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Immunisation

Should universal hepatitis B immunisation be introduced in the UK?

P English

Yes. But how?

A colleague working at a nearby desk groaned the other day. I asked why, and he told me that he'd just received a laboratory notification for a child who had been identified as needing a course of neonatal hepatitis B vaccine. It appeared that the system had failed, the vaccination hadn't been completed, and the child had become infected. Selective vaccination is not totally reliable.

So, should we have a universal vaccination programme? Before answering, we need to know:

- How important is the disease that you would prevent?
- How much of the disease would a universal vaccination programme prevent?
- What would be the costs of a vaccination programme?
- What costs would the vaccination programme prevent?
- How do the costs of the programme compare with the costs prevented?

If the costs saved exceed the costs of vaccination, the programme is worth introducing. That's the principle—in practice getting clear answers can be difficult, and the answers don't remain static.

Acute hepatitis B infection is usually asymptomatic; in a minority it is prolonged, serious, and occasionally fatal. Of those infected, 90% of infants infected at birth, 25–30% of 1–4 year olds, and 3–5% of individuals aged 5 years or more will proceed to having chronic hepatitis B (CHB). Some of those with CHB will be infectious, and some will develop cirrhosis, and/or hepatocellular carcinoma years or decades later. Each year in the UK there are an estimated 4300 acute hepatitis B infections, more than 7500 new cases of chronic infection with hepatitis B (mainly in immigrants), and up to 430 cases of hepatitis B related hepatocellular carcinoma, with estimated NHS costs of £26m–£375m.[1]

Hepatitis B can be safely and effectively prevented by vaccination.[2] The UK offers targeted vaccination for hepatitis B to people in particular risk groups, as described in the ''Green Book''.[3] Targeted vaccination programmes are harder than universal programmes to implement (especially in more disadvantaged populations) and are seldom as effective.[4–6] Some are excellent.[7–9]

Cases like the one that made my colleague groan are uncommon—over

90% of at-risk babies receive vaccine and immunoglobulin at birth.[10] A universal programme may be less likely to miss anybody; but to prevent such cases vaccination would have to start at birth, like the new US policy.[11] Without such a strategy, targeted vaccination for high risk babies will still be required; and even then targeted use of immunoglobulin needs to continue indefinitely.[2 10]

SO WHAT IS THE COST EFFECTIVENESS OF HEPATITIS B VACCINATION?

Many cost effectiveness evaluations of immunisation strategies have been published.[12–18] While hepatitis B vaccination is clearly worthwhile in high prevalence countries,[19] some conclude that transmission rates for hepatitis B infection in the UK are too low to justify a universal vaccination policy, so we should continue with our targeted vaccination policy.[20] Others emphatically recommend universal vaccination.[21 22] Universal hepatitis B vaccination is policy in many countries,[11 18] and recommended by the WHO and BMA.[2 23] Three doses are probably adequate (although some programmes use two or four), with no need for routine booster doses.[10 11 18 24 25]

Evaluating the cost effectiveness of a proposed vaccination programme is difficult, as many of the variables are complicated to estimate.[6] These include: the true costs of disease to the NHS and society; the impact, when many cases are in immigrants who were infected abroad; the importance of discounting (when the treatment has to be paid for now, to prevent costs that will be incurred many years in the future); vaccine prices; vaccine efficacy; and the proportion of cases who are treated.[1 18 26 27]

Consider the following illustration:

> It has been estimated that the NHS hospital resources consumed annually by hepatitis B patients are worth at least £26.7m; and that if all 180 000 patients with chronic hepatitis B were diagnosed and treated, the total healthcare costs would be £375m and the total societal cost would be £429m. Although only one third of cases are likely to be treated, ''the NHS could spend between £26m and £380m managing hepatitis B''.[1] Treatment options are limited, expensive, and imperfect.[28] Progress could increase or decrease the costs of treatment.
>
> About 96% of cases of hepatitis B are immigrants, infected before they entered the UK.[1] Preventing the remaining 4% of cases would save the NHS between £1.0m and £15.2m.

How much would the programme cost?

> Assume that: hepatitis B is added to the currently used primary and preschool vaccines, at an additional cost per dose of £5 (see below); three doses of hepatitis B vaccine are given; and there are 695 500 births per year in the UK.[29] This gives an additional cost of about £10.4m.[30] An adolescent vaccination programme might cost between £15m and £28m.[18]

These figures suggest that the cost of vaccination is less than the higher estimates of NHS secondary care for UK acquired hepatitis B.

The illustration assumes:

- A 100% effective vaccine, and 100% uptake (90% is probably more realistic)
- Vaccination is done along with other routine childhood vaccination, at minimal extra cost.

If a more sophisticated evaluation were to reach similar conclusions, then a universal programme would clearly be worthwhile.

Several reasons remain for questioning further whether we should adopt a universal vaccination strategy.

INCREASING RISKS

Many hepatitis B positive mothers are immigrants, who were infected before they came to the UK, so a UK based vaccination policy will have a limited impact on vertical transmission of the disease (hence the need for continued targeted immunisation). People can, however, be protected from horizontal transmission, which is increasing through:

- Travel (including, for example, student gap years). More people are putting themselves at risk through travel to countries where hepatitis B is common; and many travellers are not adequately vaccinated against hepatitis B.[31–33]
- Sexually transmitted infections.[34]
- Intravenous drug use. Markers of recent infection in intravenous drug users have increased from 3.4% in 1997 to 9.1% in 2003, despite targeted vaccination programmes.[4]

HAVE ALL COSTS AND POTENTIAL SAVINGS BEEN INCLUDED?

