caeruleus. Alterations such as nerve cell loss and atrophy, presence of Lewy bodies, and neurofibrillary tangles within nerve cells occurred to a significant extent in cases of dementia pugilistica in retired professional boxers, Parkinson's disease, Jakob-Creutzfeldt disease, and progressive supranuclear palsy; but they were minimal in normally aged control individuals (age range 30-97 years) and in those with motor neurone disease. Protein-synthesising capability, as indicated by nucleolar volume,³ was reduced significantly in remaining cells in cases of dementia pugilistica and Jakob-Creutzfeldt disease; but it was unaltered, even in the middle-aged and elderly controls, in motor neurone disease, and in the few remaining cells in cases of Parkinson's disease and progressive supranuclear palsy. A variable degree of mental impairment was common to all cases in this study where there was involvement of the locus caeruleus, ranging from mild loss of intellectual powers and confusion in cases of Parkinson's disease to overt dementia in cases of dementia pugilistica and Jakob-Creutzfeldt disease—cases of progressive supranuclear palsy being intermediate in this respect. By contrast, the control group, which was specifically screened for loss of mental ability, and the cases in the motor neurone disease group were all mentally preserved.

Adrenergic pathways from the locus caeruleus and dorsal motor nucleus of the vagus nerve, in conjunction with afferents to these regions from the supraoptic and paraventricular nuclei of the hypothalamus, form a system which through its connections with the periphery maintains homeostasis within the central nervous system against adverse extracerebral conditions.⁴ These pathways seem to regulate the permeability of the brain's microcirculation to water and water-soluble metabolites.⁴ It is, therefore, possible that the mental impairment or, more specifically, the dementia that is seen in Alzheimer's disease, and to varying extents in the other conditions we have outlined, is related to a breakdown in the functional integrity of this homeostasis-maintaining system. Such an impairment would lead to disturbed transport between brain and circulation, with widespread consequences for the nerve cells' capability to produce the proteins for correct neurophysical function.⁵

However, that is not to say, nor is it implied, that the aetiology or indeed the pathogenic mechanisms behind the changes in the locus caeruleus are the same in all conditions where dementia is a feature; rather the dementia represents a common picture of physiological outcome stemming from basically unrelated pathological causes.

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Chlormethiazole and temazepam

SIR,—Dr R S Briggs and others (1 March, p 601), in a study of the pharmacokinetics and pharmacodynamics of chlormethiazole and temazepam following single oral night-time doses, reported that the mean elimination half life of temazepam was of the order of 14 hours in a group of 10 elderly subjects (mean age 72.9 years), although insufficient data were available to permit the calculation of individual half lives. The subjects were largely symptomless and did not receive concomitant drug therapy.

We have studied the pharmacokinetics of

temazepam in a group of elderly hospital inpatients (four female, two male) (mean age 80 ± 6 (SD) years) following a single 20 mg oral dose of temazepam (Euhypnos, Montedison). Venous blood (5 ml) was obtained at frequent intervals up to 56 hours after the dose, and plasma temazepam concentrations were measured by a modification of the method of Belvedere *et al.*¹ The mean of the individual elimination half lives was found to be 17.6 ± 2.8 hours. None of the patients had acute hepatic, renal, or cardiac disease; three patients were receiving no drug therapy, two were prescribed diuretics for mild heart failure, and the remaining patient was under treatment with chlormethiazole (Heminevrin) and Distalgesic. In contrast, in an analogous study performed using healthy volunteers (four male, two female; mean age 29 ± 5 years), the mean of the individual elimination half lives was 8.0 ± 1.8 hours.

Dr A F Macklon and others (22 March, p 861) pointed out that the data of Dr Briggs and others could suggest a mean temazepam half life of up to 26 hours in the elderly subjects studied, and that accumulation of the drug on chronic daily dosage with the attendant possibility of adverse side effects was possible. Our results support this contention with respect to some elderly inpatients, since it is likely that accumulation will occur with daily dosage when the elimination half life exceeds 16 hours.² This is supported by the results of a further study, where we have observed a 1.5-fold increase in the temazepam plasma concentrations in early morning specimens after once-nightly dosage with temazepam (20 mg) for one week in elderly inpatients.

We are currently investigating the pharmacokinetics of the drug in healthy elderly subjects; but until this has been done the drug temazepam, like most other benzodiazepines, cannot be regarded as entirely safe or free from hangover effect in the elderly.

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Drugs and the elderly

SIR,—In the article "Drugs and the elderly" (10 January, p 125), by Drs Lawrence E Ramsay and Geoffrey T Tucker, though the authors accept that polypharmacy prevails in the elderly they state "What is not known is how much of prescribing is unnecessary, ineffective, or inappropriate. Indeed, we may never know. . . ." It is an everyday experience of a geriatrician to see at least half of the patients admitted taking eight to 10 kinds of tablets, more than half of these being far from essential. It has been shown that most elderly patients cannot take more than three concurrent regular medicines reliably¹ and patients who are prescribed several medicines or frequent doses are more likely to make mistakes.²⁻³

The problem of non-compliance, in the elderly at least, is too difficult to be overcome simply by giving written instructions, as suggested by authors. Poor eyesight contributes to many errors, especially so for those living alone; and small or indistinct writing makes

some labels illegible even for those with good eyesight.²⁻³ Training elderly patients, for two weeks before the date of foreseeable discharge, how and when to take their own medicine helped compliance.⁴ Also a 15-minute instruction by a designated member of the staff to the patient before discharge from the hospital was shown to reduce the errors significantly even in the poorly orientated.⁵ Further, I doubt whether a surprise raid on the home of an elderly person, as suggested by the authors, would make any difference to compliance—it would simply make the patient more apprehensive and less co-operative. Instead, a regular visit by a friendly district nurse ensures a regular intake of drugs even in the most difficult cases, as many geriatricians would agree.

Lastly, may I add that the number of people over the age of 65 in the United Kingdom is not 12% but more than 14%?

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ABC of blood pressure reduction

SIR,—If hypertension improved survival, increased intellectual capacity, or ensured physical independence there would be queues at the surgeries to find out whether the individual had hypertension or not, and if not why not.

In fact, we know from the insurance companies¹ and from the epidemiological studies in communities like Framingham in the United States² that hypertension reduces survival, may cause the multi-infarct type of dementia, and as an accelerator of the arteriosclerotic process is associated with loss of independence and indeed severe and protracted morbidity associated with stroke disease. It has been said repeatedly that there is little evidence to justify treatment of the elderly with drugs to lower the blood pressure but, since most of the drug trials have been confined to patients below 65 years of age, neither is there good evidence that preventing hypertension, or reducing hypertension, in the older patient will do any harm. It is true that Jackson *et al.*³ described cases of stroke precipitated by treatment; this paper, however, is not a reason for discarding treatment of hypertension but is simply a warning of the consequences that accrue when potent drugs are used in excessive dosage when not warranted by the clinical condition. It is always easier not to treat, especially the "symptomless," but this does not mean that it is correct. The institution of treatment, however simple the schedule, lays on the prescribing doctor the onus of supervision to ensure that the desired effect is achieved, that therapy is being taken, and that no untoward reaction has occurred.

The need to consider treatment is now more relevant than ever before as treatment regimens have been simplified to improve compliance and it has been demonstrated that blood pressure can be reduced in the elderly with simple regimens and without serious side effects.⁴ Since not only is hypertension a hypothetical risk factor in the causation of stroke⁵ but it