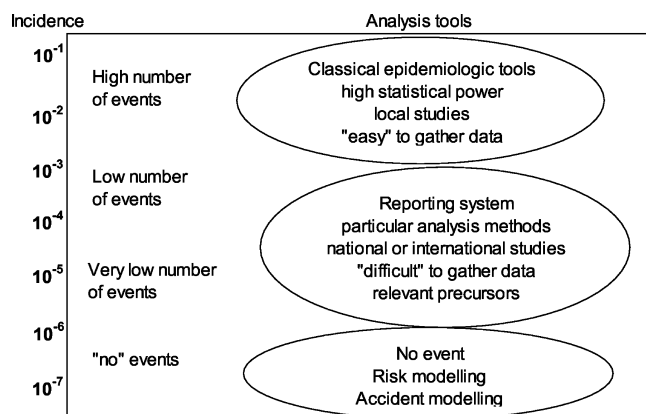


Fig. 1. Relation of occurrence of events and analysis tools.

several biases can occur when using these methods, especially because outcomes (or events) are being investigated. An outcome bias can interfere with analysis because those reporting the event are obviously aware of the clinical outcome. Propensity to a more severe judgment is often associated with a poor outcome.⁹ Hindsight bias is the exaggerated extent to which individuals indicate they would have predicted the event beforehand.¹⁰ Although reduction of this bias is difficult, a way to reduce it could be to systematically ask people to consider all other possible solutions that could explain what happened and to state all the reasons why other causes might have been correct.¹¹ For example, in the study by Moen *et al.*, only meningitis of bacterial origin was considered, although aseptic meningitis might have occurred as well.^{12,13} However, irrespective of the risk of bias, it is an added value to share not only the result (*i.e.*, the incidence) but also the content of the case analysis with a large number of practitioners. Case reports published in scientific journals are probably the best way to achieve this goal. Although they are often considered minor scientific contributions, case reports have sometimes had a greater impact on clinical practice than most randomized trials. The description by Albright¹⁴ of a small series of cardiac deaths after bupivacaine administration, the description by Schneider *et al.*¹⁵ of transient neurologic symptoms after spinal lidocaine administration, and the recent cases of cardiac arrests after administration of large doses of ropivacaine^{16,17} are three examples of how case reports can strongly impact the thinking of a whole medical specialty. Case reports can provide a view of the healthcare system, and journals should facilitate publication of clinical incidents that describe the chain of events and the contributory factors because these reports have high educational value.

Estimating the incidence of events is also relevant because strategies to control the risks differ widely at

different levels of incidence. When the system is unsafe (incidence close to 10^{-2}), the most effective safety strategies aim at increasing the constraints placed on stakeholders while providing rapid technological enhancements: increased training, more rules, more protocols, and even a strict sanction policy toward rule breakers. Technological progress is the other high-priority goal because it is commonly accepted that it eventually contributes more to improving safety than repressive measures do. At this stage, feedback on accidents and serious incidents is sufficient to foster progress. Accidents and incidents adequately represent future risks: at 10^{-3} , yesterday's accident will be tomorrow's accident, if no measure is taken.¹⁸ Between 10^{-4} and 10^{-5} , safety is much better, and events are less frequent, with the consequence that the above-mentioned strategies will be much more difficult to implement and much less effective. At this stage, any single accident or incident that occurs is unlikely to reoccur. Safety strategies logically focus on the need for an enforced culture of safety, stabilizing the effectiveness of the system among all contexts and all those involved.

To summarize, the lessons gained from the study of rare complications could be threefold:

- The more rare an event is, the greater the need is for an in-depth and professional analysis of the few existing cases to determine relevant precursors.
- Organizing a sentinel event system and detecting relevant precursors in near misses are probably the core of the most comprehensive strategy for continuous improvement.
- Reducing the risk associated with an event changes the strategies to cope with the residual risk.

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Functional Brain Imaging

Some Parameters for Success

IN 1981, Phelps *et al.*¹ published a positron emission tomography study showing that cerebral glucose utilization increases in the human visual cortex when subjects are scanned with their eyes open *versus* when they are scanned with their eyes closed. Not a dramatic finding by today's standards, but this landmark study helped found modern functional brain imaging because it demonstrated that those brain regions that are relatively more active have a regionally specific increase in metabolism, which can be noninvasively measured *in vivo* in the living human brain. Twenty-three years later, we can now image regional changes in human brain activity without the risk of radioactivity exposure that positron emission tomography imaging requires by using the widely available functional magnetic resonance imaging (fMRI) technique with blood oxygenation level-dependent (BOLD) contrast.^{2,3} This technique exploits the fact that changes in the oxygen state of hemoglobin lead to measurable changes in the local magnetic field susceptibility of the blood and surrounding tissue. By tracking these susceptibility changes over time during a physiologic manipulation (*i.e.*, a cognitive or sensorimotor challenge), one can measure localized changes in cerebral blood flow as a correlate of brain activity at finer spatial

and temporal resolution than that afforded by existing positron emission tomography techniques. Application of fMRI with BOLD contrast to pain⁴ and anesthesia research⁵ are still in their infancy, and a multitude of questions regarding the proper application of this technique remain to be determined. In this issue of *ANESTHESIOLOGY*, Ibinson *et al.*⁶ move the field forward by providing answers to three parameters that are relevant to the conduct of fMRI studies of pain.

