that, in some instances at least, the truth may be as closely approached by those housemen who record only a vague descriptive comment (or even no comment at all).

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¹ Orrego H, Blendis LM, Blake JE, Kapur BM, Israel Y. *Lancet* 1979;ii:1354-6.

SIR,—The study in your last issue by Dr I G Barrison and others (18 October, p 1040) incorporated two false premises: (a) that "heavy drinkers" are likely to reveal themselves during "routine history taking"; and (b) that a heavy drinking habit is a necessary or sufficient condition for the diagnosis of an alcoholic.

Further, one-third of the patients studied were emergency admissions. It is, therefore, hardly surprising that immediately non-relevant details, such as drinking habits, might have been overlooked in the wish to make a diagnosis and institute appropriate treatment in the very sick patient. In routine admissions—for example, for dental treatment—a drinking history might well seem out of context both to patient and houseman. It is a credit to the housemen at Charing Cross that only a relevant 15% of the patients had not been asked about drinking habits (that is the ratio of those non-teetotallers who had not been asked to the population studied).

Alcoholics are the very people that are most likely to give false drinking histories. Furthermore, in the absence of explicit admission of heavy drinking or requests of help from patient or family, it is unclear what effective action might be carried out for those heavy drinkers discovered during "routine history taking" in hospital.

There is a negative attitude to alcoholism, as the authors point out. This raises the question of who is in the best position to diagnose likely alcoholics. This must be a person who has intimate knowledge of the patient, his family, and his environment. Thus, only the general practitioner and other members within the community can be expected to substantially increase the diagnosis of the problem. It is their education on alcoholism, not the houseman's, that is of primary importance.

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Malignancies and false-positive serological results for hydatidosis

SIR,—Some authors,^{1,2} including Dr F van Knapen recently in the *BMJ* (19 July, p 195), have reported false-positive serological results for hydatidosis in patients with malignancies.

In our laboratory serological diagnosis for hydatid disease is routinely carried out by simplified counterimmunoelectrophoresis on cellulose acetate membrane with a lyophilised antigen, commercially produced for the complement fixation test (Behring, L'Aquila, Italy, code OTMN 05), as described in detail elsewhere.³ This method, in our experience, is positive in hydatidosis only.

Briefly, antigen is dissolved in 0.5 ml distilled water and is frozen (at -20°C) and thawed (at 26°C) five times. The cellulose acetate membrane (Chemetron, Milan, Italy, code 077) is immersed for 10 minutes in tris-glycine buffer, pH 9.5 (Chemetron, code 067), dried with blotting

paper, and mounted on to the plastic bridge. Each sheet is sufficient for six tests. Five microlitres of antigen are placed on the cathodic side and 5 μl of serum on the anodic side of the membrane. Counterimmunoelectrophoresis is carried out in tris-glycine buffer at 200 V for 35 minutes in an ELVI 20 apparatus (ELVI, Milan). The cellulose acetate strip is then washed four times for 15 minutes in saline with continual stirring, stained in coumassie blue (Chemetron, code 080) for 15 minutes and destained (decoloring solution Chemetron, code 092) until the precipitation bands are clearly observed. In positive sera the arcs of precipitation are generally in the form of an "upper lip" or a thick and undulating streak.

With this method we have examined sera from patients with surgically confirmed hydatidosis (69 sera), other parasitic diseases (35), malignancies of the lung (22) and liver (17), blood disorders including myeloma, leukaemia, lymphoma, etc (15), and normal individuals (50). Positive results occurred with sera from patients with confirmed hydatidosis (in 56 cases—that is, 81%) but not with any other sera.

Our method, if confirmed by other workers, could be therefore useful in the differential diagnosis of space-occupying masses. Clearly the most likely diagnosis should always be made on the basis of all available clinical and laboratory data.

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¹ Yong WK, Heath DD, Savage T. *Br Med J* 1979; i:1463-4.

² Varela-Diaz VM, Coltorti EA, D'Alessandro A. *Am J Trop Med Hyg* 1978;27:554-7.

