there is a high chance of infertility should colleagues in reproductive medicine be consulted.

There are only two established practices for fertility preservation in female patients who receive gonadotoxic cancer therapy.[4] The first method, applicable only to those patients due to receive pelvic irradiation, involves removal of the ovaries from the radiation field, a procedure known as oophoropexy, which can be done laparoscopically. In the second method, fertility can be preserved by collection of mature oocytes before therapy, for in-vitro fertilisation and subsequent embryo preservation. This method is only applicable to sexually mature females and requires a partner or donor sperm for fertilisation. For women without a partner, cryopreservation of mature oocytes is an option but subsequent pregnancy rates are much lower, since these cells sustain more damage than embryos during the freeze-thaw process.

In the case report by Donnez and colleagues,[1] it is not clear whether the patient received radiation therapy to an area that would have included her ovaries. Evidence[2,3] suggests that most young patients with Hodgkin's disease treated with hybrid chemotherapy and radiation to a field that does not include the ovaries will be fertile, albeit with a shorter fertility window than their peers.

Careful selection of patients for ovarian tissue harvesting, an experimental procedure, is vital because of the risk of reseeding cancer at the time of autotransplantation. There are no reliable screening methods to detect minimum residual tumour. Despite the reports by Donnez and colleagues, we believe that for prepubertal girls and young women without a partner, preservation of fertility remains experimental, and that harvesting and storage of ovarian tissue before commencing cancer therapy, is only applicable to a few patients who are at very high risk of infertility. We have reported[5] a spontaneous conception, despite documented evidence of ovarian failure, in a young woman successfully treated with sterilising treatment for a Ewing's sarcoma of the pelvis. In the livebirth after ovarian tissue transplantation reported by Donnez and colleagues,[1] spontaneous ovulation cannot be excluded since her ovaries were still present and she had shown evidence of ovulation in the 2 years before the transplant.

Before these experimental procedures become standard practice there are, therefore, important ethical and legal issues to be addressed.[2,3] After extensive multidisciplinary discussion, several recommendations have been made. These include ongoing structured research with centralisation of data and rapid dissemination of results, rigorous review of procedures, and development of the process of obtaining informed consent.

*W Hamish B Wallace, Jon Pritchard
hamish.wallace@luht.scot.nhs.uk

Royal Hospital for Sick Children, Edinburgh EH9 1LF, UK

1 Donnez J, Dolmans MM, Demylle D, et al. Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. *Lancet* 2004; **364:** 1405–20.
2 Royal College of Obstetricians and Gynaecologists. Storage of ovarian and prepubertal testicular tissue: report of a Working Party. London: Royal College of Obstetricians and Gynaecologists, 2000.
3 Multidisciplinary Working Group convened by the BFS. A strategy for fertility services for survivors of childhood cancer. *Hum Fertil* 2003; **6:** A1–40.
4 Wallace WHB, Anderson R, Baird DT. Preservation of fertility in young women treated for cancer. *Lancet Oncology* 2004; **5:** 269–70.
5 Bath LE, Tydeman G, Critchley HOD, Anderson RA, Baird DT, Wallace WHB. Spontaneous conception in a young woman who had ovarian cortical tissue cryopreserved before chemotherapy and radiotherapy for a Ewing's sarcoma of the pelvis. *Hum Reprod* 2004; **19:** 2569–72.

Screening of organ and tissue donors for rabies

In their Comment (Aug 21, p 648),[1] Bernhard Dietzschold and Hilary Koprowski emphasise the importance of bat rabies variants in the epidemiology of human rabies in the USA and Canada. They recommend that organ donors, especially those with neurological symptoms, be screened for rabies. I believe this recommendation is premature.

The donor they describe had a history, obtained retrospectively, of a bat bite;[2] patients with an acute neurological illness and such a history should not be organ donors. The donor had mental status changes, fever, and neuroimaging evidence of subarachnoid haemorrhage.[3] These images should be carefully reviewed. The occurrence of both rabies encephalitis and a major subarachnoid haemorrhage during the course of one illness in an organ donor is extremely unlikely.

Speculation about viral spread of rabies after solid-organ transplantation via the haematogeneous route and hypotheses about a potential role of infection of macrophages are unnecessary. Rabies virus spreads from the central nervous system to multiple organs along nerves, probably in both autonomic and sensory nerve fibres.[4] Small quantities of rabies virus could have been present within small nerves in the transplanted organs and tissues, including the liver, kidneys, and iliac artery segment from the donor. Transplantation of rabies virus into an immunosuppressed host would provide a favourable environment for replication. Indeed, rabies due to a bat rabies virus variant has been reported from Canada in an immunosuppressed patient who received a renal transplant more than 2 years earlier.[5]

Not enough information is yet available to ascertain whether donors need to be screened for the disease. Premorbid laboratory testing for rabies virus antigen or RNA on saliva, skin biopsies, and cerebrospinal fluid cannot reliably exclude rabies, though a definitive laboratory diagnosis can be made on brain tissues obtained after death. However, such post-mortem testing would likely be associated with unacceptable delays before transplantation. A careful examination of all of the evidence with respect to the rabies transmission

from the donor in the USA is needed before recommendations for screening of organ and tissue donors are seriously considered.

