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致：立法會衞生事務委員會主席李國英議員及各委員

促請立法會衞生事務委員會
盡快討論將肺炎鏈球菌疫苗納入
「香港兒童免疫接種計劃」之內

惠氏對於最近香港兒童健康疫苗關注組去信於立法會衞生事務委員會主席及各委員的文件深表關注及認同，我們亦希望在此呼籲香港政府及公共衞生決策者盡快考慮撥款，爲納入肺炎鏈球菌疫苗於「香港兒童免疫接種計劃」作準備。

作爲全球肺炎鏈球菌疫苗的領導者、服務香港社群四十年及連續 5 年獲頒「商界展關懷」標誌，惠氏一直竭盡所能爲保障本地兒童，免受肺炎鏈球菌危疾之苦而努力。

據世界衞生組織估計，肺炎鏈球菌疾病是全球最致命但能以疫苗預防的疾病中之首位。肺炎鏈球菌疾病在每一個國家及年齡組別都會發生，世衞估計每年有一百六十萬人死於此傳染病——這當中包括八十萬個五歲以下的兒童。

在很多已將肺炎鏈球菌接合疫苗納入兒童疫苗計劃的國家(包括英國、美國、歐洲等地)，已有研究肯定肺炎鏈球菌接合疫苗有助大幅減低已接種疫苗兒童及沒有接種疫苗人仕(尤其是老年人仕)患上肺炎鏈球菌疾病的發病率(群體免疫效應〝herd immunity〞)。

世衞已於 2007 年 3 月發出**全球立場書，建議推行肺炎鏈球菌疫苗兒童接種計劃**，對肺炎鏈球菌疾病帶來之危害作出了評估及確認了肺炎鏈球菌接合疫苗的安全及效益。

再者，世衞於本年 1 月的 *Weekly Epidemiological Record* 中，對還沒有被納入全民接種計劃的疫苗，就公共衞生的立場進行了一次排「優先考慮」序，並作出了指引。根據十種客觀的標準，初步確認**肺炎鏈球菌疾病爲「極優先」考慮的疾病預防級別**。

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本港兩大學院的專家亦分別作出了因肺炎鏈球菌疾病入院及接種肺炎鏈球菌接合疫苗的成本效益評估及研究，也曾先後發表了對納入肺炎鏈球菌疫苗於兒童免疫接種計劃的積極回應。

我們知悉衛生署已委託香港大學對納入一些新的疫苗(這當中包括肺炎鏈球疫苗)作出評估，而報告已接近完成階段。事實上，許多外國經濟效益研究已確認了肺炎鏈球菌接合疫苗(Prevenar®,沛兒®)的成本效益，世界著名的哈佛經濟學者 David Bloom 教授亦曾於其文獻「疫苗的價值」，強調「*疫苗是促進全民健康及福利中最有效的方法之一……。疫苗不應被看爲是增加公共衛生財政預算的重大支出，而應是列爲一項有長遠經濟效益的投資。*」

隨著新科技的發展及有效疫苗的推出，我們不能對那每年一百萬的死亡率視而不見。惠氏承諾會盡己所能，爲保障下一代及使肺炎鏈球菌疫苗普及化而努力。

隨函附上下列文件供主席及各委員細閱：

1. 世界衛生組織 2008 年 1 月發出的疫苗優先次序指引
2. David Bloom 教授的報告——疫苗的價值
3. 肺炎鏈球菌及疫苗資訊簡介

如有任何查詢，可與本人(電話: 2599-8875) 或我們的企業事務總監鄧寶蓮女士(電話:2599-8876)聯絡。

此致

美國惠氏藥廠(香港)有限公司總經理

鍾志偉

二零零八年一月二十八日

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Contents

Sommaire

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Meeting of the immunization Strategic Advisory Group of Experts, November 2007 – conclusions and recommendations

The Strategic Advisory Group of Experts (SAGE) on immunization reports to the Director-General of WHO on issues ranging from vaccine research and development, to immunization delivery. Its purview extends beyond childhood immunization to all vaccine-preventable diseases. SAGE met on 6–9 November 2007 in Geneva, Switzerland.

Report from the Department of Immunization, Vaccines and Biologicals

The Director of WHO's Department of Immunization, Vaccines and Biologicals (IVB) reported on the progress made on previous SAGE recommendations and highlighted global immunization progress. Since the April 2007 meeting, revised guidelines for bacille Calmette–Guérin (BCG) vaccination for infants at risk of HIV infection[1] and a WHO position paper on the use of rotavirus vaccines[2] have been published. A catalogue of immunization policy recommendations is now available on the IVB web site.[3] WHO's model list of essential medicines has been aligned with SAGE's recommendations and WHO's vaccine position papers. The department has made progress in implementing recommendations made by the external review of committees: terms of reference and modus operandi of committees are being revised; 1 new committee on quantitative research has been established;

[1] See No. 21, 2007, pp. 193–196.
[2] See No. 32, 2007, pp. 285–295.
[3] See www.who/immunization/documents/en/.

