

lait spots. He had no family history of testicular cancer and had no history of undescended testis. At age 15 years, right orchiectomy was done for the right testicular tumour, which was shown histologically to be an embryonal carcinoma without seminomatous component (figure). In the 10 intervening years, he had been well until he noticed swelling of his left testis. A left orchiectomy was done and histological assessment showed pure seminoma (figure).

Loss of heterozygosity was not seen through analysis of the microsatellite marker located in intron 26 of the NF1 gene (figure),<sup>3</sup> which suggests this gene might not have a principal role in the pathogenesis.

Our results, along with the histological difference between the two tumours, are consistent with the existence of only a few reported cases of NF1 with testicular cancer, including unilateral and bilateral disease. The pathogenesis of these tumours remains a conundrum.

\*Haruki Kume, Takamitsu Tachikawa, Shinji Teramoto, Koichiro Isurugi, Tadaichi Kitamura

Department of Urology, Faculty of Medicine, University of Tokyo; and \*Division of Urology and Division of Internal Medicine, Sanno Hospital, 8-10-16 Akasaka, Minato-Ku, Tokyo 107-0052, Japan (e-mail: hyykume@gol.com)

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## Antibiotic therapy and peritonitis

Sir—In his Nov 4 commentary, J Cohen<sup>1</sup> challenges the usefulness of combination antibiotic therapy for severe peritonitis compared with monotherapy with  $\beta$ -lactam antibiotics. This approach to treatment of a high-density bacterial infection such as peritonitis must, however, be questioned because of the potentially serious clinical implications.

In my hospital, a man aged 58 years was moved to the intensive-care unit with postoperative peritonitis 10 days after repair of a duodenal ulcer. *Klebsiella pneumoniae* was isolated from blood cultures and ascitic fluid. He was treated with piperacillin/tazobactam monotherapy but 36 h later he

had not improved. The isolate was sensitive to piperacillin/tazobactam on measurement of minimum inhibitory concentration by E-test (MIC=8/4 mg/L). We suspected extended-spectrum- $\beta$ -lactamase (ESBL) production and confirmed it by the ESBL disc detection test.<sup>2</sup> ESBLs are enzymes that confer resistance to newer generation cephalosporins like cefotaxime and penicillins.<sup>3</sup> The patient was started on imipenem and clinical response noted the next day.

Despite susceptibility of *K pneumoniae* to piperacillin/tazobactam on laboratory testing, clinical failure occurred. The bacterial density or inoculum size used in standard laboratory testing is  $10^5$  cfu/mL, but when the inoculum size of ESBL-producing organisms increases to  $10^7$  cfu/mL, susceptibility to  $\beta$ -lactams declines strikingly.<sup>3</sup> However, this inoculum effect does not apply to carbapenems, like imipenem, which remain active against bacteria expressing this enzyme.<sup>3</sup> Peritonitis is a high-density microbial infection,<sup>4</sup> and, therefore, if ESBL-producing organisms are present, treatment failure with  $\beta$ -lactam monotherapy is likely, unless carbapenems are used.

Gram-negative bacteria found in patients with peritonitis, especially those having long-term hospital stays or previous antibiotic therapy, may include *Enterobacter*, *Citrobacter*, *Serratia*, *Morganella*, and *Pseudomonas aeruginosa*, which characteristically produce inducible  $\beta$ -lactamases.<sup>4</sup> These enzymes are encoded on chromosomal genes, unlike ESBLs which are plasmid-mediated. Such organisms have a high spontaneous mutation rate for production of large amounts of these enzymes that confer resistance to penicillins and cephalosporins and are not inhibited by  $\beta$ -lactamase inhibitors, such as tazobactam.<sup>5</sup> Therefore, resistance emerges readily under selective pressure of treatment with penicillins or cephalosporins among these organisms. Furthermore, previous exposure to piperacillin has been associated with selection of  $\beta$ -lactam-resistant organisms but, interestingly, combination therapy that includes an aminoglycoside reduced this risk.<sup>5</sup>

Combination therapy with a  $\beta$ -lactam and an aminoglycoside may prevent resistance and, since organisms generally remain susceptible to one of the agents, possibly improve chances of survival in severely septic patients.

Brendan Crowley

Liverpool Public Health Laboratory, University Hospital Aintree, Liverpool L9 7AL, UK

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## Academic harassment

Sir—Only 7% of professors in Japanese universities are women. What is less well known is the undercurrent that might have brought about this situation—academic harassment. Such behaviour is an increasingly notorious but rarely highlighted issue in Japan, and includes all kinds of non-sexual bullying among academics.

I am a female Japanese researcher who gathered enough courage to speak out 3 years ago as the plaintiff in such a case. The verdict was issued on Oct 11, 2000, in the Osaka District Court, Japan. I won.

The five kinds of behaviour of the professor (the defendant) that the court acknowledged as bullying and for which I should be compensated are: disposal of liquid waste and other waste materials in my office while I was away from campus; moving things in and out of my office without my permission while I was gone for lunch or away from campus; unjust distribution of research funds; attempts to force me to resign or transfer; and refusal to sign documents needed for my work to be done.

According to the Japanese state redress law, the compensation pertaining to the liability of legal affairs of government workers on official duties should be given by the local prefectural government, and since the defendant is a government worker, the judge ordered the Nara prefectural government to pay me 550 000 yen.

My case, however, is just the tip of the iceberg. Bullying towards women or those who do not conform in Japan's academia is rampant and the types of bullying to my surprise, are very much like those I underwent (examples and varieties can be found at [www.kcn.ne.jp/~jjj/akahara/akahara.htm](http://www.kcn.ne.jp/~jjj/akahara/akahara.htm) accessed on Nov 16, 2000). A hostile working environment has

interfered with the exhibition and development of the victims' scientific faculties and has depressed the research activities in Japanese academic fields.