Alan C Jackson
jacksona@post.queensu.ca

Department of Medicine (Neurology) and Microbiology and Immunology, Queen's University, Kingston, ON K7L 3N6, Canada

1 Dietzschold B, Koprowski H. Rabies transmission from organ transplants in the USA. *Lancet* 2004; **364:** 648–49.
2 Centers for Disease Control and Prevention. Update: investigation of rabies infections in organ donor and transplant recipients—Alabama, Arkansas, Oklahoma, and Texas, 2004. *MMWR Morb Mortal Wkly Rep* 2004; **53:** 615–16.
3 Centers for Disease Control and Prevention. Investigation of rabies infections in organ donor and transplant recipients: Alabama, Arkansas, Oklahoma, and Texas, 2004. *MMWR Morb Mortal Wkly Rep* 2004; **53:** 586–89.
4 Jackson AC. Pathogenesis. In: Jackson AC, Wunner WH, eds. Rabies. San Diego: Academic Press, 2002: 245–82.
5 Parker R, McKay D, Hawes C, et al. Human rabies, British Columbia: January, 2003. *Can Commun Dis Rep* 2003; **29:** 137–38.

Calcium supplementation for prevention of colorectal cancer

Robert Benamouzig and Stanislas Chaussade state in their Comment (Oct 2, p 1197)[1] that "a high intake of calcium has predicted risk of kidney stones in previous cohort studies". However, the report[2] they cite in support of their statement indicates the opposite; in this large cohort study in men, the relative risk of kidney stones in the quintile with the highest calcium intake was 0·56 compared with those in the lowest. Similarly, low, rather than high, dietary calcium intake was associated with an increased risk of kidney stone formation in women; however, in the same study, ingestion of calcium supplements that were not taken with meals, or that were taken with low oxalate meals, was associated with increased risk.[3] The most likely interpretation for these findings is that calcium ingested as or with food reduces colonic absorption of oxalate, and the resulting reduction in urinary oxalate excretion reduces risk of stone formation, outweighing the effects of any increase in calcium absorption. Future studies of calcium supplementation ought to specify whether calcium is taken with or between meals.

Charlie Tomson
ctomson@ihi.org

Health Foundation Fellow, Institute for Healthcare Improvement, 37 Longwood Avenue, Boston, MA 02215, USA

1 Benamouzig R, Chaussade S. Calcium supplementation for preventing colorectal cancer: where do we stand? *Lancet* 2004; **364:** 1197–99.
2 Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 1993; **328:** 833–38.
3 Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 1997; **126:** 497–504.

Should diet be a medical intervention?

In view of Dorota Pawlak and colleagues findings in animals (Aug 28, p 778)[1] and of the nutritional data that have been known for more than 10 years,[2] should we now regard dietary intervention as a medical treatment and abandon the more laisser-faire approach?

Well before the antipsychotic era, patients with schizophrenia were recognised as being at an increased risk of type 2 diabetes. Moreover, they are more likely to smoke and use illicit drugs (notably cannabis), have a sedentary lifestyle, and have a higher body-mass index (BMI) than the average population.[3] People with schizophrenia consume larger quantities of fatty and sugary foods than controls, and can be too disorganised to shop for healthier food. In hospital, they are often permitted unlimited quantities of snack foods, take-away meals, and carbonated drinks.

Furthermore, in line with National Institute of Clinical Excellence (NICE) guidelines on the treatment of schizophrenia, patients are commonly prescribed second-generation (atypical) antipsychotic drugs. Although the evidence of a direct link between these drugs and the development of treatment-emergent diabetes is flawed, since studies generally do not take family history, ethnic origin, use of cannabis[4] and alcohol, exercise, or diet into account, they cannot be discounted as a possible risk factor.

The traditional medical view is to be as liberal as possible within the confines of treatment. As many as half of our patients are, after all, detained in hospital against their will and could see dietary control as yet another—and unjustified—infringement on their liberty. However, our experience in psychiatric intensive care units, where patients are too disturbed to be managed safely on open psychiatric wards, suggests that most people welcome, feel empowered by, and appreciate the tangible health benefits of dietary and lifestyle advice.[5]

**Maria B Isaac, Michael T Isaac*
mi@stekel.demon.co.uk

South London and Maudsley NHS Trust, Gresham Psychiatric Intensive Care Unit, Bethlem Royal Hospital, Beckenham BR3 3BX, UK

1 Pawlak DB, Kushner JA, Ludwig DS. Effects of dietary glycaemic index on adiposity, glucose homeostasis, and plasma lipids in animals. *Lancet* 2004; **364:** 778–85.
2 Jenkins DJ, Wolever TM, Collier GR, et al. Metabolic effects of a low glycaemic index diet. *Am J Clin Nutrition* 1987; **46:** 968–75.
3 Brown S, Barraclough B, Inskip H. Causes of excess mortality of schizophrenia. *Br J Psych* 2000; **177:** 212–17.
4 Isaac MB, Isaac MT. Metabolic and clinical implications of cannabis use in psychiatric intensive care units. American Psychiatric Association Annual Meeting, New York, USA, 2004 (abstr NR341).
5 Isaac MT, Isaac MB. Eat yourself happy. London: Carroll and Brown, 2004.

A thank you to an old Dutch farmer

Michael Marmot's Comment (Sept 18, p 1019)[1] made me think back to the fate of the Jews in occupied Holland. In April, 1942, all Dutch Jews were ordered to wear a yellow star over their hearts, on which in big, black, fancy, capital letters was printed the word