an informed discussion should take engineering literature into account. In urban areas, where Maimaris and colleagues recognise that most cycle accidents occur, the apparent separation of cycle paths from adjacent roads is often spurious because cycle traffic repeatedly crosses motor traffic at cross roads and junctions. Sight lines at these crossing points are typically inadequate, the right of way is unclear, and the parties may be oblivious of each other's presence. Design standards in the United States strongly discourage the construction of separate cycle paths adjacent to roads or the use of pavements as cycle paths.³

A recent study found that urban cyclists riding on a pavement or cycle path adjacent to a road were 1.8 times more likely to collide with a motor vehicle as cyclists riding on roads (a significant difference at the 1% level).⁴ Among the cyclists using a separate path, the risk of collision for those travelling against the direction of adjacent traffic was 4.5 times higher than that of cyclists travelling with the traffic flow ($P < 0.0001$). Cycling on separate paths promoted this hazardous travel: 32% of cyclists on paths rode against the flow of traffic, compared with only 5% on roads.

Cycling on roads in the same direction as adjacent traffic was not associated with increased risk for either sex of any age group. Thus, the aim of a well designed road system should be to integrate bicycles and motor vehicles, not to separate them.

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Impairment of driving by ciprofloxacin

EDITOR,—Ciprofloxacin is a 4-quinolone antibacterial agent. It is recognised to be potentially neurotoxic in both animals and man. The most commonly reported central nervous system side effects include dizziness, headache, and nervousness,^{1,2} which may impair the ability to perform skilled tasks such as driving. Appropriate counselling is therefore advised for any patient for whom ciprofloxacin is prescribed, as outlined in the *British National Formulary*. The importance of this advice was highlighted when a colleague taking ciprofloxacin felt that she was not in control of the car while driving. She had not received a warning from either her general practitioner or her pharmacist.

A postal questionnaire was sent to 204 general practitioners and 205 pharmacists in the St Helens and Knowsley District of Merseyside to determine the proportion of general practitioners and phar-

macists who routinely caution patients that their ability to drive might be affected while taking ciprofloxacin. The questionnaire listed several items of information which might be given to the patient (either verbally or written on the label) when prescribing or dispensing ampicillin, ciprofloxacin, or metronidazole. Ampicillin was included in the questionnaire as an example of a commonly prescribed antibiotic and metronidazole as a drug which has a well recognised adverse reaction with alcohol. The recipients of the questionnaire were asked to indicate the information routinely given for each antibiotic. Overall, 300 replies (73%) were received, 151 (74%) from general practitioners and 149 (73%) from pharmacists. The results are shown in the table.

Most general practitioners and pharmacists give the patient general information about antibiotics and will warn of the potential dangers of taking alcohol with metronidazole. However, only 9% of general practitioners and 43% of pharmacists routinely caution patients about driving while taking ciprofloxacin.

On 1 January 1994 regulations came into effect following a European Commission directive which requires all newly licensed medicines dispensed in an original pack to be accompanied by a patient information leaflet.³ Other products, including ciprofloxacin, will have to conform as their licenses are renewed. Until all medicines are dispensed in an original pack with a patient information leaflet, it is impossible to be certain how much information patients receive.⁴

The side effects of ciprofloxacin on the central nervous system do not seem to be widely recognised. It is essential that patients are warned of them so that potentially hazardous tasks such as driving or operating machinery may be avoided.

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Patients' rights in the Netherlands

EDITOR,—The board of the Netherlands Epidemiological Society, which has 850 members, was surprised to read Tony Sheldon's restrictive interpretation of a proposed Dutch law concerning patients' rights, which has not yet passed the First Chamber in the Netherlands.¹ Sheldon reports that the proposed law formed the basis of a document on patients' rights endorsed by 36 European nations after consultation by the World Health Organisation.

The Netherlands Epidemiological Society has collaborated closely with health lawyers, government officials, and politicians to ensure that the new law will permit non-experimental clinical and epidemiological research based on data on patients. We specifically emphasised the rights of future patients, whose treatments should be influenced by results of analyses of data on patients collected systematically in the past. Such research implies adequate access to the data. This is especially true for studies of side effects of treatments and preventive interventions. Sheldon's statement that data on patients for this type of observational research will be made available only after coding by a third party only partially reflects the proposed law. While creating the possibility that coded data can be studied (after the implicit non-refusal of patients) the law does not restrict possession of the key to the code to an independent body. Flexibility is necessary in case data on exposure to disease or on outcomes of disease need verification or interpretation direct from the records. Also, the proposed law does not require that identifiable data or material remain confidential after death.

