Vaccination greatly reduces disease, disability, death and inequity worldwide

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Abstract In low-income countries, infectious diseases still account for a large proportion of deaths, highlighting health inequities largely caused by economic differences. Vaccination can cut health-care costs and reduce these inequities. Disease control, elimination or eradication can save billions of US dollars for communities and countries. Vaccines have lowered the incidence of hepatocellular carcinoma and will control cervical cancer. Travellers can be protected against "exotic" diseases by appropriate vaccination. Vaccines are considered indispensable against bioterrorism. They can combat resistance to antibiotics in some pathogens. Noncommunicable diseases, such as ischaemic heart disease, could also be reduced by influenza vaccination.

Immunization programmes have improved the primary care infrastructure in developing countries, lowered mortality in childhood and empowered women to better plan their families, with consequent health, social and economic benefits.

Vaccination helps economic growth everywhere, because of lower morbidity and mortality. The annual return on investment in vaccination has been calculated to be between 12% and 18%. Vaccination leads to increased life expectancy. Long healthy lives are now recognized as a prerequisite for wealth, and wealth promotes health. Vaccines are thus efficient tools to reduce disparities in wealth and inequities in health.

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Introduction

Vaccination has greatly reduced the burden of infectious diseases. Only clean water, also considered to be a basic human right, performs better.[1] Paradoxically, a vociferous antivaccine lobby thrives today in spite of the undeniable success of vaccination programmes against formerly fearsome diseases that are now rare in developed countries.[2]

Understandably, vaccine safety gets more public attention than vaccination effectiveness, but independent experts and WHO have shown that vaccines are far safer than therapeutic medicines.[2,3] Modern research has spurred the development of less reactogenic products, such as acellular pertussis vaccines and rabies vaccines produced in cell culture. Today, vaccines have an excellent safety record and most "vaccine scares" have been shown to be false alarms.[4,5] Misguided safety concerns in some countries have led to a fall in vaccination coverage, causing the re-emergence of pertussis and measles.[6]

Putative vaccine safety issues are commonly reported while reviews of vaccine benefits are few. A Medline search over the past five years using the keywords "vaccine risks" scored approximately five times as many hits (2655 versus 557) as a Medline search using "vaccine benefits" as keywords.[7] This reflects the fact that negative aspects of vaccination get much more publicity than positive aspects.

How one addresses the antivaccine movement has been a problem since the time of Jenner. The best way in the long term is to refute wrong allegations at the earliest opportunity by providing scientifically valid data. This is easier said than done, because the adversary

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in this game plays according to rules that are not generally those of science. This issue will not be further addressed in this paper, which aims to show how vaccines are valuable to both individuals and societies, to present validated facts, and to help redress adverse perceptions. Without doubt, vaccines are among the most efficient tools for promoting individual and public health and deserve better press.[8]

Disease control benefits

Eradication

Unless an environmental reservoir exists, an eradicated pathogen cannot re-emerge, unless accidentally or malevolently reintroduced by humans, allowing vaccination or other preventive measures to be discontinued.

While eradication may be an ideal goal for an immunization programme, to date only smallpox has been eradicated, allowing discontinuation of routine smallpox immunization globally. Potentially, other infectious diseases with no extrahuman reservoir can be eradicated provided an effective vaccine and specific diagnostic tests are available. Eradication requires high levels of population immunity in all regions of the world over a prolonged period with adequate surveillance in place.[9] The next disease targeted for eradication is polio, which is still a global challenge.[10] Although high coverage with oral polio vaccine (OPV) has eliminated type 2 poliovirus globally, transmission of types 1 and 3 continues in limited areas in a few countries. OPV-caused paralytic disease, directly or by reversion to virulence, and persistent vaccine-virus excretion in immunodeficient individuals are problems yet to be solved. Global use of monovalent type 1 and type 3 OPV and inactivated polio vaccine (IPV) may eventually be required.[10]

Elimination

Diseases can be eliminated locally without global eradication of the causative microorganism. In four of six WHO regions, substantial progress has been made in measles elimination; transmission no longer occurs indigenously and importation does not result in sustained spread of the virus.[11] Key to this achievement is more than 95% population immunity through a two-dose vaccination regimen. Combined measles, mumps and rubella (MMR) vaccine could also eliminate and eventually eradicate rubella and mumps.[11] Increasing measles immunization levels in Africa, where coverage averaged only 67% in 2004, is essential for eradication of this disease. Already, elimination of measles from the Americas, and of measles, mumps and rubella in Finland has been achieved, providing proof in principle of the feasibility of their ultimate global eradication.[12] It may also be possible to eliminate *Haemophilus influenzae* type b (Hib) disease through well implemented national programmes, as experience in the West has shown.[13]

Local elimination does not remove the danger of reintroduction, such as in Botswana, polio-free since 1991, with importation of type 1 poliovirus from Nigeria in 2004,[14] and in the United States of America (USA) with measles reintroduced to Indiana in 2005 by a traveller from Romania.[15]

For diseases with an environmental reservoir such as tetanus, or animal reservoirs such as Japanese encephalitis and rabies, eradication may not be possible, but global disease elimination is a feasible objective if vaccination of humans (and animals for rabies) is maintained at high levels.