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, novembre 2007 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts (SAGE) rend compte au Directeur général de l'OMS sur des questions allant de la recherche-développement à l'administration des vaccins. Son domaine de compétences s'étend au-delà de la vaccination de l'enfant à toutes les maladies évitables par la vaccination. Le SAGE s'est réuni du 6 au 9 novembre 2007 à Genève (Suisse).

Rapport du Département Vaccination, vaccins et produits biologiques

Le Directeur du Département OMS Vaccination, vaccins et produits biologiques (IVB) a rendu compte des progrès accomplis dans la mise en oeuvre des précédentes recommandations du SAGE et décrit les progrès de la vaccination dans le monde. Depuis la réunion d'avril 2007, des lignes directrices révisées concernant la vaccination par le bacille de Calmette-Guérin (BCG) des nourrissons exposés à l'infection à VIH[1] ainsi qu'une prise de position de l'OMS sur l'utilisation du vaccin antirotavirus[2] ont été publiées. Un catalogue des recommandations concernant les politiques de vaccination est désormais disponible sur le site Web d'IVB.[3] La liste modèle OMS des médicaments essentiels a été alignée sur les recommandations du SAGE et les notes d'information de l'OMS sur les vaccins. Le Département a accompli des progrès dans la mise en œuvre des recommandations issues de l'évaluation externe des comités: le mandat et le mode de fonctionnement des comités sont actuellement révisés; un nouveau

[1] Voir N° 21, 2007, pp. 193-196.
[2] Voir N° 32, 2007, pp. 285-295.
[3] Voir http://www.who/immunization/documents/en/.

and a committee on technologies and logistics, and another on regulatory affairs, are under development. Linkages with regional technical consultative groups are being strengthened, and the department is working on several initiatives to help strengthen national technical advisory committees.

The Director highlighted the fact that despite progress being made in global immunization coverage, in 2006 an estimated 26.3 million children were not vaccinated with 3 doses of diphtheria–tetanus–pertussis (DTP3) vaccine, the vast majority of whom were in India and Nigeria.

The Director noted the progress that had been achieved in reducing measles mortality in 2006, with estimated deaths reduced by 68% compared with the 2000 level. Estimated routine coverage with the first measles dose reached 80%; 25 priority countries conducted supplementary immunization activities (SIAs) in 2006, the majority of which incorporated administration of vitamin A, oral poliovirus vaccine (OPV), deworming medications or distribution of insecticide-treated bed nets. This progress in mortality reduction has been paralleled by national advances in measles surveillance and the development of the global measles laboratory network, which includes 679 laboratories. There has been definite improvement in the uptake of *Haemophilus influenzae* type b (Hib) vaccine, with introduction in a further 28 countries planned for 2008. However, substantial portions of Asia and Eastern Europe have not planned to introduce the vaccine. Introduction of conjugate pneumococcal and rotavirus vaccines is also proceeding in developing countries.

SAGE was updated on the current meningococcal meningitis epidemic in the African meningitis belt. The global supply of meningococcal A vaccine is improving, with potentially increased vaccine availability from 2 manufacturers. However, the supply situation is still fragile, and the use of a fractional 1/5 dose remains an option in the event of shortage. As recommended by SAGE, WHO and Epicentre are working on a study protocol to assess the effectiveness of the 1/5 dose. There remains a funding shortfall of US$ 14 million needed to secure a stockpile for the 2007–2008 epidemic season.

SAGE acknowledged the progress made by the WHO secretariat in addressing SAGE's recommendations. SAGE requested that the Department develop a revised immunization schedule for SAGE to review in 2008. SAGE also requested a more detailed analysis of children who have not been reached by immunization services. With respect to the introduction of new vaccines, SAGE emphasized that WHO should look at achievements in coverage, in addition to decision-making processes and programmatic issues of new vaccine introduction.

Regional priorities and major policy and implementation issues

Reports were provided by the regional offices for the Americas, Europe and the Western Pacific.

comité sur la recherche quantitative a été créé; et un comité sur les technologies et la logistique ainsi qu'un autre sur les affaires réglementaires sont actuellement mis sur pied. Les liens avec des groupes consultatifs techniques régionaux sont en voie de renforcement et le Département travaille à plusieurs initiatives visant à renforcer les comités consultatifs techniques nationaux.

Le Directeur a souligné que, malgré les progrès accomplis en matière de couverture vaccinale au niveau mondial, en 2006, on estimait que 26,3 millions d'enfants n'étaient pas vaccinés par le vaccin antidiphtérique – antitétanique – anticoquelucheux (DTC3), dont la grande majorité en Inde et au Nigéria.

