haemolytic streptococci (2.9×10^5 organisms/ml) which were serologically group B (the organisms were, unfortunately, not typed). Pasteurisation at 62°C for 30 min in a purpose-built Holder pasteuriser (Oxford¹) eliminated the organisms, as predicted from their known heat sensitivity.

The early-onset, septicaemic form of group B streptococcal infection is thought to originate from colonisation in passage through the birth canal; there is little information, however, on the pathogenesis of the less common, late-onset, meningitic form of the disease. Kenny and Zedd² and Schreiner and Coates³ have suggested that in the latter disease form breast milk may be a source of infection; these authors have reported three cases of infection in neonates whose mothers' milk has grown group B streptococci. In our own studies it is not certain that the organism originated from the milk itself, but, whatever the source, the profuse growth of group B streptococci in a human milk pool again raises the important and unresolved question as to the bacteriological safety of using untreated pooled breast milk for feeding premature infants.

The advantages of untreated milk, with its live cells and intact protective properties, may be outweighed by its bacteriological disadvantages when using pooled milk from a milk bank, where cross-contamination and pathogenic bacterial overgrowth are inevitable problems. Optimal procedures in milk banking have yet to be defined, but at present pasteurisation would seem a satisfactory method of processing human milk. There is evidence for considerable preservation of the protective properties in milk with this form of heat treatment⁴ and our own preliminary data suggest that pasteurisation satisfactorily destroys most common pathogenic bacterial.

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¹ Gibbs, J H, et al, *Early Human Development*, 1977, **1**, 227.

² Kenny, J F, and Zedd, A J, *Journal of Pediatrics*, 1977, **91**, 158.

³ Schreiner, R L, and Coates, T, *Journal of Pediatrics*, 1977, **91**, 159.

⁴ Ford, J E, et al, *Journal of Pediatrics*, 1977, **90**, 29.

Changing mortality from ischaemic heart disease

SIR,—Dr C du V Florey and his colleagues (11 March, p 635) point to the associations between the recent slight decrease in mortality due to coronary disease in men and a number of concurrent changes in diet and in cigarette smoking. They draw only tentative conclusions from these associations, and this is particularly understandable in relation to a condition that has many causes.

In regard to diet the hesitation of the authors is even better founded than they themselves realise. The figures they use for food intake are those of the National Food Survey,¹ which measures only that which is consumed in the home and also omits entirely a range of items that include confectionery, ice cream, soft drinks, and alcoholic drinks. As a result the intake of some dietary constituents is considerably underestimated. For example, the survey assesses current average sugar intake at about 12 ounces (340 g) a week, but the real

total is more than twice as much as this, at around 30 ounces (850 g) a week. More importantly, the survey records a continuing smooth fall in sugar intake of some 30% between 1970 and 1976 (apart from the exceptional fall due to the world shortage of 1975), whereas total intake has changed very little over that period: less than 6% between the extremes if we again omit the figure for 1975.

To accept figures from the National Food Survey as accurately representing the amounts of food that people eat is as logical as to accept attendances at cinemas as accurately representing the number of films that people watch while ignoring those that are seen on television.

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¹ Ministry of Agriculture, Fisheries and Food, National Food Survey Committee, *Household Food Consumption and Expenditure for the Years 1968-76*. London, HMSO, 1970-7.

SI, moles, and drugs

SIR,—I read with interest your leading article on this subject (18 March, p 668). My experience is that most doctors are intelligent people who, on the whole, have made it. SI units may be "trying" initially, but "exhausting" seems an overstatement for all but the most tired.

Symbols such as kg^{-1} , meaning "per kilogram," appear straightforward. To suggest that they are ugly or even worse than they are "difficult to comprehend" could give rise to misinterpretation of the calibre of the profession by an outside observer.

The new units certainly require some work by the clinician. The difficulties outlined in the leading article are probably not insurmountable, and with a more positive attitude the new units will, like any other hurdle, be jumped successfully by the vast majority.

