Department of Public Health & Policy, London School of Hygiene & Tropical Medicine, London WC1E7HT, UK (CK, AG, KL, MM); and School for Health, University of Bath, Bath, Somerset, UK (AG)
cecile.knai@lshtm.ac.uk

CK is supported by a grant by the European Commission Research Directorate-General. AG is supported by a Health Foundation Clinician Scientist Fellowship. KL is supported by a National Institute of Health Research Fellowship. MM is an unremunerated member of the advisory board for the Community Interventions for Health Initiative of the Oxford Health Alliance, which receives funding from several food companies.

1 Biotechnology and Biological Sciences Research Council. Diet and Health Research Industry Club (DRINC). 2009. http://www.bbsrc.ac.uk/business/collaborative_research/industry_clubs/drinc (accessed Nov 16, 2009).
2 European Food Safety Authority. EFSA delivers its first series of opinions on 'general function' health claims. Oct 1, 2009. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902914361.htm (accessed Nov 16, 2009).
3 Wrieden W, Connaghan J, Morrison C, Tunstall-Pedoe H. Secular and socioeconomic trends in compliance with dietary targets in the north Glasgow MONICA population surveys 1986–1995: did social gradients widen? *Public Health Nutr* 2004; **7:** 835–42.
4 Gray L, Leyland A. A multilevel analysis of diet and socio-economic status in Scotland: investigating the 'Glasgow effect'. *Public Health Nutr* 2009; **12:** 1351–58.
5 Dowler E. Symposium on 'Intervention policies for deprived households' Policy initiatives to address low-income households' nutritional needs in the UK. *Proc Nutr Soc* 2008; **67:** 289–300.
6 Robertson A, Lobstein T, Knai C. Obesity and socio-economic groups in Europe: evidence review and implications for action. November, 2007. http://ec.europa.eu/health/ph_determinants/life_style/nutrition/documents/ev20081028_rep_en.pdf (accessed Nov 16, 2009).
7 Langley C, Parkinson S. Science and the corporate agenda: the detrimental effects of commercial influence on science and technology. Oct 12, 2009. http://www.sgr.org.uk/SciencePolicy/SGR_corp_science_full.pdf (accessed Nov 16, 2009).
8 Fooks G, Gilmore A, Collin J, Smith K. Revitalising the political authority of the tobacco industry: British American Tobacco's CSR programme. 14th World Conference on Tobacco or Health, Mumbai, India; March 11, 2009. http://www.14wctoh.org/abstract/abs_detail.asp?AbstractID=205 (accessed Nov 23, 2009).
9 Grüning T, Gilmore A, McKee M. Tobacco industry influence on science and scientists in Germany. *Am J Public Health* 2006; **96:** 20–32.
10 WHO. Tobacco industry interference with tobacco control. 2008. http://www.who.int/tobacco/resources/publications/Tobacco%20Industry%20Interference-FINAL.pdf (accessed Nov 16, 2009).
11 Cancer Research UK. Cancer Research UK code of practice on tobacco industry funding to universities. 2009. http://science.cancerresearchuk.org/gapp/terms/tobacco_policy (accessed Nov 16, 2009).
12 Vartanian L, Schwartz M, Brownell K. Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health* 2007; **97:** 667–75.
13 Knai C, Lobstein T, McKee M. Curbing the childhood obesity epidemic: the case for binding international legislation. *Eur J Public Health* 2005; **15:** 559–63.

# Monitoring of neuromuscular blockade in general anaesthesia

The use of neuromuscular blocking agents (NMBAs) remains an essential part of general anaesthesia. The muscle relaxation they produce enables interventions both by the anaesthetist and the surgeon. However, an international survey confirmed that there is considerable variation in anaesthetists' understanding of the subject, in their use of objective monitoring of the drugs' effects, and in their use of antagonists to reverse them.[1] Research evidence and advances in monitoring technology and drug development suggest that there is room for improvement in practice.