³ Mansueto S, Migneco G, Tripi S, Piccone DM. *Trans R Soc Trop Med Hyg* 1980;74:260-1.

When is it justified to stop the pill?

SIR,—I supervise contraception for a number of patients in accordance with DHSS guidelines. I have been concerned that four of my patients have recently been taken off the pill by others without my consent. I accept that this is necessary for major surgery to the pelvis, but these were young women undergoing surgery to bunions or extraction of wisdom teeth by local dentists. One patient became pregnant and had an abortion.

Comment from the local academic department of gynaecology has been noncommittal. However, to stop low-dose oestrogen pills for these sorts of very minor operations on young women seems to me to be wrong. Perhaps through your columns I may ask if surgical, dental, or family planning colleagues have seen enough cases of thrombosis and embolism in such circumstances to warrant the risk of unwanted pregnancies. In 10 years of general practice I have seen none.

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Cimetidine and ranitidine in duodenal ulcer

SIR,—Professor M J S Langman and others (16 August, p 473) conclude that "cimetidine and ranitidine give equivalent results in patients with duodenal ulcer." At week 4, 72% of cimetidine-treated patients had healed and

63% of ranitidine treated patients had healed; this is a difference of 9% in favour of cimetidine, but with only 18 patients in one group and 19 in the other the 95% confidence interval for the difference in the percentage of patients healed while on cimetidine versus those healed while on ranitidine runs from 40% to -25% .¹ In other words, subsequent studies could show a difference between cimetidine and ranitidine as great as that between cimetidine and placebo. A study with 20 patients per group will fail about half the time to show a significant difference between two treatments for which the true difference is 30%.

This study suggests that cimetidine and ranitidine may prove to give equivalent results in future tests but does not allow the conclusion that they will.

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¹ Peterson WL, Elashoff JD. *Gastroenterology* 1980;79: 585-8.

Myopathy associated with cimetidine?

SIR,—The description by Dr T J Walls and others (11 October, p 974) of two cases of motor neuropathy possibly associated with cimetidine has prompted us to report the following case.

A 71-year-old man began treatment with cimetidine (1 g daily) in the summer of 1977 for a barium-meal-proved duodenal ulcer. In August 1978 he rapidly developed painless weakness of hip and shoulder girdles such that he was unable to get out of bed or comb his hair. Other than long-standing (20 years) Raynaud's phenomenon affecting his hands, there were no other symptoms, and he was on no other medication. He had smoked 15 cigarettes daily for many years. On admission to hospital three months later general examination was normal; power was markedly reduced in all four limbs proximally (MRC grade 3-4) though not distally, with a similar distribution of wasting; sensation was normal; the lower limb tendon reflexes were absent and those in the upper limbs reduced. The following tests were normal or negative: chest radiograph, barium meal, routine haematology and biochemistry, creatinine phosphokinase, mid-stream urine examination, triiodothyronine, tetraiodothyronine, Wasserman and Venereal Disease Research Laboratory tests, and serum auto-antibody screens. Protein electrophoresis showed a slight increase in α_1 - and α_2 -globulins, a random blood sugar was 13.6 mmol/l (245 mg/100 ml) with a fasting level of 7.6 mmol/l (137 mg/100 ml), and the erythrocyte sedimentation rate (ESR) 59 mm in the first hour. Motor nerve conduction velocities in upper and lower limbs were within normal limits and coaxial needle electromyograms of forearm, hand, lower leg, and foot muscles normal. Electromyograms from deltoid and quadriceps showed a low voltage myopathic pattern with no fibrillation potentials or positive sharp waves.

The cimetidine was stopped and over the subsequent year he made a remarkable recovery. His mild maturity-onset diabetes has remained under excellent control on glibenclamide 2.5 mg daily and the ESR has fallen to 10 mm in the first hour. No evidence for any neoplastic lesion or arteritic process has appeared in the two years of follow-up. Because of a return of his ulcer symptoms he has recently recommenced cimetidine in a dosage of 200 mg twice daily without any demonstrable effect on muscle power so far.

