difference in the rate of transmission between infants fed with breast milk and those fed with formula. This is consistent with evidence from other cohort studies which indicate that most infants who acquire HCV infection do so in utero or in the peripartum period.[11 16]

The studies were all undertaken in European countries during the past 10 years. They were generally of good methodolgical quality with valid definitions of inclusion criteria and outcomes and near-complete cohort follow-up. Only one of the studies specifically examined the effect of breast feeding avoidance in mothers with HCV viraemia. Because transmission from a mother with no RNA detectable at delivery is extremely rare,[17] this may have been a confounding variable in the other studies where the HCV viral status was not assessed. We specifically aimed at evaluating the evidence in women who were not coinfected with HIV. This was possible for two studies but not for the third where 5% of participants were HIV positive. A subgroup analysis of mothers who were not infected with HIV was not possible. HIV coinfection is a contraindication to breast feeding in high-income countries.

CLINICAL BOTTOM LINE

- Approximately 6% of babies born to hepatitis C (HCV) infected mothers will develop HCV infection (grade A).
- Avoidance of breast feeding is not an effective intervention for preventing mother-to-infant transmission of HCV (grade B).

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Should children under treatment for juvenile idiopathic arthritis receive flu vaccination?

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A 12-year-old girl with rheumatoid factor negative polyarticular juvenile idiopathic arthritis (JIA) attends an outpatient appointment with her mother. Her disease has been controlled by subcutaneous methotrexate, but over the past month, she has stopped taking medication because of adverse effects—in particular, nausea and vomiting after administration of methotrexate injection. On examination, she is found to have a flare of her disease with 10 swollen inflamed joints and early morning stiffness for 2 h/day. You apply for funding for anti-tumour necrosis factor (TNF) treatment and, in the meantime, plan to treat her disease flare with a course of prednisolone. On discussion during the consultation, her mother tells you that she has had a letter from the general practitioner asking her child to attend for a flu vaccination and asks your advice.

Structured clinical questions

Do children with JIA [patient] who become infected with influenza [intervention] have a more prolonged illness [outcome] than healthy children [comparison]? In children with JIA [patient], should flu vaccinations be given [intervention] to prevent flu [outcome]? Do children with JIA respond to flu vaccination [does the vaccination have the required effect]? Does flu vaccination [intervention] cause a flare of JIA [adverse event]?

Search strategy and outcomes

Search terms used for all searches (search date 13 September 2006) were: {vaccine OR vaccination} AND {arthritis}, AND {child OR childhood OR children or juvenile} AND {influenza}.

Primary sources: Medline via Pubmed; 20 papers identified, 3 relevant. Embase: 58 articles identified, 6 relevant to vaccination but only 3 specific to influenza vaccine in JIA (table 3).

Secondary sources: Cochrane Library. Nil relevant. One review identified for influenza vaccination in healthy children (2006), but not for children immunosuppressed by disease or drugs. TRIP: 59 evidence-based articles identified, 1 relevant. Twelve guidelines were identified, 1 of which was relevant. Ten query answers, 3 e-textbooks and 1 patient information leaflet were identified, but none of these were relevant. Seventy Medline articles were identified through TRIP, but duplicated primary searches.

Commentary

Currently, there is variation in practice regarding immunisation of children with JIA owing to a lack of available published evidence.[4 5] Existing guidelines suggest that influenza may cause severe disease in patients immunocompromised by disease or drugs, and predisposes to bacterial infection.[6–9] It is therefore recommended that, each autumn, influenza vaccination should be given widely to this patient population, their family contacts and their care givers. The decision as to whether children with JIA should be vaccinated against influenza currently rests with individual doctors who balance the risk of influenza and influenza vaccination in individual patients with JIA. The present threat of an influenza pandemic,

Table 3 Influenza vaccination in patients with juvenile idiopathic arthritis

Citation	Study group	Study type	Outcome	Key results	Comments
Malleson *et al*, 1993[1]	34 patients with JIA, age 3–22 years	Prospective open-cohort study	No adverse effects except increased length of time of feeling unwell in the JIA group compared with controls	Increased number of days of feeling unwell in children with JIA ($p=0.015$) Significance lost when corrected for number of comparisons	Clearly focused study Healthy control group All patients accounted for at end of trial Follow-up complete Applicable to UK patient groups
	Active arthritis in 25/34 (74%) Prednisolone used in 7/34 (21%) and DMARD used in 9/34 (26%)	(level 4)	Increased flares after vaccine but flares easy to control	Number of flares: pre-vaccine: 4 flares/145 patient; months post-vaccine: 3 flares/34 patient months No statistical difference between mean clinical evaluation before and after vaccination	
	Compared with 13 (presumed) healthy children 1991–1992 flu season		Deterioration of JIA in 3 children after vaccine, but overall, more patients better than worse Adequate response to vaccination		**Limitations** Non-randomised Small numbers
Olson *et al*, 1994[2]	14 children with JIA, aged 5–20 years	Prospective open study: letter and abstract	Patients with JIA may have a flare of disease or adverse effects from influenza vaccination 2 patients felt they improved after vaccination	Preimmunisation and seroresponsiveness comparable in all groups No effect of prednisolone or DMARD 2/14 patients with JIA had joint pain/systemic symptoms for 7–10 days No control patients had joint pain	Control group Randomised Examiner blinded
	6 with oligo JIA, 5 poly JIA, 3 systemic onset JIA Suggests all 14 children were vaccinated, although randomisation method unclear 7 controls: 5 with asthma, and 2 siblings Abstract published in 1990	(level 4)	No significant difference in laboratory values in the two groups		**Limitations** Very small numbers No raw data shown, thus unable to analyse results Trial design unclear with poor description of methods and results
Kanakoudi-Tsakalidou *et al*, 2001[3]	70 children, aged 4–17 years	Prospective open-cohort study	No significant adverse effects identified from influenza vaccination Any effects that did occur were short lasting	5 patients (7%) reported adverse effects. 3 had local reactions and 2 systemic reactions. 9 patients had upper respiratory tract symptoms	Clearly focused Follow-up complete Applicable to UK children Discusses issues of immunosuppression and different disease types
	49 JIA 11 SLE 10 other rheumatic conditions At the time of vaccination, 17/70 had active disease	(level 4)	Influenza vaccine did not seem to affect disease activity	No patients had deterioration in disease activity, flare of disease, or change in laboratory parameters at review, 1, 3 and 6–8 months after taking vaccine Most patients developed a protective serological response to all 3 strains of influenza virus. No patients had a flu-like illness in the 6-month follow-up period	
	All children on immunosuppressants Divided into four groups according to therapeutic regimen 5 healthy children also vaccinated but did not act as a control group 1999–2000 flu season		Children with chronic rheumatic disease on immunosuppressants seem to produce a satisfactory immune response to influenza vaccine No difference between disease types and therapeutic regimens		**Limitations** No control group Not randomised or blinded Small numbers

