All determinations were done according to Gorsky and Dietz² in the Institut Pasteur, Lyons, using a Perkin-Elmer atomic absorption spectrometer model 3030 with an HGA 600 graphite furnace and a Zeeman background correction system. The intra-assay and interassay coefficients of variation were less than 5%.

Aluminium concentration in Mérieux albumin was the lowest (1.03 (SD 0.13) $\mu\text{mol/l}$). In the other products aluminium content showed a wide disparity ranging from 4.1 to 1301 $\mu\text{mol/l}$ depending on batch and manufacturer.

The source of aluminium contamination in albumin solutions is not yet known. It might originate from the extraction of filters and filter aids used to clarify fractions obtained during the manufacturing process, or from containers, glass, or bottle caps.⁴

Albumin is usually separated from other plasma components by Cohn's or Cohn's modified method. Our product is the only one to be fractionated from placental blood, however, not from plasma. This led us to improve the purification procedure by including one more step in the fractionation process: an ion exchange on diethylaminoethanol dextran and adsorption chromatography on diethylaminoethanol derivatives of silica beads.⁵ Before chromatography aluminium was found at a low concentration ranging between 0.41 and 1.68 $\mu\text{mol/l}$. It was no longer detectable after chromatography, although the protein concentration was nearly 10 times the initial value. The reappearance of a low but detectable aluminium concentration in the final albumin sample was explained by the fourfold increase in protein concentration caused by the last ultrafiltration step.

To prevent aluminium overloading, especially in patients with impaired renal function, the albumin solutions should contain very low amounts of aluminium. Chromatography is a useful additional step to the classical fractionation process to remove aluminium contamination.

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Use of ^{99m}Tc labelled sucralfate in detection of bowel disease

SIR,—It is unfortunate, but on chemical grounds not unexpected, that ^{99m}Tc sucralfate failed to function as a diagnostically useful marker for lower gut ulceration when used by Mr A George and colleagues (5 September, p 578) after preparative catharsis with PicoLax. An explanation of their observations may well involve the following.

While the main action of sucralfate is to bind to gastric mucosa and to granulation tissue in ulcer bases, some of it dissociates in aqueous solution at low pH to form sucrose sulphate and release aluminium ions.¹ As this material moves down-

wards in the intestine with a concomitant rise in pH above 5 aluminium hydroxide will be freshly precipitated in a highly surface active form, so that it will readily bind ions such as phosphate.² At least some of this aluminium hydroxide is likely to remain in association with the parent ^{99m}Tc labelled sucralfate. Luminal "hot spots" thus probably indicate the occurrence of what is well known in another context as phosphate binding by aluminium based antacids. Such phosphate binding is used therapeutically in the treatment of chronic renal failure. The characteristic pattern of the ^{99m}Tc sucralfate filled colon with haustral pattern outlined³ may well reflect the luminal distribution of ^{99m}Tc marked phosphate.

In the more acidic conditions of the stomach and proximal duodenum no such aluminium hydroxide would be formed, and no binding of phosphate would occur (R W Cargill *et al*, unpublished observations), so that ^{99m}Tc labelled sucralfate acts as a reliable marker for ulceration only in the acid secreting stomach. Beyond the pylorus in the lower intestine it is likely to be more a marker for phosphate in the lumen than for ulceration of the gut. George *et al* may be correct in suggesting that ^{99m}Tc sucralfate is not reliable as an ulcer marker in the lower gut unless the pH conditions there are rendered exceptionally low—that is, pH <4. Preparation with lactulose or mannitol is unlikely to achieve these values. Even then, however, phosphate binding to the luminal contents must greatly reduce its specificity and reliability.

Uptake of the labelled sucralfate by faecal material has already been implicated as causing confusion in this proposed diagnostic technique (31 October, p 1134). We propose that this uptake comes about through phosphate binding.

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Fetal and neonatal mortality

SIR,—The results of the survey from Curaçao (10 October, p 894) show that babies of low birth weight are the most important factor in determining the neonatal mortality rate of a population. As Dr H I J Wildschut and others have pointed out, large reductions in perinatal mortality will come as a result of long term political and socioeconomic development,^{1,2} but it is nihilistic to assume that more immediate measures cannot improve the situation. The number of babies born in hospital implies that most Curaçao mothers have ready access to antenatal care and if this is adequate then in the short term it may be wiser to examine aspects of neonatal care.

There are two areas worthy of further consideration—*asphyxia* and *infection*.

