AIDs and class II microbiological safety cabinets

SIR,—The information about class II microbiological safety cabinets presented by Sheila McKechnie (30 March, p 1006) needs correction. She states "there is sound evidence that they provide little or no operator protection."

Collins indicated that class II cabinets that satisfy the requirements of the National Sanitation Foundation Standard No 49 (1976) and British Standard 5726 (1979) are available and are effective.[1] The most pertinent information indicating the effectiveness of class II cabinets is in a table from the recent National Institutes of Health slide series that accompanies the *Fundamentals for safe Microbiological Research*, a series used to teach biosafety.

*Leak factors for safety cabinets**

Type	Activity	Leak factor
Class I	None	10^{-6} to 10^{-5}
	Simulated labwork	10^{-5} to 10^{-2}
Class IIA	None	10^{-8} to 10^{-6}
	Simulated labwork	10^{-7} to 10^{-5}
Class IIB	None	10^{-9} to 10^{-7}
	Simulated labwork	10^{-8} to 10^{-5}
Class III	Transfer through autoclave	$\leq 10^{-8}$

*The leakage factors were arrived at by sampling outside while aerosols were inside. The data were collected by placing cabinets in a wind tunnel. All air passing the cabinet was collected in a large volume sampler. A leak factor of 10^{-6} implies that one out of every million particles generated in the cabinet would escape containment under normal operating conditions.

These data indicate with simulated work conditions that the class IIA cabinet is 100 to 1000 times more effective than the class I cabinet. The class IIB cabinet is 1000 times more effective than the class I cabinet. The class III cabinet can be 1000 times more effective than the class IIA and IIB and sometimes only equally as effective as the IIB. It is very important to remember that the cabinets are effective only against aerosols. The operator still has to practice good aseptic technique.

Other factors affecting the cabinets are: (*a*) cross drafts created by walking past the cabinets; (*b*) particles brought out of the cabinet when a person withdraws his or her arms and equipment; (*c*) an operator's body close to the work opening obstructing the inflow of air and creating sufficient turbulence to cause cabinet air to spill out[2]; and (*d*) opening or closing laboratory doors.

There is no doubt that if there were convincing evidence that human lives were at risk there would be no question which cabinet should be used. At NIH Gallo's serology and tissue culture laboratories use class II cabinets (W C Saxinger, personal communication). The laboratories that supply NIH with large amounts of virus would obviously expose their workers to larger quantities of HTLV-III virus than anyone in a diagnostic laboratory, and they use class II cabinets (J Lemp and P Markham, personal communication). Levy's laboratory uses class II cabinets for all its work with material from people with the acquired immune deficiency syndrome and for producing the HTLV-III virus (J Morrow, personal communication). The experience of these four laboratories indicates there is little danger from HTLV-III as an aerosol.

Use of class III cabinets would increase the work time up to 10 times compared with work done in a class II cabinet.[3]

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1 Collins CH. *Laboratory-acquired infections*. London: Butterworths, 1982:101-5.
2 Macher JM, First MW. Effects of Airflow Rates and Operator Activity on Containment of Bacterial Aerosols in a Class II Safety Cabinet. *Appl Environ Microbiol* 1984;**48**:481-5.
3 van der Groen G, Trexler PC. A look at the P4 virus containment laboratory. *Progress in Medical Virology*. 1982;**28**:192-207.

Prognostic indicators in breast cancer

SIR,—Mr D J Holdsworth and colleagues (2 March, p 671) make the point that additional prognostic indicators should be considered in breast cancer. We would like to add parity to the independent prognostic indicators in breast cancer after considering the possible confounding effects of obesity.

Obesity has been associated with poor prognosis in breast cancer,[1] while parity associated with obesity apparently results in a good prognosis.[2] We investigated whether the presence of obesity has a modifying effect on the importance of prognostic indicators in breast cancer. The study was carried out in 331 patients with operable breast cancer who underwent mastectomy and axillary dissection in 1977-84 and had the following prognostic factors recorded: presence of histological lymph node disease (negative, 1-3 affected, ≥4 affected), tumour differentiation (well, moderate, poor), hormone receptors (positive or negative with the cut off point 10 fmol/mg cytosol protein), degree of obesity calculated by Quetelet's index (weight×100/height^2), parity (parous, nulliparous), and age (<50 years, ≥50 years).

