is legally required (107, 111). Fourthly, while Judge Munby accepts that people who are in the final phase of dying may have life prolonging treatment withdrawn lawfully without referral to a court, he seems to extend the law concerning obligatory referral to court to all cases of withholding or withdrawing artificial nutrition and hydration—and arguably all life prolonging treatments—from incompetent patients whenever there is doubt or disagreement among partners, carers, relatives, and friends.

These conclusions, with their draconian restriction of the exercise of doctors' professional skills, will surely lead to the outcomes predicted above. Doctors dislike going to court, preferring to look after patients. NHS managers are unlikely to let them go to court over the large number of cases involved: far simpler to change priorities to accommodate more provision of life prolonging treatments, especially artificial nutrition and hydration. Judge Munby assures us that "this is not a case about the prioritisation or allocation of resources, whether human, medical or financial" (27). But, although the case does not concern these issues, his judgment inevitably does, for it and its reasoning must be generalised, and this will surely inevitably lead to prioritisation of resources towards artificial nutrition and hydration and other life prolonging treatments for incompetent patients who have not rejected them in advance. If it is not overturned the ruling will delight vitalists. The rest of us—patients, doctors, and society in general—should be appalled by it. We should hope that the appeal court overturns the judgment.

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Competing interests. None declared.

1 Dyer C. GMC appeals against judgment on withholding treatment. *BMJ* 2004;329:818.
2 Oliver Leslie Burke and the General Medical Council. (Citation number [2004] EWHC 1879 (Admin)). www.courtservice.gov.uk/judgementfiles/j2775/burke-v-gmc.htm (accessed 26 Sep 2004).

Antenatal screening for Down's syndrome

Nuchal translucency plus biochemical tests has the lowest false positive rate

Many pregnant women wish to undergo antenatal testing for Down's syndrome—for reassurance that their unborn child does not have Down's syndrome, to allow the option of termination if it does, or to allow preparation for the birth of a baby with the condition. Unfortunately, invasive tests required to obtain tissue for fetal karyotyping (chorionic villus sampling, amniocentesis) cause loss of the pregnancy in about 1% of cases. The challenge of an antenatal screening programme is, therefore, to identify women in whom a risk of Down's syndrome is sufficiently high to justify such an invasive test and to minimise the risk of miscarrying a healthy baby.

Initially, invasive testing was offered only to women over 35 years, but this identified only one third of fetuses with Down's syndrome. Universal screening started with the observation that serum concentrations of α fetoprotein, used to screen for neural tube defects, tended to be lower when the fetus had Down's syndrome. Several other biochemical tests were combined with age related risk to calculate an individualised risk for Down's syndrome. Anyone with a risk of 1:250 or greater was offered amniocentesis; others were reassured with a low risk result. Another breakthrough was the advent of screening for increased nuchal translucency, a fluid filled space behind the fetal neck, which tends to be more prominent in fetuses affected by Down's syndrome between 10 and 13 weeks of pregnancy.[1] Nuchal translucency screening allowed earlier testing, but required expertise and equipment not readily available.

The competing claims of advocates of different screening approaches have not made it easy for health planners, clinicians, or pregnant women to reach a balanced decision about what should be offered, or chosen.

BMJ 2004;329:811–2

The publication of the Serum, Urine and Ultrasound Screening Study (SURUSS) has advanced our knowledge of the efficacy and safety of antenatal screening for fetal Down's syndrome and placed choices on a firmer platform of evidence.[2] Over 47 000 singleton pregnancies were studied prospectively in 25 maternity units. Ultrasound scans of fetal nuchal translucency in the first trimester and assays of several biochemical markers in the first and second trimesters combined were done to test the screening performance of various "packages."

For the principal analysis false positive rates (when the test is positive but the fetus does not have Down's syndrome) were compared for each test, and combined test packages, assuming a fixed detection rate for Down's syndrome of 85%. The best performer was the integrated test, comprising ultrasound measurement of fetal nuchal translucency and assay of serum pregnancy associated plasma protein-A (PAPP-A) at 10 weeks, combined with quadruple tests of serum α fetoprotein, unconjugated oestriol, β-human chorionic gonadotrophin (HCG), and inhibin-A during the second trimester (after 14 weeks). This two step package had a false positive rate of only 0.9%. The best first trimester screening package was a combination of nuchal translucency scan, serum free β-HCG, and pregnancy associated plasma protein A, which had a false positive rate of 4.3%. Second trimester quadruple testing alone had a false positive rate of 6.2%.