Despite adequate antepartum and intrapartum care there will be babies who require resuscitation.³ Prompt and adequate neonatal resuscitation can prevent damage due to postnatal delay in achieving normal cardiac output, blood gas pressures, and respiratory function. Hypoxic-ischaemic encephal-

opathy and other adverse effects of asphyxia may not always be fully recognised among concomitant problems in preterm or low birthweight infants but undoubtedly contribute to overall mortality.^{4,5}

Infection—an important problem in neonatal care world wide—is relegated to the miscellaneous category. In developing countries mortality from neonatal sepsis has been estimated at 80 per 1000.⁶ In Papua New Guinea, where there is a comparable situation, offering secondary care and with a similar neonatal mortality,⁷ neonatal sepsis accounts for 25% of all deaths in secondary care nurseries.⁸ As with asphyxia, for preterm or low birthweight infants septicaemia may be the terminal insult. The initial description of the Curaçao study mentions blood culture analysis, but the results of these investigations are not apparent. If the organisms cultured from the lung are a true reflection of the invasive septicaemias experienced by newborn infants in Curaçao then this may need further investigation. Geographical and temporal variations of pathogens responsible for neonatal sepsis have been well described⁹ but the predominance of *Pseudomonas* spp and *Klebsiella* spp must be worrying. The high numbers of placentas with chorioamnionitis might also implicate antepartum or intrapartum infection as a major factor in the deaths of some of the preterm babies, and data from Addis Ababa suggested that ascending amnionitis can be a major cause of perinatal death.¹⁰ Even in the tertiary care nurseries of developed countries there are still high death rates of 20 to 75% in treated cases¹¹ so that preventive measures may be more fruitful than early diagnosis and treatment.

There are short term measures aimed at preventing asphyxia and infection which might help to decrease neonatal mortality in the population described.

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HIV antigenaemia and prognosis

SIR,—Dr Court Pedersen and colleagues and Dr F de Wolf and colleagues (5 September, p 567, 569) confirm that the persistence of human immunodeficiency virus (HIV) antigen in infected homosexual patients indicates a poor prognosis and even increases the risk of asymptomatic patients developing the acquired immune deficiency syndrome (AIDS). A similar tendency might be surmised for intravenous drug abusers, and we report here the preliminary results of a prospective study of intravenous drug abusers from Barcelona, which combined specific HIV antigen and antibody detection with an assessment of clinical state.

The presence of HIV antigen was analysed¹ in

103 serum samples from 82 intravenous drug abusers, all of them seropositive for antibody against HIV: 12 were asymptomatic, 54 had the AIDS related complex, and 16 had AIDS. The samples were obtained between July 1984 and December 1986 and repeated samples were taken in 18 patients after a time interval of more than six months.

Twelve samples were antigen positive: seven out of 16 samples from patients with AIDS (44%) and four out of 75 samples from patients with AIDS related complex (6%) ($p < 0.05$). HIV antigen was not detected in any of the 14 samples from asymptomatic patients.

Study of specific antibody against the core protein (anti-p24) was performed in 12 antibody positive samples with a competitive enzyme linked immunosorbent assay (ELISA) (HTLV-III Envacore, Abbott) and showed a lack of anti-p24 in four out of 12 samples from four patients with AIDS; only one of four HIV antigen positive patients with AIDS related complex showed absence of anti-p24.

Eight patients with AIDS had oesophageal candidiasis as their sole opportunistic infection; HIV antigen was not recognised in any of them. Nevertheless, antigenaemia was present in seven out of eight patients who presented with opportunistic infections other than oesophageal candidiasis. Even though studies are required in a larger number of patients, this different incidence of HIV antigen among the patients with AIDS who presented with only oesophageal candidiasis could suggest a better prognosis for them.

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Radiological diagnosis of deep vein thrombosis

SIR,—The leading article by Professor Graham Whitehouse rightly emphasised the need for methods which avoid the use of ionising radiation and injection of iodinated contrast media (3 October, p 801).

While ultrasonography fits this bill, an alternative imaging technique, not mentioned by Professor Whitehouse, is magnetic resonance imaging. Data presented at a consensus conference last month showed that with the development of new pulsing sequences magnetic resonance imaging when compared with phlebography holds great promise in making the correct diagnosis of deep vein thrombosis.¹ In conventional spin echo magnetic resonance imaging flowing blood is known to create a signal void and, depending on slice selection, is prone to "paradoxical enhancement," which makes it unreliable in assessing the patency of vessels. With new "fast scanning" sequences flowing blood reliably shows increased signal on the cross sectional image, and clot, when present, can therefore easily be identified. From anatomical considerations magnetic resonance imaging does well in evaluating veins in the proximal lower extremities and pelvis. Like ultrasound, it has

the additional advantage that it may show conditions that mimic deep vein thrombosis, such as haematoma or abscess. Unlike ultrasound, once the correct magnetic resonance imaging pulsing sequences are set up for the imaging protocol acquisition of images does not depend on the skills of the operator.

