have always done, will continue to depend on every prescribing doctor's maintaining a high index of suspicion. The past year's explosion of interest in monitoring has generated constructive proposals; the next stage—before the CSM takes any final decisions—should surely be for the practicability of one or more of the schemes to be assessed in pilot studies.

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More about infant diarrhoea

In 1972 the infant mortality rate from gastroenteritis in Britain[1] was higher than in any other country in the European Economic Community except Italy (and possibly Luxemburg). In that year 297 children aged less than 1 year died of diarrhoeal disease in England and Wales. Since then, however, the mortality has fallen[2] to 255 in 1973, 144 in 1974, and 120 in 1975. In Newcastle upon Tyne, for example, the incidence of severe dehydration and hypernatraemia in children admitted to the gastroenteritis unit has been drastically reduced between 1971 and 1975, and physicians there believe the explanation is an increase in breast-feeding and the introduction of low-solute milks.[3]

Experience at the gastroenteritis unit of the Queen Elizabeth Hospital for Children, London, in 1971 and 1972 has recently been reviewed,[4] re-emphasising several important points. Firstly, only two of the 608 children seen there with gastroenteritis were breast-fed compared with 14% of matched infants in the community served by the hospital, showing yet again the supreme importance of breast-feeding in the prevention of this disease. Secondly, the social origins of the disease were again evident. Multiple hospital admissions, lower social class, and "social problems" were common characteristics of affected children. Thirdly, the age of the child was an important determinant of the severity of the illness. Babies aged less than 6 months were much more likely to suffer serious biochemical disturbance, and the eight deaths in the series were all in children under this age, all but one being less than 2 months. Five of the deaths were in children with other serious abnormalities, four of whom had major congenital abnormalities.

Most babies with diarrhoea will recover after a short period of oral feeding with a glucose-electrolyte mixture (72% of children in this London series were not given intravenous fluids and only 3% had persisting diarrhoea after the reintroduction of milk feeds). The management of the minority whose diarrhoea is prolonged may be difficult, and another recent analysis, this time of experience at the Hospital for Sick Children, London, gave useful practical advice.[5] There were 82 infants with diarrhoea lasting for more than two weeks. A diagnosis was made in 59 (70%), the most common being coeliac disease, secondary disaccharide intolerance, and cows' milk protein intolerance, though 12 patients had less common diseases and the full list of differential diagnoses included 28 possibilities. Prolonged diarrhoea dating from birth is a peculiar and difficult problem; of six such patients four died and a known cause for the diarrhoea was found in none. All were given prolonged intravenous nutrition, since they could not be fed by mouth. In two of these children there was a family history of similarly affected siblings who died, and another two were siblings with agenesis of the corpus callosum. No patient died whose diarrhoea did not date from birth. In the 59 patients whose diarrhoea had a specific cause long-term management was usually dictated by the diagnosis, but parenteral nutrition was sometimes necessary at first. Seventeen infants had diarrhoea not dating from birth for which no cause could be shown, but none of these needed parenteral feeding.

When faced with an infant with persisting diarrhoea most paediatricians will progress through a variety of milks beginning with a lactose-free milk such as Galactomin 18, followed by one which is lactose free and contains either altered cows' milk proteins (Nutramigen) or only soya bean protein (Velactin, Pro Sobee). Children fed with most special milks (but not Nutramigen or Pro Sobee) need added vitamins and these can best be provided as Ketovite liquid and tablets. (Liquid and tablets are different and complementary.)

For difficult, undiagnosed, prolonged diarrhoea various synthetic and semisynthetic diets have been advocated, but none has been entirely satisfactory. The Great Ormond Street team[5] had considerable success with a fluid diet based largely on comminuted chicken—all 17 infants with non-specific diarrhoea not dating from birth responded to it promptly.

If, indeed, the life-threatening complications of gastroenteritis have become less common with the introduction of low-solute milks and with renewed efforts to promote breast-feeding it may be possible in future to avoid admission to hospital in all but a few cases, though in young babies under the age of 6 months close and careful supervision will be necessary if they are to be nursed at home. Only a small minority of babies will have persisting diarrhoea, but these require specialised investigation and care in hospital.

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Chemotherapy in bladder cancer

Bladder cancer accounts for much of a urologist's work load and requires not only the co-operation of radiotherapists, chemotherapists, and pathologists but also the use of costly technological resources. Experience has shown that clinically there is a clear separation between two parts of the range of urothelial cancer.[1 2] Some 80% of the lesions are papillary, non-invasive, T1 lesions; the remaining 20% are solid, invasive cancers classed as T2, T3, and T4. In both types the end results leave little cause for satisfaction or complacency.

