

Clinical experience suggests that as with all problems of addiction the patient must take some initiative and positively be seeking assistance for any treatment to produce worthwhile results. I would further suggest that in Britain the fact that prescriptions of nicotine chewing gum are not covered by the National Health Service itself filters out some half hearted potential recipients.

D G WILLIAMS

Aylsham,
Norfolk NR11 6EH

SIR,—We are conducting a randomised trial on 600 subjects aimed at evaluating smoking withdrawal in three groups: one group given acupuncture, one nicotine chewing gum, and a control group receiving no treatment at all. The abstinence rates of self reported non-smoking after one month of follow up were significantly greater ($p < 0.001$) in both the chewing gum group (22%) and the acupuncture group (19%) than in the control group (8%). Intermediate results on 270 subjects with 12 months of follow up showed a fall in success rates to around 6% for all groups.¹

As stated by Dr Konrad Jamrozik and others, the effect of nicotine chewing gum is better when used in special smokers' clinics than in general practice. In fact our results suggest an even lower effect when tested on the general population—that is, among people who had not taken the initiative but who had been approached to take part in the trial. Moreover, in order to obtain the 600 smokers for the trial we had to contact 35 000 smokers.

FRANCOISE CLAVEL
SIMONE BENHAMOU

Département de Statistique
Médicale,
Institut Gustave Roussy,
94805 Villejuif,
France

1 Clavel F, Benhamou S. Désintoxication tabagique. Comparaison de l'efficacité de différentes méthodes. Résultats intermédiaires d'une étude comparative. *Nouv Presse Med* 1984;13:975-7.

SIR,—I report a patient who successfully stopped smoking but is now as irrevocably hooked on nicotine chewing gum.

A 59 year old middle class businessman used to smoke 60 cigarettes a day and drink heavily. He gave up alcohol in 1968 and by his own efforts reduced his cigarette consumption to "under 10 a day." In November 1982 he gave up smoking entirely and treatment with 4 mg nicotine chewing gum was started.

Within two months he was using 8-10 pieces of gum a day and was finding that he was psychologically as dependent on the gum as he had been on cigarettes. He was changed on to the 2 mg strength of the gum, and since that time he has used 107 boxes each of 105 pieces giving a net consumption of 11 235 pieces. Looked at another way, the number of pieces consumed over about two years works out at over 16 a day.

We have been able to monitor the progress of his business affairs and domestic stresses and strains by the frequency with which he asks for repeat prescriptions. Our efforts to reduce his consumption have failed, and he is at present undergoing treatment by hypno-

therapy in an effort to cure him of his addiction to this substance.

J SHAPIRO

Nuneaton, Warwicks CV12 9LX

*.*Professor Fowler and others reply below.—
Ed, *BMJ*.

SIR,—Mr Raw's criticism is that our trial was too small to have had much of a chance of detecting a treatment effect of the size it might have been reasonable to expect in general practice. At the time that our study was planned the only results available were the encouraging ones from a clinic trial comparing nicotine gum users with historical controls who had received psychological treatment,¹ and subsequently there were implications that similar results might be achieved in general practice. Our findings indicate that this is not the case, but they are nonetheless consistent with a modest beneficial effect of nicotine gum in general practice. We agree with Mr Raw that even small effects may be clinically important when an intervention is offered to many people.

In response to Dr Williams's suggestion that our trial subjects lacked motivation, we point out that those recruited had already shown some motivation by participation in a previous advice study, by their claim to have tried unsuccessfully to have stopped smoking, and by their response to an invitation to try the gum. But we would, of course, agree that motivation is of prime importance in smoking cessation.

Dr Clavel and Dr Benhamou report findings which again indicate that with any antismoking intervention in the population at large the expectation must be that any effect is likely to be modest. Finally, as Dr Shapiro says, smoking cessation may be achieved at the price of being hooked on nicotine gum, but we do not know the size of this problem.