Panel members at the National Institutes of Health consensus conference were of the opinion that at present magnetic resonance imaging for the evaluation of deep vein thrombosis could not be recommended for general clinical practice. This is, nevertheless, a fertile area for clinical research. Those concerned in performing efficacy studies for assessing technological advances should consider including magnetic resonance imaging in their trial designs, since it is a non-invasive technique which provides the relevant information about deep vein thrombosis without the use of contrast media or ionising radiation.

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Repeat prescribing of non-steroidal anti-inflammatory drugs

SIR,—In October 1986 we carried out an audit of our prescribing of non-steroidal anti-inflammatory drugs by examining a range of data similar to those of Dr K Steele and others (17 October, p 962) and relating to all patients receiving these drugs in our practice over one month (list size 13 500, total doctor-patient contacts for the period 3154).

We examined the records of all patients who received non-steroidal anti-inflammatory drugs during the study period, taking care to include all those who received prescriptions at home visits or prescriptions written by hand without the patient being seen as well as those issued by our computerised repeat prescribing system and at face to face consultations. We found 22 patients who received a repeat prescription for non-steroidal agents other than via the computerised system, including seven who had had prescriptions for these drugs renewed at a home visit.

In the month of the study we issued 108 prescriptions for these agents to 3.42% of all doctor-patient contacts and at 3.1% of all face to face contacts. Of these 52 were issued for the first time in the month of the study and 56 were reissues. Like Dr Steele and others we found that more prescriptions were issued to women and to people over 65 years, though the differences between sexes and age groups were less pronounced. Thus 64 of 108 prescriptions for these drugs were issued to women and of the 56 which were reissues 24 were to people aged over 65.

The indications for long term use—that is, reissuing of a further prescription for a non-steroidal anti-inflammatory drug—were similar to those found in the Belfast study: osteoarthritis 28; rheumatoid arthritis 8; soft tissue problems 11. The small differences from the authors' finding may well be accounted for by our different definition of long term treatment.

Three drugs—ibuprofen, naproxen, and indomethacin—accounted for 90 of the items prescribed, and a total of seven different agents were used. Our use of indomethacin was twice that of the doctors in the Belfast study (15 out of 108 v 15 out of 198).

We divided gastrointestinal problems into three categories: peptic ulceration with confirmatory documentation, peptic ulcer recorded in the notes

without further evidence other than suggestive symptoms, and patients taking antacids or H_2 antagonists without diagnosis. When we examined the records of the patients having prescriptions renewed we found evidence of confirmed peptic ulceration in 10, suggestive symptoms in 3, and 3 taking concurrent antacids or H_2 antagonists without a diagnosis. Thus, up to 29% of our patients had some indication of gastrointestinal problems of relevance to their use of non-steroidal anti-inflammatory agents. Ten of the 56 patients being reissued with prescriptions had concurrent hypertension, one concurrent renal impairment, and one a documented history of congestive cardiac failure. Nine were taking antihypertensive agents and 14 diuretics. Only 16 were taking other analgesics excluding aspirin.

We also investigated the monitoring of patients who had been taking these drugs for more than a year. Eight of 34 had had their urea concentration measured or other renal function tests, three had had hepatic function tests performed, and 11 had had a full blood count within the previous year. However, many of these blood tests may have been done for reasons not connected with the monitoring of non-steroidal anti-inflammatory medication. Certainly the monitoring of patients on indomethacin was no better than that of those on less toxic agents. Side effects were recorded in the notes of eight patients who had been taking the drugs for more than a year. All were gastrointestinal and none had been reported to the Committee on Safety of Medicines. Only one had led to a change of treatment. While the recording of indications for long term non-steroidal anti-inflammatory use was satisfactory the recording of contraindications and side effects was poor.

Overall our small study largely confirms that of Dr Steele and others. It indicates that the prescribing of non-steroidal agents in this practice is for appropriate indications and from a small range of drugs. The use of indomethacin was greater and fewer patients were taking simple analgesics. There were important deficiencies in our recording and monitoring of side effects and contraindications, particularly in relation to gastrointestinal problems.

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Cytotoxic drug expenditure

SIR,—Professors T J McElwain and J S Malpas (31 October, p 1136) assert that the appointment of a medical oncologist reduces expenditure on cytotoxic drugs and refer to the Royal College of Physicians 1986 comitia document on this subject.

The Royal College of Physicians document, which is entitled *Cost Effectiveness of Medical and Paediatric Oncology*, lists the costs of cytotoxic chemotherapy in three hospitals before and after the appointment of medical oncologists. For one of these hospitals the costs given refer to one drug only. Many factors can have a bearing on drug expenditure, including loss of patents and commercial sponsorship of clinical research. No analysis is given which could lead to the conclusion that the change in expenditure was wholly or partly due to a change in prescribing habits, and no information is given on changes in chemotherapy costs at other institutions.

The credibility of this document is further undermined by the robust implications that skill in cytotoxic chemotherapy is the prerogative solely of medical oncologists and that no patients with metastatic germ cell tumours and only 5% of