draws much of its support, the citizens (whipped on by the media) are much more worried about illicit drug abuse than they are about abuse of alcohol and tobacco. They may have very little experience of illicit drug abuse, but paradoxically they are so used to their friends dying of tobacco and alcohol related diseases that they think it "normal." The citizens and the government are right to be concerned about illicit drug abuse, but they may need to be more intelligent in their response. Furthermore, they need to recognise that it is neither "normal" nor necessary for so many to die from, and have their lives ruined by, tobacco and alcohol. Already public attitudes have changed greatly on smoking, and the government is following, not leading, on this issue. Soon it will be possible to say the same of alcohol, and already pregnant women are very wary of the toxin.

The government should thus hurriedly revise its programme for next week's conference and give much more prominence to tobacco and alcohol abuse. It should then follow this up by putting its money where the problems are. Oddly this might enhance its struggle against illicit drug abuse—because the young, who make up most of the drug users, are very sensitive to the hypocrisy that says "your drugs are killers but ours are pleasures."

# Tumour markers in germ cell tumours

Over three quarters of patients with metastatic non-seminomatous germ cell tumours have a raised serum concentration of human chorionic gonadotrophin or α fetoprotein or both. These markers may be used both as diagnostic aids and in monitoring the growth of the tumours.[1 2] For most to be gained from tumour markers, however, estimations need to be frequent and clinicians need accurate results as soon as possible. Patients with gestational trophoblastic tumours have regular estimations of human chorionic gonadotrophin organised in a national screening programme.[3] A similar national scheme for patients with germ cell tumours would give clear benefits; at present many patients have only infrequent marker estimations.

A pilot scheme has been set up at the Cancer Research Campaign Laboratories at the Charing Cross Hospital and is already used by many hospitals.[4] Patients diagnosed as having non-seminomatous germ cell tumours and those with seminomas and a raised human chorionic gonadotrophin concentration or metastatic disease are eligible. They are registered when a completed form (which may be obtained on request) is returned with the first blood sample. Once the patient is registered a postage prepaid box with addresses printed on it is sent to his or her home. The box contains a letter of instructions to the patient, the venesectionist, and the local laboratory and sample tubes. The patient is asked to have a blood sample taken by the specified date at the most convenient hospital. An automated radioimmunoassay is used to measure the serum concentrations and the results are available within 36 hours of receipt of the sample for posting to the referring consultant and general practitioner.

Further requests for samples from registered patients are generated automatically by the computer. These tumours may have doubling times of less than two weeks, and in consequence samples are requested weekly during treatment and for the first 10 weeks of follow up, but then less frequently. Since there are no hold ups caused by the laboratory waiting for batches consultants usually obtain results within a week. There is an automatic check system on failures in follow up.

All patients in Britain with germ cell tumours could be monitored if there were two or three properly equipped centres providing the sort of service offered at Charing Cross Hospital—and regardless of the clinical and epidemiological benefits of such a system the financial savings of such a scheme when compared with the use of assay kits in each hospital should commend the system to the Department of Health and Social Security.

Other tumour markers of value in this group of diseases can be included in the scheme. At least half the patients with active seminoma have raised activities of serum placental alkaline phosphatase,[5 6] and this enzyme is also raised in some women with dysgerminomas. Lactate dehydrogenase activity is raised in some patients with germ cell tumours, especially in those with more advanced disease, and has been used to predict the outcome in patients with non-seminomatous germ cell tumours.[7 8]

The initial serum concentrations of human chorionic gonadotrophin and α fetoprotein may also be used as powerful indicators of which patients will be rendered free of disease by current treatment.[9] A recent Medical Research Council study has shown that equal importance should be given to the clinical stage (which takes account of both size and sites of disease) and the serum markers (human chorionic gonadotrophin greater than 1000 IU/l or α fetoprotein greater than 500 kU/l, or both); the two assessments may be combined to produce a staging classification with three risk categories.[10] In those patients treated at six centres between 1980 and 1982 the survival rates for the low, middle, and high risk groups were 95%, 85%, and 54% respectively. The centre with the best results in the high risk group found that those patients with very bulky disease had a poor prognosis only if they also had very substantially raised marker concentrations.[11]

Lives are likely to be saved if those patients found to have marker concentrations in the high risk range after orchidectomy are immediately referred to a specialist centre without time being wasted in staging investigations. Once patients in poor prognostic groups are recognised their treatment may be modified to compensate for their more aggressive tumours.[11]