The five-year survival[3-5] for T1 lesions is about 70-80%. Nevertheless, as over half of these papillary cancers are multiple and recurrent, diagnosis and treatment require repeated cystoscopies under general anaesthesia. Here the main problem is preventing recurrence—and knowing what to do when the recurrences are too frequent and too numerous to be controlled by endoscopic surgery. We need more trials

to evaluate alternative treatments such as intravesical chemotherapy or hydrostatic pressure in managing these papillary lesions.[6 7]

At the other extreme, T4 bladder tumours which have invaded other organs or are fixed within the pelvis have a hopeless prognosis, and one unlikely to be much improved by treatment. The aim here can be only the palliation of symptoms. The most perplexing problem is treating T2/3 tumours, with or without extension to the local lymph nodes, but with no overt distant metastases. These lesions can be resected completely by radical cystectomy. They also respond to radiotherapy, yet the results of treatment are disappointing even in the absence of known spread to the local lymph nodes: five-year survival figures[8] after cystectomy are 16-28%, and the results of radiotherapy are equally poor.[9 10] A combination of preoperative radiotherapy and cystectomy may improve results, but so far the advantage has seemed small and the figures are probably biased by patient selection.[11 12] Surgery and radiotherapy are capable only of ablating the local lesion. When the complications of primary treatment and urinary diversion after a cystectomy are excluded, death occurs from local recurrence or metastatic disease; and clearly many T2/T3 lesions without clinical metastases must in fact have micrometastases at presentation. If the results are to be improved then we need to add some form of systemic treatment to the conventional management of the primary lesion.

Nevertheless, it would be wrong to believe that we can now forge ahead with chemotherapy: advance will come only from carefully planning adequate clinical trials. Unfortunately, we have few hard facts about the chemotherapy of the bladder cancer other than a general impression that it is a difficult tumour to treat. Trials in patients with T4 lesions have helped in finding active drugs for combination chemotherapy—and the advantages of even temporary regression certainly outweigh the disadvantages for the patients in such trials. Bladder cancer poses special problems, with drug toxicity added to the metabolic disturbances of the surgical and radiotherapeutic treatment of the primary tumours. An estimate of toxicity is a vital prerequisite to any adjuvant trial. Only when we know this can we begin randomised clinical trials in T2/T3 bladder cancer.

Over 30 chemotherapeutic agents are available to be evaluated, and this task requires co-operation by large clinical groups. Such an approach has already been made by the US National Cancer Institute, the European Organisation for Research on the Treatment of Cancer, and here in Britain the Yorkshire Urological Cancer Research Group. Some progress has been made. In 1975 only three drugs—adriamycin, 5-fluorouracil, and mitomycin C—were known to have shown significant activity in bladder cancer.[13] Since then the Yorkshire group has confirmed[14] the value of the combination of adriamycin and 5-FU, and more recently VM26, bleomycin, cyclophosphamide and methotrexate have been added to the lists of drugs active against bladder cancer.[15-17] Attention is now focused on cis-dichlorodiamine platinum,[18 19] which is an active drug but is highly nephrotoxic.

If the clinical trials are to be adequately designed and co-ordinated the first step must be agreement among different centres on the criteria of response. Many patients are going to be needed for each study, and that means co-operation on a national or international basis. Furthermore, those responsible for managing trials need to ensure a free exchange of intentions and results on a worldwide basis, so avoiding unnecessary reduplication of effort and the fruitless exploration of the same blind alleys.

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Dopamine in cardiac failure and shock

Two factors have limited the value of sympathomimetic amines in treating circulatory disturbances: firstly, their lack of specificity, and, secondly, the consequent high rate of unwanted side effects. Noradrenaline causes peripheral vasoconstriction, whereas isoprenaline increases the heart rate and may predispose to impaired coronary perfusion, increased myocardial ischaemia, and arrhythmias.[1] Dopamine is a less familiar, endogenous catecholamine which is an immediate precursor in the synthesis of noradrenaline,[2] and its therapeutic value is a matter of current concern. In man dopamine infusion increases myocardial contractility and cardiac output by a direct action and also indirectly by releasing endogenous noradrenaline.[3] It increases renal blood flow, the glomerular filtration rate, and sodium excretion, and it also causes vasodilatation of the mesenteric vessels.[4 5] At higher doses dopamine may have a vasoconstrictor effect due to alpha-adrenergic stimulation; this is associated with an increase in arterial blood pressure and peripheral resistance.[6] The effects of dopamine on coronary blood flow and myocardial oxygen utilisation are also influenced by dosage and by its several haemodynamic actions, and for that reason its use requires caution, especially in patients with ischaemic heart disease.[4]

The action of dopamine in increasing cardiac output and in redistributing visceral blood flow has led to its use in treating severe refractory cardiac failure and shock. Unfortunately there are real difficulties in mounting satisfactory controlled clinical studies in patients with these conditions: as well as problems over patient selection, comparisons are complicated by the inevitable continuous changes in haemodynamics and concomitant drug treatment and by the need for carefully titrating infusions against response.

In patients with severe congestive cardiac failure dopamine infusion improves indices of myocardial function, such as the cardiac index, total pulmonary resistance, mean aortic pressure, and left ventricular tension/time index.[1 7] But we have no conclusive evidence that in such patients either dopamine or dobutamine[1 8] (a synthetic analogue of dopamine) improves survival beyond what can be achieved by traditional methods: bed rest, diuretics, and the careful use of digoxin. Nevertheless, individual patients may benefit from prolonged dopamine infusion, and some patients with acute and chronic cardiac