Letters

Bovine spongiform encephalopathy threatens drugs in European Union

EDITOR—While the debates about bovine spongiform encephalopathy periodically have a high profile in public health, food safety, and agricultural and political environments, the pharmaceutical environment is now becoming seriously entangled in the web of controversy. On 20 February this year the pharmaceutical council of the European parliament accepted the European Commission's proposed revisions to directive 75/18/EEC.

If the revisions are accepted by the European Union's Council of Ministers it will mean that drugs for human consumption that have bovine, ovine, or caprine ingredients, or ingredients derived from such, will (with one exception) not be allowed on any member state's market after 31 December. Over 200 drugs with gelatin capsules will be affected, as will specific products such as HibTITER (*Haemophilus influenzae* type b vaccine), Hyalase (hyaluronidase), and Hypurin (insulin).[1]

The only exception to the ban will be drugs with such ingredients that have or secure a pan-European Union product licence through the European Medicines Evaluation Agency's centralised route and for which no alternative drug is available. This escape route shows another aspect of the growing importance of the pan-European Union drug licensing system.[2]

On 10 June this year Emma Bonino, the commissioner for fisheries, consumer policy, and the European humanitarian office, announced the creation of another committee of the European Union, the scientific steering committee. This will act as the supreme source of expertise for the commission and offer excellence, independence, and transparency.

The first task for the scientific steering committee must be to make available the scientific evidence and rationale underpinning the decision to revise directive 75/18/EEC. If there is a scientific basis for the policy the committee should, being excellent and independent, produce it for all to see. The more obvious reason for the commission's actions is that the European parliament had earlier threatened by 422 votes to 49 to force the commission to resign in a body if it did not act on the crises over bovine spongiform encephalopathy. Whether the emerging responses are justified or prudent remains questionable. Who is going to benefit from this malaise in policy and this lack of evidence based decision making: the millions of consumers of meat, jellies, sweets, and drugs?[3-5]

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1 Association of the British Pharmaceutical Industry. *Compendium of data sheets and summaries of product characteristics.* London: ABPI, 1996.
2 Earl-Slater A. Recent developments in regulating the pharmaceutical business in the EU. *European Business Review* 1996;96(1):17-25.
3 Belcher P, Mossialos M. Health priorities for the European intergovernmental conference. *BMJ* 1997;314:1637-8. (7 June.)
4 Coghlan T. New Labour, new Europe. *BMJ* 1997;314:1506. (24 May.)
5 Davis P. Managing medicines: public policy and therapeutic drugs. Buckingham: Open University Press, 1997.

Figures given for bed complement in Edinburgh were wrong

EDITOR—In a letter the chief executive and chairman of the Royal Infirmary of Edinburgh object to the figures that Allyson M Pollock and colleagues used when they considered the implications of a private finance initiative in Edinburgh.[1] Included in their letter was a table that documented the bed status at 31 March 1997. This table included the bed status of the Eastern (not Edinburgh as printed) General Hospital. Unfortunately, the figures for the Eastern General Hospital that John J Owens and Cairns Aitken used were incorrect; the table shows the correct figures.

The figures that Owens and Aitken used were projected figures that had been calculated on the basis of several assumptions and were not the actual staffed bed complement at 31 March 1997. Contrary to what Owens and Aitken state in their letter, these were not discussed with the clinicians involved.

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1 Owens JJ, Aitken C. What happens when the private sector plans hospital services for the NHS. *BMJ* 1997;314:1619-20. (31 May.)

Delays in diagnosing oesophagogastric cancer

Attempts to reduce delays in diagnosis should be done in controlled trial

EDITOR—The finding that gastric cancer detected early has a long doubling time (several years) whereas that diagnosed in an advanced stage has a short doubling time (several months)[1] is consistent with the well known length bias. A non-aggressive course is associated with a long subclinical period with a high chance of early detection, whereas aggressive growth with a rapid onset of severe clinical symptoms leaves little chance of recognition of disease in an early stage. This confounds the observation that "early" cancer has a better prognosis than "late stage" cancer. The low case fatality from gastric cancer in Japan is a logical consequence of such biases, given that over six million Japanese people (presumably a selection of healthy people) have stomach screening annually. The suggestion that "patients with new onset dyspepsia and with changes in long standing dyspepsia must be referred promptly [for gastroscopy]" [1] is therefore not evidence based.

