angina.^{1,24} Both studies were multicentre, randomised, and double blind. In the Veterans' Administration study of 1266 men buffered aspirin 325 mg daily was compared with placebo,¹ whereas in the Canadian study the 555 patients received aspirin 1300 mg daily, sulfinpyrazone 800 mg daily, or both, or neither.²⁴ Patients were entered into the trials by 51 hours and eight days after admission respectively. In the Veterans' study there was a 51% reduction in death or acute myocardial infarction in the active treatment group at 12 weeks. The Canadian study found an identical reduction in the aspirin treated groups compared with the others after 18 months' follow up; the absolute numbers in the groups receiving aspirin either alone or in combination were 17 cardiac deaths or non-fatal myocardial infarcts out of a total of 276 patients compared with 36 events in 279 patients in the other groups. In both studies the patient groups were comparable and similar to those patients seen elsewhere; for example, the mortality for the untreated patients in the Veterans' study who were followed up for one year was 9.6%. In both studies withdrawals were few, and the incidence of side effects in the various groups was similar apart from the increased frequency of gastrointestinal symptoms in those taking aspirin in the Canadian study.

So for our patients with unstable angina medical management remains appropriate; only those with persisting pain need be referred for angiography. For subsequent treatment a credible maxim might be that a coated or buffered aspirin a day keeps the coronary at bay.

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Use of molar units for drugs and toxins?

The chemical, physiological, and pharmacological activity of any natural or artificial constituent of body fluids (and its comparison with the activity of similar constituents) is almost always directly related to the concentrations of the relevant molecules, radicals, or ions expressed in amount of substance (mole) units, and not to the concentrations in mass units such as grams. The *BMJ* made the change from using mass concentrations to (amount of) substance concentrations in 1975; but this change implies more than just a switch in numerical values, as in converting from calories to joules. The use of molar units requires a conceptual change in dimensions, for when using moles we are in effect counting the number of relevant functioning entities—for example, one molecule, one receptor site. Both substance concentrations and mass concentrations, usually per litre, are part of the *Système International d'Unités* (SI), each to be used when most appropriate; in popular medical jargon, however, "SI" has come to mean the preferential use of substance concentrations, typically as mmol/l.

In most medically advanced countries, including Britain, the results of assay of almost all substances in plasma (or other body fluids) are quoted as substance concentrations if they are naturally occurring constituents of the body and have a known relative molecular mass. The main exception has been the plasma proteins, but the changeover has started for them. There has been no move to abandon the advantages

of this system and return to mass units, for this would now be regarded as a retrograde step; the biological importance of the concept of the mole is taught from schooldays. The initial British recommendations did not, however, give guidance for plasma (or urine) constituents that were not normally present, particularly drugs and toxins.¹ So we have the anomaly that in patients plasma lactate and cholesterol concentrations, for example, are measured in mmol/l, while plasma salicylate and ethanol concentrations are usually measured in mg/dl—and some drug concentrations are confusingly given per millilitre. In pharmacological research substance concentrations for drugs are already widely used, particularly in experimental animals.

In the United States the American Medical Association has now decided to recommend the change from using mass concentrations to substance concentrations.² These intentions will extend both to natural constituents and to drugs. The time seems right, therefore, to plan the change for drug and toxin concentrations in Britain,³ and the Association of Clinical Biochemists has issued recommendations for drugs.⁴ These read: "Rationalisation is paramount in the interests of patient safety. The units adopted should be based on the litre as the unit of volume. As no particular unit is used by a substantial majority of laboratories, molar units should be the units of choice because of the strong scientific arguments in their favour."

An increasing part of the work of chemical pathology laboratories in district general hospitals is measuring drug concentrations in plasma, both for toxicological (overdose) diagnosis and for therapeutic monitoring. It is these laboratories, and not specialised toxicological units or departments of pharmacy or clinical pharmacology, that now carry out most such tests on patients.

Are clinicians (including nurses), clinical pharmacologists, pharmacists, and the pharmaceutical industry prepared to support the changeover now that substance concentrations are almost universally used for constituents other than drugs and are familiar for drugs in basic research studies? For example, as the molar mass of phenobarbitone is 232 g a plasma phenobarbitone concentration of 4.6 mg/dl becomes 0.2 mmol/l. New ranges for treatment or toxicity would have to be known, but this caused scarcely any problems for the natural constituents. For toxic substances such as ethanol there would be legal implications from the change of units.