Although muscle pains are recorded with cimetidine therapy¹ to our knowledge there are no recorded cases of an associated myopathy. Until Walls *et al* had demonstrated a possible neurotoxic property of cimetidine we were reluctant to believe that this was the causal factor in our patient. The timing of the

myopathy and the lack of a similar myopathic effect so far on restarting the drug suggests a dose-related effect, which was obviously not the mechanism in the two cases of motor neuropathy. Millions of people must by now have been treated with cimetidine and it is possible that other isolated cases of toxic neuromyopathy have gone unrecognised because of the apparent rarity of the association. We wonder if our case is unique or whether others have also seen unexplained weakness in patients on long-term cimetidine?

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¹ Burland WL. In: Creutzfeldt W, ed. *Proceedings of the third international symposium on histamine H₂-receptor antagonists*. Amsterdam: Excerpta Medica 1978:238-58.

Fulminant hepatic failure in childhood

SIR,—Your leading article on fulminant hepatic failure in childhood (27 September, p 823) is certainly a tribute to the efforts made at King's College Hospital over the last decade to improve the outlook in this desperate condition. Essentially patients die of encephalopathy, which is due to the effects of accumulating toxins on the integrity of the blood-brain barrier; and if appropriate care is taken renal failure, haemorrhage, hypoglycaemia, infection, and plasma volume depletion should now be only terminal and less usual events.

The mainstay of current support is charcoal perfusion,^{1,2} with prostacyclin infusion to prevent platelet destruction and if necessary haemodialysis (again preferably with a charcoal membrane). Both of these techniques can now be done by experts in regional centres. Why then should sick patients ever be transported over long distances? Such patients do not stand the journey well and even to consider it shows a lack of concern for relatives, who also have to travel and then "camp around" in London.

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¹ Engle WD, Jacobs JF, Swartz RD. *J Pediatrics* 1978;**93**:972-4.
² Gimson A, Hughes RD, Canalese J. *Lancet* 1980;ii:173-5.

Test reduction

SIR,—The need to find optimal (or at least second-best) groupings of "indicants" as a (partial) means of more rational cost control in the medical sector is no less pressing for the United States than it is for the British National Health Service. The papers by Professor W I Card and Dr P A Emerson (23 August, p 543 and 6 September, p 656), and Dr C C Spicer (30 August, p 592) on test reduction were commendable for their brevity and clarity in addressing these issues, and one hopes that they will find a wide audience on both sides of the Atlantic.

One might take exception to two points in their presentations. The first relates to what seemed to be an implicit assumption—namely, that the physician is the only relevant decision maker. Needless to say, the patient has a non-trivial stake in the choice of therapy or the decision to use or to forego one more diagnostic procedure. In the face of mounting

sentiment for greater patient autonomy, the patient's beliefs or preferences in the matter should be taken more formally into account. (If the objection is that the patient is uninformed, the answer may be that it is incumbent on the physician to provide the information, not to be paternalistic and make the decision in the patient's "best interest.") Secondly, patients and physicians differ among and between themselves in the degree to which they are "risk takers." Some, for example, might prefer surgery for the gastric ulcer regardless of the probability that it is benign (or malignant), because they view the "risk" of cancer as being so much greater than any possible "risk" of the operative procedure itself; others might take a quite opposite view. One trusts that the authors will, in coming years, present us an equally lucid description of more refined statistical methods for calculating expected utilities and cost effectiveness that take some of these factors into account.

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Recurrent urinary infection with microaerophilic and anaerobic bacteria

SIR,—I was interested in the article by Professor W Brumfitt and colleagues (4 October, p 910) on a case of recurrent microaerophilic and anaerobic infection. They were certainly successful in treating the infection, but was it justified since they say that the patient was always symptom free? The fact that she had had a cystoplasty would have accounted for the "sterile pyuria" and this in itself would hardly warrant further investigation. In some hospital laboratories it is normal practice not to report on the presence, or absence, of pus cells or red cells; and since the standard cultures would in this case be reported as being sterile the matter would not be taken further.

More important than treating esoteric, asymptomatic infection in patients with a cystoplasty is to make sure that they are able to empty the bladder to completion. This may require urethral dilatation, sphincterotomy, or a bladder neck procedure.