Control of mortality, morbidity and complications

For the individual

Efficacious vaccines protect individuals if administered before exposure. Pre-exposure vaccination of infants with several antigens is the cornerstone of successful immunization programmes against a cluster of childhood diseases. Vaccine efficacy against invasive Hib disease of more than 90% was demonstrated in European, Native American, Chilean and African children in large clinical studies in the 1990s.[13] In the United Kingdom, no infant given three doses developed Hib disease in the short-term (boosters may be required for long-term protection), and recent postmarketing studies have confirmed the high effectiveness of vaccination of infants against Hib in Germany and pertussis in Sweden.[13,16,17]

Many vaccines can also protect when administered after exposure – examples are rabies, hepatitis B, hepatitis A, measles and varicella.[18]

For society

Ehreth estimates that vaccines annually prevent almost 6 million deaths worldwide.[19] In the USA, there has been a 99% decrease in incidence for the nine diseases for which vaccines have been recommended for decades,[20] accompanied by a similar decline in mortality and disease sequelae.

Complications such as congenital rubella syndrome, liver cirrhosis and cancer caused by chronic hepatitis B infection or neurological lesions secondary to measles or mumps can have a greater long-term impact than the acute disease. Up to 40% of children who survive meningitis due to Hib may have life-long neurological defects.[13]

In field trials, mortality and morbidity reductions were seen for pneumococcal disease in sub-Saharan Africa and rotavirus in Latin America.[21,22]

Specific vaccines have also been used to protect those in greatest need of protection against infectious diseases, such as pregnant women, cancer patients and the immunocompromised.[18]

Mitigation of disease severity

Disease may occur in previously vaccinated individuals. Such breakthroughs are either primary – due to vaccine failure – or secondary. In such cases, the disease is usually milder than in the non-vaccinated. In a German efficacy study of an acellular pertussis vaccine, vaccinated individuals who developed whooping cough had a significantly shorter duration of chronic cough than controls.[23] Such findings were confirmed in Senegal.[24] Varicella breakthroughs exhibit little fever, fewer skin lesions and fewer complications[25] than unvaccinated cases. Milder disease in vaccinees was also reported for rotavirus vaccine.[22]

Prevention of infection

Many vaccines are primarily intended to prevent disease and do not necessarily protect against infection. Some vaccines protect against infection as well. Hepatitis A vaccine has been shown to be equally efficacious (over 90% protection) against symptomatic disease and asymptomatic infections.[26] Complete prevention of persistent vaccine-type infection has been demonstrated for human papillomavirus (HPV) vaccine.[27]

Such protection is referred to as "sterilizing immunity". Sterilizing immunity may wane in the long term, but protection against disease usually persists because immune memory minimizes the consequences of infection.[28]

Protection of the unvaccinated population

Herd protection

Efficacious vaccines not only protect the immunized, but can also reduce disease among unimmunized individuals in the community through "indirect effects" or "herd protection". Hib vaccine coverage of less than 70% in the Gambia was sufficient to eliminate Hib disease, with similar findings seen in Navajo populations.[29,30] Another example of herd protection is a measles outbreak among preschool-age children in the USA in which the attack rate decreased faster than coverage increased.[31] Herd protection may also be conferred by vaccines against diarrhoeal diseases, as has been demonstrated for oral cholera vaccines.[32]

"Herd protection" of the unvaccinated occurs when a sufficient proportion of the group is immune.[33] The decline of disease incidence is greater than the proportion of individuals immunized because vaccination reduces the spread of an infectious agent by reducing the amount and/or duration of pathogen shedding by vaccinees,[34] retarding transmission. Herd protection as observed with OPV involves the additional mechanism of "contact immunization" – vaccine viruses infect more individuals than those administered vaccine.[10]

The coverage rate necessary to stop transmission depends on the basic reproduction number (R_0), defined as the average number of transmissions expected from a single primary case introduced into a totally susceptible population.[34] Diseases with high R_0 (e.g. measles) require higher coverage to attain herd protection than a disease with a lower R_0 (e.g. rubella, polio and Hib).

Because of herd protection, some diseases can be eliminated without 100% immunization coverage.

Source drying

Source drying is a related concept to herd protection. If a particular subgroup is identified as the reservoir of infection, targeted vaccination will decrease disease in the whole population.

In North Queensland, Australia, there was a high incidence of hepatitis A in the indigenous population. Vaccination of indigenous toddlers, with catch-up up to the sixth birthday, had a rapid and dramatic impact in eliminating the disease in the indigenous population and in the much larger non-indigenous population (who were not vaccinated) across the whole of Queensland.[35] Similar approaches have been very successfully applied in several other larger settings, including Israel and the USA.[36]

The success of source drying justifies vaccination of special occupational groups, such as food handlers, to control typhoid and hepatitis A.[37]

Pertussis vaccine boosters for close contacts (such as parents, grandparents, nannies, siblings and baby unit nurses), who are the most common sources of transmission to infants, protect those too young to be given primary vaccination with a surrounding "pertussis-free cocoon".[38]