One of the arguments given against the change is that drugs are administered in mass units, except for intravenous electrolytes; therefore it would be confusing and illogical to quote resultant plasma concentrations in substance units. In practice no confusion arises—for example, in the oral glucose tolerance test, when we investigate whether a dose of 75 g of glucose will raise the two hour blood concentration above 7.0 mmol/l—though, of course, we should say “a dose of 400 mmol.”

The logical final reform—perhaps hard to accept for clinicians—is that drug dosages should also be stated in

substance units; this would require a considerable upheaval in most doctors' and nurses' thinking. Yet a dose as prescribed, in milligrams of active drug X, is a round number that often bears little relation to the total mass of tablet which may contain several other pharmaceutical ingredients. The mass of X itself need not be the same as the mass of drug compound X' in the tablet, which may be present as an ester or hydrated salt—but in substance units X and X' would be identical. If we have round numbers to remember, let them be scientifically consistent and relate to the desired concentrations in plasma. Such an evolutionary change will raise many problems, particularly of safety and of manufacturers' costs, but it could be made. A generation ago, when we changed from imperial (grains and minims) to metric units of dosage (milligrams and millilitres) and everyone had to learn new numbers, were there any lethal consequences or serious cost implications?

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Left brain, retrotransposons, and schizophrenia

In 1915 E E Southard, Bullard professor of neuropathology at Harvard, wrote on schizophrenia: “The disease must be conceded to be in some sense structural, since at least 90% of all cases examined [50 cases, data of 1910 and 1914] give evidence of general or focal atrophy when examined post-mortem... the atrophies and aplasias when focal show a tendency to occur in the left cerebral hemisphere. The coarse atrophy is usually of moderate degree, and often does not appreciably alter the brain weight, at least outside the limits of expected variation. More remarkable... is the high proportion of cases of internal hydrocephalus (at least nine cases)... Aside from left-sidedness of lesions and internal hydrocephalus, very striking is the preference of these changes to occupy the association centers of Flechsig.”¹

With remarkable prescience this 70 year old contribution reflects contemporary foci of research. Recent work based on computed tomography (CT) and earlier findings from air encephalograms—all in apparent ignorance of Southard's work—provide strong evidence of some internal hydrocephalus, particularly in the more chronic forms of schizophrenia.^{2,4} Enlargement of the ventricles, most prominent in the temporal horn, has been confirmed in a recent necropsy study and may reflect atrophic changes in limbic structures.⁵ The weight of the brain was reduced by 5-6% in patients with schizophrenia by comparison with those with affective disorders.

Most striking is Southard's insistence that the disease has a predilection for the left hemisphere. Laterality was introduced into discussions of psychosis in 1969 by Flor-Henry's report that when psychosis develops in association with an

epileptic focus in the left hemisphere it is schizophrenia like, while when the focus is in the right hemisphere the changes are primarily affective.⁶ These observations were widely seen to be relevant to temporal lobe epilepsy and its associated psychiatric changes rather than to the pathophysiology of the functional psychoses. Yet recent research has re-emphasised that schizophrenia itself may be a disease of the left, or dominant, hemisphere. The evidence comes from four sources.

Firstly, differences in laterality have been reported in some CT scan studies. For example, Largent *et al* found reductions in scan “density” on the left side in patients but no difference between the sides in controls.⁷ This observation has been replicated in a study of monozygotic twins discordant for schizophrenia (M A Reveley and A M Reveley, paper to Fourth World Congress of Biological Psychiatry, 1985). It seems less likely that reduced CT scan density reflects a change in actual brain density than that it indicates that cerebrospinal fluid spaces (not identifiable on the image) are increased in the left hemisphere—in other words that there is a reduction in tissue mass. An early air encephalogram study reported that nine of 27 chronic psychotic patients had ventricular enlargement restricted to the left side.⁸

Secondly, two recent studies using computer controlled topographic electroencephalographic mapping (the BEAM (brain electrical activity mapping) technique) reported differences in laterality. Morihisa *et al* found increased fast beta activity in the left posterior quadrant in institutionalised patients with chronic schizophrenia and taking no drugs; this