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# Ampoules, infusions, and filters

Particulate contamination of intravenous fluids has been recognised for years.[1] It is mostly due to manufacturing and packaging debris—rubber, cotton, plastic, particles of drug, and glass. Improvements in the manufacturing processes have reduced the numbers of these particles but not eliminated them.[2-4] When drugs (including multivitamin preparations) or electrolyte solutions are added to an intravenous infusion there is a disproportionately large increase in particulate contamination.[4] Some at least of this is associated with the opening of ampoules, the breaking of container seals, and the insertion of syringes or needles during transfer of the additive to the infusion. The risks of these particles have not been well defined.

Particulate contamination plays a part in the development of phlebitis related to infusion, the most common complication of intravenous treatment. The many other factors include the site of infusion, the size of the vein, the composition of the solution being infused (especially its tonicity), the duration of the infusion, the nature of the cannula, and the rate of flow or injection of material through this.[5] The contribution of particulate matter may be reduced by "in line filters," with pore sizes varying between 0·2 and 0·5 μm. This type of filtration reduces the incidence of phlebitis during infusions of large volumes,[6-9] and similar reductions have occurred with in line filtration of antibiotic infusions.[7 10] Uncertainty remains about the relative importance of particles in the infusion fluid and those contributed by the additives. Dorris *et al* showed that filtrates of a solution of cephalothin sodium produced more inflammatory changes in the vein wall than did filtrates of a solution of dextrose.[11] This was consistent with observations by Allcutt *et al,* who found that a filter prolonged "phlebitis free survival" of the drip only in those patients who had antibiotics injected above the filter.[12] Persistence of the drip at five days was improved from about 17% to 58%. No such difference was noted, however, in a similar study by Falchuk *et al.*[9] They concluded that filtration reduced phlebitis from 58% to 25% after three days irrespective of the addition of antibiotics.

Even less is known about the systemic effects of infused particles. Garvan and Gunner described the formation of granulomas in rabbits' lungs after intravenous infusion, and they suggested that these might represent a long term foreign body reaction to particulate matter.[1] They described similar granulomas in human lungs removed at necropsy. Other reports of pulmonary lesions have appeared, and infused particles have also been linked with lesions of the kidney, spleen, liver, and brain.[13] The clinical importance of these lesions is unknown, and improvements in manufacturing processes since they were first identified may be sufficient to prevent similar complications occurring with modern intravenous treatment.

Turco and Davis first noted that glass fragments greater than 5 μm could be aspirated from opened ampoules of frusemide.[14] A paper by Shaw and Lyall published last year in the *BMJ* reopened the debate on the importance of this contamination from intravenous additives drawn up from glass ampoules.[15] These workers identified glass particles with diameters of over 20 μm—and some visible to the naked eye, which are probably over 75 μm diameter. Such particles might lodge in the pulmonary capillaries, which have an average size of 10-12 μm. Clearly further research is needed into the possible consequences of these particles being injected intravenously. Until such studies have been carried out what conclusions or recommendations may be made? Firstly, in line filtration will reduce the risks of contamination with micro-organisms and may prolong the phlebitis free survival of intravenous drips. It follows that filtration is a sensible precaution in any patient who needs a prolonged infusion and who is susceptible to infection either by virtue of systemic disease or as a result of cancer chemotherapy. Most patients of this type will be located in "high care" areas of the hospital, and most will be receiving regular intravenous treatment. Phlebitis may also, however, be prevented by regular resiting of the infusion, and this may be more appropriate in many patients.

The potential benefits of in line filters must be weighed against their possible disadvantages. They cost more, they restrict the flow of colloid solutions and lipid suspensions, and they add an extra potential site for disconnection. Some "final in line" filters are produced with injection ports below the filter itself. Use of these ports for injections drawn from glass ampoules may diminish any gains to be expected from filtering infusions. Some drugs may be retained in filters, notably insulin and vincristine sulphate.[16] The latest filter designs, however, do not greatly restrict flow of crystalloids and microvent air bubbles to prevent their infusion.

Another approach may be to look for alternatives to glass for drug packaging. Not only might these overcome any problems associated with the infusion of glass particles but they should also prevent the problems of injury to staff. Lacerations occurring during the opening of glass ampoules represent an important potential site of entry of bacteria and viruses.

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