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SIR,—Your leading article (18 March, p 668) will restimulate interest in SI unit practice, which is good. However, I am now convinced you are wrong in opposing the recommended change in the method of indicating concentration per litre, from "/l" to $\text{"l}^{-1}\text{"}$. "/l" is perfectly safe when typed or in print, but about one in five of our young staff find it almost impossible to make the solidus ($/$) diagonal and they write it vertical, which is very dangerous next to a figure 1. It is not difficult to manipulate a typewriter in full flood to introduce the symbol for the inverse power of a litre, that is, l^{-1} . A slight turn of the left wrist and simultaneous tapping upon the - followed by the 1 (not, of course, by the l) makes a quick neat job of this symbol. If necessary a key can be made to do it in one jab. All the youngsters from school and university nowadays are trained in the use of this symbol. Where safety and speed matter we older ones must try to catch on.

Another point. We in this laboratory have used grams per litre for haemoglobin concentrations for several years now and are delighted that it is to be recognised as more desirable than grams per decilitre with its decimal point and general ability to confuse among the indices. We recognise that milli-

moles may come when a way round the monomer/tetramer controversy is thought out. A tip when changing over the grams per litre from grams per decilitre: always state the unit in full every time a haemoglobin concentration is mentioned, never just the figure. It's dangerous to answer, "What's the haemoglobin?" with "a hundred"; but perfectly safe if you say the unit out in full, "grams per litre."

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SIR,—I would like to correct an unfortunate error which crept into my letter (1 April, p 853), in which I stated that 513.5 mg of chlormethiazole edisylate and 161.65 mg of chlormethiazole base both provide 10 mmol of chlormethiazole (as edisylate or base). This should, of course, be 1.0 mmol. As I stated, care is needed in conversion!

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Serum IgE in mycosis fungoides

SIR,—After reading the paper by Dr P L Amlot and Mr L A Green on IgE in Hodgkin's disease and other lymphomas we considered it of relevance to collect the knowledge available of the relation between IgE and mycosis fungoides. Mycosis fungoides is a T-cell lymphoma originating in the skin, sometimes disseminating to lymph nodes and viscera. In three reports an elevation of serum IgE concentration (>1000 U/ml) has been found in mycosis fungoides, occurring in about 20% of cases.¹⁻³ However, the numbers of patients reported on were rather small—14, 22, and 23 respectively.

In the Scandinavian Mycosis Fungoides Study Group we have collected data on serum IgE levels in cases of mycosis fungoides since July 1974. Our findings are presented in the accompanying table. Among 75 patients the serum IgE level exceeded 1000 U/ml in only eight cases, and four of these had levels above 4000 U/ml. Neither a family or personal history nor clinical evidence of atopy (eczema, hay fever, or asthma) was recorded in these cases. In this series no relation could be found between the clinical type, stage, or response to treatment and the occurrence of elevated serum IgE concentration. In one of the cases the IgE level increased during treatment (from 1200 to 5200 U/ml) and in another case the level decreased (from 4000 to 300 U/ml); both patients were treated with psoralen and long-wave ultraviolet light (PUVA) to complete remission. No correlation was found in the series between IgE and the other immunoglobulins (IgA, IgG, IgM). At present we are not able to draw any conclusions from these

Serum IgE concentrations in mycosis fungoides

Stage of MF	Serum IgE concentrations (U/ml)			Total
	<500	500-1000	>1000	
Plaque stage	42	10	7	59
Tumour stage	8	2	1	11
Tumour stage with extracutaneous involvement	5	—	—	5
Total	55	12	8	75

findings except that the frequency observed is lower than previously reported. We consider the elevated IgE concentration as a non-specific expression of the inflammatory process in the skin, as has been discussed in other skin diseases.^{4,5}

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- ¹ Tan, R S H, *et al*, *British Journal of Dermatology*, 1974, **91**, 607.
² Zachariae, H, *et al*, *Acta Dermatovenereologica*, 1975, **55**, 466.
³ MacKie, R, *et al*, *British Journal of Dermatology*, 1976, **94**, 173.
⁴ Arbesman, C E, *et al*, *Archives of Dermatology*, 1974, **110**, 378.
⁵ Bruns, G R, and Ablin, R J, *Archives of Dermatology*, 1977, **113**, 1461.