In practice, early detection of cancer means not only the possible advantage of better curability in some cases but also the possible disadvantage of overdiagnosis and overtreatment in many other cases. Necropsy

Bed complement at Eastern General Hospital, Edinburgh, at 31 March 1997

	Bed complement at Eastern General Hospital		
	As stated by Owens and Aitken	Actual	60% of complement at Eastern General Hospital*
General surgery	10	42	25
Gneral medicine	48	107	64
Gynaecology	15	13	8
Obstetrics	15	37	37 (all to RIE)
Neonatology	8	7	7 (all to RIE)
Subtotal	96	206	141

*Calculations assume that 60% of beds at Eastern General Hospital are moved to Royal Infirmary of Edinburgh (RIE) and 40% to Western General Hospital, Edinburgh, except where otherwise stated.

studies show that 25% of women have cancerous breast tissue at the time of death, but in only 29% of these was it diagnosed during their lifetime.[2] Screening or case finding has invariably resulted in a considerable increase in diagnosed breast cancer. The incidence of malignant melanoma, similarly, has doubled in places where early detection campaigns took place, with no subsequent change in mortality being observed. "It is possible that earlier diagnosis has uncovered a pre-existing nonmetastasising, nonfatal form of melanoma, and that this accounts for a substantial proportion of increases in incidence." [3] Furthermore, necropsy studies indicate that prostate cancer is present in nearly half of older men, suggesting that many occult cancers detected through screening would not manifest themselves during the patient's lifetime.[4]

The medical community has hesitantly learnt to accept that screening for prostate cancer is not useful.[4] We will perhaps be forced to accept that even the benefit of screening for breast[2] and cervical cancer[5] is equivocal. It is time to stop publishing papers suggesting that more should be done about early detection of cancer without suggesting that length and lead time bias and the dilemma of overdiagnosis should be addressed. The important question is not whether cancer statistics can be improved but whether interventions truly do more good than harm to patients. If Britain is to rush to "improve" on delays in the diagnosis of gastric cancer it should be done in a controlled trial.

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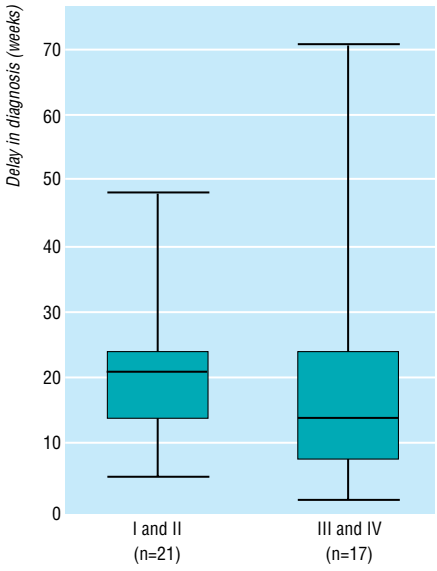
1 Martin IG, Young S, Sue-Ling H, Johnston D. Delays in the diagnosis of oesophagogastric cancer: a consecutive case series [with commentaries by T Sano and K Maruyama and R Siewert and U Fink]. *BMJ* 1997;314:467-70. (15 February.)
2 Schmidt JG. The epidemiology of mass breast cancer screening: a plea for a valid measure of benefit. *J Clin Epidemiol* 1990;43:215-25, 235-9.
3 Burton RC. Analysis of public education and the implications with regard to nonprogressive thin melanomas. *Curr Opin Oncol* 1995;7:170-4.
4 US Preventive Services Task Force. *Guide to clinical preventive services.* Baltimore: Williams and Wilkins, 1989.
5 Raffle AK, Alden B, Mackenzie EF. Detection rates for abnormal cervical smears: what are we screening for? *Lancet* 1995;345:1469-73.

Small study showed no difference in delay with stage

EDITOR—We agree with Iain G Martin and colleagues' wish to see more patients at an earlier stage of their disease.[1] We are, however, unhappy about their conclusion from such a small number of patients with oesophageal cancer and its implication.