It is easier to estimate the cost of a vaccination programme than the savings that might accrue, with the risk that savings may be omitted. Many evaluations—like the illustration above—focus on measurable costs (sometimes only inpatient NHS costs). Other possible costs and savings include:

- Other ''costs'' of disease (which push the balance further in favour of universal vaccination), such as:
  - Loss of years of life or quality adjusted life years (QALYs).
  - Loss of productivity and earnings due to illness, time off work, and informal care.
  - Distress and anxiety caused by actual or possible disease (distress and anxiety caused by vaccination needs to be offset against this).
  - Management of possible exposure to hepatitis B; for example, counselling, testing, and post-exposure prophylaxis. (Such incidents are rarely written up or reported, which makes their impact hard to cost. One incident involving a looked-after child caused great distress, and generated hundreds of hours of work for professionals: the cost of the meetings alone exceeded £1.5k; and many additional hours were spent writing and reading reports and correspondence. This incident was more involved than most, but the costs of dealing with smaller incidents are not trivial.)
- Savings from not having to vaccinate people who would otherwise have entered target groups. (The NHS alone employs over a million people, and healthcare workers in a target group make up a considerable proportion of the UK population.)

Discounting is another, controversial, aspect of the cost of a vaccination programme: vaccination would be paid for at today's prices, and the benefits accrued later, so discounting the benefits would considerably reduce their value (although some argue that health benefits should be discounted at a reduced rate, if at all).[26 27]

CHANGES TO THE COST OF VACCINATION

Vaccine technology is developing rapidly. Multi-component vaccines are becoming commonplace. The cost of maintaining different product lines means that manufacturers may prefer to rationalise their products: MMR is cheaper than single-component vaccines.

UK infants receive a five-component vaccine to protect against diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (Hib), and polio. Many countries

now use similar six-component vaccines, which also contain hepatitis B vaccine. Evidence of the likely cost of as-yet unlicensed vaccines is hard to obtain; but six-component vaccines are likely to cost little more than five-component vaccines, especially if they are marketed internationally. (Existing six-component vaccines use three-valent acellular pertussis component (aP_3) instead of the five-valent component (aP_5) that some think is essential.[35] In countries using aP_3 this is not perceived as a problem—the protection provided seems adequate, perhaps because they include more booster doses. It may be possible to develop a six-component vaccine that contains aP_5.)

HOW MIGHT WE INTRODUCE UNIVERSAL HEPATITIS B VACCINATION?

The cost of a vaccination programme will depend on the precise strategy adopted.

Whichever strategy for universal hepatitis B vaccination policy were adopted, targeted vaccination of unvaccinated individuals and at-risk neonates would continue to be required for some time; and targeted administration of immunoglobulin will be required indefinitely.

Before considering a universal programme, one might consider limiting universal vaccination to areas with a high proportion of immigrants from high prevalence countries, as with BCG.[36]

Choosing a strategy involves weighing up the costs and benefits of each possible strategy. More effective strategies may be more expensive. The practicalities of each must be considered—for example, would it have an impact on other vaccinations?

One approach might be to *replace current primary immunisations with vaccines incorporating an added hepatitis B component*. This would be simple and relatively cheap to implement, but it would leave today's older children vulnerable to infection, and would rely on targeted interventions to provide protection from birth; but it would reduce infection at ages at which chronic disease is most likely to arise.

Another, more expensive, strategy that would more quickly prevent sexual transmission of hepatitis B would be a *schools based programme for adolescents*.[18] Other vaccines, such as a human papillomavirus vaccine, might be given at the same time, reducing the overall programme costs. The recent cessation of the BCG schools programme might create space for this.[36] The vaccine may be more effective in this age group;[24] but waiting until the teenage years leaves children vulnerable until then, requires additional targeted neonatal vaccination, and misses the opportunity to prevent CHB.

The USA has recently adopted a strategy of *universal vaccination at birth*, to minimise vertical transmission, combined with catch-up programmes for unvaccinated older children, teenagers, and at-risk adults.[11] This strategy would be very effective, but has additional costs including the catch-up programmes and the need for a single-component hepatitis B vaccine to be given at birth.

PATIENT CHOICE

The value individuals will place on uncertainty and illness varies, so an intervention that is not cost effective for one may be cost effective for another.

Where the benefit to the population does not clearly justify a universal vaccination programme it can be difficult for individuals to obtain vaccination for themselves or their children. This applies, even when vaccination would provide some population benefit, and the individuals perceive themselves to be at risk.

Individuals who perceive themselves at risk of hepatitis B, but who are not (or do not want to admit to being) in an official ''target group'' have to pay for it privately. Some travel vaccinations (including hepatitis B) have to be prescribed privately; others (including hepatitis A) are available on the NHS. There is little apparent logic to the distinctions, and the NHS pays for treatment if people return to the UK having been infected while abroad.

There is a strong case for reviewing arrangements for ''optional'' vaccination (for travel, and vaccinations that are not provided universally); and for facilitating people who choose to, to have them conveniently, and without paying the full, for-profit, private costs.

SUMMARY

Although the UK has a low prevalence of hepatitis B, a universal vaccination programme would be beneficial, and should be introduced—but the best strategy is not yet clear, and we might need new combination vaccines.

As many infections are imported it remains vital for the UK to work with others to improve vaccination programmes in countries with a high prevalence of hepatitis B. This could, in the long term, be more cost effective than anything we do in the UK.

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