Maternal pethidine and neonatal depression

SIR,—We are grateful to Dr M Rosen and his colleagues (18 February, p 438) for a more complete description of the methods used in their trial of naloxone in neonates (23 July 1977, p 229). Following their censure we have earnestly endeavoured to give their paper a "proper" reading, but we feel that their letter fails to answer the points which we previously raised.

Our main concern was that a relatively new drug was used in this trial on babies who appeared to be perfectly healthy and that a large dose was administered in a situation in which pethidine antagonists would not normally have been considered. We wholeheartedly support their view that no drug should be given without a clinical indication and this is especially true in neonates. In their letter they mention that naloxone was not given routinely to babies included in the trial but only to those who had a clinical problem associated with pethidine used in labour. We are unable to find an explanation of exactly what this problem was. The criteria mentioned by the authors in their paper seem only to emphasise what fine fettle the babies were in at birth and it is difficult to envisage what problem occurred in the first 60 s of life that necessitated the use of naloxone. Furthermore, the authors persistently refer to the subjects of the trial as "healthy mature neonates." It seems to us of fundamental importance that normal babies should not be exposed to the unnecessary risks associated with trials of new drugs. That drug effects may be more clearly demonstrated in healthy babies is hardly a justification for such conduct, for the effects of prematurity, asphyxia, and birth trauma should be excluded by subjecting the results of a large trial to conventional statistical analysis.

Their trial failed to show how naloxone acts in the clinical situations in which pethidine antagonists are conventionally employed. It would be unethical to use a placebo in such instances, but most paediatricians have used nalorphine and levallorphan quite successfully for years, and this was why we suggested that a trial comparing naloxone with the older antagonists would have given more meaningful results. What effect a drug has on adults or anaesthetists may be irrelevant to the neonate and is certainly not a justification for dismissing the conventional antagonists out of hand. Similarly, substances innocuous in the adult may be toxic to the newborn and one need only quote bilirubin and oxygen to illustrate the point. On what grounds Dr Rosen and his colleagues abandoned use of conventional pethidine antagon-

ists "years" ago is uncertain. A safe and well-established drug should be superseded by a newer one only after scientific proof of superior efficacy or safety.

At the present time we question whether there is sufficient evidence to justify widespread use of naloxone. For the most part significant pethidine depression is easy to diagnose and, in our experience, responds well to nalorphine. We have had very few problems with the older antagonists. If pethidine toxicity is in doubt—for example, if asphyxia has also occurred—and if further depression would be deleterious then we use intravenous naloxone as a diagnostic aid. With these restrictions we use the newer drug rarely but have been impressed with its performance.

Pethidine antagonists have a small role to play in neonatal medicine, but at times they may be life saving. Their widespread use for trivial depression will put an unacceptably high number of healthy babies at risk. All drugs have side effects and any talk of safety of a drug after animal testing and small clinical trials is spurious. Unless we learn our lessons from thalidomide and practolol avoidable iatrogenesis will continue to occur. Practolol was widely prescribed in conditions in which its selectivity was completely unnecessary. It would be a pity if naloxone succumbed to the same fate.

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Cimetidine and serum prolactin

SIR,—Firstly, we thank Dr M C Bateson (18 March, p 718) very much for pointing out the error in the calculation of the mean value of our observations on serum prolactin reported earlier (18 February, p 409); however, the corrected mean value lies well within the normal limit and hence does not alter our conclusions. We sincerely regret this unintentional error and offer our apology to readers for the confusion it might have created.

