with cimetidine is appropriate for those found to have either an ulcer crater or scarring.⁴

The Danish workers conclude that when patients with a pre-existing ulcer crater are excluded cimetidine reduces the incidence of gastrointestinal bleeding—largely from erosions—occurring during the first four postoperative weeks in patients given high dose prednisolone (prednisolone 1 mg/kg/day as in the Danish study is about four times greater than a low dose prednisolone regimen).⁵ The study does not allow the implied recommendation that cimetidine should be given as a routine third drug after renal transplantation. It is a fundamental principle that the renal patient should be given as few drugs as possible; recommendations to the contrary should be resisted.

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Nocturnal deaths among patients with chronic bronchitis and emphysema

SIR,—I agree with Dr Walter T McNicholas and Professor Muir X Fitzgerald that nocturnal death is common among patients with chronic bronchitis and emphysema (6 October, p 878). Smolensky *et al* reported that death in the general population is most common between 5 and 6 am.¹ We observed severe hypoxaemia and associated cardiac arrhythmias among patients with type 2 respiratory failure (hypoxaemia with hyper-

capnoea) during the night.² The findings of Dr McNicholas and Professor Fitzgerald could be explained by nocturnal hypoxaemia and consequent cardiac damage. They found the highest death rate among patients with type 2 respiratory failure between 11 pm and 7 am. Some time during this period most of these patients are in rapid eye movement sleep, and they hypoventilate and develop hypercapnoea.³ Patients with type 2 respiratory failure are often overweight,⁴ and they develop hypoxaemia, hypoventilation, and sometimes sleep apnoea.^{3,5}

We have noticed these changes more often between 1 and 5 am.² During this time patients develop several electrocardiographic changes such as prolonged QTc interval (figure), tachycardia, ST-T depression, heart block, and various arrhythmias.^{2,5} Prolonged QTc interval associated with hypoxaemia was found in most of these patients.^{2,5} Schwartz *et al* reported that a prolonged QTc interval is arrhythmogenic and also a predictor of sudden death in patients with myocardial infarction.⁶ Severe hypoxaemia, hypercapnoea, hypoventilation, and acidosis probably insult the myocardium and result in widespread electrocardiographic changes,^{2,5,7} and these changes may predispose to nocturnal death among these patients.

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Electrocardiographic changes with corresponding oxygen saturation levels between 10 pm and 9 am. Oxygen saturation was reduced progressively between midnight and 4 am, and a corresponding increase in heart rate and prolongation of the QTc interval was observed during this time.

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Midazolam in intensive care

SIR,—Dr C M Byatt and colleagues (29 September, p 799) made an important contribution to our knowledge of midazolam in defining conditions in which its action can be prolonged. In defence of this newer benzodiazepine we would like to point out that it accumulates much less than diazepam. Gamble *et al* found that the administration of diazepam 10 mg every four hours to patients in intensive care produced plateau plasma concentrations after two to three days. After 17 days of administration the elimination half life was about five days for diazepam and nine days for the metabolite *N*-desmethyl diazepam.

Similar pathological conditions were present in both the patients of Gamble *et al* and those of Dr Byatt and his colleagues, and the findings reported with midazolam may well apply to all the benzodiazepines. To describe a drug as "accumulative," however, Dr Byatt and colleagues should have performed analyses during administration.

We have studied the pharmacokinetics of midazolam 0.3 mg/kg given intravenously to over 200 patients undergoing elective surgery. In patients aged under 50 years (and in young volunteers) the elimination half life was about three hours.^{2,3} In older patients undergoing major operations, including open heart surgery, the elimination half life was increased to six hours.^{4,5} Out of the 76 patients in this latter study, however, six had atypical elimination half lives of 10-22 hours. Such phenomena have been demonstrated with other drugs,⁶ where the pharmacokinetic indices of some individuals are at variance with those of the rest of the population.

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Pulmonary thromboembolism presenting as abdominal pain

SIR,—Further to the lesson of the week by Dr A F Henderson and others (6 October, p 902) we report a further case of pulmonary thromboembolism presenting as abdominal pain.

A 62 year old man had a left upper lobectomy for an adenocarcinoma of the bronchus. On the sixth day after operation he developed right hypochondrial pain, exacerbated by deep inspiration. Clinical

examination of the chest and abdomen showed nothing abnormal. A chest radiograph showed no focal lesion in the right lung field, but he was given anticoagulants because we suspected a pulmonary embolus. This was confirmed the next day by a ventilation-perfusion lung scan, which showed two unmatched perfusion deficits in the apical and posterior segments of the right upper lobe. The pain persisted for four days and remained localised to the right hypochondrium. He had no haemoptysis and was discharged home on oral anticoagulants.

The localisation of the embolus to the right upper lobe contrasts with the findings in the previous report, in which the left base was affected in both cases. It is difficult to understand why such a lesion should produce only abdominal pain, but diaphragmatic pleurisy was clearly not implicated in this case. Irritation of the parietal pleura may cause referred pain in the dermatomes of the lower thoracic nerves and thus produce upper abdominal pain. Visceral pleura and lung parenchyma are said not to have a sensory innervation.¹ The lungs are foregut derivatives, and visceral pain from other foregut structures is mediated by sympathetic afferents with cell bodies at the mid-thoracic level. This type of pain is poorly localised in the somatic sensory distribution from the same level of the spinal cord and thus perceived in the upper abdomen. Such a visceral innervation would explain the abdominal pain associated with these cases of pulmonary thromboembolism.

