Stochasticity in Clinical Medicine

Paul Myles, Alfred Hospital and Monash University, Melbourne

Making predictions of future events can be difficult. In medicine, as in life, most real-world systems are stochastic, uncertain or poorly understood. How do we deal with uncertainty?

Stochasticity refers to the quality of lacking any predictable order, and, to me at least, summarizes the inherent unpredictability of patients undergoing surgery and anaesthesia. Although we can expect anaesthetic drugs to work, we are never certain that any drug or technique is totally effective, or that adverse events will be avoided. The complexity multiples when considering every component of the perioperative process, the patient and their co-morbidity, the constant threat of serious complications, and the wide variation in clinician practices throughout.

Humans are inherently intuitive thinkers, judging problems on their merits and deciding upon actions according to their experience and beliefs. Implicit in such decision-making are assumptions of cause and effect. But how certain can we be, and more importantly, do we reliably consider alternative explanations and weigh each of them up in an objective fashion? Our brains attempt to create a complete story from the fragments of information that are available. Can we truly practice evidence-based medicine?

This presentation will consider some of the errors in human thinking, and how this relates to anaesthesia. Flawed thinking, biased information and misuse of statistics abound in our lives and in our work. Do you know of regression to the mean, the prosecutor's fallacy, Simpson's paradox, or mathematical coupling? We are all prone to confirmation bias.

If a novel anaesthetic technique works well in one patient, or a series of patients, does this mean it is truly effective? If the benefits of a new treatment are reported in a peer-reviewed publication, does this mean it is truly effective? When any of us have a strong belief, based on experience, objective facts, published data, or any mixture of these, instead of searching for ways to prove our ideas wrong, we more often look for reasons to prove our ideas correct.

Statistical techniques are meant to help but more often mislead most clinicians. A P value is no more than a statement of probability of an event occurring. It describes the likelihood of it being a random finding, not a *true* finding. P(event)=0, means that the event is impossible, P(event)=1.0 means that the event is certain. A P value less than 0.05 is a statement of probability of the observed event being due to chance alone being less than 5%. Clinicians do not consider a trial result in isolation. They generally consider what is already known and judge whether the new trial information modifies their belief and practice.

A recent study found a marked reduction in breast cancer recurrence with paravertebral block. The investigators did a retrospective analysis of 129 consecutive patients undergoing mastectomy for breast cancer, to compare 50 patients who had paravertebral block (and GA) with 79 patients who had GA and postoperative

morphine analgesia. Recurrence- and metastasis-free survival was higher in the paravertebral block group: 94% (95% CI: 87-100%) and 82% (74-91%) at 24 months, and 94% (87-100%) and 77% (68-87%) at 36 months, respectively (P = 0.012). Regional block may reduce the risk of cancer recurrence after surgery.

Is this true? Should we change our practice on the basis of this finding, or even a series of similar findings? Are there alternative explanations for the findings? Could epidural block provide similar benefits in abdominal cancer surgery?

We are testing this hypothesis in the original MASTER trial cohort. The MASTER trial was primarily designed to test the effectiveness of epidural block in reduce postoperative complications after abdominal surgery, but given that cancer surgery was common in this cohort, it provides a unique opportunity to investigate long-term cancer recurrence rates now that it has been more than 10 years since the original randomised trial was done.

Acknowledgements
The MASTER cancer recurrence study is funded by the Australian and New Zealand College of Anaesthetists, the Department of Outcomes Research at the Cleveland Clinic (Dan Sessler), and the Alfred Research Trust (Alfred Hospital, Melbourne, Australia).

References

1. Mlodinov L. The Drunkard's Walk: how randomness rules our lives.
2. Sackett DL. Bias in analytic research. J Chron Dis 1979; 32:51-63.
3. Abramson NS, Kelsey SF, Safar P, Sutton-Tyrrell K. Simpson's paradox and clinical trials: what you find is not necessarily what you prove. Ann Emerg Med 1992; 21:1480-2.
4. Archie JP. Mathematical coupling of data: a common source of error. Ann Surg 1981; 193:296-303.
5. Hill AB. The environment and disease: association or causation? Proc Roy Soc Med 1965:295-300.
6. Browner WS, Newman TB. Are all significant p values created equal? The analogy between diagnostic tests and clinical research. JAMA 1987; 257:2459-63.
7. The James Lind Library. www.jameslindlibrary.org
8. Evans I, Thornton H, Chalmers I. Testing treatments: better research for better healthcare. The British Library 2006.
9. Jadad AR. Randomised controlled trials: a user's guide. London, England: BMJ Books, 1998.
10. Exadaktylos AK, Buggy DJ, Moriarty DC, Mascha E, Sessler DI. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? Anesthesiology 2006;105:660-4.
11. Rigg JRA, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, Collins KS, and the MASTER Anaesthesia Trial Study Group. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. Lancet 2002;359:1276-82.