cells), may be lost after exposure to IgG immune complexes, the cells usually converting to Fc-IgM receptors, which express a helper population (Tμ cells).[1] Exposure to such immune complexes in the summer may account for the apparent reduction in OKT8 cells. We might have expected a concomitant increase in helper cells, but this was not observed. Nevertheless, cells characterised by OKT4 and OKT8 monoclonal antibodies bear little relation to those characterised by Fc-IgG and Fc-IgM receptors.[2]

We would be cautious in interpreting abnormalities and variation in T cell subsets defined by monoclonal antibodies. Firstly, in organ specific diseases, such as Graves' disease, where abnormalities in subsets have been described,[3] it is perhaps surprising that gross changes are observed, since T cells are highly antigen specific and any abnormality should affect only a small fraction of the T cell subset. Secondly, the commonly used monoclonal antibodies do not adequately define function —for example, the OKT4 population is known to harbour a group of cells capable of suppressor function.[4]

The conflicting reports of T cell subset abnormalities in hay fever sufferers may be explained by their seasonal nature and serve to emphasise the importance of considering not only the time of day but also, in some diseases, time of year when reporting data using monoclonal antibodies.

A G FENNERTY
K P JONES
B H DAVIES

Asthma and Allergy Unit,
Sully Hospital,
Penarth, South Glamorgan CF6 2YA

1 Pichler W, Lum L, Broder S. Fc receptors on human T lymphocytes. 1. Transition of TY to Tμ cells. *J Immunol* 1978;**121**:1540-8.
2 Reinherz EL, Moretta L, Roper M, *et al.* Human T lymphocyte subpopulations defined by Fc receptors and monoclonal antibodies. A comparison. *J Exp Med* 1980;**151**:969-74.
3 Ludgate EM, McGregor AM, Weetman AP, *et al.* Analysis of T cell subsets in Graves' disease: alteration associated with carbimazole. *Br Med J* 1984;**288**:526-30.
4 Thomas Y, Rogozinski L, Irigoyen OH, *et al.* Functional analysis of human T cell subsets defined by monoclonal antibodies IV induction of suppressor cells within the OKT4 + population. *J Exp Med* 1981;**154**:459-67.

SIR,—The recent leading article by Dr Martin S Knapp and Mr Roy Pownall (17 November, p 1328) correctly behoves investigators to report not only the discovery of biological rhythms but also their absence. The lack of a rhythm may not only be of fundamental importance but also be of immediate value in that the variable lacking a rhythm can be measured at any time without the possibility of a misleading result due to an unidentified rhythm. This is of particular importance in routine clinical chemistry and immunology tests. If any of these were shown to exhibit notable rhythms then sampling times during clinical trials could be critical. If a given test has not been investigated for rhythmic changes then it would be a wise precaution to take samples at the same time of day throughout a trial. Some biochemical tests used to monitor patients with rheumatoid arthritis have been shown to lack rhythmic changes during "clinic hours," when blood samples are usually taken, hence eliminating circadian variation as a source of error in clinical trials.[1] This does not, however, eliminate the possibility of biologically important changes during the night in these or other tests, and some clinical features of rheumatoid arthritis, such as grip strength, certainly do show such changes.

Some apparent rhythms may be a consequence of variable factors such as food intake and changes in social habits. These factors might easily give misleading results in studies with only small numbers of subjects. The limitations of accuracy, precision, inter-observer and intraobserver variation, and day to day variation of the method used to assess the particular feature under investigation need to be thoroughly elucidated in advance.

Rhythms are often ignored in pharmacokinetic studies, where, for single dose studies, the dose is invariably given at the start of the day so that blood samples can be conveniently collected throughout normal working hours. Studies with indomethacin[2] and prednisolone[3] have shown clinically significant variations in kinetic variables in relation to the time of day of drug intake. A recent investigation of ibuprofen in normal volunteers has shown considerable intersubject and intrasubject variation in kinetics when single doses are given at 8 00 am, 12 00 noon, 6 00 pm, and 12 00 midnight (K E Surrall, unpublished observations). This may have clinical importance—for example, in the more efficient alleviation of early morning stiffness in patients with rheumatoid arthritis. Conversely, rhythms may contribute to drug side effects or, in turn, drugs may affect rhythms, and this then leads to toxic reactions.

