Vaccine Against Mumps

Mumps is a common infectious disease of childhood and adolescence, and as the alternative name, epidemic parotitis, implies it has a predilection for the parotid and other salivary glands. When these are affected alone little harm comes to the patient, but mumps is a generalized infection as a result of which other organs may be damaged, notably the brain, testes, pancreas, and ovaries. Infection of these organs carries a greater risk to the patient's health and life than uncomplicated mumps. Consequently there is justification for specific prophylaxis.

Passive immunization with convalescent serum, pooled gamma-globulin, and convalescent immune globulin has been tried at various times without any clearcut evidence of efficacy. It has been reported that the incidence of orchitis\(^1\) can be reduced two- to threefold by the use of convalescent immune globulin, but even such a limited protective effect is offset by the fact that protection is only temporary. Killed virus vaccines have been used with some evidence of a reduction in the attack rate, but again immunity appears to be brief.\(^2\)

More recently virologists have been turning their attention to the development of a live virus vaccine in the hope that a more effective and durable immunity would result. Reports from a recent conference in Washington\(^3\) indicate that considerable progress has been made in the past few years, both in the United States\(^4\) and in the Soviet Union.\(^5\)

From the United States comes a series of reports from investigators at the department of pediatrics in the University of Pennsylvania and virologists from the Merck Institute for Therapeutic Research on a live attenuated vaccine prepared in chick-embryo tissues.\(^6\) The vaccine was developed from a strain of virus attenuated by passage in embryonated hens' eggs and chick-embryo tissue culture derived from leukosis-free flocks, and was subjected to safety requirements at present in use for live measles vaccine.\(^6\) Two vaccines were tested in children aged 1 to 10 years (average 5 years)—one obtained at the 12th passage ("A level") and the other at the 17th passage ("B level").\(^6\) Both were prepared in freeze-dried form and administered by subcutaneous injection. Of 16 children without detectable mumps antibody given the A level vaccine four developed a parotid swelling, and three were found to be excreting virus in the throat between the 10th and 14th days. All 16 showed a rise in mumps antibody. None of the 32 uninoculated susceptible control children in contact with the vaccinees developed mumps antibody. In a further series of tests 14 seronegative children were given the further attenuated B level vaccine. None showed any sign of mumps infection or excreted virus, and all developed antibody. In this series the incidence of febrile reactions was no greater than in the controls and certainly less than with the A level vaccine. Further studies with varying dilutions of the B level vaccine regularly produced mumps antibody in susceptible children even when the virus was diluted 10 to 100 times. These tests indicated that the B level vaccine was suitable for further investigation.
The same investigators have now carried the story a stage further by observing the effect of the vaccines on children in families and classroom groups. Altogether 1,337 children, whose ages ranged from 1 to 11 years (average 3.6 years) were included in the study. Of these, 482 had a negative history of mumps and 362 were found to be without antibody. Thus the parents’ negative history given by the parents was accurate in 75% of cases. Three hundred and fifty-nine of the 362 susceptible children developed an immune response after inoculation of 1 ml. of the freeze-dried vaccine—a sero-conversion rate of 98%. None of the 500 uninoculated control children in contact with the vaccinated children in the family or classroom groups showed evidence of mumps or developed mumps antibody. No excess of reactions was noted between the inoculated groups and the controls, and no interference with the response to mumps vaccine was detected in children who were also administered a killed polyvalent respiratory virus vaccine. The antibody levels after the mumps vaccine were considerably lower than those usually encountered after natural mumps. Nevertheless, from the experience with attenuated measles vaccine this is to be expected, and the low levels may still be protective. It was found that the serum neutralization test was more specific and sensitive for detecting low levels of antibody than was the haemagglutination-inhibition test.9

Soon after these studies had been completed a chance arose to evaluate the protective effect of the vaccine. Mumps, which had been endemic at the time of the first trial, became epidemic a few months later. One hundred vaccinated and 100 unvaccinated children at risk to natural mumps were observed. The overall attack-rate among the control group was 61%, in contrast to 2% in the vaccinated children, the protective effect being 97%.10 If the clinically diagnosed cases are included with the virologically proved cases of mumps in the families and classrooms, the overall protective effect was 98%.

Experience with live mumps vaccine in the Soviet Union extends over several years. More than one million children have now received a lyophilized vaccine also prepared in chick embryo fibroblasts. The reduction in morbidity has been 10%. A. A. Smorodintsev12 recommends that as a result of waning immunity revaccination would be necessary after four to five years.

These reports are encouraging, but it is too early to say how long protection from such a vaccine will last. From the analogy with measles vaccine—and there are many points of similarity between these two vaccines not only in the method of their development but in the immune responses they evoke—there is every hope that immunity will be of long duration. If not, it can be reinforced by further immunization.

What is the need for a mumps vaccine? This is a more difficult question to answer. In the past few years amazing progress has been made in the development of viral vaccines, and before long nearly all the common infectious diseases will be preventable by immunization. Measles vaccine is already being widely used in the United States, and the incidence of the disease there is the lowest on record for many years. Preliminary data indicate that mumps vaccine appears to be safe and protective, and there are good prospects that a vaccine against rubella will be developed in due course. Each disease presents its own special problems, and the development of a safe and effective vaccine must be considered in relation to the need for a vaccine, the age of immunization, and the extent to which this should be carried out, and more especially the safety of a vaccine in relation to the cell substrate in which the virus is propagated. In this connexion the choice of chick embryo tissue as the source for the mumps vaccine would appear to be a distinct advantage in view of the knowledge already gained about the safety of such vaccines from experience with live measles vaccine.

Mumps is a relatively benign disease in children, but it is a considerable nuisance, particularly from time lost at school. The importance of complications is more difficult to assess. Infections of the central nervous system occur in mumps more often than in any other infectious disease, but rarely are they serious. Cranial nerve palsies, transverse myelitis, and occasionally death from demyelinating encephalitis have been reported, but these are rare. The commonest neurological complication is aseptic meningitis, which carries a good prognosis. Deafness also follows mumps; it is uncommon but can be severe. Orchitis is a common complication and is supposed to lead to sterility, but the risks of this are not great because most cases of mumps orchitis are unilateral. Other complications such as pancreatitis followed by diabetes and myocarditis have been reported, but they too are rare in relation to the frequency of mumps infection. The only method of preventing complications in either children or adults is by immunization, preferably carried out in childhood. The preliminary results are distinctly encouraging, but there is no obvious need immediately for mass immunization with a view to eradication of the disease. It will be necessary to feel our way with further studies on duration of immunity. A mumps vaccine might be useful for groups of people at special risk such as in the armed Forces and in an outbreak. A further interesting development in this field comes in a report from the U.S.S.R.13 of preliminary results of a combined attenuated vaccine against measles and mumps.

Isoniazid and Cancer

Isoniazid, first used clinically in 1951, has proved a major therapeutic success. It is generally regarded as the most active and least toxic of the antituberculosis drugs. It is also cheap. Its usefulness in the control of what is still a formidable killing disease in many parts of the world is unsurpassed. But just because the drug is so exceptionally effective and so widely used it is specially important to evaluate laboratory reports which seem to cast doubt on its safety. Many investigators have shown that oral or parenteral administration of isoniazid results in the appearance of tumours of the lung, predominantly adenomas, in certain strains of mice. While results in other strains of mice and in other animals have been negative,14 the evidence that the drug can induce lung tumours in mice appears conclusive. It poses the question of how far, if at all, this finding is relevant to the use of...