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Analysis and comment

Child health

Should all children be immunised against hepatitis A?

Jonathan L Temte

Is the recent US recommendation for vaccination of all children against hepatitis A one shot—or rather two shots—too many?

In October 2005, the Advisory Committee on Immunization Practices—an advisory panel to the United States Centers for Disease Control and Prevention—recommended immunisation of all children aged 12-23 months against hepatitis A.¹ This policy replaced the 1999 recommendation for targeted vaccination of children in states and communities with a consistently high prevalence of hepatitis A.²

The 1999 recommendations were effective. Coverage among children aged 24-35 months was 51% where vaccination of all children was recommended and 25% where it should be considered, compared with 1.4% for areas with no recommendation.³ Vaccination reduced the incidence of infection by 80% between 1999 and 2003.^{4 5}

Is recommending vaccination for hepatitis A in all children one immunisation too many? The answer is complex and must take into account the changing epidemiology of the virus, the complex schedule of vaccinations for children in the US, cost issues, and other diseases that can be prevented by vaccination.

A clinician's perspective

Ruby is typical of many of my new paediatric patients. She was born in the People's Republic of China and at her postadoption consultation I found it difficult to decide on the appropriate array and sequence of vaccines for her. Because of immunisation, children across much of the world (especially in the West) are now free from smallpox, diphtheria, paralytic poliomyelitis, measles, and rubella. In my practice, the last case of *Haemophilus influenzae* type B in a child occurred 14 years ago and today I rarely see chickenpox. Nevertheless, the question of sustainability arises with each new vaccine.

Changing epidemiology

The reduced incidence of hepatitis A has had some unintended consequences. The average age at infection has increased, resulting in more clinically severe infections,^{6 7} as in the 2003 outbreak in Pennsylvania, which resulted in three deaths.⁸ The reduction in

hepatitis A infections is greater in areas where vaccination is recommended for all children than in other areas.⁹

Vaccination of all children for hepatitis A will eventually protect against endemic and imported viruses (such as viruses brought in via agricultural products). Hepatitis A has devastating consequences when superimposed on chronic hepatitis C infection. About 2.7 million Americans have chronic hepatitis C infection,⁴ so reducing hepatitis A infections in children should benefit this vulnerable group. Consequently, the recommendation for immunisation for all children is probably justified.

A vast array of vaccinations

Under the current recommendations, by the age of 18 children in the US will have received up to 44 vaccine injections (fig 1), 28 of which are recommended for all. Immunisations are mostly concentrated into narrow windows of time and coincide with usual health visits at 0-2 years and prekindergarten stage (4-5 years), and since June 2005 at 11-12 years.¹⁰

The number of recommended vaccines in the US has risen by about three per decade, from seven in 1985 to 13 in 2005. New vaccine technologies and applications are about to expand this array. An unprecedented number of childhood and adolescent vaccines are currently being introduced, most of which have substantial merit.

In 2005, the Advisory Committee on Immunization Practices approved two new vaccines—meningococcal polysaccharide conjugate (MCV4) and a pertussis booster (Tdap)—and the new strategy of immunising 11-12 year olds.¹¹ Effective campaigns of targeted vaccination and realistic expectations for elimination have led to the two dose vaccination for hepatitis A also being recommended for all children aged 12-23 months.¹ Vaccines for human papillomavirus and rotavirus are likely to be licensed soon, and recommendations will probably follow. In comparison, vaccines for only two diseases—smallpox and rotavirus—have been retired from routine recommendation in the past 40 years.

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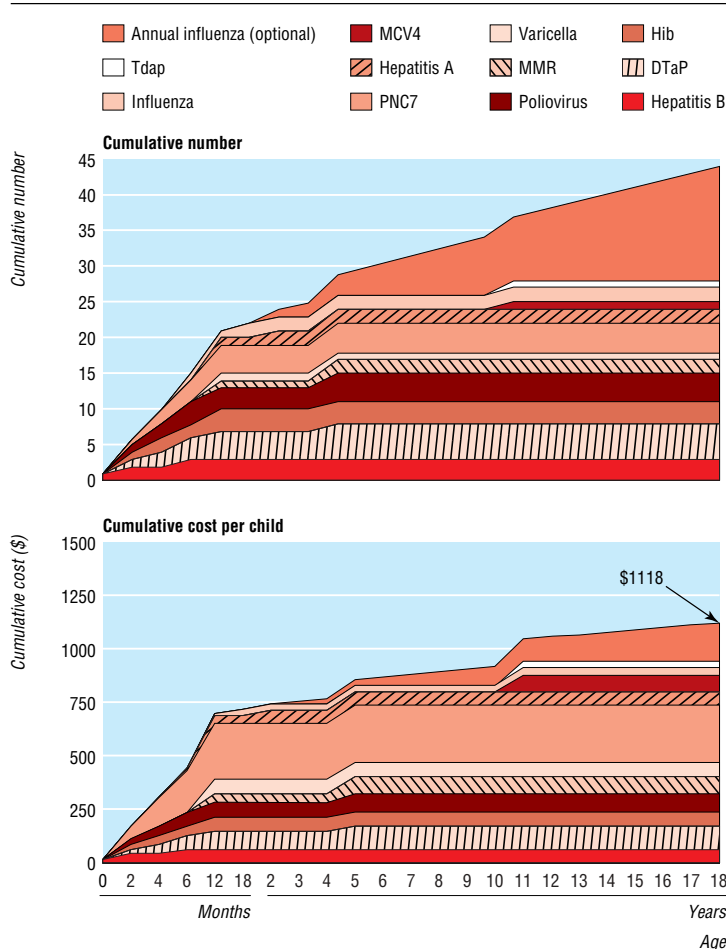


