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accept second best and opt for the cheaper natural surrogacy, which at present is almost a do it yourself procedure, requiring no medical intervention.

An ideal solution?

It would be ideal to monitor all forms of surrogacy through the provision of treatment by a few, well chosen, licensed in vitro fertilisation units, covering all regions of the country. An all inclusive fee could include counselling and medical screening. Couples requiring surrogacy could pay a fee to register. Potential surrogates would register too, but for no charge, and be carefully matched to the couple. All expenses incurred by the surrogate mother would be paid out of administrative funds held by the clinic, from the couple's registration fee. We could adopt the professionalism of the surrogate agencies in the United States, but not the commercialism.

The only drawback would be the cost. Infertile couples are ordinary people from all walks of life. Many cannot afford to pay their surrogate mother's expenses, let alone the cost of in vitro fertilisation or artificial insemination procedures in a clinic. Straight surrogacy arrangements go surprisingly well despite the huge hazards attached. I believe infertile couples should have the choice. They can go through a clinic and meet all the protocols imposed and feel safe in the clinicians' hands. Other couples may prefer to take matters into their own hands and feel that they are back in control. They can proceed in their own time, with artificial inseminations taking place in the more intimate surroundings of their own homes or the home of their surrogate mother.

Whichever method they choose, the benefits experienced by all parties after the successful birth and handover of a long awaited surrogate baby are immeasurable.

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Recommendations for using MMR vaccine in children allergic to eggs

G A Khakoo, G Lack

The measles virus used in the MMR (measles, mumps, rubella) and single measles vaccine is grown in cultures of fibroblasts from chick embryos, and there have been concerns raised about the possible presence of egg protein in the vaccines and the advisability of administration to individuals who are allergic to eggs. We review the evidence for egg as the agent responsible for allergic reactions to MMR or measles vaccine and propose recommendations based on the evidence. The arguments presented also apply to the single mumps vaccine and all other vaccines derived from egg. The recommendations presented have been reviewed and endorsed by the Committee on Infection and Immunisation of the Royal College of Paediatrics and Child Health, and the British Society of Allergy and Clinical Immunology.

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Summary points

The majority of life threatening (cardiorespiratory) allergic reactions to MMR vaccine have been reported in children who are not allergic to eggs; these are more likely to be explained by the gelatin or neomycin contained in the vaccine than the ovalbumin

MMR vaccine is as safe as any other vaccine, and an allergy to eggs should not delay measles vaccination

The only children who need to be vaccinated in hospital are those with an allergy to eggs in whom previous exposure led to cardiorespiratory reactions and those with coexisting active, chronic asthma

Children with milder forms of allergy to eggs can be safely vaccinated without additional precautions

Any child experiencing an acute allergic reaction to MMR vaccine must have the reaction clearly defined and be evaluated for other allergies

Methods

References were found by performing a Medline search (for the years 1966-99), which identified 51 references, and by searching issue 3 of the 1999 *Cochrane Library*, which identified no references. We also reviewed the reference list of each study identified. Thirty four of the studies identified by the Medline search were relevant; they reported either allergic reactions to MMR or measles vaccine in individuals who were allergic to eggs or reactions in those who were not or examined the components of the vaccine that have the potential to cause an allergic reaction. None of the studies could be classed as meeting the criteria for category I-III evidence since they consisted of reports of isolated or consecutive cases; however there were reports from respected authorities and expert committees (category IV evidence).[1]

Current recommendations

In the United Kingdom immunisation guidelines recommend that all children, except those in whom there is a contraindication, should receive two doses of MMR vaccine: the first shortly after their first birthday and the second before starting school.[2] The uptake rates

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for the vaccine are 90% for the first dose and less than 50% for the second dose.[3 4] Using annual data on live births and a conservative estimate of a 1% prevalence rate of allergy to eggs in early childhood, we calculated that in England and Wales at least 5760 vaccinations against measles, mumps, and rubella are administered to children aged between 1 and 2 years who are allergic to eggs.[5–7] Figures for preschool children are lower because vaccine uptake rates are lower, and many children will have outgrown their allergy to eggs. Between 10% and 25% of these children will have had severe cardiorespiratory reactions to eggs.[8 9]

