cigarettes with unventilated filters may be a little higher than those of plain cigarettes. But even if some filter-tipped brands do have slightly higher CO yields than plain cigarettes, it is surely not beyond the intelligence of smokers to choose the ones with the lower CO yields. They could be instructed to pay more attention to tar yields but within each tar yield group to go for the brands with the lower CO yields. Besides, there are a number of brands which have low tar, low nicotine, and low CO yields and smokers would have little difficulty in identifying these as the least harmful brands to smoke.

We have found that the CO yields of different brands of cigarette range from 5 mg to more than 20 mg per cigarette.⁵ Any assessment of the degree of hazard of a particular brand cannot, therefore, be complete without knowledge of its CO yield. The manufacturers know the CO yields of their cigarettes, the Government laboratories have already measured them, but the public remain uninformed. It requires only a word from the Secretary of State for Health and Social Security for this important information to be released.

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¹ Russell, M A H, *et al*, *Lancet*, 1973, 2, 687.

² Wald, N J, and Smith, P G, *Lancet*, 1973, 2, 907.

³ Wald, N J, *Lancet*, 1976, 1, 136.

⁴ Russell, M A H, *Lancet*, 1976, 1, 301.

⁵ Russell, M A H, *et al*, *British Medical Journal*, 1975, 3, 71.

Laparoscopy explosion hazards with nitrous oxide

SIR,—Drs G B Drummond and D B Scott (6 March, p 586) have suggested that explosion is not a significant hazard in laparoscopy when nitrous oxide is used unless intestinal gas is released into the peritoneal cavity by puncture of the bowel wall. They carried out analyses of gas samples in 12 laparoscopies only. It is unlikely that the bowel was punctured at all in this small series of cases, but nevertheless there is evidence that there is a significant known incidence of bowel puncture probably of at least 2%. In addition there are a few cases which escape detection at the time of induction of the pneumoperitoneum but which are found by careful routine laparoscopic inspection of the bowel at the conclusion of sterilisation.

The risk of bowel puncture is increased if the Verres needle, which has a locking pin, is employed to enter the abdomen. This needle was originally designed as an all-purpose needle for use in several procedures, including venepuncture, in which the inner cannula needed to be locked outwards. This locking device is not needed by the gynaecological laparoscopist, and if it accidentally becomes locked the risk of bowel puncture is increased. The manufacturers should omit the locking pin, and the inner cannula should also have two side exits for the passage of gas, so reducing the risk of obstruction if the thread of the collar becomes defective.

It is my opinion that nitrous oxide for the pneumoperitoneum should be reserved for those cases in which high-frequency electrical diathermy is not to be used. It has been shown that the minor disturbances caused by carbon dioxide are readily controlled by good general

anaesthesia, but that nitrous oxide has some advantages if local anaesthesia alone is employed. For those who prefer to use nitrous oxide always it would be advisable to employ thermal coagulation and division, elastic rings, or clips for sterilisation procedures. Even then the occasional bleeding hazard may necessitate rapid use of electrocoagulation.

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Use of pressurised aerosols by asthmatic patients

SIR,—It was interesting to read the short reports by Dr J Orehek and others and Drs I C Paterson and G K Crompton (10 January, p 76) concerning the problems associated with the correct use of pressurised aerosols by asthmatic patients. The former study showed that 15 out of 20 patients (75%) failed either to inspire deeply or hold their breath afterwards, or both, or poorly co-ordinated the puff and the inspiration. In these 15 patients the degree of bronchodilatation achieved after self-administration was significantly smaller than that achieved after administration by the physician. The latter workers identified 45 out of 321 patients (14%) as having doubtfully efficient or inefficient techniques as classified by the trained respiratory technician.