A major problem is persistent weakness in the recovery period, so-called postoperative residual curarisation. This effect is thought to affect up to 30% of patients receiving these drugs to some degree,[2] although clinically significant events are less common. Residual blockade causes decreased chemoreceptor sensitivity to hypoxaemia, and pharyngeal and oesophageal muscle dysfunction.[3] The ventilatory response to hypoxaemia is thus blunted[4] and the airway less patent and more at risk of regurgitation and aspiration, leading to critical respiratory events in the recovery room[2] with the risk of postoperative pulmonary complications. If the patient is aware of the residual weakness, it is uncomfortable and distressing. Contributory factors include the substantial variability in individual response to a given dose of a given NMBA,[5] making it impossible to predict how long the drug's effect will last, and the possibility of persisting blockade even when an antagonist is given.[2] Evidence now links reversal of neuromuscular blockade and reduced postoperative mortality.[6]

Naguib and colleagues' survey[1] revealed that 19·4% of European and 9·4% of US respondents did not routinely use a neuromuscular monitor. There was also substantial variation in the use of reversal agents and in the appreciation of the poor value of clinical tests for predicting adequate recovery of neuromuscular function.[5] If anything, the findings of this survey might paint too rosy a picture: in a study from the UK, over 60% of respondents did not routinely use a monitor.[7] As Naguib and colleagues state,[1] practice will vary widely within a given average, both throughout Europe and within the USA. It is also likely that those who respond do so because they are aware their practice is more in line with current standards and thinking.

Until now, reversal of blockade has been achieved with anticholinesterases such as neostigmine, which requires the co-administration of an antimuscarinic agent such as

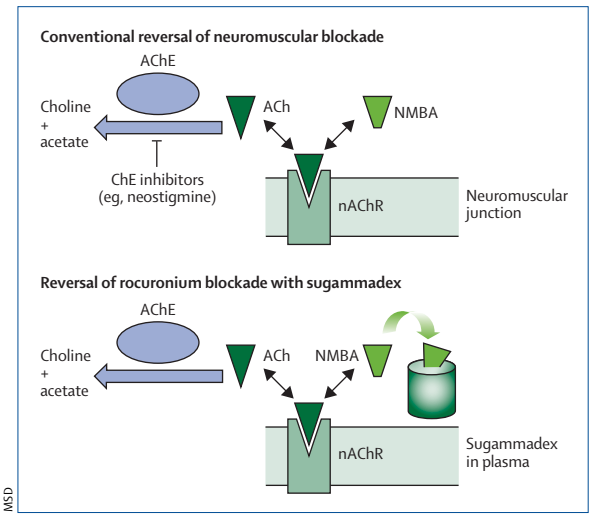



***Figure:*** **Pharmacological reversal of neuromuscular blockade**
ACh=acetylcholine. AChE=acetylcholine esterase. NMBA=neuromuscular blocking agent. nAChR=nicotinic ACh receptor. Adapted from slide supplied by MSD.

glycopyrronium to mitigate the undesirable side-effects of bradycardia, nausea, increased salivation, and bronchoconstriction.[8] Sugammadex, is a novel "doughnut-shaped" modified γ-cyclodextrin which works by irreversibly binding molecules of rocuronium in the plasma into its "hole" to form a biologically inert complex.[8] Unbound drug then diffuses rapidly away from the neuromuscular junction, allowing the patient's own acetylcholine to act to restore muscle activity (figure). Apart from the avoidance of muscarinic side-effects, sugammadex offers the possibility of immediate reversal of rocuronium neuromuscular blockade in the life-threatening situation in which endotracheal intubation is difficult or impossible, helping to avoid hypoxia and possible resulting organ damage. The drug can also be used if surgery finishes more rapidly than expected, potentially saving operating-theatre time. Clinically, sugammadex more rapidly reverses rocuronium-induced neuromuscular blockade than does neostigmine, regardless of the depth of the block, with no significant difference in the prevalence of drug-related adverse events.[9] However, at present, sugammadex is expensive (about £60 per patient for routine reversal) and does not act against all currently used NMBAs.