Finally, all organisations in the Netherlands that have collaborated to arrive at this balanced solution have agreed, with the support of representatives of all political parties in the Chamber of Commons, that possible harmful effects of this law on the quality of health care and research should be monitored. Using this law as the basis for an international patient charter seems premature; the best course for the Department of Health in Britain may indeed be to "wait for the WHO report, then consider it."

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Genesis of apoptosis

EDITOR,—H Konrad Muller's preoccupation with historical accuracy in his letter on apoptotic priorities¹ would be served better by studying an earlier period.

Robert Schröder described the phenomenon in 1914 in a paper on menstruation² regularly cited in earlier monographs on gynaecological pathology³ for its originality, merit, and acclaimed diagnostic value. With exemplary deduction he described the presence, significance, and immense predictive power of the minute particles of pyknotic chromatin which appear in the subnuclear zone of the endometrial glands in the two or three days before menstruation.

Although well aware that the chromatin granules were products of individual cell death (Kernzerfallsfigurin), Schröder wisely named them without any hint of functional speculation or interpretation. His very simple descriptive term, Pyknosen, describes vividly and unerringly exactly what is seen—pyknotic bodies.

Schröder's illustration, made without the benefit of photomicrography, is executed to perfection in pen and ink, aided only by a drawing prism. Instantly recognisable, it leaves no doubt that the Pyknosen are identical to the apoptotic bodies subsequently published without reference to his original description.⁴ He enjoyed the obvious antithesis and, with less contrivance than his successors, wrote, "Die Erscheinung der Pyknose steht in einem direkten Gegensatz zur Mitose."

Information routinely given by general practitioners and pharmacists when prescribing or dispensing ampicillin, metronidazole, or ciprofloxacin

Information given	Antibiotics	No (%) of GPs	No (%) of pharmacists
Dose and duration	Ampicillin, metronidazole, ciprofloxacin	140 (93)	142 (95)
Complete the course	Ampicillin, metronidazole, ciprofloxacin	119 (79)	143 (96)
Avoid alcohol	Metronidazole	122 (81)	148 (99)
Take before food	Ampicillin	36 (24)	137 (91)
Possible impairment of skilled tasks (driving, etc)	Ciprofloxacin	14 (9)	64 (43)

In airing Schröder's work I am completely convinced that neither Kerr, Currie, Wyllie, Hopwood, nor Levison had any knowledge of it at the time their early papers were published. It has also escaped Muller's historical researches.

Independent and unwitting rediscovery is quite common: its benefits include fresh minds, new points of view, confirmation by repetition, and, often, greatly advanced techniques. It is not an occasion for shame. The contributions of the Australian and Scottish schools to the understanding of cell death have been imaginative, enthusiastic, and manifold. Schröder would reel in amazement at what they have uncovered; yet, perhaps felicitously, he has eliminated both schools from the claim to priority.

Muller would do well to study Schröder's paper, retrieve its incomplete reference,³ and perhaps reconsider his own views. Instead of inciting destructive rivalry, his historical inclinations might be employed more benevolently to promote a Robert Schröder Memorial Lecture at the next major meeting on cell death. In suitable hands, the story of Schröder's simple, useful, outstandingly reliable observation might enrich, inspire, and even graciously redress, a debt long overdue.

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Nocturnal ambulatory blood pressure measurement

Authors' reply

EDITOR,—If we have understood Shennan *et al*'s letter about our recent paper on ambulatory blood pressure during sleep² correctly, then the main problem is that they have assumed that the orienting reflex which is activated during arousal from sleep is due to the same physiological mechanism as the "white coat effect" while the subject is awake. There is no evidence to support this, and the time courses of the two vascular responses are very different. In addition, Shennan *et al* suggest that the haemodynamic response to ambulatory blood pressure measurement during the day is less likely to habituate to repetition than the haemodynamic response to measurements during sleep. This is incorrect, since the autonomic effects of arousal from sleep do not habituate with repetition at all (see references 4, 11, and 12 in our original paper), while the "white coat effect" does.