The 1996 edition of *Immunisation Against Infectious Disease* states that "over 99% of children who are allergic to eggs can safely receive MMR vaccine. Dislike of egg, or refusal to eat it, is not a contraindication. If there is concern, paediatric advice should be sought with a view to immunisation under controlled conditions such as admission to hospital as a day case."[2] In 1997, the advice from the Health Education Authority was that "if a child has had a serious reaction when eating eggs, or food containing egg, then the parent should talk to their doctor about making special arrangements for the child's immunisation. This can usually be done as a day-case at the Paediatric Department of the local hospital."[10] The definition of a serious reaction is not provided nor are the specific precautions for vaccinating these patients defined. This has resulted in inconsistent and widely differing practices, and the inevitable caution exercised has led to inappropriate admissions and unnecessary intravenous cannulation. A lack of focus on the individuals who are at greatest risk may lead to inadequate supervision of them.

The guidelines from the American Academy of Paediatrics and the Canadian National Advisory Committee on Immunisation are in broad agreement with those in the United Kingdom and provide no further clarification about individuals who may be at risk.[11 12]

Constituents that may cause allergic reactions

Many different preparations of the measles vaccine are available, all containing small amounts, at most, of the egg protein ovalbumin. Several analyses of MMR II (Pasteur Mérieux MSD, Maidenhead), one of the two MMR vaccines used in the United Kingdom, have found that it contains none, picogram quantities, or 0.5-1 ng of ovalbumin per 0.5 ml dose.[13–15] These discrepancies may reflect either a lack of standardisation between batches of the vaccine or the different methods used to measure the egg protein. In most double blind, placebo controlled food challenges the minimum oral doses that elicit objective reactions are between 50 mg and 100 mg, although they can occasionally be as low as 2 mg.[16] Therefore, the amount of ovalbumin in the vaccine seems to be far too small to cause an allergic reaction in the majority of individuals even considering the parenteral route of exposure.

There are, however, other potential allergens in measles vaccine. Each 0.5 ml of MMR II also contains 14.5 mg of gelatin and 25 μg of neomycin[17]; both agents are known to cause severe allergic reactions and are present in larger doses than ovalbumin.[18–20]

Evidence that egg causes allergic reactions

Since 1963 there have been numerous published reports looking at the incidence of allergic reactions to MMR or measles vaccine occurring in a total of 1803 children allergic to eggs.[9 14 15 21–38] There have also been reports of allergic reactions occurring in children who were not allergic to eggs.[14 21 22 39–46] Many of these are selected case reports of reactions. The only population based study of type I hypersensitivity reactions occurring after vaccination is by Kalet et al.[46] This study found that five allergic reactions occurred during the administration of 2789 doses of MMR vaccine, although two children had had other vaccinations at the same time. Whether the children were allergic to eggs was not assessed.

The largest reported series of consecutive patients allergic to eggs who received MMR or measles vaccine involved 500, 410, and 140 children.[14 24 27] No severe cardiorespiratory reactions were reported. The literature probably has a bias towards the reporting of severe reactions; there are only 14 reported cases of mild reactions (erythema, wheal or induration at the injection site, puffy eyes, facial swelling, perioral and localised urticaria, flushing, and vomiting) after measles vaccination both in children allergic to eggs and in children not allergic to eggs. The table summarises reports of systemic allergic reactions including both severe cardiorespiratory reactions and non-severe (generalised urticarial) reactions. In all 10 of the cases in which cardiorespiratory reactions to vaccination occurred, the clinical criteria for defining allergy to eggs was weak. Not all children had skin testing or specific IgE testing. Furthermore, neither open nor double blind food challenges were used in any child to confirm the presence of an allergy to eggs.