Fig 1 Recommended immunisations up to age 18 in the United States.¹⁰ Vaccine costs from Centers for Disease Control vaccine price list (www.cdc.gov/nip/vfc/cdc_vac_price_list.htm). See box for abbreviations

Despite the complexity of the immunisation schedule, vaccine coverage of children aged 19-35 months has risen consistently and significantly in the US. Currently, by their third birthday about 76% of children receive vaccinations for diphtheria, tetanus, and acellular pertussis (DTaP; four doses); poliovirus (three doses); mumps, measles, and rubella (MMR; one dose); *H influenzae* type B (Hib; three doses); hepatitis B (three doses); and varicella (one dose).¹² In addition, 73.2% receive at least three doses of pneumococcal conjugate vaccine (PNC7).¹²

The acceptability and feasibility of an increasingly complicated schedule of vaccination may have limits. Non-paediatric doctors in Switzerland were less likely than paediatricians to have their own children immunised because of concern over immune overload, safety issues, and low prevalence of target disease.¹³ Two thirds of parents in the US felt that no more than two immunisations should be given at one visit, and underimmunisation was significantly associated with the complexity and inconvenience of the vaccination schedule.¹⁴

Sustainable cost?

Between 1998 and 2003, after the recommendation for pneumococcal conjugate vaccine in all children,

invasive pneumococcal disease caused by the seven serotypes in the childhood vaccine dropped by 94% in children under 5.¹⁵ As a result of herd immunity, the disease was reduced by 55% in adults (age >50) during the same period, whereas the prevalence of disease caused by the other 16 serotypes in the adult polysaccharide vaccine remained fairly stable.¹⁶

The full schedule of immunisations for children and adolescents in the US costs about \$1118 (£642; €940) per child, excluding administration charges (fig 1)—about \$4.47bn per year. Benefits include reduced invasive pneumococcal disease in target and non-target populations; the global eradication of smallpox; and the elimination of polio, measles,¹⁷ and rubella in the US.¹⁸ I would argue that currently this expense is justified.

An economic analysis of the basic series of seven vaccines (DTaP, Tdap, poliovirus, MMR, hepatitis B, Hib, and varicella; see box) in childhood in the US defined the cost savings.¹⁹ The direct and net savings were estimated at \$9.9bn and \$43.3bn, with benefit to cost ratios of 5.3 and 16.5. Vaccination for hepatitis A has been shown to be cost effective in Chile and the US, although benefit is greatest in areas of highest prevalence.^{20 21} Regardless of economic models, protection of all children in the US through use of all currently recommended vaccines would use less than 0.5% of overall healthcare expenditure. Childhood immunisation is one of the most cost effective interventions in modern medicine.

Issues relating to vaccine policy

Older vaccines and the first ones to be recommended for all were for common diseases with high morbidity and mortality (smallpox, measles, and polio; fig 2). More recently, vaccines have been developed for diseases that are prevalent but have low mortality (varicella and rotavirus) or are rare but highly lethal (meningococcal disease).

It is against this background that we should carefully consider vaccine policy. The 1999 recommendation on hepatitis A significantly affected prevalence and altered the characteristics of the disease (fig 3).^{2 4} A line drawn between tetanus and varicella forms an arbitrary but traditional boundary. Vaccines for diseases that lie above this line deserve serious consid-

Vaccines currently recommended for children in the US

DTaP: diphtheria, tetanus, and acellular pertussis
 Tdap: tetanus, diphtheria, and acellular pertussis booster
 Poliovirus
 MMR: mumps, measles, and rubella
 Hib: *Haemophilus influenzae* type B
 Hepatitis A
 Hepatitis B
 Varicella
 PNC7: pneumococcal conjugate vaccine
 MCV4: meningococcal polysaccharide conjugate
 Influenza (6-23 months)
 Annual influenza (optional 2-18 years)

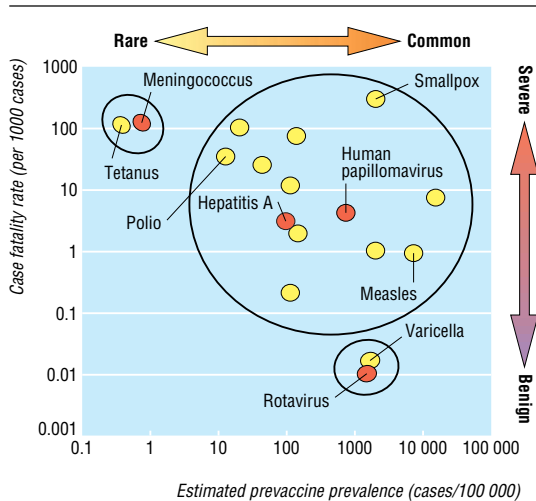


Fig 2 Mortality and prevaccine prevalence of vaccine preventable diseases in the United States. Recently recommended and future candidate vaccines shown in red^{11 22-25}

eration, whereas vaccines for diseases below must be justified in terms of cost, additional complexity, and efficacy. The vaccine for hepatitis A has been displaced to a position close to but still above this line.