GODFREY FOWLER
MARTIN VESSEY

Department of Community
Medicine and General
Practice,
Radcliffe Infirmary,
Oxford OX2 6HE

NICHOLAS WALD

Department of Environmental
and Preventive Medicine,
St Bartholomew's Hospital,
London EC1M 6BQ

1 Raw M, Jarvis MA, Feyerabend C, Russell MAH. Comparison of nicotine chewing-gum and psychological treatments for dependent smokers. *Br Med J* 1980;281:481-2.

More ballast!

SIR,—Dr Bernard J Freedman takes a narrow view of the uses of a medical dictionary (22 September, p 757). Rather than complain of redundancy he should have taken the compiler to task for parsimony. Here in Enfield we recognise, with Guy de Chauliac, that "there be 6 names of symple apostemes. And of compounede apostemes, there beeth endles names." But this dictionary, seemingly, giveth only one, and even that he would excise.

Does it contain that marvellously useful collective attributed to Aretaeus for those who from an internal abscess void pus downwards, *apostematiai*, as in "If you don't move your suppurating apostematiai out of my ward by

lunchtime . . . ?" Sadly Dr Freedman regards such expressions as obsolete and archaic, as ballast, and therefore to be thrown overboard; but without ballast how is one to keep on an even keel? I agree that modern bones such as the clavicle can be found in any old glossary, but to write in the notes that the patient is in a state of extreme eremacausis is the surest way to get the operation postponed for at least a fortnight. And there must be many whose first language is German and who have been waiting all these years for a key to the *Ancrene Riwele*, or Arderne on *Fistula in Ano*, or Lanfranc's *Science of Chirurgie* as edited by von Fleischhacker—yes, really!—Early English Text Society No 102. I think the compiler of this dictionary should be congratulated for making so much accessible to so many.

As I have observed before, to read the writings of our predecessors is neither an eccentricity nor an irrelevance.¹ In some fields it is becoming a necessity. For example, there can no longer be any doubt that the Harveian hypothesis, based as it was on the study of the animal model only, is not universally applicable to man. Quite often nowadays I, in common I gather with many of my colleagues elsewhere, am asked to anaesthetise patients in whom there is no detectable communication between the arteries and the veins; in whom it is only the gentle, barely perceptible without the aid of the latest high power ultrasonic detector, diurnal flow and ebb of the Gilbertian fluid in the separate sets of vessels communicating only through a leaky interventricular septum that distinguishes the quiver from those already gathered unto their fathers. In such a situation the troubled anaesthetist gets no help whatever from modern cardiovascular physiology. To find out what is going on he has to turn to Galen, and in the *De usu partium* he will find much that is both informative and reassuring.

As far as I am aware this is the first occasion on which the historical reversion from the Harveian to the Galenic mode of blood flow has been described. It is not an uncommon condition; and let me be the first to say, unless others are already saying it behind my back, that I think I can even detect the beginnings of it in myself. Of course it gets you in the legs; even Galen knew that all the best stuff goes to the cerebrum.

DAVID ZUCK

Chase Farm Hospital,
Enfield EN2 8JL

1 Zuck D. Reading Harvey. *Lancet* 1978;ii:928-9.

Hyponatraemia and Moduretic (amiloride plus hydrochlorothiazide)

SIR,—Dr A M Zalin and others (15 September, p 659) describe eight patients who developed hyponatraemia while taking chlorpropamide and Moduretic (amiloride 5 mg plus hydrochlorothiazide 50 mg). While chlorpropamide may well have contributed to the hyponatraemia, we believe that severe hyponatraemia from Moduretic alone deserves wider recognition. Many of the elderly patients referred to us on this drug could just as well, and more safely, have been managed solely with a thiazide diuretic. The problem must be much more common than the few reports to the Committee on Safety of Medicines suggest. (Eleven reports of hyponatraemia with amiloride and eight with hydrochlorothiazide, which include reports for the combined preparation.) It appears to occur much more

often with this particular preparation than with thiazides used on their own.¹

In our department we recently looked at the drugs taken on admission by a random sample of 30 patients (mean age 81.9 years). Diuretics were the most commonly used drugs (11 patients), and four patients had been taking Moduretic—of these, two were profoundly hyponatraemic (plasma sodium less than 125 mmol(mEq)/l). No other diuretics were associated with hyponatraemia, but hypokalaemia (less than 3.4 mmol(mEq)/l) was noted in four patients on diuretics—including one on Moduretic.