Prevention of related diseases and cancer

Protection against related diseases

Vaccines will also protect against diseases related to the targeted disease. For example, in Finland, the USA and elsewhere, influenza vaccination has been found protective for acute otitis media in children, with a vaccine efficacy of more than 30%.[39] Measles vaccination protects against multiple complications such as dysentery, bacterial pneumonia, keratomalacia and malnutrition.[40] An enterotoxic *Escherichia coli* vaccine demonstrated protection against diarrhoea due to *Salmonella enterica*.[41]

Cancer prevention

Infective agents cause several cancers. Chronic hepatitis B infection leads to liver cancer. Vaccination against such pathogens should prevent the associated cancer as already observed for hepatocellular carcinoma in Taiwan, China.[42] These results could be replicated in Africa.[43]

Reduction of the incidence of cervical cancer is expected with the use of HPV vaccines against serotypes 16 and 18, responsible for over 70% of the global cervical cancer burden, as reduction in precancerous lesions has been demonstrated in vaccinees.[27]

Societal and other benefits

Health-care and other savings for society

Immunization programmes require funding for infrastructure (e.g. cold-chain maintenance), purchase of vaccines and adequate staffing. However, the mortality and morbidity prevented translates into long-term cost savings and potential economic growth. Globally, the savings from vaccines were estimated by Ehreth in 2003 to be of the order of tens of billions of US dollars of direct savings.[19] Malaria (for which there are currently several promising vaccines in development) costs sub-Saharan Africa US$ 100 billion worth of lost annual gross domestic product (GDP).

Savings are enhanced if several antigens are delivered in a single vaccine. Combination vaccines bring the added benefit of better compliance, coverage, and injection safety. Introduction of a new antigen is facilitated with combination vaccines, ensuring early high coverage by maintaining previous immunization schedules, without compromising (and sometimes improving) immunogenicity and reactogenicity.[44,45]

When taking into account indirect costs, savings are higher for common diseases with lower mortality and morbidity (such as varicella) than for more severe diseases (such as polio).[46] Indirect costs, such as lost productivity (as well as direct medical costs) have been emphasized by eminent health economists in assessing the full value of vaccination.[47]

Immunization programmes, compared to other common public health interventions such as wearing seat-belts and chlorination of drinking water, are a good investment and more cost effective than, for example, advice on smoking cessation.[48]

Cost savings will be achieved with the new live-attenuated rotavirus and conjugated pneumococcal vaccines, as well as wider use of hepatitis B and Hib vaccines.[49]

Preventing development of antibiotic resistance

By reducing the need for antibiotics, vaccines may reduce the prevalence and

hinder the development of resistant strains. Introduction of a conjugate pneumococcal vaccine for infants in the USA in 2000 saw a 57% decline in invasive disease caused by penicillin-resistant strains and a 59% decline in strains resistant to multiple antibiotics by 2004 across a broad age spectrum: 81% among children under 2 years of age and 49% among persons aged 65 years and older.[50]

Vaccines against typhoid can prevent primary infection and the spread of antibiotic-sensitive as well as multidrug-resistant strains.[51] The development of new vaccines against infectious pathogens where antibiotic resistance is a global threat (e.g. *Staphylococcus aureus*) is viewed as a better long-term option to control the problem of increasing resistance.[52]

Extending life expectancy

Vaccines can increase life expectancy by protecting against diseases against which one would not expect benefit. Elderly individuals given influenza vaccine in the USA had approximately 20% less chance of suffering cardiovascular and cerebrovascular disease and 50% lower risk of mortality from all causes compared to their unvaccinated counterparts.[53]

In Sweden, administration of polysaccharide pneumococcal vaccine and inactivated influenza vaccine significantly reduced the risk of in-hospital mortality for pneumonia and cardiac failure among elderly persons, with an additive effect when both vaccines had been administered.[54]

Safe travel and mobility

With global air travel rising, there is an increased risk of exposure to infectious diseases abroad. Travellers transmit and disseminate disease, as has been observed in the case of polio and in the dispersal of meningococcal strains by returning pilgrims from Saudi Arabia.[55] In the case of the Muslim Hajj (the largest annual human gathering in the world), local authorities require meningococcal ACWY vaccination and recommend various other vaccinations, such as influenza and hepatitis B, for pilgrims.[56]

The most common vaccine-preventable diseases among travellers are influenza and hepatitis A.[57] Other vaccines to consider for travel include rabies, hepatitis B, typhoid, cholera, yellow fever, Japanese encephalitis and measles.[57] Many vaccines can be given by flexible accelerated schedules to ensure early protection.[58] Thus the traveller seeking health advice, even within a few weeks of departure, can travel overseas without vaccine-preventable health risks to themselves and others.

Other public health benefits

In developing countries, vaccination programmes are cornerstones of primary health-care services. The infrastructure and personnel required for an effective and sustainable immunization programme give opportunities for better primary health-care services, particularly in the critical perinatal and early infancy period.[59–61]

Empowerment of women

With improvements in infant and child mortality, women tend to opt for fewer children as the need to have many children to ensure that some will reach adulthood is reduced. This has significant health, educational, social and economic benefits.[59]

Protection against bioterrorism

The current concern about the potential use of smallpox virus in bioterror is due to the cessation of vaccination (and of vaccine manufacture) following the monumental achievement of smallpox eradication. The potential of vaccines to protect populations from bioterrorism threats such as smallpox and anthrax has led many governments to ensure an adequate supply of the necessary vaccines in preparation against such an attack.[62] Surveillance and response systems for vaccine-preventable and other diseases play a critical role in identification, characterization and response to biological weapons.