Over the past two years, one of us (WG) personally visited over 50 patients before intended oesophagectomy at four West Midlands hospitals. A brief questionnaire was administered, which included an inquiry about the onset of relevant symptoms in each patient so that the interval between that time and both diagnosis and treatment could be estimated. We had hoped to reach a conclusion identical with that of Martin and colleagues to justify a nationwide awareness campaign to the public as well as to primary carers. Thirty eight of the interviewed patients had a full resection so that the tumour, node, metastases (TNM) status and grade could be recorded.



Delay in diagnosis of oesophageal cancer according to stage

The figure shows that we found no difference in delay; delay in presentation was not related to prognosis. Now that the incidence of adenocarcinoma exceeds that of squamous carcinoma,[2] perhaps screening of certain patients with a Barrett's oesophagus will be the next hope. Wright et al, however, showed that this was not cost effective as it cost £14 868 to detect an asymptomatic man and £42 084 to detect a woman with early cancer.[3] Van der Burgh et al also found screening not to be cost effective, though they suggested that patients with either an ulcer or columnar epithelium longer than 7 cm were more vulnerable to malignant change.[4]

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1 Martin IG, Young S, Sue-Ling H, Johnston D. Delays in the diagnosis of oesophagogastric cancer: a consecutive series [with commentaries by T Sano and K Maruyama and J R Siewert and U Fink]. *BMJ* 1997;314:467-71. (15 February.)
2 Powell J, McConkey CC. The rising trend in oesophageal adenocarcinoma and gastric cancer. *Eur J Cancer Prev* 1992;1:265-9.
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4 Van der Burgh A, Dees J, Hoop WCJ, van Bankenstein M. Oesophageal cancer—an uncommon cause of death in patients with Barrett's oesophagus. *Gut* 1996;37:5-8.

Provision of endoscopy in primary care speeds diagnosis

EDITOR—Iain G Martin and colleagues highlight the delays in reaching a histological diagnosis of upper gastrointestinal cancer in a specialised hospital with open access gastroscopy.[1] They suggest a one stop service as a remedy. Most hospital units, however, are already struggling to provide an open access service and would be overwhelmed if 1% more of the population were examined annually, as recommended by the British Society of Gastroenterology. Increasing endoscopy services in hospitals also has cost implications.

An alternative is to establish diagnostic endoscopy clinics from within primary care that are run by experienced general practitioner endoscopists in accordance with the guidelines set out by the British Society of Gastroenterologists. Such units would cater for a more local population. During the past two years over 700 patients have had gastroscopy at our two surgeries, with an average waiting time of two weeks from the date of referral. Excellent "turn round" times from our local pathology department add, on average, a further week to obtain a histological diagnosis. Speed of communication between the referring general practitioner and the endoscopist is enhanced by the use of fax to transfer details of referrals and reports. Our cost per case is much less than that charged by our local trust hospitals because of reduced overheads and the omission of sedation.

Faster, cheaper, and easier local access to diagnostic endoscopy is one key element in the earlier diagnosis of upper gastrointestinal malignancy. Although in its infancy, the provision of endoscopy in primary care is highly efficient and looks set to expand, provided support continues from our political masters.

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1 Martin I, Young S, Sue-Ling H, Johnston D. Delays in the diagnosis of oesophagogastric cancer: a consecutive series [with commentaries by T Sano and K Maruyama and R Siewert and U Fink]. *BMJ* 1997;314:467-71. (15 February.)

Misconceptions exist over whether delay in diagnosis influences survival

EDITOR—Iain G Martin and colleagues report the causes of delays in the diagnosis of oesophagogastric cancer.[1] Against a background of a median delay of 17 weeks, the authors argue that long delays matter to outcome. With respect to gastric cancer, this extrapolation should be interpreted with caution.

The basic assumption is that advanced cancers presenting after long delays in diagnosis were potentially earlier stage tumours when their symptoms began; this assumption is questionable. Using a model of tumour doubling times is simplistic. Tumour stage is related more to invasion and spread than simply to tumour size,[2] and a tumour may double in size but not be upstaged. Equally, this model assumes that the doubling time occurs within the window of delay, and clearly this is not so for some "early" cancers, where doubling times may be very long (up to 10 years; references 11 and 12 in the paper).