DMARD, disease-modifying anti-rheumatic drug; JIA, juvenile idiopathic arthritis; SLE, systemic lupus erythematosus.

and government pressure on general practitioners to vaccinate against influenza in target groups, provides a good reason to review available evidence.

Complications of influenza infection that can be avoided by vaccination include bronchitis or secondary bacterial pneumonia, otitis media, and meningitis or encephalitis. An increased risk of complications is found in children with chronic illness and in those who are immunocompromised.[8] Risks of infection need to be balanced with any adverse effects of vaccination. Common adverse effects are usually mild and

short lasting, such as pain, swelling and redness at the injection site, formation of a small painless nodule, or low grade fever, shivering, headache, myalgia and arthralgia. Other rare adverse effects such as neuralgia, paraesthesia, convulsions, transient thrombocytopenia, Guillain—Barré syndrome, vasculitis and encephalomyelitis have been reported.[8] Contraindications for vaccination include a previous anaphylactic reaction to the vaccine or component of the vaccine, or a confirmed anaphylactic reaction to egg products.

Several types of influenza vaccination are available. In the UK, inactivated types are most commonly used (whole virion vaccine, subunit vaccine or split virion vaccine).[10] There is evidence that inactivated vaccines are effective in healthy adults, and vaccination between September and November is said to offer 70–80% protection for 1 year.[8] Children <13 years of age may need two doses, and there may possibly be a suboptimal response in immunocompromised patients.[10]

There are no randomised controlled trials addressing the issue of vaccination against influenza in patients with JIA. Two small prospective open-cohort studies (table 3) suggest that vaccination is safe, and that children with JIA are able to develop a protective response to vaccination equivalent to that of healthy children.[1 3] Vaccination does not seem to have a noticeable effect on disease activity. Another small study suggests that children can have short-lasting but significant adverse effects after vaccination including a flare of their arthritis, although the study methodology is poorly documented.[2] All studies occurred before 2000 and therefore do not address the issue of effect of immunosuppression with anti-TNF treatments, but there is documentation of seroconversion despite immunosuppression with other disease-modifying anti-rheumatic drugs such as methotrexate, ciclosporin and azathioprine, in addition to prednisolone.

Influenza vaccination changes each year to reflect changes in influenza strain, and hence some influenza strains may be more rheumatogenic and thereby more likely to precipitate a flare of arthritis. However, there is no evidence for this. In fact, evidence from other vaccinations, such as hepatitis B vaccination in children with JIA, suggests that children develop an adequate response without aggravation of their arthritis.[11] Evidence in adults with rheumatoid arthritis, including adults treated with anti-TNF medication, suggests that influenza vaccination is safe, effective and generates a good antibody response.[12–14]

In the absence of a large double-blind, placebo-controlled trial, it is impossible to be certain that influenza vaccination does not cause a flare of arthritis in some children. However, the current available evidence suggests that children with arthritis are not at a significantly increased risk of adverse reactions or disease flare after inactivated influenza vaccination. Children with JIA seem to be able to produce an antibody response similar to healthy children after vaccination, even when they are taking steroids or disease-modifying drugs. No children were taking anti-TNF medication, and therefore the effect of immunosuppression by these newer medicines on seroconversion after vaccination has not been addressed. However, evidence from adult studies indicates adequate seroconversion in rheumatoid arthritis. Evidence from cohort studies in healthy children suggests that inactivated vaccines have a reasonable efficacy (up to 64%) and effectiveness (57%) in children over 6 years of age.[15]

The current evidence does not indicate whether influenza vaccination is actually protective against developing symptoms of influenza illness, or whether children with JIA are more at risk of developing severe influenza infection with secondary complications. Until this is addressed, the risk:benefit ratio of influenza vaccination in patients with JIA is uncertain. However, available evidence suggests that influenza vaccination is safe in children with JIA and produces a satisfactory protective response.

CLINICAL BOTTOM LINE

- There is an increased risk of secondary bacterial infections from influenza disease in patients immunocompromised by disease or drugs (grade C).
- Flu vaccination seems to be safe in children with JIA; it is unlikely to cause a flare of disease (grade C).
- Flu vaccination may be effective in JIA; children seem to produce an adequate antibody response (grade C).
- Flu vaccination should be given in all children with JIA (grade C).

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