shown congestion in various organs, suggesting death from congestive heart failure. L1 and its iron complex are not mutagenic and do not increase the growth of yersinia in vitro.³

Toxic side effects observed during multicentre clinical trials with L1 in over 200 patients known to have mainly thalassaemia and other volunteers in the United Kingdom, India, Switzerland, Canada, the Netherlands, Italy, and Czechoslovakia include transient episodes of agranulocytosis in two patients; musculoskeletal and joint pains in 19 patients; one fatal incident with a patient who developed a lupus-like syndrome; gastric intolerance in 12; and an increased requirement for transfusions of red cells in a patient who had not had a splenectomy.^{3 6 10} A more detailed report on the efficacy and toxicity of L1 and other chelators in humans is given elsewhere.¹¹

The prospect of identifying the few people who may be susceptible to L1 requires further attention. Such screening has been suggested for other drugs—for example, screening for the production of sulphoxide in patients treated with penicillamine. Other measures might include withdrawing L1 during acute inflammation and infection—both of which activate neutrophils and monocytes¹²—and introducing protocols of low doses given often. Toxicity long term and not efficacy is the major issue that needs to be addressed with L1 now and possibly other related oral chelators in the near future. Formal long term studies of toxicity in animals and clinical trials will possibly be required before all patients switch from desferrioxamine to L1 or some other oral chelator. Such studies, however, are expensive and may never be supported by pharmaceutical companies because of the

classification of L1 and related chelators in the “orphan drugs” category.

The potentially life saving benefits of treatment with L1 in patients loaded with iron who are not adequately treated with desferrioxamine may outweigh the risks of its possible toxicity, and its introduction in such patients may now be appropriate.

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Camelford revisited

Still not the last word

The Cornish town of Camelford is again in the news. In July 1988, 20 tonnes of concentrated aluminium sulphate was accidentally discharged into a local reservoir. Drinking water was heavily polluted for up to three days, not only by the primary contaminants but also by copper, zinc, and lead dissolved from domestic plumbing. The acute effects on the town's inhabitants included gastrointestinal disturbances and oral ulceration.

In response to persistent public concern, in January 1989 the government appointed an independent group of experts to advise on the possible long term consequences of the episode. The advisory group, chaired by Dame Barbara Clayton, reported in July 1989.¹ While conceding uncertainties, it concluded that long term toxic effects were unlikely on the basis of current knowledge. It did, however, support the collection of further information—for example, on outcomes of pregnancy—as well as making recommendations about the handling of any similar incidents in future.

Despite the advisory group's reassuring conclusion public anxiety was not allayed. Furthermore, new information emerged which suggested that people living in Camelford at the time of the accident had persistent symptoms and clinicopathological abnormalities. In particular, there were reports of raised serum aluminium concentrations several months after the incident, of sensitivity to aluminium in some people, of a high prevalence of perceived difficulties with memory, and of abnormalities on neuropsychological testing. The advisory group was therefore reconvened to examine the

fresh evidence, and its second report was published two weeks ago.²

Like the first, the report is carefully considered and clearly reasoned, and it again concludes that long term toxicity is unlikely. The limitations of the new data are discussed. For example, much of the information derives from self selected and highly unrepresentative samples or is inadequately controlled. The advisory group accepts that the accident has led to real mental and physical suffering but suggests that the excess of reported symptoms may be attributable to anxiety and heightened awareness rather than a direct toxic effect. There are specific recommendations for further research but not for the large scale epidemiological survey that some have advocated. This conclusion is unlikely to satisfy those who believe that the community has been seriously poisoned.

The task of the advisory group was always going to be difficult. In some ways its situation is similar to that which clinicians face when presented with an anxious patient whose symptoms seem after routine investigation to signify nothing sinister. How far should one go in trying to exclude improbable diagnoses before offering reassurance? Prolonged investigation may throw up spurious abnormalities that increase the patient's conviction of major pathology. On the other hand, just occasionally there will indeed be serious underlying disease.

Epidemiological investigation of the alleged health effects is far from straightforward. There is no reliable way of measuring exposure to the contaminated water retrospectively.

Studies must therefore compare people living in the area supplied by the polluted reservoir with controls from elsewhere. But people who drank the contaminated water are aware of their exposure, and this could bias comparisons based on subjective end points such as reported symptoms and performance in certain neuropsychological tests. Objective indicators that would unambiguously measure the postulated toxic effects are not readily available.