In a study of 77 elderly patients with hyponatraemia collected over 10 months by Sunderam and Mankikar drug treatment was found to be the most common cause (49 cases) followed by intravenous infusion (11 cases). Moduretic was most commonly implicated (19) followed by frusemide (12).¹

The combination of thiazide and amiloride was devised to prevent hypokalaemia, but it appears that while this is less of a problem, save in patients on digoxin,² drug induced hyponatraemia may cause grave deterioration in health with mental confusion, asthenia, nausea "going off the feet," and so forth without being recognised as due to the treatment. Hyperkalaemia may also occur with Moduretic,³ but in our experience is very much less common and was not mentioned either by Dr Zalin and others or by Sunderam and Mankikar.

We think that this preparation should not be in general use with elderly patients and favour simply a thiazide with potassium supplement when indicated.

DAVID MILLSON
COLIN BORLAND
PETER MURPHY
WILLIAM DAVISON

Department of Geriatric Medicine,
Addenbrooke's Hospital,
Cambridge CB2 2QQ

- 1 Sunderam SG, Mankikar GD. Hyponatraemia in the elderly. *Age and Ageing* 1983;12:77-80.
- 2 Harrington JT, Isner JM, Kassiere JP. Our national obsession with potassium. *Am J Med* 1982;73:155-9.
- 3 Jaffey L, Martin A. Malignant hyperkalaemia after amiloride/hydrochlorothiazide treatment. *Lancet* 1981;ii:1272.

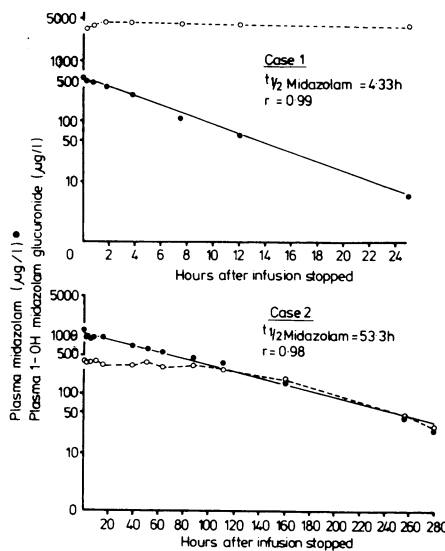
Accumulation of midazolam in patients receiving mechanical ventilation

SIR,—A similar experience to that of Dr C M Byatt and others (29 September, p 789) with a few patients in our intensive care unit prompted us to study the elimination kinetics of midazolam and its principal metabolite, 1-hydroxy midazolam glucuronide, after infusions of what we now consider to be inappropriately large doses of midazolam.

Our first patient was a 77 year old woman who required artificial ventilation after suffering multiple injuries in a road traffic accident. She received a total of 502 mg of midazolam over six days and after the infusion was stopped woke up within a few hours.

The second patient was a 71 year old man who developed respiratory failure secondary to multiple rib fractures. He received 372 mg of midazolam over seven days and took three days to wake up when the infusion was stopped.

The figure shows that the level of 1-hydroxy midazolam glucuronide was 10 times greater in case 1 than in case 2. This evidence suggests that the elimination half life of midazolam depends on the ability of the patient to metabolise the drug. Although in



Serial plasma midazolam (●) and 1-hydroxy midazolam glucuronide (○) concentrations in two patients after a midazolam infusion was stopped.

case 2 there was no biochemical evidence of liver dysfunction, there are many possible explanations for the low plasma concentrations of the metabolite—for example, reduced hepatic blood flow, drug interaction, or pharmacogenetic variation.