Promoting economic growth

Poor health has been shown to stunt economic growth while good health can promote social development and economic growth. Health is fundamental to economic growth for developing countries and vaccinations form the bedrock of their public health programmes.[47,59,60] The annual return on investment in vaccination has been calculated to be in the range of 12% to 18%, but the economic benefits of improved health continue to be largely underestimated.[47,63,64]

Enhancing equity

The burden of infectious, including vaccine-preventable, diseases falls disproportionately on the disadvantaged. Vaccines have clear benefits for the disadvantaged. Pneumococcal immunization programmes in the USA have at least temporarily removed racial and socioeconomic disparities in invasive pneumococcal disease incidence, while in Bangladesh, measles vaccination has enhanced equity between high- and low-socioeconomic groups.[65,66]

Promoting peace

There were at least seven United Nations Children's Fund (UNICEF) vaccine-mediated ceasefires during civil conflicts.[67] These conflicts were in diverse parts of the world, from Liberia to Afghanistan, where even warring factions see the benefit of immunization programmes.

During protracted conflict it is possible to ensure that vaccination coverage remains high. This is seen in Sri Lanka, where despite unrest for the last two decades coverage in 2005 for both three doses of diphtheria–tetanus–pertussis vaccine and one dose of measles vaccine was 99%.[68]

The high cost-effectiveness and multiple benefits of relatively modest resource investments in immunization contrast starkly with profligate global military expenditures, currently over US$ 1 trillion annually.[69]

Conclusions

The benefits of vaccination extend beyond prevention of specific diseases in individuals. They enable a rich, multifaceted harvest for societies and nations. Vaccination makes good economic sense, and meets the need to care for the weakest members of societies. Reducing global child mortality by facilitating universal access to safe vaccines of proven efficacy is a moral obligation for the international community as it is a human right for every individual to have the opportunity to live a healthier and fuller life. Achievement of the Millennium Development Goal 4 (two-thirds reduction in 1990 under-5 child

mortality by 2015) will be greatly advanced by, and unlikely to be achieved without, expanded and timely global access to key life-saving immunizations such as measles, Hib, rotavirus and pneumococcal vaccines.

We conclude that a comprehensive vaccination programme is a cornerstone of good public health and will reduce inequities and poverty. ■

Competing interests: Bock and Datta are current employees of a vaccine manufacturer. Other coauthors have, in the past or now, either been employees of a vaccine manufacturer (Andre and Ruff) and have been or are consultants to or chief investigators in studies sponsored by different vaccine manufacturers as well as national and international health agencies. In detailed statements they have all indicated that they do not have any relevant conflict of interest.

Résumé

La vaccination réduit fortement la morbidité, les incapacités, la mortalité et les inégalités dans l'ensemble du monde

Dans les pays à faible revenu, les maladies infectieuses représentent encore une forte proportion des décès, mettant en lumière des inégalités sur le plan sanitaire résultant dans une large mesure d'écarts économiques. La vaccination peut faire baisser les coûts des soins de santé et réduire ces inégalités. La lutte contre les maladies, leur élimination ou leur éradication permettent aux communautés et aux pays d'épargner des milliards de dollars des Etats-Unis. Les vaccins ont également fait baisser l'incidence du carcinome hépatocellulaire et permettront d'endiguer le cancer du col utérin. Les voyageurs sont protégés contre les maladies « exotiques » par une vaccination appropriée. Les vaccins sont considérés comme indispensables dans la lutte contre le bioterrorisme. Ils peuvent s'opposer au développement d'une résistance aux antibiotiques pour certains agents pathogènes. La vaccination antigrippale pourrait aussi faire reculer des maladies non transmissibles, comme les cardiopathies ischémiques.

Les programmes de vaccination ont permis d'améliorer l'infrastructure de soins de santé primaire dans les pays en développement, de faire baisser la mortalité infanto-juvénile et de favoriser l'autonomie des femmes dans le cadre d'une meilleure planification familiale, avec des bénéfices sanitaires, sociaux et économiques conséquents.

La vaccination contribue partout à la croissance économique, grâce aux baisses de morbidité et de mortalité. On a calculé que le retour annuel sur investissement de cette intervention se situait entre 12 et 18 %. Elle entraîne également une augmentation de l'espérance de vie. Il est maintenant reconnu que des vies longues et en bonne santé sont un préalable à la richesse et la richesse favorise à son tour la santé. Les vaccins constituent ainsi des outils efficaces pour réduire les inégalités en matière de richesse et de santé.

