

control, this time in critically ill medical patients,⁸ and showed no overall benefit on mortality (37.3% v 40% in the control group; P = 0.33).

Why might tight glycaemic control reduce mortality in critically ill patients after surgery but not in critically ill medical patients, where the much higher mortality might be associated with a larger effect? Firstly, the prevention of nosocomial infection, thought to be a major reason for the mortality reduction in the original Van den Berghe study in uninfected surgical patients, did not occur in the medical trial, where established infection was commonly the reason for admission. Secondly, the treatments tested were different. The original surgical study used an unusual feeding regime with 9 g intravenous glucose per hour⁹ overnight usually followed by parenteral nutrition. This was not repeated in the medical study, where patients were started on enteral feeding once stable. Possibly both insulin and intravenous supplementary glucose are required for benefit. Finally, recent work suggesting that hyperglycaemia on admission is an independent risk factor in patients undergoing intensive care after cardiothoracic surgical procedures but not in those with medical conditions is compatible with blood glucose control showing benefit only in the surgical patients.¹⁰

The continuing use of tight glycaemic control in all critically ill patients presupposes that this treatment is harmless. But this may not be the case. In the original surgical study 5.1% of the patients receiving tight glycaemic control had one or more episodes of hypoglycaemia (<2.2 mmol/l), but they were all also receiving intravenous glucose, and a dedicated doctor cared for the study group. In the subsequent medical study, without glucose infusions or medical support, the figure was 3.7 times this (18.7%), exceeding even the 12.1% seen in the SepNet study. As in the SepNet study, there were more deaths in patients who had hypoglycaemic episodes in the tight glycaemic control group, though this may simply reflect hypoglycaemia as a marker of disease severity.

Trials are underway both to determine the mechanism for the benefit of tight glycaemic control seen in the surgical patients, and to see if the benefit extends to the mixed medical-surgical populations treated in British, European, Canadian, and Australasian intensive care units. In the meantime how should glucose control in the critically ill be managed?

For now tight control (target blood glucose 4.4-6.1 mmol/l) is probably best reserved for critically ill patients after elective surgery in intensive care units with aggressive feeding policies and a high staffing ratio. In the remaining heterogeneous group of critically ill patients, where tight glycaemic control has no proved benefit but the potential of harm through hypoglycaemia, this treatment should be avoided. Instead we should use the common, vigorously contested¹¹ but reasonably supported,¹² practice of using less aggressive regimens⁴ until trials on appropriate populations have reported.

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- 1 Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;345:1359-67.
- 2 Malmberg K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenstrom A, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 1995;26:57-65.
- 3 Krinsley JS. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. *Mayo Clin Proc* 2004;79:992-1000.
- 4 Mackenzie I, Ingle S, Zaidi S, Buczaski S. Tight glycaemic control: a survey of intensive care practice in large English hospitals. *Intensive Care Med* 2005;31:1136.
- 5 Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2004;32:858-73.
- 6 Brunkhorst FM, Kuhnt E, Engel C, Meier-Hellmann A, Ragaller M, Quintel M, et al. Intensive insulin therapy in patient with severe sepsis and septic shock is associated with an increased rate of hypoglycemia—results from a randomized multicenter study (VISEP). *Infection* 2005;33:19-20.
- 7 Mehta SR, Yusuf S, Diaz R, Zhu J, Pais P, Xavier D, et al. Effect of glucose-insulin-potassium infusion on mortality in patients with acute ST-segment elevation myocardial infarction: the CREATE-ECLA randomized controlled trial. *JAMA* 2005;293:437-46.
- 8 Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, et al. Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006;354:449-61.
- 9 Van den Berghe G. Beyond diabetes: Saving lives with insulin in the ICU. *Int J Obes Relat Metab Disord* 2002;26:S3-8.
- 10 Whitcomb BW, Pradhan EK, Pittas AG, Roghmann MC, Perencevich EN. Impact of admission hyperglycemia on hospital mortality in various intensive care unit populations. *Crit Care Med* 2005;33:2772-7.
- 11 Van den Berghe G, Bouillon R. Optimal control of glycemia among critically ill patients. *JAMA* 2004;291:1198-9.
- 12 Finney SJ, Zekveld C, Elia A, Evans TW. Glucose control and mortality in critically ill patients. *JAMA* 2003;290:2041-7.

Regulating the collection and use of fetal stem cells

They currently lie in a regulatory limbo

The British government is committed to supporting stem cell science and industry.¹ An important part of that commitment is a strong regulatory environment, seen as being embodied in the Human Fertilisation and Embryology Authority (HFEA), which oversees a strict but permissive regulatory framework and contains public concerns about the use in research and treatment of human embryos. However, the HFEA regulates only the use of embryos created in vitro. It has no jurisdiction over the use of aborted fetuses, which are still subject to guidelines

drawn up 17 years ago and have been neglected in recent discussions around stem cell research.