Disease free survival was evaluated in 323 of these patients (eight were lost to follow up) with the Cox proportional hazards model after stratification by presence of obesity. Quetelet's index of 3·5 or more was the cut off point for presence of obesity.

The univariate analysis showed that the degree of axillary lymph node disease and poor tumour differentiation were significant prognostic indicators in both lean and obese women. Among obese women positive hormone receptors and parity were significant prognostic indicators as well ($p=0·05$). In the stepwise analysis lymph node disease, tumour differentiation, and hormone receptors entered the model in both the lean and the obese groups. In addition, Quetelet's index entered the model in the lean group while parity and age entered in the obese group (table).

These findings indicate a modifying effect of obesity at least in the prognostic significance of parity and of age in breast cancer. Increased Quetelet's index among the lean is apparently associated with poor prognosis while increases in the index in the obese does not seem to affect prognosis. Nulliparity appears to be associated with poor prognosis only among obese women and in that group it is the most significant prognostic indicator after lymph node disease. Women over 50 years of age who are obese seem to have a worse prognosis, while no such age effect was noted among the lean. The association between parity and obesity was more pronounced and was significant only in the older age group. Among the young obese 25/31 (81%) were parous compared with 59/77 (77%) in the young lean. The respective numbers among the older group were 83/101 (82%) and 80/122 (66%) ($\chi^2=7·79$, $p<0·01$).

These findings suggest that in obese women parity should be considered in defining subgroups for adjuvant treatment and the same applies for tumour differentiation and hormone receptors in the lean group. These observations underline the heterogeneity of patients with breast cancer and the pitfalls when results are evaluated without considering the peculiarities of different subsets.

Results of univariate and stepwise analyses

	Lean (n=195/DFS=159)			Obese (n=128/DFS=86)		
	Univariate p	Stepwise p	Coefficient/SE	Univariate p	Stepwise p	Coefficient/SE
Degree of lymph node disease	0·0096	0·0076	2·67	0·0097	0·0075	2·67
Poor tumour differentiation	0·0057	0·0106	2·62	0·0190	0·0984	1·66
Positive hormone receptors	0·1339	0·0267	−2·26	0·0464	0·0701	−2·46
Parity	0·9881			0·0248	0·0209	−2·46
Age	0·8175			0·3072	0·0483	1·84
Quetelet's index	0·0785	0·0394	2·02	0·5811		

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1 Tartter PI, Papatestas AE, Ioannovich J, Mulvihill MN, Lesnick G, Aufses AH Jr. Cholesterol and obesity as prognostic factors in breast cancer. *Cancer* 1981;**47**:2222-7.
2 Papatestas AE, Mulvihill MN, Josi C, Ioannovich J, Lesnick G, Aufses AH Jr. Parity and prognosis in breast cancer. *Cancer* 1980;**45**:191-4.

Peptic ulcer and piroxicam

SIR,—I am sure that Drs W H W Inman and N S B Rawson are correct in questioning the validity of comparative analyses of the gastrointestinal toxicity of non-steroidal anti-inflammatory drugs which are based on spontaneous reports of adverse reactions (23 March, p 932). It is well known that these sources of data may be heavily biased. I am, therefore, surprised at their interpretation of the prospective data which they have collected from a large group of recipients of non-steroidal anti-inflammatory agents. We are told that the frequency of upper gastrointestinal bleeding or perforation ranged from 3 to 6 per 1000 patient years but that "only a minority (were) attributed to the drugs by the reporting doctor"; furthermore, we are told that these events "were very rarely caused by these drugs." Based on published evidence[1,2] my calculations give an expected frequency of upper gastrointestinal haemorrhage and perforation for the population of England and Wales of less than 1 per 1000 patient years. Although this figure is for all age groups and may not accurately represent the "background" risk for the subjects of Drs Inman and Rawson, it suggests that the relative risk of these events in users of non-steroidal inflammatory agents is greater than 3.

By making statements about causality which are based on clinical impressions are they not introducing exactly the same type of bias which contaminates spontaneous reporting? Surely it is the ratio of the observed to the expected event frequency which matters.

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2 Coggon D, Lambert P, Langman MJS. 20 years of hospital admissions for peptic ulcer in England and Wales. *Lancet* 1981;i:1302-4.

**Drs Inman and Rawson reply below.—ED, *BMJ*.

SIR,—Dr Henry estimates that the expected frequency of upper gastrointestinal haemorrhage and perforation for the population of England and