Electronic monitoring has become standard during general anaesthesia. Monitoring augments and quantifies the anaesthetist's clinical observation of the patient, allowing moment-to-moment balancing of different streams of information to ensure patients' safety.[10] However, the effect of NMBAs is only clinically visible when blockade is incomplete—for instance, when the patient moves or coughs. The only way to ensure that blockade is sufficiently deep for smooth endotracheal intubation or for satisfactory muscle relaxation for surgery, or, conversely, shallow enough to be safely antagonised at the end of surgery, is to use electronic monitoring of neuromuscular function. Such monitors, available for clinical use for over 20 years, stimulate a peripheral nerve, allowing anaesthetists to judge the degree of blockade by tactile or visual evaluation of the movement in the corresponding muscle. Quantitative monitors are now commercially available which provide a more objective numerical display of this response and evidence is accumulating to support the use of quantitative over conventional monitoring,[2,11] making it easier to justify the greater cost (£600) of a quantitative monitor. Monitoring is also needed to establish the correct dose of sugammadex required for reversal, to ensure that costly overdose is avoided. In view of these recent developments, it is perhaps strange that, when other monitoring modalities have been so rapidly and enthusiastically adopted, many anaesthetists have been reluctant to use neuromuscular monitoring. Some might still believe that there is no evidence to support such use. Even if that were true, lack of evidence has not prevented the widespread adoption of other modes of monitoring (eg, pulse oximetry[12]).

Current professional guidance in the UK is simply that a neuromuscular monitor be available when NMBAs are used.[13] This advice should be revisited. A case can now be made for monitoring every patient, especially those at high risk of problems from residual blockade. Monitoring should start after induction of anaesthesia to establish a baseline. Additionally, quantitative monitors offer a further dimension of understanding and should be used more widely.

*Andrew Smith*
Department of Anaesthesia and Patient Safety Research Unit, Royal Lancaster Infirmary, Lancaster LA1 4RP, UK
andrew.f.smith@mbht.nhs.uk

I have received a gift of a quantitative monitor of neuromuscular function from Schering-Plough, manufacturers of rocuronium and sugammadex.

1 Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular blockade in the United States and Europe. *Anesth Analg* 2010; **111:** 110–19.
2 Murphy GS, Szokol JW, Marymont JH. Intraoperative acceleromyographic monitoring reduces the risk of neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* 2008; **109:** 389–98.

3 Sundman E, Witt H, Olsson R, Ekberg O, Kuylenstierna R, Eriksson LI. The incidence and mechanism of pharyngeal and upper esophageal dysfunction in partially paralyzed humans. *Anesthesiology* 2000; **92:** 977–84.

4 Eriksson LI, Lennmarken C, Wyon N, Johnson A. Attenuated ventilatory response to hypoxaemia at vecuronium-induced partial neuromuscular block. *Acta Anaesthesiol Scand* 1992; **36**: 710–15.

5 Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology* 2003; **98:** 1042–48.

6 Arbous MS, Meursing AEE, van Kleef JW, et al. Impact of anaesthesia management characteristics on severe morbidity and mortality. *Anesthesiology* 2005; **102:** 257–68.

7 Grayling M, Sweeney BP. Recovery from neuromuscular blockade: a survey of practice. *Anaesthesia* 2007; **62:** 806–09.

8 Srivastava A, Hunter JM. Reversal of neuromuscular block. *Br J Anaesth* 2009; **103:** 115–29.

9 Abrishami A, Ho J, Wong J, Yin L, Chung F. Sugammadex, a selective reversal medication for preventing postoperative residual neuromuscular blockade. *Cochrane Database Syst Rev* 2009; **4:** CD007362.

10 Smith AF, Mort M, Goodwin D, Pope C. Making monitoring 'work': human-machine interaction and patient safety in anaesthesia. *Anaesthesia* 2003; **58:** 1070–78.