Sustaining in vitro a human embryo beyond 14 days is legally and technically impossible, so investigators seeking embryonic material older than 14 days usually collect it after abortion (or, less often, after miscarriage or surgery for an ectopic pregnancy). The collection and use of aborted fetuses has been governed by the Polkinghorne guidelines,² which were drawn up in 1989 in response to controversy provoked by transplants of fetal neural tissue into the brains of people

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with Parkinson's disease. The Polkinghorne committee decided that professional self regulation overseen by research ethics committees offered the public sufficient reassurance about the proper collection and use of aborted fetuses. The following year, parliament gave human embryos in vitro the protection of the criminal law by passing the Human Fertilisation and Embryology Act 1990.

The Polkinghorne guidelines rest on the principle of separation and operationalise it in four ways. Firstly, decisions relating to abortion and to the subsequent use of fetal tissue must be made separately, and consent for the use of the fetus in research or therapy can be sought only after a woman has agreed to the termination. Secondly, a woman's consent to the use of the fetus in research is general: she is not allowed to specify how her fetal tissue may or may not be used. Thirdly, the practice of abortion must be physically separate from the use of fetal tissue in research or therapy. Fourthly, separation of source and user must be complete: the source records the identity of the woman but does not divulge it to the user, thereby ensuring that the user knows nothing of the provenance of the material. An intermediary is recommended as the best way of achieving separation.

Review of the Polkinghorne guidelines is long overdue. In excluding clinical investigators from the clinical care of women undergoing pregnancy termination the guidelines codified distrust of clinicians who undertake research, and, according to the Royal College of Obstetricians and Gynaecologists, inhibit the progress of modern fetal medicine and the collection of stem cells at the time of termination.³ The Polkinghorne approach of non-specific consent is also "increasingly out of step with modern expectations."⁴

The Medical Research Council (MRC) fetal tissue bank until recently acted as intermediary between the abortion clinic and the laboratory. A study of stem cell scientists' views on the ethics of stem cell science in the laboratory noted that they trusted the MRC tissue bank for ensuring that fetal material had been ethically sourced (S Wainwright et al, BSA Medical Sociology Conference, 2005). However, the bank was closed in 2005.

The Human Tissue Act 2004 established the Human Tissue Authority as the regulatory body responsible for overseeing of the collection, storage, and use of human tissues. Embryos are not covered by the act, but, although not explicitly specified, aborted fetuses seem to fall within it and qualify as "relevant material." New standards and practices relating to con-

sent, donation, and storage of human tissues are being implemented, but how these relate to aborted fetuses is unclear and clarification by the Human Tissue Authority would be welcome.

The MRC is seeking to standardise procedures for seeking informed consent for donation of human embryos in assisted conception clinics in order to meet the ethical requirements of the UK stem cell bank.⁵ However, termination of pregnancy takes place in different clinical environments from fertility clinics and so far no fetal stem cells have been deposited in the stem cell bank.

If fetal stem cells are to be used in stem cell therapy then procedures for dealing with traceability, quality control, and risk management at the point of tissue collection need to be considered in order to comply with European Union's regulatory requirements on clinical grade tissue banks⁶ and advanced cell therapies.⁷ As the UK's authority responsible for implementing these European regulations, the Human Tissue Authority's remit with regard to abortion practices and the collection of fetal material for stem cell derivation remains to be clarified and the implications for clinical practice widely discussed.

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- 1 Pattison J. *UK Stem cell initiative: report and recommendations*. London: DoH, 2005. www.advisorybodies.doh.gov.uk/uksci. (accessed 14 Mar 2006).
- 2 Polkinghorne J. *Review of the guidance on the research use of fetuses and fetal material*. London: HMSO, 1989.
- 3 Royal College of Obstetricians and Gynaecologists. *Response to MRC consultation on the Code of Practice for the Use of Human Stem Cell Lines*. www.rcog.org.uk 2004 (accessed 30 Jun 2005).
- 4 Department of Health. *Human bodies, human choices. The law on human organs and tissue in England and Wales. A consultation report*. London: DoH, 2002.
- 5 Minger S, Braude P, Franklin S. *Derivation of both research and clinical grade human embryonic stem cell lines*. London: Guy's and St Thomas NHS Foundation Trust, 2005.
- 6 Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, storage, and distribution of human tissues and cells. *Off J European Union* L 102/48. http://europa.eu.int/eur-lex/pri/en/oj/dat/2004/l_102/l_10220040407en00480058.pdf (accessed 14 Mar 2006).
- 7 European Commission DG Enterprise and Industry. *Human tissue engineering and beyond: proposal for a community regulation on advanced therapies*. Brussels: EU, 2005. <http://pharmacos.eudra.org/F2/advtherapies/index.htm> (accessed 14 Mar 2006).

The care of older people

Wanless might offer a politically acceptable compromise to paying for care

The latest "Wanless report" on securing good social care for older people in England¹ is a welcome contribution to the debate about caring for older people, and in particular about paying for their care. It completes a trilogy of reports by Sir Derek Wanless, a former banker who was initially commis-

sioned by the Treasury to provide an evidence based assessment of the long term resource requirements of the NHS² and later reviewed the wider determinants of health.³ The latest report attempts to find a middle way between complete state funding of social care for older people and strict means testing.