Resumen

La vacunación reduce considerablemente la morbilidad, las discapacidades, la mortalidad y las inequidades en todo el mundo

En los países de ingresos bajos, las enfermedades infecciosas representan todavía una gran proporción de las defunciones, lo que pone de manifiesto unas inequidades sanitarias cuya causa fundamental son las desigualdades económicas. La vacunación puede reducir los costos de la atención de salud y reducir esas inequidades. El control, la eliminación y la erradicación de enfermedades permiten ahorrar miles de millones de dólares estadounidenses en beneficio de las comunidades y los países. Las vacunas han reducido la incidencia de carcinoma hepatocelular y permitirán controlar el cáncer cervicouterino. Los viajeros pueden protegerse contra enfermedades «exóticas» mediante la vacunación apropiada. Las vacunas son un arma imprescindible contra el bioterrorismo. En el caso de algunos agentes patógenos, pueden dificultar la aparición de resistencia a los antibióticos. Algunas enfermedades no transmisibles, como la cardiopatía isquémica, también podrían reducirse mediante la vacunación contra la gripe.

Los programas de inmunización han mejorado la infraestructura de atención primaria en los países en desarrollo, reducido la mortalidad en la niñez y empoderado a las mujeres para planificar mejor su familia, con los consiguientes beneficios sanitarios, sociales y económicos.

La vacunación contribuye al crecimiento económico en todas partes, debido a la menor morbilidad y mortalidad. Se estima que las ganancias que reportan anualmente las inversiones en inmunización ascienden a un 12%-18%. La vacunación propicia una mayor esperanza de vida, y es un hecho admitido hoy día que las vidas longevas y sanas son una condición de la riqueza, y que ésta favorece a su vez la salud. Las vacunas constituyen por consiguiente un instrumento eficiente para mitigar las disparidades de riqueza y las inequidades en salud.

ملخص

التلقيح يقلِّص بشكل كبير الأمراض، والعجز، والوفاة، والجور في أنحاء العالم المختلفة

ماتـزال الأمراض المعدية مسؤولة عن نسبة كبيرة من الوفيات في البلدان المنخفضة الدخل، مما يلقي الضوء على جوانب الجور الصحي الناجم، في جزء كبير منه، عن الفوارق الاقتصادية. ويمكن أن يخفِّض التلقيح من تكاليف الرعاية الصحية، ويقلِّص جوانب الجور فيها. ويمكن توفير بلايـين الدولارات للمجتمعات والبلدان من خلال مكافحة الأمراض أو التخلُّص منها أو اجتثاثها. فقد قلَّصت اللقاحات وقوع سرطانة الخلايا الكبدية، وستضع سرطان عنق الرحم تحت السيطرة. ويمكن توفير الحماية للمسافرين ضد الأمراض الأجنبية من خلال تلقِّيهم للّقاحات المناسبة. ولا غنى عن اللقاحات لمواجهة الإرهاب البيولوجي. فاللقاحات قادرة على مكافحة المقاومة للمضادات الحيوية لدى عدد من الـمُمرضات. ومن الممكن كذلك تقليص الأمراض غير السارية مثل أمراض القلب الإقفارية وذلك عن طريق لقاح الإنفلونزا. وتسهم برامج التمنيع في تحسين البنية الأساسية للرعاية الأولية في البلدان النامية، كما تسهم في خفض وفيات الأطفال، وتمكين المرأة كي تخطط لأسرتها بشكل أفضل، مما يفضي إلى تحقيق منافع صحية واجتماعية واقتصادية لهذه الأسر.

والتلقيح يعزِّز النمو الاقتصادي في جميع البلدان لما ينتج عنه من انخفاض في المراضة والوفيات. وحُسب المردود السنوي للاستثمار في التلقيح، فوجد أنه يتـراوح بين 12% و18%. ويؤدي التلقيح إلى زيادة مأمول الحياة. ويُنظر الآن إلى طول الحياة الصحية على أنه شرط أساسي للثروة، فالثروة تؤدِّي إلى تعزيز الصحة. وعلى ذلك، فإن اللقاحات تُعد من الأدوات الفعَّالة لتقليص التفاوت في الثروة والجور في الصحة.