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1 Last RJ. *Anatomy regional and applied*. Edinburgh: Churchill Livingstone, 1981:242.

SIR,—The article by Dr A F Henderson and others correctly alerts the young surgeon to the diagnostic problem of pulmonary thromboembolism presenting with abdominal pain. We would also like to reiterate the dangers inherent in diagnosing pulmonary thromboembolism in the presence of abdominal pain.

We have recently reported a series of patients in whom empyema occurred in association with abdominal sepsis.¹ Eight out of 10 patients were erroneously thought to have pulmonary thromboembolism, and correct treatment was therefore delayed. While pulmonary thromboembolism may undoubtedly present with acute abdominal pain, complications of intra-abdominal sepsis may also masquerade as pulmonary thromboembolism.

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Day hospital rehabilitation—effectiveness and cost

SIR,—Dr M A Tucker and his colleagues (3 November, p 1209) should be commended for their attempt to assess the cost effectiveness of a day hospital. It is a pity, however, that they chose to assess a unit which has just been opened. In our experience it takes considerable time to achieve optimum efficiency. In the case of the day hospital in Islington, which

also opened in July 1981, it took nearly 18 months to resolve most of the issues relating to transport and operational policies, and the "corrected new patient index" reached 1 only in the third year.

It is not surprising that the cost of attendance nearly equalled that of inpatient treatment, since the average attendance at their day hospital was 23.4 days, whereas the average (calculated by Millard¹) is 10 days. Our own average is about 8 days. The greater length of attendances, which, of course, increases the cost, suggests that the day hospital in Auckland is providing more a social than a therapeutic function. We agree that the day hospital is not a cheap form of treatment, but if used efficiently with input from physicians trained in geriatric medicine it compares well with the cost of inpatient treatment and, of course, reduces the risks of mortality and morbidity associated with inpatient treatment.²

Lastly, a day hospital is not just a unit to provide rehabilitation. The functions of a day hospital, according to Brocklehurst and Tucker, are rehabilitation, maintenance, assessment, and medical, nursing, and social care.³

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Do emergency tests help in the management of acute medical admissions?

SIR,—The evidence presented by Dr Gerald Sandler (13 October, p 973) about the use of urgent tests in the management of acute medical admissions is valuable, but the data presented raise several questions. The tests requested seem to fall into two groups on the basis of the proportion of abnormal values detected—namely, urea, potassium, and other electrolytes and all others (table).

Type of test	No (%) of tests	No (%) of abnormal results
Urea and electrolytes	1223 (52)	70 (6)
Other biochemistry	458 (19)	126 (28)
Non-biochemistry	691 (29)	199 (29)
Totals	2372 (100)	395 (17)

This discrepancy in detection rate is difficult to explain assuming that the usual definition of normal is applied—that is, mean and two standard deviations in a non-selected population. This always produces 5% abnormal values outwith the 2SD range, which may or may not relate to a clinical disorder. Discussion and comparison of tests as different as electrocardiography, chest radiography, and various biochemical, haematological, and microbiological tests require that the criteria used to describe normal are clearly indicated, which they are not in Dr Sandler's paper. When only 6% abnormal urea and electrolyte values are found in a selected hospital population this certainly calls into question the definition of normality used for these

and all other tests and hence much of the derived data and discussion.

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Total and free thyroid hormone concentrations in patients receiving replacement treatment with thyroxine

SIR,—Dr J H Marigold and colleagues (15 September, p 699) report measurements of serum free thyroid hormone concentrations in a group of patients receiving maintenance replacement with thyroxine. Their results are similar to those we presented earlier this year (3 March, p 693). Their broad conclusion parallels our own, but they take us to task for suggesting that the history and clinical examination remain an important part of patient assessment. They imply that almost complete reliance can be placed on the results of biochemical tests of thyroid function. This negation of clinical medicine is in general unwelcome and, in thyroid medicine, potentially dangerous. There are well recognised circumstances in which radioimmunoassays for both total and free thyroid hormones give grossly misleading results owing to interference by abnormal thyroid hormone binding proteins or by endogenous iodothyronine antibodies.¹ In these circumstances patients will be classified as hypothyroid or hyperthyroid depending on the interference with the assay, and unless due regard is given to the clinical findings inappropriate treatment may be given. There can be little doubt that radioimmunoassays have transformed the practice of clinical endocrinology, but surely they have not replaced it.

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The care of infants with gastroenteritis

SIR,—Dr D C A Candy's leading article (10 November, p 1245) prompts a question that has lingered since it was reported that increasing numbers of infants with gastroenteritis are being admitted to hospital,¹ even though most need no treatment at all except, of course, provision of food and water. Why do so many mothers seem to be incapable of providing for their infants' basic needs?

Of possible answers, two are especially important because, if valid, a remedy would be ready to hand: that there is widespread misuse of oral rehydration solution coupled with failure to understand that the principle of feeding on demand holds true whether there is diarrhoea or not.

The traditional treatment for gastroenteritis is to give nothing but clear fluid, such as oral rehydration solution. But since only dehydrated patients can be given oral rehydration therapy, when oral rehydration solution and nothing else is given to those who are not dehydrated the procedure can be justified only by assuming, firstly, that because it is best to rest the intestines² other food is harmful when there is diarrhoea and, secondly, that the food value of oral rehydration solution is sufficient for it to serve instead. The first assumption lacks supporting