By studying a further three patients with prolonged elimination half lives we have come to the following conclusions. (1) During infusions of midazolam extensive redistribution of the drug occurs—for example, we have consistently measured 10 fold or greater concentrations of midazolam in gastric aspirate compared with plasma. (2) Initially the plasma concentrations of metabolite may be low, but a gradual rise to a maximum is seen. When the infusion of midazolam is stopped this plateau plasma concentration of metabolite is maintained for some hours.

We believe that the long recovery times in cases 2-5 (table) are due to a combination of impaired metabolism and redistribution from body depots. Further studies are needed to identify the mechanisms of impaired metabolism and to determine its relative importance in these types of patient.

A J BYRNE
P M YEOMAN
P MACE

Queen's Medical Centre,
Nottingham NG7 2UH

SIR,—Dr C M Byatt and others have shown that midazolam may accumulate after repeated dosage in patients receiving artificial ventilation. The findings were not, however, sur-

Plasma concentrations of midazolam and its metabolite, 1-hydroxy midazolam glucuronide, when a midazolam infusion was stopped in five patients

Case No	Age (years)	Elimination half life of midazolam (h)	Plasma concentration of midazolam when infusion was stopped (µg/l)	Plasma concentration of 1-hydroxy midazolam glucuronide when infusion was stopped (µg/l)	Total dose (mg) of midazolam	No of days over which midazolam was given
1	77	4.33	520	4225	502	6
2	71	53.3	1285	375	372	7
3	75	36.5	480	2080	150	4
4	60	12.2	560	360	72	3
5	62	28.9	690	2115	190	2

prising given the pharmacokinetics of midazolam. The elimination half life of all benzodiazepines tends to increase in elderly people and more so in those who may have liver disease. Recent work has shown that benzodiazepines, such as temazepam, which are eliminated from the body by glucuronidation, which does not involve the liver, may be a better choice for premedication or induction anaesthesia in minor surgical procedures including dentistry. Temazepam is converted into a water soluble breakdown product which can be excreted by the kidneys. The glomerular filtration rate and renal tubular activity in the elderly, however, tends to be slower, which contributes to the increase in the elimination half life of such drugs as temazepam in these patients. The pharmacokinetic properties of temazepam indicate that it would be the drug of choice since it is less likely to accumulate.

CHARLES A L MOON

Redruth,
Cornwall

Diabetes care: whose responsibility?

SIR,—The study in Cardiff by Dr T M Hayes and Dr J Harries (22 September, p 728) comparing the care of type II diabetics by hospital and general practitioners concludes that routine care in general practice is less satisfactory than care by a hospital diabetic clinic. This conclusion deserves comment from a local and general practice perspective.

The general practice cohort is biased in that there is an increased incidence of ischaemic heart disease and heavy smoking, which would have contributed to the increased death rate in this group. General practitioners participating in the study had originally referred their type II diabetics to the clinic, which could mean that they were less interested or skilled than those who do not refer such patients; alternatively the referred patients may have been more difficult to manage. Dr Hayes and Dr Harries should not give the impression that their findings are valid for GPs who did not take part in the study.

It is hardly surprising that the general practitioners should have performed less well in such a study when there has long been a tradition of hospitals monopolising the care of diabetics. Unloading diabetics on to GPs unused to diabetic care shows that they performed surprisingly well. It is arrogant of Dr Hayes and Dr Harries to hold hospital care as the gold standard when in fact the standard of care received by type II diabetics has been termed "benign neglect."

We think this study shows that if local GPs received relevant postgraduate education in managing diabetics they would be confident enough to provide the care these patients need. It is surprising that the differences noted were