In order to obtain objective evidence we monitored the relationship between inspiration and release of the dose in 103 patients attending routine outpatient clinics. A standard pressurised aerosol was modified by the attachment of transducers to provide an electrical analogue of the release of the metered dose and of inspiration. The separate signals were fed to a two-channel recorder. The patient's technique was regarded as satisfactory if the tracing showed that the metered dose was released during inspiration. Thirty-three patients (32%) failed to synchronise and the majority of these had been receiving bronchodilator and/or steroid aerosol therapy as part of their treatment.

We are concerned that many patients may not be receiving maximum benefit from these drugs despite initial instruction, and it is now our policy to repeat the tuition at intervals. We have developed a device that detects and indicates, by means of a light, correct synchronisation. The patient practises until he can light the lamp on every attempt.

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Hypertriglyceridaemia and abdominal pain

SIR,—We read with interest the description by Dr R S Elkeles and Mr D Horwell (21 February, p 435) of a case of abdominal pain associated with transient hypertriglyceridaemia and a normal serum amylase level. There have been several recent reports of patients with an elevated serum triglyceride level, abdominal pain, and normal serum amylase activity who

were shown at laparotomy to have acute pancreatitis.¹ Cameron *et al*² were of the opinion that abdominal pain associated with hypertriglyceridaemia was as indicative of acute pancreatitis as an elevated serum amylase.

Warshaw *et al*³ reported six patients with the clinical features of acute pancreatitis, minimally elevated serum amylase levels, and hyperlipidaemia. The hyperlipidaemic serum was serially diluted and they demonstrated a mean rise in amylase activity of 232% at 16 dilutions. This is not seen in sera with a high amylase level and normal serum triglyceride levels and suggests that inhibition of the amylase activity in the serum can occur in the presence of an elevated serum triglyceride level.

We have recently seen a patient admitted with abdominal pain whose serum triglyceride level was 112 mmol/l (9911 mg/100 ml) (normal <2 mmol/l (<170 mg/100 ml)). The amylase level in undiluted serum (1165 IU/l) was below that acceptable for a diagnosis of acute pancreatitis but rose 338% to 3936 IU/l, a level diagnostic of acute pancreatitis, when serial dilutions of the serum up to 32 times were performed. Further dilution of the serum resulted in no significant increase in amylase activity, indicating that a plateau had been reached.

It thus appears that in the presence of hyperlipidaemia serial dilutions of serum are necessary to obtain a true serum amylase level. This has obvious importance in the diagnosis of abdominal pain associated with an elevated serum triglyceride level.

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¹ Cameron, J L, *et al*, *Surgery*, 1971, 70, 53.

² Cameron, J L, *et al*, *Annals of Surgery*, 1973, 177, 483.

³ Warshaw, A L, Bellini, C A, and Lesser, P B, *Annals of Surgery*, 1975, 182, 72.

Reticuloendothelial phagocytosis in nephritis

SIR,—Dr I I Onyewotu (13 March, p 646), together with Dr E J Holborow, has written a classic on the uptake of complexes by macrophages. Nevertheless he is unwise to criticise the in-vivo test without having the appropriate experience. In the long term an in-vivo patient test will be likely to have greater clinical relevance.

The points that he raises may be answered as follows: (1) Only in shock is uptake by the Kupffer cells dependent on hepatic blood flow. In other situations clearance is remarkably independent of liver blood flow.¹ (2) The free iodide levels in our tests, as we originally stated,² are less than 1% and can be ignored. Correction is in any case simple. (3) Polyvinylpyrrolidone is certainly not an advantage. Its stated molecular weight is 40 000, which means not only that large amounts will be lost in the urine, but that it is not a macromolecule, only a foreign molecule. The molecular weight of our aggregated albumin is about 760 000. (4) Our patients with mesangio-capillary nephritis show impaired reticuloendothelial system (RES) clearances, as mentioned briefly in our paper (7 February, p 321). This is shown quite clearly by an "RES stress test" that we have used latterly. (5) Dr Onyewotu may be correct in thinking

that this is due to competition by circulating immune complexes, but there are many possibilities, which might of course have to be analysed in vitro.