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The anaesthetist and the pain clinic: dextromoramide analgesia

SIR,—I was interested to read the comment by Dr Lesley A M Wills (20 September, p 809) that it is a myth that tolerance and habituation to opiate analgesics occur if pain is properly managed. In the same letter Dr Wills perpetuated a similar myth—namely, that dextromoramide is a very short-acting, strongly habituating drug with little or no place in the management of terminal pain. Although Dr Wills provided a bibliography to support the comments made on the first myth, similar support was noticeably absent with regard to the second. Comments similar to those of Dr Wills on dextromoramide are published with regularity, the latest originating from an area health authority.¹ Such publications are also similar in another respect—namely, the complete lack of clinical evidence to substantiate the opinions they contain.

This lack of reference to published (or unpublished) clinical evaluations of dextromoramide is surprising as there are many reports on the use of the drug for the relief of both acute and chronic severe pain. It is known from controlled clinical studies^{2,3} that dextromoramide (Palfium) provides a relief of severe acute and chronic pain equivalent in quality to that of morphine and other opiate drugs. Dextromoramide was recently independently recommended as an alternative to oral morphine, particularly for the ambulant, working patient.⁴ When pain is properly managed with dextromoramide there appears to be little tendency for habituation to occur. Kolodny⁵ in a study of 102 patients found no evidence of tolerance, habituation, or primary addiction; while Calesnick⁶ treated patients for up to 14 months with similar results. One case of habituation, although without withdrawal symptoms when the treatment was stopped, was supported by Flavell-Matts⁷ during a study of 60 patients. Den Otter⁸ found no evidence of habituation in more than 350 patients.

With regard to the duration of dextromoramide analgesia, data in a large number of published reports indicate a range from 2 to 12 hours, with a median value of the order of four to six hours, independent of the type of patient studied and independent of the route of administration of the drug. For example, in postoperative pain relief, Swerdlow² demonstrated that dextromoramide provided analgesia with a duration equivalent to that of morphine, oxymorphone, and phenazocine. In pain relief associated with various medical conditions, including carcinoma, the mean duration of dextromoramide analgesia typically is reported to be from four to six hours.⁶⁻⁷ Objective pharmacokinetic studies by Caddy⁹ (also personal communication) indicated that the mean plasma half life of dextromoramide is approximately 45 hours (range 13.3-86.6 hours), which is inconsistent with a short duration of analgesia in the average patient.

"Let us dispel all myths about these drugs" was the exhortation by Dr Wills. I believe that this letter will help to do exactly that.

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¹ Leeds Area Health Authority. *Drug Information Bulletin*. Leeds AHA, March 1980.

² Swerdlow M, Murray A, Daw RM. *Acta Anaesth Scand* 1963;**7**:1-19.

³ Bauer RO, Free SM, Bowen EH. *J Pharmacol Exper Therap* 1961;**131**:373-80.

⁴ Anonymous. *Drug and Ther Bull* 1980;**18**:69-72.

⁵ Kolodny AL. *Antibiot Med Clin Ther* 1960;**7**:695-701.

⁶ Calesnick B. *J Chron Dis* 1959;**10**:58-66.

⁷ Flavell-Matts SG. *Practitioner* 1962;**188**:524-6.

⁸ Den Otter G. *Ned Tijdschr Geneesk* 1958;**102**:1637-41.

⁹ Caddy B, Idowu R. *Analyst* 1979;**104**:328-33.

Bayes's theorem and the evaluation of tests

SIR,—In his article on Bayes's theorem (30 August, p 592), Dr C C Spicer is correct to say that the theorem is named after the Rev Thomas Bayes, but not that Bayes discovered it in about 1760. Bayes's fame is due to his having invented a particular method of inductive argument that happened to involve a manipulation of probabilities, which may be written (following Dr Spicer) as: $P(D|S) = P(D) \times P(S|D) \div (PS)$, where D is the disease, S is the pattern of symptoms and signs observed, and the upright bar (|) is read as