Le Directeur du Département IVB a souligné les progrès accomplis en matière de réduction de la mortalité rougeoleuse en 2006, le nombre estimatif des décès ayant été réduit de 68% par rapport au niveau de 2000. La couverture systématique par une première dose de vaccin antirougeoleux atteindrait 80% selon les estimations; 25 pays prioritaires ont conduit des activités de vaccination supplémentaires (AVS) en 2006, dont la majorité comportait l'administration de vitamine A, du vaccin antipoliomyélitique oral VPO, de vermifuges ou la distribution de moustiquaires imprégnées d'insecticide. Ces progrès en matière de réduction de la mortalité vont de pair avec des progrès au niveau national en matière de surveillance de la rougeole et la mise en place d'un réseau mondial de laboratoires de la rougeole qui compte 679 laboratoires. Le recours au vaccin anti-*Haemophilus influenzae* de type b s'est nettement amélioré et il est prévu de l'introduire dans 28 autres pays en 2008. Toutefois, des zones importantes d'Asie et d'Europe orientale n'ont pas prévu d'adopter le vaccin. L'introduction des vaccins antipneumococcique conjugué et antirotavirus se poursuit également dans les pays en développement.

Le SAGE a été mis au courant de l'épidémie actuelle de méningite méningococcique dans la ceinture africaine de la méningite. L'approvisionnement mondial en vaccin antiméningococcique A s'améliore, avec une offre potentielle accrue de vaccins de 2 fabricants. Toutefois, la situation de l'approvisionnement est encore fragile et l'utilisation d'un cinquième de dose demeure une option en cas de pénurie. Comme l'avait recommandé le SAGE, l'OMS et Epicentre travaillent à un protocole d'étude visant à évaluer l'efficacité d'un cinquième de dose. Un déficit de financement de US$ 14 millions subsiste en vue de la constitution d'un stock pour la saison épidémique 2007-2008.

Le SAGE a reconnu les progrès accomplis par le Secrétariat de l'OMS dans la mise en oeuvre de ses recommandations. Il a demandé au Département d'élaborer un calendrier de vaccination révisé à lui soumettre en 2008. Il a également demandé une analyse plus détaillée portant sur les enfants que les services de vaccination n'atteignent pas. En ce qui concerne l'adoption de nouveaux vaccins, le SAGE a souligné que l'OMS devrait examiner les réalisations en matière de couverture, et pas uniquement les processus décisionnels et les questions programmatiques.

Priorités régionales et principales questions concernant l'élaboration et la mise en œuvre des politiques

Les Bureaux régionaux des Amériques, de l'Europe et du Pacifique occidental ont présenté des rapports.

Region of the Americas

The presentation focused on the Regional Immunization Vision and Strategy, which is based on the *Global Immunization Vision and Strategy* document, that aims to contribute to the Millennium Development Goals (MDGs) by optimizing the use of immunization to reduce child mortality, improve women's and children's health, promote high-quality surveillance, achieve effective programme management, and strengthen partnerships and alliances. The Regional Immunization Vision and Strategy document has 3 strategic areas: protecting the achievements made, completing the unfinished agenda, and meeting new challenges.

The region has made tremendous gains in eradicating polio, eliminating measles and controlling diphtheria, pertussis, hepatitis B and Hib disease. Protecting these achievements is critical, along with introducing new vaccines and technologies. The 2 main unfinished issues are the elimination of rubella and congenital rubella syndrome (CRS) and making the transition from a childhood immunization programme to a family immunization programme. The Directing Council of the Region of the Americas and the Pan American Health Organization recently endorsed the goal of eliminating rubella by 2010. The region has seen a 98% reduction in rubella cases as a result of high coverage with a routine dose of measles–mumps–rubella vaccine and campaigns with measles–rubella vaccine extended to adults and adolescents. Several campaigns were conducted in 2007. In 2007, only 5 cases of CRS were reported in all of the Americas. It was recognized, however, that CRS surveillance was hospital based and may lack sensitivity; other more sensitive options are being explored in some countries. The region has also successfully implemented an "immunization week"in the Americas, which targeted older age groups, including the elderly. The vaccines used vary between countries based on national priorities. Future immunization weeks will be synchronized with immunization weeks in the European Region.

The third strategic area in the Region of the Americas is to contribute to achievement of MDGs by introducing new vaccines, namely rotavirus, pneumococcal and human papillomavirus (HPV) vaccines. To meet the new challenges associated with this strategic area, the region is developing tools and building capacity for evidence-based decision-making, strengthening the immunization infrastructure, promoting technical excellence and positioning the revolving fund for the future. In order to meet the requirements for introducing pneumococcal and rotavirus vaccines, the capitalization of the revolving fund needs to be increased to US$ 126 million by 2012, and additional resources will need to be mobilized.