As usual when studies have been carried out by less than ideal methods, scientists disagree on their interpretation. Such differences do not help the credibility of the advisory group. Just as patients seeking a diagnosis may visit several doctors until they get the answer they want, so people will seize on the opinion that best fits their view. Moreover, patently misleading advice given out by the water authority at the time of the accident has promoted a distrust of official pronouncements. Despite the independence of its members the advisory group has been unfairly perceived as an organ of the establishment brought in to carry out a whitewash. Public

anxieties have been further provoked by journalists seeking to generate controversy rather than present a balanced overview.

The latest report is a fair evaluation of the evidence now available, but it will not be the last word. The new studies recommended by the advisory group will require evaluation, and further information—for example, on the absorption and metabolism of aluminium—may emerge from other sources. Meanwhile, I have every sympathy with the residents of Camelford who continue to suffer from distressing symptoms and whose anxieties cannot at the moment be satisfactorily resolved.

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Bile duct stones and laparoscopic cholecystectomy

Selective intraoperative cholangiography is the best strategy

Laparoscopic cholecystectomy is now the best operation for patients with symptomatic gall bladder stones,^{1,4} and many surgeons use it in over 90% of patients.^{4,9} Patients with gall bladder stones may also have stones in the bile duct, but controversy exists over the best way of identifying such stones and then removing them.^{10,11}

Ductal stones are reported less commonly in patients undergoing laparoscopic cholecystectomy (<2%)^{8,9} than in those undergoing open cholecystectomy (13-20%),^{12,13} which suggests that stones are being missed. Operative cholangiography is technically more difficult during laparoscopic cholecystectomy than during open operation, and, although success rates of 90% have been achieved,^{6,14} most authors report rates below 50% with technical failure rates of 10-25%.^{4,8,9}

Some ductal stones will be identified on initial ultrasound scanning, but this is an insensitive technique.^{12,15,16} For the remaining patients a policy of selective cholangiography is well supported by many studies of open cholecystectomy.¹⁷⁻¹⁹ The criteria for selecting patients for cholangiography (history of jaundice, raised serum alkaline phosphatase or bilirubin values, bile duct diameter >10 mm) are reliable, with low rates of undetected ductal stones (0-3%), a reduced risk of false positive findings on cholangiography, and reduced cost.²⁰⁻²² The diameter of the bile duct, previously assessed at open operation, may be easily measured before operation by ultrasound scanning. There is no direct evidence that the increased incidence of injury to the bile duct associated with laparoscopic cholecystectomy^{4,7} would be reduced by routine cholangiography.

Preoperative cholangiography shows the ductal anatomy and identifies those ductal stones that may be difficult to remove endoscopically (because of their size or because of a distal bile duct stricture). Intravenous cholangiography is least invasive and has a high sensitivity for ductal stones.^{16,23} Its selective use minimises the risk of hypersensitivity.²⁴ Preoperative identification of bile duct stones allows either an attempt at endoscopic treatment or a decision to opt for open operation. Screening by endoscopic cholangiography is not

recommended as it subjects 85-90% of patients to non-therapeutic endoscopic retrograde cholangiopancreatography^{19,22} with its own small morbidity²⁵ and also results in a substantial additional cost and endoscopic workload.

Intraoperative cholangiography avoids the need for preoperative cholangiography and results in minimal morbidity,¹⁴ but the identification of bile duct stones during laparoscopic cholecystectomy raises the problem of how best to proceed. If the stones look as though they may be difficult to remove endoscopically the surgeon should convert to open exploration of the bile duct. In other cases the decision may be difficult but should be based on the estimated risks of alternative strategies. By the time the surgeon has reached the stage of performing operative cholangiography, however, he or she is under considerable psychological pressure not to convert to an open procedure.

Laparoscopic exploration of the common bile duct is currently performed in only a few centres. For most surgeons performing laparoscopic cholecystectomy the choice of treatment for patients with stones in both the gall bladder and the bile duct is either an open operation or laparoscopic cholecystectomy preceded or followed by endoscopic removal of the ductal stones. Exploring the bile duct during open cholecystectomy seems to add little to the risk of death in patients at low risk from surgery (less than 1% aged under 60), but it does increase mortality in patients aged over 60 (2.6-4.7%).²⁶⁻²⁸ Though the mortality (0.8-2%), morbidity (7-8%), and duct clearance rates (86-93%) associated with endoscopic treatment are comparable with those associated with open exploration of the bile duct, the endoscopic complications are largely independent of age.^{25,29,30} Thus patients at low risk from surgery who undergo laparoscopic cholecystectomy and endoscopic treatment of duct stones may suffer greater morbidity and mortality than they would if they underwent open operation.³¹

For clinical and economic reasons a policy of selective intraoperative cholangiography with postoperative intra-venous cholangiography for the technical failures is recommended. If preoperative cholangiography is performed the