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Prevention of mumps

"Mumps is a preventable disease. Why should any child have it?" asked an American speaker at a conference ten years ago.[1] In the United States a live attenuated mumps vaccine (Jeryl Lynn strain) has been available since 1967 and over 40 million doses have been distributed.[2] Singly or combined with live measles and/or rubella vaccine, it produces satisfactory seroconversion.[3] Clinical reactions are negligible,[4] and protection may persist for up to 12 years.[2] In the United States mumps/measles/rubella vaccine is now given routinely to children of both sexes at the age of 15 months.

The notification of mumps is not uniform in the United States but in Massachusetts a mumps vaccination campaign starting in 1969 was followed by a 99% reduction in cases.[5] In Seattle-King County, Washington, increased vaccination of preschool and school children in 1976 was followed by the lowest incidence of mumps ever recorded in children aged 5-9.[6] The overall incidence of mumps in the United States is now said to have been cut by 90%.[5] Mumps vaccine is recommended by the US Immunisation Practices Advisory Committee for all susceptible children, adolescents, and adults in the absence of contraindications[2]—and susceptibility is assumed unless a doctor has diagnosed mumps or there is laboratory evidence of immunity.

Should mumps vaccine be used in Britain? A monovalent mumps vaccine of the same strain has been available since 1971, but combinations with other vaccines are not, though these are licensed and could be obtained from the United States. Mumps is not notifiable in Britain and neither its incidence nor its infectivity is known, since up to 40% of cases are asymptomatic.[7] Deaths are few; 48 were reported between 1968 and 1978,[8 9] 28 in patients aged over 64. Complications include meningitis (usually mild and self-limiting); orchitis in about a fifth of boys after puberty; and encephalitis, which, though less common with mumps than with other common virus diseases, may have a severe prognosis.[7]

In a retrospective study of 2482 cases of mumps admitted to hospital between 1958 and 1969, half were aged 15 or more.[10] The central nervous system was affected in 22% of cases, but the only permanent damage was eighth-nerve deafness in five patients, four of them adults. One in four of the male patients developed orchitis, but there were no recorded sequelae. This study concluded that mumps was relatively benign and that vaccination of the whole population did not seem warranted.

So again we may ask: is the introduction of yet another vaccine in infancy justifiable? A combination product might be the answer. Measles vaccine is now routinely offered —though not routinely accepted—at 15 months, and could be combined with mumps vaccine. Would the half of parents who currently accept measles vaccine also accept the combination, or might it prove more popular? The combined vaccine could also be offered at school entry to those with no history of infection. Ideally, susceptible adults should be identified and vaccinated, but though screening by radial haemolysis is cheap, quick, and reliable[11] it is not realistic as a routine. Another possible use of the vaccine would be to protect the individual after exposure, since mumps hyperimmune gammaglobulin neither reduces the attack rate nor prevents complications.[12] Whether the vaccine is effective in these circumstances is, however, doubtful,[13 14] partly because the wild virus is excreted for some days before symptoms appear, making the time of exposure uncertain.[7] Finally, vaccination would be of value for groups of susceptible adults in confined conditions, such as military servicemen.

What would be the effect of offering combined measles/mumps vaccine at 15 months? Unless the ill-founded[15–17] but commonly held dread of sterility from mumps orchitis overcomes the British distrust of new vaccines the acceptance rate would almost certainly be low. Nevertheless, the effect might be enough to modify the pattern of the disease and so increase the number of susceptible adults. In the United States, where vaccine acceptance is high, a slight upward trend in age distribution has already been observed.[18] For the seronegative individual the vaccine might be a boon. For the general population it might be the reverse, since the pattern of natural infection resulting in a current 95% of immune adults[10] would be altered. The disease, though painful, is rarely dangerous at present. To attempt its prevention on a mass scale might well increase its incidence in adults with all the troubles and risks which that implies.

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Chasing the unknown primary

ACUP is not a Cockney version of hiccup, nor even a close relative: it is yet another oncological abbreviation which describes a common clinical problem—adenocarcinoma from an unknown primary site. The approach to management of a patient who so presents varies widely according to the accompanying clinical clues—and also to the physician's attitude and experience. Some prefer simple symptomatic treatment, while others opt for vigorous investigation up to and including surgical assault. The negative prognostic implications of the first approach (adenocarcinomas are incurable, so keep the patient comfortable) can be defended more easily if the histological findings are unequivocal, tests for markers for tumours of the prostate and testis are negative, and examination of the breast and pelvis has shown no abnormalities. Systemic treatment is warranted for lymphomas, which may masquerade as adenocarcinomas, and for carcinomas of the prostate, testis, breast, and ovary. Treatment with hormones and cytotoxic drugs has a high chance of shrinking the tumour; survival is usually prolonged in patients who show a response. On the other hand, these are all tumours that are uncommon in most series of ACUP.[1-3] Much more likely primaries are carcinomas of the pancreas, lung, colon, and liver, all of which stubbornly resist the attentions of physicians, surgeons, and radiotherapists.

This poor prognosis is the first reason why the zealous hunt for the site of an elusive primary may not always be in the patient's interest. The second reason is that the search is so often inconclusive. A recent large series of 266 patients with unidentified adenocarcinomas had a battery of tests, including chest radiography, skeletal survey, intravenous pyelography, barium meal and enema, sigmoidoscopy, liver scan, and multichannel biochemical analysis of plasma and urine.[4] One hundred and thirty of them were further investigated post mortem. In 23 cases the primary site was not found even at necropsy. In only 22 cases was an antemortem diagnosis proved correct at necropsy, while in 25 cases it was proved wrong. In other words, this plethora of investigations gave a correct result in only a small minority of cases. Logically, therefore, the search should be drastically limited. What seems reasonable is to try to exclude the cancers mentioned above with careful clinical examination; to take a further look at the histological appearance (including immunoperoxidase and other special stains); to measure serum α-fetoprotein and human chorionic gonadotrophin concentrations and acid phosphatase activity; and perhaps mammography and ultrasound examination of the pelvis.

Most patients with ACUP have tumours resistant to conventional treatment. One early study of their clinical course showed that the median survival was around three months.[3]

A recent report from the same institute has described the outcome of blind blanket cytotoxic treatment in patients with ACUP.[5] Two regimens were compared in a random fashion and, surprisingly, one resulted in some encouraging responses. Nine out of 25 patients receiving doxorubicin together with mitomycin responded, and three remain alive and well over a year later. Non-responding patients, including all but one of 22 who were given cyclophosphamide, methotrexate, and 5-fluorouracil, had a median survival of 13 weeks. Possibly the drugs in the first combination might be applied more widely—with the proviso that they are discontinued promptly if no response is seen within two months or so, so avoiding prolonged toxicity. A trial of such an approach compared with symptomatic measures would be the best way to prove its real benefit.

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Centrally acting drugs in chronic airways obstruction

Any drug that affects the central nervous system may influence the respiratory centre. In most cases this is incidental to the main action, and for bronchodilators such as salbutamol[1] and aminophylline[2] is a bonus as these drugs stimulate respiratory drive. On occasion, however, drugs are given specifically for their central effect on respiration: for example, amylobarbitone sodium has been used to suppress the ventilatory disturbance associated with anxiety,[3] and progesterone is an effective central respiratory stimulant for treating the obesity-hypoventilation syndrome.[4] Nevertheless, many patients with chronically