European Region

Regional priorities include strengthening national immunization systems, sustaining polio eradication, achieving measles and rubella elimination by 2010, supporting the introduction of new and under-utilized vaccines and strengthening surveillance. In order to

Région des Amériques

Le rapport s'articulait autour de la stratégie régionale de vaccination, inspirée de *La vaccination dans le monde: vision et stratégie (GIVS)*, et le but étant de contribuer aux objectifs du Millénaire pour le développement (OMD) en optimisant l'utilisation de la vaccination afin de: réduire la mortalité de l'enfant, améliorer la santé des femmes et des enfants, promouvoir une surveillance de qualité, assurer une gestion efficace des programmes, et renforcer les partenariats et les alliances. La stratégie régionale de vaccination (RIVS) comporte 3 domaines stratégiques: protéger les acquis, terminer le programme en cours et relever de nouveaux défis.

La Région a accompli des progrès énormes en ce qui concerne l'éradication de la poliomyélite, l'élimination de la rougeole et la lutte contre la diphtérie, la coqueluche, l'hépatite B et l'infection à Hib. La protection de ces acquis est donc essentielle, de même que l'introduction de nouveaux vaccins et de nouvelles technologies. Les 2 principaux domaines dans lesquels les activités vont se poursuivre sont l'élimination de la rubéole et du syndrome de rubéole congénitale (SRC) et le passage d'un programme axé sur la vaccination de l'enfant à un programme de vaccination familiale. Le Conseil directeur de l'Organisation panaméricaine de la Santé et de la Région OMS des Amériques a récemment approuvé l'objectif de l'élimination de la rubéole d'ici 2010. La Région a enregistré une réduction de 98% du nombre de cas de rubéole suite à une couverture élevée par une dose de routine du vaccin rougeole- oreillons- rubéole et l'extension des campagnes de vaccination contre la rougeole et la rubéole aux adultes et aux adolescents. Plusieurs campagnes ont été organisées en 2007. En 2007, 5 cas seulement de SRC ont été signalés dans l'ensemble de la Région des Amériques. Il a toutefois été reconnu que la surveillance du SRC, basée dans les hôpitaux, pourrait manquer de sensibilité; d'autres solutions plus sensibles sont à l'étude dans certains pays. La Région a, par ailleurs, organisé avec succès la semaine de vaccination dans les Amériques, ciblée sur des groupes d'âge plus âgés, y compris les personnes âgées. Les vaccins utilisés varient selon les pays en fonction de leurs priorités nationales. Les futures semaines de vaccination seront synchronisées avec les semaines de vaccination dans la Région européenne.

Le troisième domaine stratégique dans la Région des Amériques vise à contribuer à la réalisation des OMD par l'introduction de nouveaux vaccins, à savoir les vaccins antirotavirus, antipneumococcique et antipapillomavirus humain (HPV). Afin de relever les nouveaux défis associés à ce domaine stratégique, la Région met au point des outils et développe ses capacités de prise de décision fondée sur des données factuelles, renforce l'infrastructure de vaccination, encourage l'excellence technique et positionne le fonds de roulement pour l'avenir. Afin de répondre aux besoins liés à l'introduction des vaccins antipneumococcique et antirotavirus, le capital du fonds de roulement doit en effet être augmenté de US$ 126 millions d'ici 2012 et des ressources supplémentaires devront être mobilisées.

Région européenne

Les priorités régionales sont le renforcement des systèmes nationaux de vaccination, le maintien de l'éradication de la poliomyélite, l'élimination de la rougeole et de la rubéole d'ici 2010, le soutien à l'introduction de vaccins nouveaux ou sous-utilisés et le renforcement de la surveillance. Pour atteindre

achieve these objectives, the regional office has developed a plan of action that has 3 strategic areas: immunization systems strengthening; targeted disease initiatives; and surveillance, laboratory and monitoring.

Currently, all countries in the region have achieved DTP3 coverage of >80%, with most countries having DTP3 coverage of >90%. However, the timeliness of vaccination remains a problem in some countries, and around 500 000 infants remain unimmunized. Delays partly result from the application of erroneous contraindications by physicians. In addition to these issues being directly addressed in the region, vaccinology modules need to be included in medical curricula. Under-immunized groups include the urban poor, remote populations, mobile groups and minorities. Reaching these subpopulations has been, and will remain, a priority in the region.

Large measles outbreaks continue to occur in the region despite high coverage of routine vaccination. The reasons for this, and the groups affected, vary between countries. Targeted SIAs have been carried out in 13 countries and are planned for 2008 in 2 additional countries with high measles incidence.

Sustaining polio-free status remains a priority through the support of surveillance for acute flaccid paralysis, the polio laboratory network, and other containment measures in countries at high risk of importation and transmission of poliovirus.