Unable to stand by and watch the situation, some victims and I are now preparing to establish a non-governmental organisation to fight academic harassment. This landmark ruling might pave the way for justice to be done in favour of the victims.

Messages are welcome at kogoshi@naramed-u.ac.jp or jijj@kcn.ne.jp. Opinions can be voiced at the Science Council of Japan (info@scj.go.jp) and the Japanese Ministry of Education, Science, Sports and Culture (voice@monbu.go.jp). Information about discriminatory promotion towards women can be found at the site of the Japanese Prime Minister's Office for Gender Equality (www.sorifu.go.jp/danjyo/index2.htm accessed on Nov 16, 2000).

Kumiko Ogoshi

Department of Public Health, Nara Medical University, Kashihara City, Nara 634, Japan

## Presentation of in-vitro fertilisation results

Sir—The Human Fertilisation and Embryology Authority (HFEA) is required to publish the outcome of licensed treatments. The format of the data presentation has evolved since publication of the first annual report in 1991, but still does not meet with the universal approval of the purchasers and providers of these services.

We accept the fundamental importance of showing in-vitro fertilisation (IVF) outcome by the number of treatment cycles started, but are concerned that too much emphasis has been placed on this denominator. Expressing results by cycles started may encourage clinics to adopt treatment policies which give them a maximum apparent success rate, mainly by avoiding the cancellation of cycles before egg recovery or embryo replacement. With

the number of episodes of embryo replacement limited by private finance or health-authority funding, this practice might not be in the best interest of individual couples. Furthermore, although much effort is expended in verifying the accurate reporting of treatment cycle *outcomes*, the HFEA has no mechanism to verify the number of cycles *started*.

We believe that it is essential for IVF treatment data to be published in a format that is readily understood by all interested parties, and that the dataset is as comprehensive as possible. We propose a format (table) that meets the HFEA requirement to show livebirth outcome by the number of cycles started (17.5% overall in one of our centres in 1999). The format also includes: the number of cycles cancelled before embryo replacement (27.8% [94 of 337]), the number of embryos replaced in the centre, and the effect of the age of the woman—the major determinant of outcome.<sup>1</sup> Patients and purchasers can assess pregnancy rates in like groups of patients, and the impact of cycle cancellation and embryo-transfer policies of the unit. The current form of HFEA data presentation is inadequate in this respect, since it lists only the proportion of treatment cycles started that culminate in the transfer of two embryos. This figure is misleading since it is dependent on the abandoned-cycle rate and the proportion of patients who have only one embryo transferred.

The HFEA remains concerned about the high rate of multiple births and advises that two rather than three embryos are replaced when four or more embryos have been created. The Royal College of Gynaecologists has recommended that the maximum number of embryos replaced be reduced to two. It is important for units to show, therefore, the relative proportion of two-embryo and three-embryo transfer cycles.

With customised data-collection software now widely available, we suggest that units use this format to report interim clinical pregnancy data for a 12-month period. We further

believe that there is no reason why this format should not be used for livebirth data by the HFEA in their Annual Report and Patient's Guide to OI and IVF units.

B A Lieberman, D Falconer, \*D R Brison

\*Department of Reproductive Medicine, St Mary's Hospital, Manchester M13 0JH, UK; and Manchester Fertility Services, BUPA Hospital, Manchester

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## BSE report

Sir—Your Nov 4 editorial on the Phillips report on bovine spongiform encephalopathy (BSE)<sup>1</sup> is inaccurate in claiming that the Food Standards Agency “quietly lifted part of the ban on calves' offal entering the human and animal food chain”.

The whole issue was put on public record at the second open board meeting on June 22, and is recorded in the minutes, which remain available on our website (www.foodstandards.gov.uk accessed on Dec 6, 2000). We issued a News Release on Aug 21, in which we formally announced that UK legislation was to be changed to embrace new BSE protection measures covering the whole of the European Union.

The Spongiform Encephalopathy Advisory Committee (SEAC) discussed these new measures at its meeting in May, 2000, and published their advice. As we stated in June and in our news release in August, the SEAC concluded that the benefits of introducing controls across the European Union outweighed any potential slight increase in the theoretical risk caused by a small reduction in the amount of material previously designated in the UK as specified risk material.

I hope you will agree that the publishing of a change 6 months before it is due to take effect, an advisory committee publishing their advice, and the laying out of regulations before Parliament is about as open as we can get. This approach is entirely consistent with the Phillips recommendations.

Finally, you believe that the Government would do well to put research money into BSE (and scrapie). The Food Standards Agency draft report on BSE controls recommends better coordination of the large sums already being spent on research and a speeding up of the research in several critical areas. In the

Embryos replaced	Maternal age (years)									
	<30		30–35		36–39		≥40		Totals	
	LB per cycle	LBR (%)	LB per cycle	LBR (%)	LB per cycle	LBR (%)	LB per cycle	LBR (%)	LB per cycle	LBR (%)
None	0/3	..	0/31	..	0/39	..	0/21	..	0/94	..
1	0/1	0.0	1/5	20.0	1/8	12.5	0/3	0.0	2/17	11.6
2	5/21	23.8	20/65	30.8	8/44	18.2	0/9	0.0	33/139	23.7
3	2/4	50.0	11/30	36.7	10/36	27.8	1/17	5.9	24/87	27.6
Totals	7/26	26.9	32/131	24.4	19/127	15.0	1/50	2.0	59/337	17.5

LB=livebirths; LBR=livebirth rate.

**Livebirth rate per cycle started, by age of woman and number of embryos replaced**