References

1. Plotkin SL, Plotkin SA. A short history of vaccination. In: Plotkin SA, Orenstein WA, eds. *Vaccines*, 4th edn. Philadelphia: WB Saunders; 2004: 1-15.
2. Global Advisory Committee on Vaccine Safety. 3–4 December 2003. *Wkly Epidemiol Rec* 2004;79:16-20. PMID:15024856
3. Zhou W, Pool V, Iskander JK, English-Bullard R, Ball R, Wise RP, et al. Surveillance for safety after immunisation: Vaccine Adverse Event Reporting System (VAERS) – United States, 1991–2001. *MMWR Surveill Summ* 2003; 52:1-24. PMID:12825543
4. MacIntyre CR, Leask J. Immunisation myths and realities: responding to arguments against immunisation. *J Paediatr Child Health* 2003;39:487-91. PMID:12969200 doi:10.1046/j.1440-1754.2003.t01-1-00200.x
5. Folb PI, Bernastowska E, Chen R, Clemens J, Dodoo AN, Ellenberg SS, et al. A global perspective on vaccine safety and public health: the Global Advisory Committee on Vaccine Safety. *Am J Public Health* 2004;94:1926-31. PMID:15514229
6. Atkinson P, Cullinan C, Jones J, Fraser G, Maguire H. Large outbreak of measles in London: reversal of health inequalities. *Arch Dis Child* 2005;90:424-5. PMID:15781939 doi:10.1136/adc.2003.048892
7. Medline website. Available from: http://www.pubmed.gov
8. Andre FE. What can be done to make vaccines more trendy? *Expert Rev Vaccines* 2005;4:23-5. PMID:15757470 doi:10.1586/14760584.4.1.23
9. Henderson DA. Lessons from the eradication campaigns. *Vaccine* 1999; 17:S53-5. PMID:10559535 doi:10.1016/S0264-410X(99)00293-5
10. Fine PE, Griffiths UK. Global poliomyelitis eradication: status and implications. *Lancet* 2007;369:1321-2. PMID:17448799 doi:10.1016/S0140-6736(07)60533-9
11. Muller CP, Kremer JR, Best JM, Dourado I, Triki H, Reef S. WHO Steering Committee for Measles and Rubella. Reducing global disease burden of measles and rubella: report of the WHO Steering Committee on research related to measles and rubella vaccines and vaccination, 2005. *Vaccine* 2007;25:1-9. PMID:17262908 doi:10.1016/j.vaccine.2006.07.039
12. Peltola H, Davidkin I, Paunio M, Valle M, Leinikki P, Heinonen OP. Mumps and rubella eliminated from Finland. *JAMA* 2000;284:2643-7. PMID:11086376 doi:10.1001/jama.284.20.2643
13. WHO position paper on *Haemophilus influenzae* type b conjugate vaccines. *Wkly Epidemiol Rec* 2006;81:445-52. PMID:17124755
14. *Polio reported in Botswana.* Geneva: WHO; 2004. Available from: http://www.who.int/mediacentre/notes/2004/np11/en
15. Parker AA, Staggs W, Dayan GH, Ortega-Sanchez IR, Rota PA, Lowe L, et al. Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *N Engl J Med* 2006;355:447-55. PMID:16885548 doi:10.1056/NEJMoa060775
16. Schmitt HJ, von Kries R, Hassenpflug B, Hermann M, Siedler A, Niessing W, et al. *Haemophilus influenzae* type b disease: impact and effectiveness of diphtheria-tetanus toxoids - acellular pertussis (-inactivated poliovirus)/*H. influenzae* type b combination vaccines. *Pediatr Infect Dis J* 2001;20:767-74. PMID:11734739
17. Olin P, Gustafsson L, Barreto L, Hessel L, Mast TC, Rie AV, et al. Declining pertussis incidence in Sweden following the introduction of acellular pertussis vaccine. *Vaccine* 2003;21:2015-21. PMID:12706691 doi:10.1016/S0264-410X(02)00777-6
18. Succi RC, Farhat CK. Vaccination in special situations. *J Pediatr (Rio J)* 2006; 82:S91-100. PMID:16683052 doi:10.2223/JPED.1474
19. Ehreth J. The global value of vaccination. *Vaccine* 2003;21:596-600. PMID:12531324 doi:10.1016/S0264-410X(02)00623-0
20. Anon. Impact of vaccines universally recommended for children. 1900–1998. *Mortal Morb Wkly Rep* 1999;48:243-8.
21. Cutts FT, Zaman SM, Enwere G, Jaffar S, Levine OS, Okobo JB, et al. Gambian Pneumococcal Vaccine Trial Group. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial. *Lancet* 2005;365:1139-46. PMID:15794968 doi:10.1016/S0140-6736(05)71876-6
22. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, Abate H, Breuer T, Clemens SC, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Engl J Med* 2006;354:11-22. PMID:16394298 doi:10.1056/NEJMoa052434
23. Schmitt HJ, von Konig CH, Neiss A, Bogaerts H, Bock HL, Schulte-Wissermann H, et al. Efficacy of acellular pertussis vaccine in early childhood after household exposure. *JAMA* 1996;275:37-41. PMID:8531284 doi:10.1001/jama.275.1.37
24. Preziosi M-P, Halloran ME. Effect of pertussis vaccination on disease: vaccine efficacy in reducing clinical severity. *Clin Infect Dis* 2003;37:772-9. PMID:12955637 doi:10.1086/377270
25. Vazquez M, LaRussa PS, Gershon AA, Niccolai LM, Muehlenbein CE, Steinberg SP, et al. Effectiveness over time of varicella vaccine. *JAMA* 2004; 291:851-5. PMID:14970064 doi:10.1001/jama.291.7.851
26. Innis BL, Snitbhan R, Kunasol P, Laorakpongse T, Poopatanakol W, Kozik CA, et al. Protection against hepatitis A by an inactivated vaccine. *JAMA* 1994; 271:1328-34. PMID:8158817 doi:10.1001/jama.271.17.1328
27. Harper DM, Franco EL, Wheeler CM, Moscicki AB, Romanowski B, Roteli-Martins CM, et al. HPV Vaccine Study Group. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. *Lancet* 2006;367:1247-55. PMID:16631880 doi:10.1016/S0140-6736(06)68439-0
28. Banatvala J, Van Damme P, Oehen S. Lifelong protection against hepatitis B: the role of vaccine immunogenicity in immune memory. *Vaccine* 2000; 19:877-85. PMID:11115711 doi:10.1016/S0264-410X(00)00224-3
29. Adegbola R, Secka O, Lahai G, Lloyd-Evans N, Njie A, Usen S, et al. Elimination of *Haemophilus influenzae* type b (Hib) disease from the Gambia after introduction of a Hib conjugate vaccine: a prospective study. *Lancet* 2005;366:144-50. PMID:16005337 doi:10.1016/S0140-6736(05)66788-8