The introduction of Hib-containing vaccines shows a marked difference between countries in Western Europe and some of those in Eastern Europe and the Newly Independent States, with low uptake in countries in the Newly Independent States. Lack of recognition of the burden of Hib disease and relatively high vaccine prices are largely responsible. The approaches being taken to address these issues include finalizing a regional plan of action for the introduction of new vaccines, developing a regional strategic direction, and providing support for evidence-based decision-making for introduction.

In addition to the diversity in epidemiology, health-care systems and immunization programmes that characterize this region, the lack of governmental and partner support for surveillance, the lack of a comprehensive regional strategy, and inadequate financial, technical and strategic support have been a challenge. The region proposes to develop regional surveillance objectives; support national surveillance systems, especially sentinel surveillance for diseases targeted by new vaccines; and support laboratory networks. Links and collaboration have been established with the European Centre for Disease Prevention and Control to collaborate in surveillance activities, and a memorandum of understanding has been signed between the centre and WHO.

Western Pacific Region

The presentation by the Western Pacific Region focused on controlling hepatitis B. Recognition of the very high burden of disease in the region has led to an increased effort to control hepatitis B. Initial efforts in the 1990s

ces objectifs, le Bureau régional a élaboré un plan d'action qui comporte 3 domaines stratégiques: renforcement des systèmes de vaccination; initiatives ciblées contre des maladies; et surveillance, laboratoire et suivi.

A l'heure actuelle, tous les pays de la Région ont atteint une couverture par le DTC3 >80%, la plupart pouvant même se prévaloir d'une couverture >90%. Toutefois, la rapidité de la vaccination demeure un problème dans certains pays et près de 500 000 nourrissons ne sont pas vaccinés dans les temps. Les retards sont dus en partie à l'application de contre-indications erronées par les médecins. Outre ces questions, que la Région traite directement, des modules de vaccinologie doivent être inclus dans les programmes des études de médecine. Parmi les autres groupes mal vaccinés figurent des urbains pauvres, des populations isolées, des groupes mobiles et des minorités. La couverture de ces groupes de population est et restera une priorité dans la Région.

D'importantes épidémies de rougeole continuent de se produire dans la Région malgré une couverture vaccinale systématique élevée. Les raisons de ces phénomènes et les groupes touchés varient selon les pays. Des AVS ciblées ont été organisées dans 13 pays et sont prévues en 2008 dans 2 pays supplémentaires à forte incidence de la rougeole.

Le maintien de la situation lorsqu'une zone est exempte de poliomyélite grâce au soutien de la surveillance de la paralysie flasque aiguë, au réseau des laboratoires de la poliomyélite et à d'autres mesures d'endiguement dans les pays à fort risque d'importation et de transmission du poliovirus reste une priorité.

L'introduction de vaccins contenant le vaccin anti-Hib fait apparaître une nette différence entre les pays d'Europe occidentale et certains pays d'Europe orientale et les nouveaux Etats indépendants, où ces vaccins sont peu utilisés. Le manque de prise de conscience de la charge que représente l'infection à Hib et le prix relativement élevé du vaccin en sont largement responsables. Les approches suivies pour remédier à ce problème sont les suivantes: finaliser un plan d'action régional pour l'introduction de nouveaux vaccins, définir une orientation stratégique régionale et apporter un appui à la prise de décision fondée sur des données factuelles en faveur de l'introduction de ces vaccins.

Outre la diversité des tableaux épidémiologiques, des systèmes de soins de santé et des programmes de vaccination qui caractérise la Région, le manque d'appui des pouvoirs publics et des partenaires en faveur de la surveillance, l'absence de stratégie régionale d'ensemble et le manque de soutien financier, technique et stratégique posent problème. La Région propose d'établir des objectifs régionaux de surveillance, de soutenir les systèmes nationaux de surveillance, notamment la surveillance sentinelle pour les maladies cibles des nouveaux vaccins, et de soutenir les réseaux de laboratoire. Des liens et une collaboration ont été établis avec le Centre européen de Prévention et de Contrôle des Maladies pour collaborer aux activités de surveillance, et un mémorandum d'accord a été signé entre le Centre et l'OMS.

Région du Pacifique occidental

Le rapport régional a essentiellement porté sur la lutte contre l'hépatite B. La reconnaissance de la très forte charge que représente la maladie dans la Région a conduit à accroître les efforts de lutte contre celle-ci. Les efforts commencés dans les

focused on overcoming the high cost of vaccine by building regional consensus, increasing the number of manufacturers within the region, and introducing the vaccine on a cost-sharing basis and subsequently through the support of the GAVI Alliance. Since 2000, the main challenges have been suboptimal coverage of vaccines; financing problems in countries that have relatively low gross national income, notably the Philippines, and are not eligible for funds from the GAVI Alliance; failure to administer the birth dose in some countries and hence prevent perinatal transmission; and coincidental severe adverse events at the time of the birth dose.