Such studies are, however, clearly just the tip of the iceberg in terms of a more efficient application of the available therapeutic armoury, and much more work is needed to make use of recognised biological rhythms.

J S DIXON
N G SITTON
K E SURRALL
A J TAGGART

Clinical Pharmacology Unit
(Rheumatism Research),
Royal Bath Hospital,
Harrogate HG1 2PS

1 Sitton NG, Taggart AJ, Dixon JS, Surrall KE, Bird HA. Circadian variation in biochemical assessments used to monitor rheumatoid arthritis. *Ann Rheum Dis* 1984;**43**:444-50.
2 Reinburg A, Smolensky MH. Circadian changes of drug disposition in man. *Clin Pharmacol* 1982;**7**: 401-20.
3 English J, Dunne M, Marks V. Diurnal variation in prednisolone kinetics. *Clin Pharmacol Ther* 1983; **33**:381-5.

Certifying death in infancy

SIR,—The World Health Organisation recommended a modified certificate to record both maternal and infant causes or conditions for early neonatal deaths. Dr Maureen J Scott (1 December, p 1511) argues that the new certificate should be introduced to cover deaths throughout the first year of life. Her table II indicates that 59 (42%) out of 140 deaths occurring from 28 days to 1 year were "birth determined."

There appears, however, to be a misunderstanding of the additional information that will be available from this new certificate. Forty three of the 59 deaths were from congenital malformations and it is not clear that any different information would be recorded for these deaths whatever style of certificate were to be used. By requesting maternal and fetal causes, the form may allow additional conditions to be recorded for at least some of the 15 deaths Scott recorded as due to prematurity. The gain in information for deaths from 28 days to 1 year that are due to prematurity has to be balanced against the use of a certificate which would be inappropriate for most of the deaths (about 88% from the material presented by Dr Scott).

Postneonatal deaths by cause in England and Wales in 1982

ICD codes	Cause	No	(%)
740-759	Congenital malformations	542	(19·5)
760-763, 773	Relating to maternal conditions	2	(0·1)
764-766	Relating to gestation and birth weight	4	(0·1)
767-768	Relating to the birth	13	(0·5)
769-772, 774-779	Other perinatal conditions	92	(3·3)
798	Sudden infant death syndrome	1066	(38·4)
140-239	Neoplasms	25	(0·9)
E800-E999	Injury and poisoning	110	(4·0)
001-139, 240-739, 780-797, 799	All causes other than above	919	(33·1)
	Total	2773	(100·0)

The table shows the underlying cause of death for the 2773 deaths between the ages of 28 days and 1 year that occurred in England and Wales in 1982. This suggests that about 111 (4%) might have fetal and maternal conditions recorded as contributing to the cause of death. For the small proportion of deaths after 28 days of life where maternal factors are relevant the diagnoses can be recorded in part II of the traditional death certificate. From 1 January 1985 the Office of Population Censuses and Surveys will be coding all diagnoses recorded on the death certificate; it will then be feasible to produce counts of maternal conditions contributing to death after the neonatal period.

M R ALDERSON
BEVERLEY BOTTING
M MURPHY

Office of Population Censuses
and Surveys,
London WC2B 6JP

Consensus development conference: coronary artery bypass grafting

SIR,—Your publishing the report of this consensus meeting so quickly and the tone of your leader both implied approval of such deliberations (1 December, pp 1477, 1527). Surely it is ridiculous to expect that starting from scratch, or possibly from preconceived prejudices, two experts with 10 laymen (four of whom were medically qualified) should arrive at correct conclusions about so complicated a subject as this. The data presented by the "experts" were incomplete and contradictory and from the audience often irrelevant and emotional.

The reasonableness of the final report does not nullify the stupidity of the concept. It was probably a tribute to the cardiologist and cardiac surgeon, who must have directed the "jury" well, including introducing material which had not been given in the open meeting.

The problem of such a gathering is that with the names of the King's Fund and the *BMJ* backing it, conclusions are liable to be thought to be weightier than is the case, just as the debate in the Oxford Union about not fighting for King and country misled German thinking before the war, so such trials of debating skills could produce conclusions which are hopelessly wrong and should not be thought to carry any authoritative message. The *BMJ* should think carefully before lending its weight to any further entertainment of this sort.

R B PRIDIE

Harefield Hospital,
Uxbridge, Middlesex UB9 6JH