30. Moulton LH, Chung S, Croll J, Reid R, Weatherholtz RC, Santosham M. Estimation of the indirect effect of *Haemophilus influenzae* type b conjugate vaccine in an American Indian population. *Int J Epidemiol* 2000;29:753-6. PMID:10922355 doi:10.1093/ije/29.4.753
31. Schlenker TL, Bain C, Baughman AL, Hadler SC. Measles herd immunity: the association of attack rates with immunization rates in preschool children. *JAMA* 1992;267:823-6. PMID:1732654 doi:10.1001/jama.267.6.823
32. Ali M, Emch M, von Seidlein L, Yunus M, Sack D, Rao M, et al. Herd immunity conferred by killed oral cholera vaccines in Bangladesh. *Lancet* 2005; 366:44-9. PMID:15993232 doi:10.1016/S0140-6736(05)66550-6
33. John TJ, Samuel R. Herd immunity and herd effect: new insights and definitions. *Eur J Epidemiol* 2000;16:601-6. PMID:11078115 doi:10.1023/A:1007626510002
34. Anderson RM, May RM. *Infectious diseases of humans: dynamics and control*. Oxford: Oxford University Press; 1991.
35. Hanna JN, Hills SL, Humphreys JL. Impact of hepatitis A vaccination of indigenous children on notifications of hepatitis A in north Queensland. *Med J Aust* 2004;181:482-5. PMID:15516191
36. Andre FE. Universal mass vaccination against hepatitis A. In: Plotkin SA, ed. *Mass vaccination: global aspects – progress and obstacles. Current Topics in Microbiology* 2006; 304: 95-114.
37. Fiore AE. Hepatitis A transmitted by food. *Clin Infect Dis* 2004;38:705-15. PMID:14986256 doi:10.1086/381671
38. Crowcroft NS, Booy R, Harrison T, Spicer L, Britto J, Mok Q, et al. Severe and unrecognised: pertussis in UK infants. *Arch Dis Child* 2003;88:802-6. PMID:12937105 doi:10.1136/adc.88.9.802
39. Manzoli L, Schioppa F, Boccia A, Villari P. The efficacy of the influenza vaccine for healthy children: a meta-analysis evaluating potential sources of variation in efficacy estimates including study quality. *Pediatr Infect Dis J* 2007; 26:97-106. PMID:17259870 doi:10.1097/01.inf.0000253053.01151.bd
40. Strebel PM, Papania MJ, Halsey NA. Measles vaccine. In: Plotkin SA, Orenstein WA, eds. *Vaccines*, 4th ed. Philadelphia: WB Saunders; 2004; 389-440.
41. Peltola H, Siitonen A, Kyronseppa H, Simula I, Mattila L, Oksanen P, et al. Prevention of travellers' diarrhoea by oral B - subunit/whole-cell cholera vaccine. *Lancet* 1991;338:1285-9. PMID:1682684 doi:10.1016/0140-6736(91)92590-X
42. Chang MH. Decreasing incidence of hepatocellular carcinoma among children following universal hepatitis B immunization. *Liver Int* 2003;23:309-24. PMID:14708890 doi:10.1034/j.1478-3231.2003.00865.x
43. Kirk GD, Lesi OA, Mendy M, Akano AO, Sam O, Goedert JJ, et al. The Gambia Liver Cancer Study: Infection with hepatitis B and C and the risk of hepatocellular carcinoma in West Africa. *Hepatology* 2004;39:211-9. PMID:14752840 doi:10.1002/hep.20027
44. Aristegui J, Usonis V, Coovadia H, Riedemann S, Win KM, Gatchalian S, et al. Facilitating the WHO Expanded Programme of Immunization: the clinical profile of a combined diphtheria, tetanus, pertussis, hepatitis B and *Haemophilus influenzae* type b vaccine. *Int J Infect Dis* 2003;7:143-51. PMID:12839717 doi:10.1016/S1201-9712(03)90011-7
45. Decker MD. Principles of paediatric combination vaccines and practical issues related to use in clinical practice. *Pediatr Inf Dis J* 2001;20:S10-8. doi:10.1097/00006454-200111001-00002
46. Lieu TA, Cochi SL, Black SB, Halloran ME, Shinefield HR, Holmes SJ, et al. Cost effectiveness of a routine varicella program for US children. *JAMA* 1994; 271:375-81. PMID:8283587 doi:10.1001/jama.271.5.375
47. Bloom DE, Canning D, Weson M. The value of vaccination. *World Econ* 2005; 6:15-39.
48. Chabot I, Goetghebeur MM, Gregoire J-P. The societal value of universal childhood vaccination. *Vaccine* 2004;22:1992-2005. PMID:15121312 doi:10.1016/j.vaccine.2003.10.027