The regional response to these issues has been to revise the regional action plan in order to achieve the regional goal for hepatitis B control and to reduce chronic hepatitis B infection in children aged <5 years to <2% by 2012 (and ultimately <1%). This goal was chosen to provide also the opportunity to improve immunization delivery, serve as an indicator for programme performance, and link the delivery of other interventions to improvements in neonatal and maternal health. Efforts currently being made to achieve these goals include producing field guidelines for delivering the birth dose and supporting countries in implementing the guidelines. As a result, vaccine coverage has improved and an increasing number of countries are providing the birth dose in a timely manner.

The region has developed processes for monitoring progress towards achieving the regional goal, particularly by using national serosurveys to determine the prevalence of surface hepatitis B antigen and by using vaccination coverage data. Future steps include improving delivery of routine services, ensuring financial sustainability after the end of GAVI Alliance support, implementing the certification process and the regional action plan, collecting empirical data to support policies on the timing of the birth dose, co-administering the birth dose with BCG, using hepatitis B vaccine outside the cold chain and introducing other new vaccines.

SAGE endorsed the region's goals and action plan and recognized the need to clarify remaining issues about the timing of delivery of the birth dose and the use of vaccines outside the cold chain.

Report from the GAVI Alliance

The GAVI Alliance's Executive Secretary noted that there has been strong growth in the introduction of new vaccines, with most eligible countries having been approved to introduce hepatitis B and Hib vaccines. The first country applications for support for pneumococcal and rotavirus vaccines have been approved. A recent analysis of applications by the Alliance's Independent Review Committee demonstrated that an increased number of countries have greater capacity to pay, there have been improvements in the completeness of information (including new vaccine introduction plans) and there has been an overall improvement in the quality of applications. WHO's technical assistance to these countries was commended. Countries were increasingly availing themselves of the new opportunities for health-system support funds.

années 90 visaient surtout à surmonter le coût élevé du vaccin en favorisant un consensus au niveau régional, en accroissant le nombre de fabricants dans la Région et en introduisant le vaccin sur la base d'un partage des coûts, puis avec un appui de l'Alliance GAVI. Depuis 2000, les principaux problèmes ont été une couverture vaccinale laissant à désirer, des problèmes financiers dans les pays qui n'ont pas droit à un soutien de l'Alliance et qui ont un revenu national brut relativement faible – les Philippines notamment –, la non-administration de la dose à la naissance et donc l'absence de prévention de la transmission périnatale dans certains pays, et la survenue de manifestations indésirables graves coïncidant avec l'administration de la dose à la naissance.

La réponse de la Région a consisté à réviser le plan d'action régional en vue d'atteindre l'objectif régional pour la lutte contre l'hépatite B, de ramener le taux d'infection chronique par l'hépatite B chez les enfants de <5 ans à <2% d'ici 2012 (puis à <1%). Cet objectif a été choisi afin d'offrir également la possibilité d'améliorer l'administration des vaccinations, de servir d'indicateur de l'efficacité du programme et de lier la fourniture d'autres interventions à des améliorations en matière de santé de la mère et du nouveau-né. Parmi les efforts actuellement déployés pour atteindre ces objectifs figurent la production de guides de terrain pour l'administration de la dose à la naissance et l'appui aux pays pour l'application de ces directives. Grâce à cela, la couverture vaccinale s'est améliorée et un nombre croissant de pays administrent la dose à la naissance dans les délais voulus.

La Région a mis au point des processus permettant de suivre les progrès vers la réalisation de l'objectif régional, en particulier grâce à des enquêtes sérologiques nationales sur la prévalence de l'antigène de surface de l'hépatite B (Ag HBs) et à des données sur la couverture vaccinale. A l'avenir, il s'agira d'améliorer la fourniture des services de vaccination systématique, d'assurer la fiabilité financière une fois le soutien de l'Alliance arrivé à son terme, de mettre en oeuvre le processus de certification, d'appliquer le plan d'action régional, de recueillir des données empiriques à l'appui des politiques sur le moment où doit être administrée la dose à la naissance, de coadministrer la dose à la naissance et le BCG, d'utiliser le vaccin anti hépatite B en dehors de la chaîne du froid et d'introduire d'autres vaccins nouveaux.

Le SAGE a approuvé les objectifs et le plan d'action de la Région et reconnu la nécessité de clarifier les questions en suspens concernant le moment de l'administration de la dose à la naissance et l'utilisation du vaccin en dehors de la chaîne du froid.