The first parameter addressed by Ibinson *et al.* concerns the question of signal attenuation. In an fMRI pain study where a pain stimulus is presented to subjects in an on-and-off manner (a so-called boxcar design), does the fMRI BOLD signal get smaller from one boxcar to the next as the session continues? Some studies suggest that it fades or attenuates from one block to the next,^{7,8} whereas other studies have not reported this effect.^{9,10} Ibinson *et al.* found the BOLD signal in the fourth "on" block to be significantly lower than that seen in the first "on" block in the three brain regions of the anterior cingulate cortex, the somatosensory cortex, and the cerebellum, with the greatest attenuation (*i.e.*, as much as 50%) occurring in the somatosensory cortex.

The second parameter addressed by Ibinson *et al.*⁶ concerns the period of time over which the BOLD signal might remain suppressed, given within-session signal attenuation. Ibinson *et al.* determined whether the attenuation from one session would continue into another session that starts 4 min after the first. If so, this might be problematic for any study in which the experimental conditions are changed between sessions. If there is an attenuation carryover effect, the second imaging session would start with a reduced BOLD signal and, if an investigator did not counterbalance the active and

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control scan sessions, a systematic error might be falsely attributed to an experimental manipulation. Fortunately, for future studies, a signal attenuation carryover effect is not evident when a 4-min between-session break is used.

The third parameter addressed by Ibinson *et al.* concerns the most effective echo time to use in a pain study. These investigators determined whether a 40-ms or a 60-ms TE time would provide the most robust BOLD signal for imaging pain, given a repetition time of 3 s on a 1.5-T scanner. Their results do not reveal much difference between an echo time of 40 or 60 ms, and either seems appropriate.

The source of the within-session BOLD signal attenuation is not known, and many postulates have been offered. Activation of descending pain modulation pathways is one postulate, but this seems unlikely because the psychophysical perception of pain does not fade over a 30-s block of time,^{7,11} and it may actually increase near the end of that time window.⁹ Pain-induced global changes in cerebral blood flow have also been postulated,^{6,8,12} and this idea deserves further study. Another possibility may be stimulus-induced motion that directly varies with the BOLD signal. This is an important additional parameter for future fMRI studies to consider.

The studies showing BOLD signal attenuation have also noted some difficulty with pain-induced subject movement. Indeed, 31% of the scan sessions in the study of Ibinson *et al.* were eliminated from analyses after applying an exclusion threshold limiting head motion to less than 1 mm of movement from one scan to the next and excluding sessions showing significant task-correlated motion. In the pain study of Kurata *et al.*,⁸ pain “on” stimulation periods were limited to 15 s, as opposed to 30 s for visual and motor tasks, to reduce pain-induced movement artifact and suggested that “more sophisticated techniques to correct head-motion artifacts . . . might permit longer duration of pain stimulus.” All of these studies applied the motion correction technique of realigning all of the session scans to the first scan in the series, but is this sufficient to correct for stimulus-induced motion artifact in the fMRI time series? As stated by Friston *et al.*¹³ in reference to their retrospective motion correction procedure, “This [motion correction] approach is predicated on the observation that movement-related effects are extant even after perfect realignment.”

The studies that did not report a within-session pain-induced attenuation of the BOLD response used slightly different techniques that may have minimized motion-related effects. Pain-induced motion artifact may have been reduced in the study by Apkarian *et al.*⁹ because they used a surface head coil and they had their subjects move their own hands onto the pain stimulus, which allowed their

subjects to anticipate and prepare for the pain. In a recent study by our group, we used the approach of Friston *et al.*¹³ for motion correction. With this approach, the within-session time series movement parameters that were used to realign the time series are entered into the design matrix of the study such that the linear translations and rotations of the image volume are treated as confounds within the statistical model. This procedure effectively eliminates the signal covariance that is directly due to subject movement and is particularly effective at minimizing or removing stimulus-induced movement effects. Friston *et al.*¹³ claim that, using their motion correction technique, their own “empirical analyses suggest that (in extreme situations) over 90% of fMRI signal can be attributed to movement, and that this artifactual component can be successfully removed.”

Motion-induced artifact in the fMRI time series will continue to pose a problem for pain researchers well into the future. This is especially true for studies that attempt to precisely quantify changes in the evoked hemodynamics caused by various pain stimuli. Perhaps recent developments in prospective motion correction techniques will help to minimize concern related to stimulus-evoked motion.¹⁴

The potential for functional imaging to help elucidate mechanisms of pain and elucidate anesthesia is enormous. The work of Ibinson *et al.* reminds us that that any field of research moves forward sometimes with giant steps and sometimes by simply understanding the basic parameters that produce the experimental signals of interest.

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