49. Miller MA, McCann L. *Policy analysis of the use of hepatitis B, Haemophilus influenzae* type B, *Streptococcus pneumoniae conjugate and rotavirus vaccines in immunization schedules. Health Econ* 2000;9:19-35. PMID:10694757 doi:10.1002/(SICI)1099-1050(200001)9:1<19::AID-HEC487>3.0.CO;2-C
50. Kyaw MH, Lynfield R, Schaffner W, Craig AS, Hadler J, Reingold A, et al. Active Bacterial Core Surveillance of the Emerging Infections Program Network. Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *N Engl J Med* 2006;354:1455-63. PMID:16598044 doi:10.1056/NEJMoa051642
51. Parry CM. Typhoid fever. *Curr Infect Dis Rep* 2004;6:27-33. PMID:14733846 doi:10.1007/s11908-004-0021-6
52. Lieberman JM. Appropriate antibiotic use and why it is important: the challenges of bacterial resistance. *Pediatr Infect Dis J* 2003;22:1143-51. PMID:14688589 doi:10.1097/01.inf.0000101851.57263.63
53. Nichol KL, Nordin J, Mullooly J, Lask R, Fillbrandt K, Iwane M. Influenza vaccinations and reductions in hospitalisations for cardiac disease and stroke among the elderly. *N Engl J Med* 2003;348:1322-32. PMID:12672859 doi:10.1056/NEJMoa025028
54. Christenson B, Hedlund J, Lundbergh P, Ortqvist A. Additive preventive effect of influenza and pneumococcal vaccines in elderly persons. *Eur Respir J* 2004;23:363-8. PMID:15065822 doi:10.1183/09031936.04.00063504
55. Klaber R, Booy R, El Bashir H, Mifsud A, Taylor S. Sustained outbreak of W135 meningococcal disease in east London, UK. *Lancet* 2002;360:644. PMID:12241960 doi:10.1016/S0140-6736(02)09795-7
56. Ahmed QA, Arabi YM, Memish ZA. Health risks at the Hajj. *Lancet* 2006; 367:1008-15. PMID:16564364 doi:10.1016/S0140-6736(06)68429-8
57. Steffen R, Banos A, de Bernardis C. Vaccination priorities. *Int J Antimicrob Agents* 2003;21:175-80. PMID:12615383 doi:10.1016/S0924-8579(02)00286-8
58. Nothdurft HD, Zuckerman J, Stoffel M, Dieussaert I, van Damme P. Accelerated vaccination schedules provide protection against hepatitis A and B in last-minute travelers. *J Travel Med* 2004;11:260-1. PMID:15541232
59. Shearley AE. The societal value of vaccination in developing countries. *Vaccine* 1999;17:S109-12. PMID:10559542 doi:10.1016/S0264-410X(99)00303-5
60. Ruff TA, Gertig DM, Otto BF, Gust ID, Sutanto A, Soewarso TI, et al. Lombok Hepatitis B Model Immunisation Project: Toward universal infant hepatitis B immunisation in Indonesia. *J Infect Dis* 1995;171:290-6. PMID:7844364
61. Martines J, Paul VK, Bhutta ZA, Koblinsky M, Soucat A, Walker N, et al. Lancet Neonatal Survival Steering Team. Neonatal survival: a call for action. *Lancet* 2005;365:1189-97. PMID:15794974 doi:10.1016/S0140-6736(05)71882-1
62. Hassani M, Patel MC, Pirofski LA. Vaccines for the prevention of diseases caused by potential bioweapons. *Clin Immunol* 2004;111:1-15. PMID:15093546 doi:10.1016/j.clim.2003.09.010
63. Press release, 8 July 2004. Pan American Health Organization. Available from: http://www.paho.org/English/DD/PIN/pr040708.htm
64. Wagstaff A. Poverty and health sector inequalities. *Bull World Health Organ* 2002;80:97-105. PMID:11953787
65. Flannery B, Schrag S, Bennett NM, Lynfield R, Harrison LH, Reingold A, et al. Impact of childhood vaccination on racial disparities in invasive *Streptococcus pneumoniae* infections. *JAMA* 2004;291:2197-203. PMID:15138241 doi:10.1001/jama.291.18.2197
66. Bishai D, Koenig M, Ali Khan M. Measles vaccination improves the equity of health outcomes: evidence from Bangladesh. *Health Econ* 2003;12:415-9. PMID:12720258 doi:10.1002/hec.732
67. Hotez PJ. Vaccines as instruments of foreign policy. *EMBO Rep* 2001;2:862-8. PMID:11600443 doi:10.1093/embo-reports/kve215
68. *Immunization profile – Sri Lanka*. Geneva: WHO. Available from: http://www.who.int/vaccines/globalsummary/immunization/countryprofileresult.cfm?C=
69. Stalenheim P, Fruchart D, Omitoogun W, Perdomo C. Military expenditure. In: *Stockholm International Peace Research Institute (SIPRI). SIPRI Yearbook 2006*. Oxford: Oxford University Press; 2006: 295-386.