Rapport de l'Alliance GAVI

Le Secrétaire exécutif de l'Alliance GAVI a noté la forte progression de l'adoption de nouveaux vaccins, l'introduction des vaccins anti-hépatite B et anti-Hib ayant été approuvée dans les pays où ceux-ci se justifient le plus. Les premières demandes d'appui à l'introduction des vaccins antipneumococcique et antirotavirus ont été approuvées. Une analyse récente des demandes par le Comité d'examen indépendant de l'Alliance a fait apparaître de plus grandes capacités financières pour des pays de plus en plus nombreux, une information beaucoup plus complète (y compris s'agissant des plans d'introduction de nouveaux vaccins) et une amélioration générale de la qualité des demandes. L'OMS a été félicitée de l'assistance technique qu'elle apporte à ces pays. Les pays mettent de plus en plus à profit les nouvelles possibilités de financement à l'appui du système de santé.

Several SAGE and regional technical advisory group members raised concerns about the GAVI Alliance's eligibility criteria. The potential exists for non-eligible middle-income countries to fail to find resources to introduce new vaccines. The Alliance's Executive Secretary noted that any revision to the eligibility criteria would have to be initiated by the GAVI Alliance's Board. Similarly, the matter of the long-term sustainability of financing for new vaccines by countries was raised. Both the co-financing policy and the long-term financing outlook provided by the GAVI Alliance were important steps taken towards ensuring sustainability. More information was sought about how investment in health systems is improving immunization programmes.

Reports from other immunization-related advisory committees

SAGE was provided with reports from the Global Advisory Committee on Vaccine Safety, WHO's Expert Committee on Biological Standardization and the Advisory Committee of WHO's Initiative for Vaccine Research.

SAGE was presented with a report of the September 2007 meeting of the HPV Expert Advisory Group. SAGE had requested that the group review the evidence to be included in a WHO position paper on HPV vaccines and to identify outstanding questions on vaccine performance and delivery. The Chair summarized the committee's accomplishments. There was a strong consensus that evidence is now sufficient to draft recommendations on the use of HPV vaccine for consideration by SAGE. WHO's first consultations in the regions of the Americas, Europe and South-East Asia have shown there is great interest in HPV vaccines, but concerns about affordability, access and the development of delivery systems for pre-adolescents remain. The 2007 60th World Health Assembly noted the Executive Board's reports referred to in WHA60(12) that make reference to the progress report on *Cancer prevention and control (Resolution WHA58.22): cervical cancer* that recommended integrating HPV vaccines into existing immunization, cancer control and reproductive and adolescent health programmes; accelerating affordability and sustainable financing in the context of financing existing screening programmes; and using opportunities offered by HPV vaccination programmes to strengthen other pre-adolescent health interventions. In June 2007, the Global Advisory Committee on Vaccine Safety concluded that the safety data are reassuring.[4] SAGE concluded that it should expeditiously discuss HPV vaccines after receiving a detailed background paper.

Target product profile for pneumococcal conjugate vaccines

The advanced market commitment (AMC) involves a financial commitment made by donors to subsidize vaccine demand by GAVI-eligible countries at a set

[4] See No. 28/29, 2007, pp. 252–259.

Plusieurs membres du SAGE et des Groupes consultatifs techniques régionaux ont exprimé leur préoccupation au sujet des critères d'admissibilité appliqués par l'Alliance. Il existe un risque potentiel pour les pays à revenu intermédiaire qui ne répondent pas aux critères de l'Alliance de ne pas parvenir à trouver les ressources nécessaires à l'introduction de nouveaux vaccins. Le Secrétaire exécutif de l'Alliance a noté que toute révision des critères d'admissibilité devrait être entreprise à l'initiative du Conseil de l'Alliance. De même, la question du maintien à long terme du financement de nouveaux vaccins par les pays a été soulevée. Tant la politique de cofinancement que les perspectives de financement à long terme fournies par l'Alliance sont des pas importants pour assurer la viabilité à terme. De plus amples informations ont été demandées au sujet de l'amélioration apportée aux programmes de vaccination du fait des investissements dans les systèmes de santé.

Rapports d'autres comités consultatifs liés à la vaccination

Le SAGE a été reçu des rapports du Comité consultatif mondial de la Sécurité vaccinale, du Comité d'experts de la Standardisation biologique et du Comité consultatif OMS de l'Initiative pour la Recherche sur les Vaccins.