Secondly, the suggestion by Dr W L Burland and others (18 March, p 717) of involvement of the dopaminergic receptors in the hypothalamus (prolactin-inhibiting factor, PIF) in cimetidine-induced hyperprolactinaemia in healthy male subjects is a provocative hypothesis. It may be relevant to mention that certain non-phenothiazinic antihistaminics (H₁-receptor antagonists), meclozine and tripeleminamine, stimulate prolactin secretion.¹ Meclozine is a piperazine derivative and tripeleminamine an ethylenediamine; it may be postulated that H₁-receptors and dopaminergic receptors have some structural or stereochemical similarities and it could even be true for H₂-receptors as well. Of course, cimetidine is an amidazoline derivative with a cyanoguanidine group attached to the side-chain. Receptors, in the present state of our knowledge, are, however, pharmacological concepts engraved in a philosophical mosaic.

Prolactin was the first hormone shown to be predominantly under the control of hypothalamic PIF but, though unelucidated yet, a prolactin-releasing factor (PRF), probably a polypeptide dependent on serotonin as the intrahypothalamic neurotransmitter, has also been proposed.² Balance between PIF and PRF could be the final regulating mechanism of prolactin secretion and release; in view of this the effect of cimetidine on both factors needs to be examined.

Thirdly, circulating prolactin has normally a circadian rhythm and levels rise during the early part of the night; it may also be secreted during stress.³ The time of collection of blood samples and the stress factor, though of minor importance, might deserve some consideration. Further study on these lines is in progress.

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- ¹ Williams, R R, *Lancet*, 1976, **1**, 996.
² Mortimer, C H, and Besser, G M, in *Recent Advances in Medicine—17*, ed D N Baron *et al*, p 441. London and Edinburgh, Churchill Livingstone, 1977.
³ Besser, G M, and Thorner, M O, in *Advanced Medicine Symposium—11*, ed A F Lant, p 225. Tunbridge Wells, Pitman Medical, 1975.

Subarachnoid haemorrhage in patients over 59

SIR,—I refer to Dr B V Martindale and Mr J Garfield's article (25 February, p 465) and subsequent correspondence (25 March, p 783).

There is no particular mystique about the age of 60. In an aging population many of our citizens lead active, useful lives for a further one or two decades and an arbitrary age limit imposes a check on both thought and effort. Each patient should be considered according to the clinical condition.

In a personal series of 694 patients with cerebral aneurysms and angiomas presenting with subarachnoid haemorrhage, 75 were aged 60 or over (mean age 62.6 years); 42 of these were operated upon (craniotomy for 40) and nine died within three months. Thirty-three (mean age 63.9 years) were not operated on and 10 of these were dead within three months. Survivors of both groups were followed up for an average of 6.3 years. In the operated series the quality of life was distinctly improved compared with the unoperated.

Factors other than arbitrary age are more important in selection of patients—for example, coma, multiple ruptures, hypertension. It is hoped that these and other considerations will be presented soon in a prospective study of over 900 personal cases of spontaneous subarachnoid haemorrhage seen during a period of 17 years.

Finally, in the context of the above and with reference to the article by Stewart *et al*¹ on neurosurgery in the older patient (over the age of 65), I do not think the resources available for neurosurgery are being used unwisely.

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- ¹ Stewart, I, Shephard, R H, and Millac, P, *Postgraduate Medical Journal*, 1975, **51**, 453.

Typhoid and its serology

SIR,—Your leading article (18 February, p 389) states that "serology plays a minor part in the diagnosis of enteric fever." May I mention an outbreak¹ in which serology was very helpful?

Knowing of two cases of paratyphoid fever, apparently unrelated, a practitioner submitted blood from four persons ill for a few days. Within four hours a presumptive diagnosis of paratyphoid infection was made in three cases,