What our paper does show is that ambulatory cuff measurements raise the sleeping blood pressure variably between recording machines and subjects. Therefore they do not measure undisturbed sleeping blood pressure, but a combination of sleeping blood pressure plus an arousal component whose influencing factors and relevance to vascular risk are not yet adequately understood. The severity of this arousal component may be an important vascular risk factor, but it should be seen for what it is and not confused with an attenuated fall in blood pressure overnight.

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Periocular steroid ointments may cause ocular damage

EDITOR,—Jeremy M Butcher and colleagues point out the dangers of long term unsupervised use of topical steroid drops but only briefly refer to topical, periocular steroid ointments as a potential source of ocular damage.¹ Several reports have implicated periocular steroid preparations in the genesis of raised intraocular pressure and glaucomatous damage²⁻⁴ as well as the formation of cataracts.⁵ Although most of these cases have resulted from long term, periocular use of strong steroid ointments, Aggarwal *et al* reported a case of extensive visual loss after long term periocular use of 1% hydrocortisone ointment.⁴ This is particularly alarming as such a preparation is available from pharmacies without a prescription.

As Butcher and colleagues point out, the *British National Formulary* warns that topical steroid preparations should be used only under expert supervision. It should be made clear that the warning applies to both steroid drops and periocular ointments. Pharmacists dispensing 1% hydrocortisone ointment over the counter to unsupervised patients should warn them not to use the preparation periocularly for more than two weeks.

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Complementary medicine in Germany

EDITOR,—In their overview of the diverse situation regarding complementary medicine in Europe Peter Fisher and Adam Ward mention the German "Heilpraktiker" (health practitioner), stating that these practitioners "have passed an examination in basic medical knowledge."¹ This is misleading.

There is no mandatory training to become a Heilpraktiker, and, even though every candidate has to pass a test, the Heilpraktiker's qualifications are pitifully low.^{2,4} The only guideline for the test is to "exclude danger to the health of the nation."³ If a candidate fails the test he or she can take it again, at the same place or elsewhere, as often as desired. Failure rates vary from 0 to 100%, with an average of around 60%.³ Thus a thriving "examination tourism" has developed to those authorities with high average pass rates.³ The test may be oral or written, lasts from 20 minutes to five hours, and covers mostly legislation; essentially, candidates

must know which procedures they are not legally allowed to perform. Medical knowledge is rarely included.³

A Heilpraktiker practises predominantly (but by no means solely) methods that are unlikely to cause direct harm (there is, however, much concern about indirect risks—that is, missed diagnoses and otherwise incompetent behaviour). While complementary practitioners in Britain usually specialise in one or two complementary treatments, Heilpraktiker normally use many or all such treatments as well as diagnostic techniques of unproved or disproved validity. Heilpraktiker may also give subcutaneous and intramuscular injections. Complications and deaths occur.⁵

In Britain the call for registration of and control over providers of complementary medicine is becoming louder. The Osteopaths' Bill and the proposed Chiropractors' Bill are important steps towards control over educational and professional standards. The example of the Heilpraktiker suggests that registration without proper training (which should mean not merely a minimal amount of knowledge but also the right sort of knowledge) will not lead to acceptable standards of safety. Even an intrinsically safe remedy may become unsafe when not applied with competence. Thus professional competence is essential and must be considered when complementary medicine is discussed.

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Hopeful newspaper article was justified

EDITOR,—John R Petrie argues that an article by me in the *Times* drawing attention to a new cancer drug that is undergoing phase III trials in 26 centres in Britain and elsewhere in Europe is an example of "sensational reporting by poorly informed journalists."¹ Petrie is from Scotland; it is unfortunate that before writing his article he did not consult colleagues at Glasgow Royal Infirmary, Aberdeen Royal Infirmary, and Ninewells Hospital in Dundee, all of which hospitals are participating in the phase III study of lithium gammalinolenate in pancreatic cancer.

It is also a pity that the databases Petrie consulted during his literature search seem to have failed him. I can provide a list of more than 25 studies of lithium gammalinolenic acid in cancer, several of which are in well known publications such as the *Journal of the National Cancer Institute*. A phase II trial of lithium gammalinolenate in pancreatic cancer has been conducted in 48 patients at Edinburgh Royal Infirmary and Addenbrooke's Hospital in Cambridge. Partial results from this study were presented at a meeting of the American Association for Cancer Research last May and at a joint conference on cancer held by the National Cancer Institute and the European Organisation for Research and Treatment of Cancer in Amsterdam in March. The results of this phase II study were summarised in an earlier article in the *Times*, to which I would happily have referred Petrie had he contacted me.