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¹ Normann, S J, *Journal of the Reticuloendothelial Society*, 1973, 13, 47.

² Drivas, G, Uldall, P R, and Wardle, E N, *British Medical Journal*, 1975, 3, 743.

Aplastic anaemia and hair dye

SIR,—Following the recent report by Drs P J Toghill and R G Wilcox (28 February, p 502) we would like to recount a similar case in this hospital

The patient was a 54-year-old housewife who developed aplastic anaemia of undetermined aetiology. As in the case reported, she had been using a new hair dye prior to this. This contained *para*-toluene diamine sulphate. She showed no response to prednisolone or oxymetholone, being maintained by blood and platelet transfusions. Five months later she remains well and is taking ethamsylate 500 mg four times daily.

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Exchange transfusion in prevention of iron overload

SIR,—Your leading article (1 November, p 244) entitled "Blood transfusion and iron overload" states that children suffering from chronic aplastic anaemia or homozygous thalassaemia requiring frequent blood transfusions usually die during adolescence or early adult life and treatment must be directed to preventing iron accumulation by all available means. I wish to report a method of exchange blood transfusion which I have found to be successful in this regard.

Case 1—A boy aged 16 had required frequent blood transfusions since infancy to sustain life. He was suffering from a haemoglobinopathy and showed the full syndrome of haemochromatosis with involvement of skin, bone marrow, liver, heart, pancreas, kidneys, and testes. The serum iron was 54 $\mu\text{mol/l}$ (300 $\mu\text{g}/100\text{ ml}$), with 100% saturation of iron-binding protein. A series of 14 exchange blood transfusions were given at intervals of 2-3 months. Two direct blood transfusion pumps were used simultaneously to take blood from a femoral vein and give blood into the other femoral vein from 6-8 consecutive donors.¹ There was marked clinical improvement and serum iron fell to 35 $\mu\text{mol/l}$ (195 $\mu\text{g}/100\text{ ml}$), with 55% saturation of the iron-binding protein. He died suddenly after a transfusion in February 1963.

Case 2—A woman aged 40 suffering from aplastic anaemia and paroxysmal nocturnal haemoglobinuria received, over a period of 12 years, 131 regular blood transfusions. Her skin became pigmented and she showed an increased amount of iron in the bone marrow, liver, and kidneys. In October 1958 her serum iron was 47 $\mu\text{mol/l}$ (260 $\mu\text{g}/100\text{ ml}$), with 98% saturation of the iron-binding protein. Regular exchange blood transfusions, given by the direct method using two donors, were then started. As a result of this treatment her clinical condition improved and by December 1967 the serum iron was reduced to 11 $\mu\text{mol/l}$ (64 $\mu\text{g}/100\text{ ml}$), with 26% saturation of iron-binding protein. During the period of 10 years until the patient's death in February 1969 from a subarachnoid haemorrhage she received 94 exchange transfusions. With

exchange transfusions her haemoglobin level ranged from 6 to 13.4 g/dl compared with 4.3-7.6 g/dl during the period of non-exchange transfusions. Post-mortem histological examination showed increased fibrosis of the liver with moderate deposition of haemosiderin. There was no excess iron in the bone marrow or kidney.

It is concluded that the exchange transfusions given in these two cases were beneficial because abnormal red cells were removed and replaced by normal erythrocytes with normal cell life span and normal haemoglobin.

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¹ McLean, J A, and Luke, H A, *British Medical Journal*, 1967, 4, 78.

Carcinoma-in-situ of cervix in sisters

SIR,—May I support Mr S Bender's suggestion of investigating sisters in patients with an intraepithelial carcinoma of the cervix (28 February, p 502)? In 1959¹ I reported the simultaneous cytological diagnosis of cervical cancer in three sisters, the third of whom we "waylaid" while she was visiting her other two sisters, then in hospital. All these three women are still alive and well. In over 25 years' experience in my department we have at least six other examples of preinvasive carcinoma of the cervix and clinical carcinoma of the cervix in sisters and we have at least 12 examples of the same in mother and daughter.

