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We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters must be signed personally by all their authors. We cannot acknowledge their receipt unless a stamped addressed envelope or an international reply coupon is enclosed.

Interpretation of clinical laboratory data

SIR,—An ever-increasing number of laboratory tests are being carried out every day—and night—in hospital laboratories. All those involved in requesting these tests and those actually carrying out the analyses must be aware of the fact that several sources of error may threaten the reliability of the final results. There are the blood sampling technique, clerical errors, analytical errors, etc. Time and energy of numerous staff members of various disciplines are invested to conquer these problems and minimise the risks.

Why then is it that so often when results of laboratory investigations are published in the literature a considerable lack of care is demonstrated? Why not ascertain that the reader of the paper is able to interpret correctly the data presented? One simple but important piece of information missing too often is the nature of the material that was analysed. The terms "blood," "serum," and "plasma" frequently are so exuberantly mingled that

one hesitates to believe that this was all actually sent to the laboratory. For instance, we find the following examples in the *BMJ*: serum calcium, plasma parathyroid hormone (4 August, p 309); blood urea, plasma urate, serum potassium (11 August, p 360); serum bilirubin, plasma albumin, plasma bilirubin (18 August, p 416)—despite a perfect example of full information (4 August, p 235).

Current textbooks on clinical chemistry¹ point out how and when these materials should be collected and handled. The point is always stressed that, depending on the material, analytical findings may be significantly different. Even results from plasma depend on whether it was made with the use of heparin, (EDTA), citrate, oxalate, or fluoride. An important part of the extensive literature on this subject was reinvestigated and reviewed a few years ago.² Such facts as a 10% difference in K⁺ in serum or plasma and several mmol/l difference in the Na⁺ levels are described.

Plasma and serum glucose may differ 1 mmol/l (18 mg/100 ml). Cholesterol values of serum and plasma made with oxalate are 17-20% different.³ Another matter is the various temperatures at which the enzyme activity is measured. Values found at 37°C are often twice those measured at 25°C. No one can interpret such values unless this temperature is stated, or the reference range as obtained by the laboratory in a defined, healthy sample of the population is given for comparison.

Probably these important details might be presented in a much improved manner if the manuscript were to be checked by the clinical chemist or chemical pathologist, who without doubt will be perfectly ready to do so. With approval we quote Dent, who once wrote⁴: "Surely it is not asking too much for people to state what has been analysed in any particular case and make sure that they get it right. Only in this way can we eventually educate people to send the right samples to the pathology

laboratories for analysis, and also later make sure the results can be compared with those of other workers."

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¹ Henry, R J, Cannon, D C, and Winkelman, J W, *Clinical Chemistry—Principles and Techniques*, 2nd edn, ch 14. London, Harper and Row, 1974.

² Lum, G, and Gambino, S R, *American Journal of Clinical Pathology*, 1974, **61**, 108.

³ Boerma, G J M, et al, *Clinical Chemistry*, 1978, **24**, 1126.

⁴ Dent, C E, *Lancet*, 1976, **2**, 866.

Ethics of drug promotion

SIR,—Most doctors are aware that some pharmaceutical companies tend to make over-extravagant claims for the therapeutic properties of their drugs. In a highly competitive commercial market this is perhaps inevitable, but the code of practice imposed on its members by the Association of British Pharmaceutical Industries (ABPI) clearly indicates that it actively discourages methods of advertising and promotion which would bring discredit upon the industry. It is to be hoped that the recent promotional launch of ketotifen (Zaditen) by Sandoz Products Ltd will be subjected without delay to the scrutiny of the ABPI.

Ketotifen is an antihistamine-like drug which is believed to have mast-cell-stabilising properties and a prophylactic action in the treatment of asthma. The clinical trial data in support of the claim for ketotifen's clinical value are scanty. Indeed, the lurid double-page advertisements now appearing in most medical journals quote only one published controlled trial and the other claims are based on undisclosed "data on file." Nevertheless, a national press release, organised by inviting members of the press to a briefing outside this country, has stimulated many patients to ask their medical advisers to prescribe ketotifen for them. General practitioners are also being persuaded to use this drug by advertising material which relies on manifestly inadequate evidence and in which the dangers of the treatment are displayed in very small print.

Furthermore, general practitioners are being offered £15 for each patient for whom a history card and three-month follow-up form are completed, and £5 for three-monthly follow-up information at six, nine, and 12 months.

The advertising campaign also includes the issue of patient instruction leaflets, which inform patients that ketotifen is "a new kind of treatment which helps to stop attacks," although antihistamines and mast-cell-stabilising drugs are, in fact, not new. These leaflets contain advice on the withdrawal of "a powder inhaler," thus tacitly boosting the claim that ketotifen is superior to established forms of treatment. This would appear to represent an attempt to supplant an effective safe drug administered by inhalation by a new oral preparation of doubtful therapeutic activity, already known to cause systemic side-effects, for treatment of a disease which in the majority of cases can be completely controlled by drugs used topically by inhalation.

Most respiratory physicians would agree that there is not, as yet, convincing evidence of either the efficacy or the safety of ketotifen and that the premature publicity given to this drug could have unpredictable and possibly serious consequences.