There was evidence of a coexisting allergy to gelatin in 5 of the 10 children who were allergic to eggs and who had severe cardiorespiratory reactions to MMR vaccine; whether this allergy coexisted in the other five children was not assessed. Seven children who were allergic to gelatin but were not allergic to eggs have been reported to have had severe allergic reactions after being vaccinated against measles.[22 39 45] One case

Systemic reactions to MMR or measles vaccine in children who are allergic and children who are not allergic to eggs. Most studies were isolated case reports or consecutive case series

Study	No of children with systemic reaction: Cardiorespiratory	No of children with systemic reaction: Generalised urticaria	Presence of egg allergy	Presence of gelatin allergy
Reactions in children allergic to egg				
Sakaguchi et al[22]	5	0	5	5
Herman et al,[15] Baxter,[23] Puvvada et al,[25] Trotter et al,[28] Lavi et al,[9] Freigang et al,[24] Horner et al[26]	5*	6†	11	NA
Reactions in children not allergic to egg				
Sakaguchi et al,[22] Kelso et al,[39] Kumagai et al[45]	7	0	0/3	7
Fasano et al,[14] Pollock et al,[40] Aukrust et al,[41] Van Asperen et al,[42] McEwen,[43] Thurston,[44] Kalet et al[46]	36	1	0/8	NA

NA=not assessed.
*Two reactions occurred after full dose of the vaccine administered and three occurred during graded vaccination (desensitisation) or skin testing.
†One reaction occurred after full dose of the vaccine administered; five occurred during graded vaccination (desensitisation) or skin testing.

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of a possible allergy to neomycin has been reported in a patient receiving MMR vaccine.[18] Another 36 children have been reported to have had cardiorespiratory reactions to MMR or measles vaccine; of these, eight had no evidence of being allergic to eggs and it was not determined whether the remaining 28 were allergic to eggs.[14 40–44 46]

Although these figures do not reflect true incidence rates in the general population, the larger number of severe reactions to MMR or measles vaccine occurring in children who were not allergic to eggs and in children who were allergic to gelatin suggests that predicting which children are at risk of having an allergic reaction is difficult because reactions are not limited to those who are allergic to eggs.[47]

Predicting and preventing allergic reactions

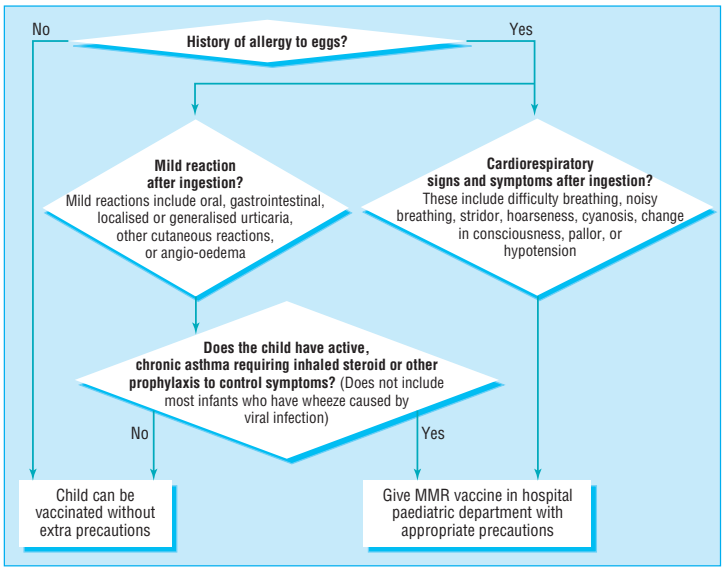
For 3 of the 10 children who had severe reactions after being vaccinated, adequate clinical details are given of the child's allergy to eggs. All three children had a history of exposure to eggs leading to a life threatening reaction or they also had asthma. This supports reports that coexisting asthma is a risk factor for anaphylaxis.[14 48]

Skin prick and intradermal testing have been used to try to predict allergic reactions to measles vaccinations. There have also been attempts to "desensitise" children to the vaccine using graded injections. However, there have been as many reports of adverse systemic reactions to these procedures as to the single dose vaccine (table), and these procedures have no place in the management of children who are allergic to eggs and who require vaccination against measles.[27 41 49]