11 Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology* 2008; **108:** 1117–40.

12 Pedersen T, Hovhannisyan K, Møller AM. Pulse oximetry for perioperative monitoring. *Cochrane Database Syst Rev* 2009; **4:** CD002013.

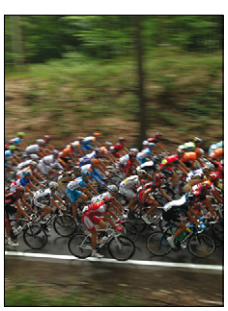
13 Association of Anaesthetists of Great Britain and Ireland. Recommendations for standards of monitoring during anaesthesia and recovery, 4th edn. March, 2007. http://www.aagbi.org/publications/guidelines/docs/standardsofmonitoring07.pdf (accessed April 9, 2010).


# The biological passport and doping in athletics

The head of the French anti-doping agency (AFLD) has questioned the effectiveness of the biological passport to detect doping at the Tour de France, which started on July 3.[1] A biological passport monitors an athlete's blood and body chemistry values over time to assess whether there has been a deviation from an established baseline, thus indirectly detecting illegal manipulation.[2]

Implemented by the International Cycling Union for the 2008 cycling season and approved for widespread use by the World Anti-Doping Agency (WADA) in December, 2009,[3] the biological passport was criticised by AFLD's Pierre Bordry, who says cyclists consistently taking small amounts of doping substances can go undetected.[1] Although Bordry's comments have merit and will need to be taken into consideration as the biological passport system is modified over time, the biological passport might well prove to be an improvement over the traditional method of direct detection of doping. Traditional tests have searched for direct evidence of known doping agents, but the biological passport can look for changes from baseline that might result from doping, even if the specific drug or tactic is unknown.[2] Some drugs, such as erythropoietin, which increases erythrocyte production, can only be detected for a few days, but the performance benefits last for weeks,[2] producing a suspicious blood profile indicative of previous use of erythropoietin. Also, traditional tests compare concentrations of a banned substance with averages for an entire population, but the biological passport's emphasis on many readings from an individual should make it easier to catch a doped athlete.[4]

The biological passport is a breakthrough in the anti-doping fight, and WADA's Athlete Biological Passport Operating Guidelines should be implemented by all anti-doping organisations. Monitoring biological variables that indirectly reveal the effects of doping should make it more difficult to take banned substances.[3] The biological passport has already been used against elite cyclist Franco Pellizotti, who won the prestigious honour of being the best mountain climber in last year's Tour de France, to keep him out of the Tour of Italy in May.[2] In advance of the London 2012 Olympics, it is encouraging to see that all UK athletes will receive biological passports.[4] The UK's example should be followed by all countries participating in the 2012 Olympics in the effort to combat doping in athletics.



Getty Images


*Michael Wozny*
Loma Linda University School of Medicine, Loma Linda, CA 92350, USA
mwozny@llu.edu


I declare that I have no conflicts of interest.


1 McGrath M. Tour de France dope tests 'flawed' says French agency. *BBC News Channel* July 1, 2010. http://news.bbc.co.uk/1/hi/world/europe/10484158.stm (accessed July 5, 2010).

2 Niiler E. Biological passport nabs cheating cyclists. *Discovery News* May 7, 2010. http://news.discovery.com/tech/biological-passport-cycling-doping.html (accessed July 5, 2010).

3 World Anti-Doping Agency. Questions and answers on the Athlete Biological Passport. December, 2009. http://www.wada-ama.org/en/Science-Medicine/Athlete-Biological-Passport/Questions-Answers (accessed July 5, 2010).

4 Anon. British athletes to get biological passports in move to curb doping. *Guardian.co.uk* Feb 5, 2010. http://www.guardian.co.uk/sport/2010/feb/05/biological-passports-london-2012-olympics (accessed July 5, 2010).