Implications

What does this panoply of vaccines mean for doctors and their patients? For Ruby it meant four separate injections at her first visit and an extra visit for three more injections (we have yet to consider vaccination for hepatitis A). For the doctor it means a confusing matrix of potential vaccine combinations. For policy makers, it will soon force the current schedule of recommended immunisations to be divided into childhood and adolescent sets. For healthcare insurance companies it is another component of increasing costs. For vaccine manufacturers it represents an often favourable return on investment.

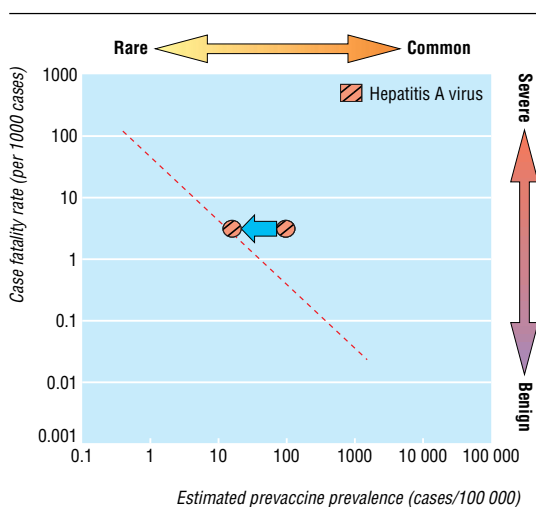


Fig 3 Shift in prevalence of hepatitis A after the 1999 vaccine recommendation. Vaccines for diseases that lie above the broken line deserve serious consideration, whereas vaccines for diseases below must be justified in terms of cost, additional complexity, and efficacy

Summary points

Vaccination of all children aged 12-23 months for hepatitis A virus has been recommended in the United States

This raises the total number of recommended immunisations for children and adolescents from 26 to 28

The estimated cost for full childhood and adolescent immunisation is \$1118 per child, but will probably be cost saving

Recommendations for vaccinations are based on the prevalence and severity of disease caused by infection but because targeted vaccination has reduced the prevalence of hepatitis A this vaccine is now only just above the cut-off margin

Changes are needed to maintain sufficient coverage with the increasingly confusing and complex schedule of immunisation. Firstly, vaccine manufacturers should develop more combination vaccines.²⁶ Secondly, vaccine providers should use immunisation information systems to help manage the selection and timing of vaccinations.²⁷ Thirdly, all children and adolescents should receive the recommended vaccines. This requires a willingness of society to pay and good economic assessments before vaccinations are recommended for all children, which will depend on enhanced transparency in the manufacture and pricing of vaccines.

Conclusions

The new recommendation for vaccination for hepatitis A in all children aged 12-23 months is based on strong epidemiological evidence of its effectiveness but is compromised by the reduced prevalence of the virus due to the success of targeted vaccination. Adding two more injections to an already crowded schedule may reduce compliance. Although additional costs are incurred, childhood immunisations have generally been cost saving and vaccine related expenses are dwarfed by other spending. This recommendation is probably justified, but future childhood vaccine recommendations should be scrutinised carefully.

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Health policy

Contracting out health services in fragile states

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Non-governmental organisations are contracted to provide most of Afghanistan's health services. What can we learn from their approach and is it sustainable in the longer term?

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Many Western health systems contract out healthcare services, including the NHS. Contracts are less common in low income countries, but contracts with non-governmental organisations (NGOs) to deliver health services are increasingly being promoted in so called fragile states—countries affected by conflict, emerging from conflict, or otherwise lacking the will or capacity to implement pro-poor policies.¹ Contracts with NGOs are seen as an effective way to expand services quickly. This is important to reach many of the poorest people living in these countries and thus to make progress towards the millennium development goals for health, but many questions about contracting remain unanswered.

Use of contracts

In a pilot project in Cambodia, NGOs were contracted to provide district health services on behalf of the government. An extensive evaluation showed that districts with health services that were contracted out to NGOs delivered care more efficiently and equitably than those that remained under government control.² These findings have encouraged promotion of the contracting out approach in weaker health systems.³

Many low income countries that are implementing or discussing contracting of health care belong to the



The challenge of outsourcing

group of around 40 countries currently referred to as fragile states—for example, Cambodia, Afghanistan, Pakistan, Southern Sudan, and Democratic Republic of Congo.¹ The contracts are usually funded by a donor in response to the need to expand services rapidly and the lack of functioning government infrastructure and workforce to deliver these services. As a result, perhaps paradoxically, the weaker the country's government capacity, the more likely it is that contracting is