Any screening programme package needs to include a risk cut-off point with an expectation that "high risk" women will opt for an invasive prenatal diagnostic test while the rest will be sufficiently reassured not to seek further testing. The UK National Screening Committee has set a screening programme target of a detection rate of at least 75% with a false positive rate of 3% or less by April 2007. Using a

currently recommended cut-off of 1:250, the estimated performance of the two step integrated test is clearly superior, with a detection rate of 91% and false positive rate of only 2.6%. But we know that some women ask for the one stop first trimester package, accepting a slightly inferior screening performance (85% detection rate, 4.2% false positive rate). Also we should not forget that some women access maternity services for the first time in the second trimester and others will request definitive diagnosis by chorionic villus sampling or amniocentesis irrespective of their risk. The integrated test may be the most cost effective, but any "one size fits all" policy sits uncomfortably with pregnant women and clinicians.

The main challenge for pregnant women is to absorb all the relevant information in early pregnancy to allow them to make an informed choice about which, if any, screening option they wish to undergo. The main challenge to health systems will be to ensure that there are enough adequately trained sonographers to deliver an ultrasound based screening programme on a national basis—certainly a major issue.[3]

Other remaining questions are behavioural and contextual. How many women will tolerate the delay between the two gestational stages of the integrated tests? And what is the importance of establishing top quality Down's syndrome screening programmes, relative to other priorities in the maternity services—notably tackling inequalities and ensuring that all women in labour have enough midwives to meet their needs?[4 5]

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1 Snijders RJM, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. *Lancet* 1998;351:343-6.
2 Wald NJ, Rodeck C, Hackshaw AK, Rudnicka A. SURUSS in perspective. *Br J Obstet Gynaecol* 2004;111:521-31.
3 Crossley JA, Aitken DA, Cameron AD, McBride E, Connor JM. Combined ultrasound and biochemical screening for Down's syndrome in the first trimester: a Scottish multicentre study. *Br J Obstet Gynaecol* 2002;109: 667-76.
4 Lewis G, Drife J, Botting B, Carson C, Cooper G, Hall M, et al. Why mothers die 1997-1999. *The fifth report of the confidential enquiries into maternal deaths in the United Kingdom.* London: RCOG Press, 2001.
5 Hodnett E, Gates S, Hofmeyr GJ, Sakala C. Continuous support for women during childbirth *Cochrane Database Syst Rev* 2004;(3):CD003766.

Managing metastatic bone pain

Radiotherapy and bisphosphonates are effective for metastases and pain

Patients associate advanced cancer with pain, and for many such patients the source of the pain will be metastatic bone disease. Bone is one of the most frequent sites of spread for many common cancers such as breast, prostate, lung, and kidney and is usually affected in multiple myeloma.[1] Active management of metastatic bone disease can, however, control the symptoms and in many cases prevent further complications such as pathological fracture or compression of the spinal cord.[2]

What can be done? Firstly, patients should be given analgesics and considered for appropriate systemic treatment for the underlying cancer, usually hormonal treatment or chemotherapy. Secondly, patients should be considered for specific treatment for the bone metastases, the principal modalities being radiotherapy and bisphosphonates.

Radiotherapy has long been used. It is most commonly given as external beam to the most painful site or sites. Does it work, and how should it be given? Assessing reduction in pain in patients with advanced cancer is difficult because of changes in their analgesia, changes in the cancer itself, and high dropout rates in patients with advanced cancer. Nevertheless, the data on fractionation trials have been subjected to two overviews (and, for aficionados, an overview of the overviews).[3–5] Both overviews are consistent and show a response rate (pain reduction) in about 60% of patients, which is complete in about 33% (and rises to about 72% and 40%, respectively, if the analysis is of evaluable patients rather than on an intention to treat basis). These response rates are the same whether the radiotherapy is given as a single fraction (usually 8-10 Gy) or as multiple fractions (most commonly 20-30 Gy in 5-10 fractions). The pressure on facilities for radiotherapy in the United Kingdom as well as convenience for the patient in attending only once are strong arguments to use single fractions.[6] The main difference between single and multiple fractions is the higher rate of repeated treatment in the single fraction studies (21.5% *v* 7.4%). The higher re-treatment rate in the single fraction arms may not necessarily lower therapeutic efficacy since time to progression was the same in those studies that examined it. Rather, it may reflect clinicians' greater willingness to repeat treatment after a single rather than after the higher dose of multiple fractions. Whatever the reason, even with single fractions, nearly 80% of patients will not need repeat treatment.

For some patients, especially for those with cancer of the prostate, using a radioisotope such as strontium 89 that localises to bone will relieve pain, albeit with risk of leucopenia and thrombocytopenia.[7]

Given that most patients will have multiple bony metastases, what are the systemic options specifically for treating bone metastases? The most widely used agents are bisphosphonates, for which good evidence indicates that they will reduce the incidence of fractures, the need for palliative radiotherapy, the risk of hypercalcaemia, and the need for orthopaedic surgery (often collectively called skeletal related events), but not the risk of compression of the spinal cord.[8] These benefits are seen mainly after six months of treatment, and the reduction in orthopaedic surgery

BMJ 2004;329:812–3