Recommendations for children allergic to eggs

A case can be made for taking no special precautions when giving MMR vaccine to children who are allergic to eggs. The vast majority of children can safely be given the vaccine regardless of whether they are allergic to eggs. As with all vaccines, the Department of Health's guidelines, which advise that adrenaline (epinephrine) should be available, must be followed.[2] In administering all vaccines there are cases in which the protocol needs to be modified. In the specific case of the MMR vaccine it is advisable to take special precautions for the small subgroup of children in whom there is the remote possibility that an allergic reaction may occur. Children who have previously had life threatening reactions to foods or children who have food allergies and active, chronic asthma may be at risk for future life threatening reactions on subsequent exposure to the food.[48] Theoretically these children might also have a lower threshold for reacting to very low doses of an allergen. Although the numbers are small, our review of the literature shows that only children with a history of life threatening reactions to eggs or who have an allergy to eggs and coexisting asthma had life threatening reactions after being vaccinated against measles.

Our recommendations for vaccinating children allergic to eggs against measles, mumps, and rubella, developed in consultation with the Committee on Infection and Immunisation of the Royal College of Paediatrics and Child Health, and the British Society of Allergy and Clinical Immunology, are summarised in the figure. They represent safe practice and will allay parental anxiety. In the small subgroup of children requiring supervision in hospital, monitoring for an allergic reaction must include monitoring of cardiorespiratory values for two hours after vaccination.[50] This monitoring should be performed by a suitably qualified paediatric nurse and there should be continuous observation for the first 20 minutes after vaccination and an assessment immediately before discharge. Resuscitation facilities and an anaphylaxis management protocol must be available but routine siting of an intravenous cannula is not required.



Algorithm for administering MMR vaccine in children who are allergic to eggs

Any child who is suspected of having had an allergic reaction to MMR vaccine should have further assessments to define the timing and nature of the reaction and to evaluate the possible allergens involved in the reaction.

Conclusions

Despite the recommendations of previous guidelines, practices for the administration of MMR vaccine to children who are allergic to eggs vary across the United Kingdom. Data on the incidence of allergic reactions to the vaccine are unclear. The amount of ovalbumin in the vaccine is so small that it is highly unlikely that it would cause a serious allergic reaction in the majority of individuals. The possibility that allergens other than egg have a role in the aetiology of systemic allergic reactions to MMR or measles vaccine is supported by the larger number of these reactions reported as occurring in children who are not allergic to eggs. Only a few of the reports have looked for other potential allergens, such as neomycin and gelatin, which are present in larger quantities in the MMR vaccine and are known to cause serious reactions during measles vaccination. Skin testing for reactions to the vaccine lacks specificity and sensitivity in predicting a serious allergic response, and desensitisation is a procedure that lacks scientific rationale. Both procedures are associated with a risk of allergic reaction and should be

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abandoned. Children with a history of a cardiorespiratory reaction to eggs or who have coexisting active, chronic asthma are the only small subgroups of children allergic to eggs who require hospital supervision during vaccination against measles. The MMR vaccine is as safe as any other vaccine, and children with an allergy to eggs must not have their vaccinations delayed.

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One hundred years ago

The war in South Africa: Mr Kipling's hospital sketches

In the *Daily Mail* of May 1st and 2nd Mr. Rudyard Kipling continues his graphic sketches of the wounded in the military hospitals which he has recently visited. Incidentally he bears witness to the splendid stuff, physical and mental, of which the Colonial volunteers, who are fighting their Mother's quarrel so bravely, are made. He sees in these young men the best hopes for the future development of the land which has been "starved by policy and craft through many years lest an incompetent race should be found out before the face of the nations." We may assume, he says, that among the hospitals there are 300 Canadians of the very stamp and breed we require—young, sound, clean, intelligent, well educated, of whom 75 per cent hold or have held land. These men, he urges, should be induced to settle in South Africa. Mr. Kipling gives a vivid picture of the sufferings and hopes and fears of our wounded soldiers now lying in the hospitals of South Africa, and of the efficiency and devotion with which they are tended.

(*BMJ* 1900;i:1112.)