It is also to be hoped that the Code of Practice on such matters which is being drawn up by the Minister of State for Health in conjunction with the profession will provide adequate safeguards against the risk of trials of this kind being used as a means of promoting a new drug.

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Babesiosis in man

SIR,—We write on behalf of our colleagues to clarify the position regarding the Scottish case of babesiosis we described (25 August, p 474). The misunderstanding has arisen because we omitted the word "acquired" and thus appeared to suggest that this was the first case occurring in the United Kingdom.

We were, of course, well aware of the Irish case Dr C C Kennedy and others mention (6 October, p 867)—indeed, the memorable photomicrographs associated with that case alerted us to the diagnosis in the Scottish one. The Irish patient, however, apparently contracted the disease in Eire by Lough Corib in County Galway and this has been referred to before as a case from Eire.¹ So far as we are aware the Scottish case is the first instance where definitive *Babesia divergens* infection has been acquired in the United Kingdom.

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¹ *Lancet* (1976), **1**, 1001.

SIR,—May I supplement the letter from Dr C Cotton Kennedy and others (6 October, p 867) and the report by Dr J H Entrican and others (25 August, p 474) by referring to a possible case of babesia infection in Northern Ireland in 1939? The following excerpt from a chapter that I wrote for a pathology book¹ is reproduced by permission of its publisher.

At a laboratory meeting in the Institute of Pathology of the Queen's University of Belfast in 1939, blood films and sections of a lymph node biopsy specimen were demonstrated by a physician from a county hospital in Northern Ireland as an instance of indigenous malaria, a disease that had long since disappeared from Ireland. The patient had presented with anaemia, and had been found to have enlargement of cervical lymph nodes and of the spleen. There was a history of a tick bite, and the physician suggested the transmission of "malaria" by this means. The minute parasites in the red cells in the blood film and in red cells in the sections of the lymph node, including cells that had been engulfed by macrophages in the sinuses, had been interpreted as trophozoites of a malarial plasmodium: in retrospect, it seems possible that this was an example of babesia infection, as was suggested during discussion of the demonstration by Dr N C Graham [lecturer in bacteriology] and Sir Thomas Houston [consulting clinical pathologist, Royal Victoria Hospital, Belfast].

The patient had been treated with anti-malarial drugs (probably quinine and mepacrine at that time) and after a succession of febrile relapses, accompanied by uraemia,

recovered. Inquiries a few years ago disclosed that the case notes and pathological preparations were not traceable. While there is no doubt that absence of the spleen predisposes to the development of babesia infection in man, there are published proved cases of the disease in individuals who have not lacked this organ: it is a mistaken belief that splenomegaly precludes the diagnosis.

Although the possibility of babesia infection can be no more than suggested in the tantalisingly uncertain case summarised above, the observation may be of interest to those whose awareness of this rare disease of man has been revived by the two recent mentions in your pages.

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¹ *Systemic Pathology*, ed W St C Symmers, 2nd edn, vol 2, p 668. Edinburgh, Churchill Livingstone, 1978.

Concanavallin A—non-reactive alpha-fetoprotein and communicating fetal malformation

SIR,—Dr E Ruoslahti and others¹ have confirmed our demonstration² of the concanavallin A (con A)-binding heterogeneity of human alpha-fetoprotein (AFP) and recently have supported (29 September, p 768) our conclusion that the determination of the percentage of the total amniotic fluid AFP not reactive with con A is a valuable adjunct in the diagnosis of communicating fetal malformations.³ Several other recent reports also agree with the usefulness of the con A-binding assay for enhancing the reliability of the testing for the leakage of fetal serum into amniotic fluid.⁴⁻⁶

In contrast to our data, Ruoslahti and colleagues failed to demonstrate a difference between the percentages of con A-non-reactive AFP in amniotic fluids from normal and abnormal pregnancies after the 18th week. We have extended our study so that the gestational age ranges of the normal pregnancies (14.6 to 36 weeks) and abnormal pregnancies (14.6 to 28 weeks) are comparable.^{7,8} These recent results confirm our initial conclusion that the percentage of con A-non-reactive amniotic fluid AFP in normal gestations is independent of gestational age and that the presence of a fetus with a communicating abnormality is associated with a lower-than-normal percentage of con A-non-reactive AFP throughout the age range tested. Dr D J H Brock presented similar findings at the recent meeting in Guildford of the International Society for Oncodevelopmental Biology and Medicine. In his study, three of the four false-positives and three of the six false-negatives by total AFP assay, which subsequently were predicted correctly by the con A-binding assay, were later than 18 weeks of gestation.⁶ During normal gestation no difference was found between the percentage of con A-non-reactive AFP present in amniotic fluid at 14 to 16 weeks and the percentage of con A-non-reactive AFP present at 20 to 24 weeks (D J H Brock, personal communication).

Maintenance of the difference between the proportions of the con A-non-reactive AFP and con A-reactive AFP in fetal serum and amniotic fluid during normal gestation beyond the period of yolk sac function is most likely owing to the slow degradation rate of AFP in amniotic fluid and to the very small amount of