As Mr Bender states, there are no cancer families in which the cervix has been the organ affected, but, knowing what we now know about the epidemiology of this disease, it appears to be a case of "like mother, like daughter."

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¹ Way, S, Hetherington, J, and Galloway, D C, *Lancet*, 1959, 2, 890.

Immunological findings in multiple sclerosis

SIR,—The study reported by Dr G Lamoureux and others (24 January, p 183) is interesting with regard to the broad spectrum of tests performed. Unfortunately, the number of patients with multiple sclerosis (MS) investigated (23) was small and because of the criteria applied for selection (young adults with a remitting course and a CSF IgG value exceeding 0.035 g/l) the conclusions drawn apply only to a particular group of MS patients.¹

We have attempted to obtain detailed information from all patients with MS in a defined area of Lower Saxony² concerning the incidence of the following childhood infections: measles, mumps, rubella, varicella, poliomyelitis, fifth disease, herpes zoster, herpes simplex, exanthema subitum, rickettsioses, scarlet fever, encephalitis, meningitis, and hepatitis. Two control groups consisted of 53 patients with disc lesions or psychiatric illnesses in the same area and 17 relatives or friends of the MS patients who had lived with or close to them during childhood and were not more than three years older or younger.

No statistically significant difference was found between the three groups in the incidence of any infections with the single exception of fifth disease, of which eight

members of the first control group but none of those of the other two groups had a history. These results are in contrast to those of Dr Lamoureux and his colleagues, though the small number of their cases makes the interpretation difficult.

As MS is a disease common enough in northern Europe (prevalence about 50 per 100 000 inhabitants) it is possible to include as many patients and controls in a study as the level of significance requires. Conclusions should be drawn with caution from studies in which a small number of highly selected patients are investigated.

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¹ Olsen, J E, et al, *Journal of Neurological Sciences*, 1976, 27, 233.

² Firnhaber, W, *Vorkommen der Multiplen Sklerose und epidemiologische Aspekte in einem umschriebenen Gebiet Südniedersachsens*. Göttingen, Habil.-Schrift, 1969.

Failure of phenobarbitone to prevent febrile convulsions

SIR,—I was brought up on the conventional teaching that phenobarbitone was the most useful single drug for treating most cases of epilepsy in children, a statement that regrettably continues still to be repeated in books and review articles. Experience gradually led me to the exactly opposite conclusion—that phenobarbitone was worse than useless for this purpose. Worse not only because does one seldom come across a child whose fits have been benefited by it but also because so often the child's behaviour deteriorates noticeably (He's become so irritable, say the parents).

Hard evidence to disprove the effectiveness of an anticonvulsant drug is never easy to obtain or collect. Greatly to be welcomed, therefore, is the evidence that Dr J Z Hackmatt and his co-workers from Glasgow (6 March, p 559) have provided to counter the widely held notion that phenobarbitone is effective in one context at least—the prevention of febrile fits.

If phenobarbitone ceased altogether to be regarded as a drug for treating children with fits would there be anything but gain?

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Hazards of ergotamine tartrate

SIR,—Experience in the headache clinic at this hospital lends support to the note of caution sounded by Drs F C Rose and Marcia Wilkinson (28 February, p 525). I have seen many instances of the characteristic nausea and headache, present all day and every day and relieved briefly only by further ergotamine. These symptoms are due both to ergot toxicity and to the invariably coexistent tension (muscle contraction) headache; they are similar to the migraine that the patient has had in the past but are distinguished by the fact that uncomplicated migraine almost never occurs continuously every day. This complex picture is important because it is a sign not only of ergot toxicity but also of habituation.¹