Le SAGE a été saisi d'un rapport de la réunion de septembre 2007 du Groupe consultatif d'experts sur le vaccin antipapillomavirus humain (HPV). Il a demandé au Groupe de passer en revue les données factuelles à faire figurer dans une prise de position de l'OMS sur les vaccins anti-HPV et de recenser les questions en suspens concernant l'efficacité et l'administration du vaccin. Le Président du Groupe a récapitulé les réalisations du Comité. Un net consensus s'est dégagé pour affirmer que les connaissances sont désormais suffisantes pour rédiger des propositions de recommandations concernant l'utilisation du vaccin anti-HPV et les soumettre au SAGE. Les premières consultations de l'OMS dans les Régions des Amériques, européenne et de l'Asie du Sud-Est ont fait apparaître un vif intérêt pour les vaccins anti-HPV, mais des questions subsistent quant à leur coût, l'accès à ceux-ci et la mise au point de systèmes de distribution pour les préadolescents. En 2007, la Soixantième Assemblée mondiale de la santé a pris note du rapport du Conseil exécutif de l'OMS (document WHA60(12)) qui fait référence au rapport de situation relatif à la résolution WHA58.22: *Prévention et lutte anticancéreuse: cancer du col de l'utérus*, recommandant d'intégrer des vaccins anti-HPV dans les programmes existants de vaccination, de lutte anticancéreuse et de santé génésique et des adolescents, d'accélérer l'accès et le financement durable en même temps que le financement des programmes de dépistage existants; et d'utiliser les possibilités offertes par les programmes de vaccination anti-HPV pour renforcer d'autres interventions pour la santé des préadolescents. En juin 2007, le Comité consultatif mondial de la Sécurité vaccinale a conclu que les données disponibles concernant l'innocuité étaient rassurantes.[4] Le SAGE a estimé qu'il devait rapidement examiner la question des vaccins anti-HPV dès qu'il aurait reçu un rapport de fond détaillé.

Profil de produit cible (TPP) pour les vaccins antipneumococciques conjugués

L'engagement d'achat à terme (AMC) suppose un engagement financier des donateurs qui subventionnent la demande de vaccins des pays répondant aux critères GAVI à un prix fixé,

[4] Voir N° 28/29, 2007, pp. 252–259.

price as long as the vaccine in question meets a specific target product profile (TPP). The goal of an AMC is to motivate suppliers and accelerate vaccine introduction. In November 2006,[5] SAGE was tasked with providing recommendations to the AMC independent advisory committee on a TPP for pneumococcal conjugate vaccines. The independent advisory committee will determine whether vaccines proposed by manufacturers comply with the TPP and are eligible for purchase by the GAVI Alliance with AMC funds.

An AMC/TPP is a formal document setting the minimum acceptable performance criteria for AMC-eligible vaccines for the duration of the AMC. It may be modified only in exceptional circumstances. The TPP for pneumococcal conjugate vaccines was developed by an ad hoc expert committee building on WHO's guidelines and technical background documents and informed by the report by the Global Serotype Distribution Project.[6] SAGE reviewed the TPP proposed by the ad hoc expert group.

The Global Serotype Distribution Project estimates the incidence and proportion of the various serotypes of *Streptococcus pneumoniae* causing disease and death globally and regionally, and is based on an extensive review of published and unpublished data. The analysis shows variation in the distribution of serotypes across the different regions: in North America, 6–7 serotypes account for 80% of cases of invasive disease, whereas in Asia 11 types account for 80% of cases. However, the 8 most common types are the same in Africa and Asia. It was noted that serotypes 1, 5 and 14 are the most common in GAVI-eligible countries, and that the 6 most prevalent serotypes are the same across all regions, with differences in the ranking of these serotypes among regions. A vaccine formulation based on only 6 serotypes (1, 5, 6B, 14, 19F, 23F) would provide coverage in Africa and Asia only moderately inferior to that provided by the forthcoming 10-valent and 13-valent formulations. Moreover, it appears that useful regional formulations could be developed with only 3–5 serotypes.

The proposed TPP is composed of a master table listing the minimum acceptable performance criteria for AMC eligibility and a supplementary information document that provides the scientific rationale for the set criteria and proposes more demanding non-binding product characteristics. The TPP stipulates that eligible vaccines should cover at least 60% of the invasive disease isolates and must include serotypes 1, 5 and 14. Immunogenicity should be established according to existing WHO criteria, and the vaccine schedule should comprise no more than 3 doses in the first year of life. Moreover, the vaccine must be compatible for integration into national immunization schedules. Vaccine presentation should be in mono-dose or low multi-dose form, using liquid formulations only. Storage, packaging and labelling should follow WHO's guidelines. Vaccines need to be prequalified by WHO, and post-marketing surveillance should be conducted as per national regulation and WHO requirements.

[5] See No. 1/2, 2007, pp.1–16.

[6] See http://www.preventpneumo.org/pdf/GSP%20Summary%20for%20SAGE%20Nov6-8%202007_Oct%2019-07.pdf

pour autant que le vaccin en question réponde au profil de produit cible. Le but d'un AMC est de motiver les fournisseurs et d'accélérer l'introduction du vaccin. En novembre 2006,[5] le SAGE a été chargé de formuler des recommandations à l'intention du Comité consultatif indépendant (IAC) concernant un TPP pour les vaccins antipneumococciques conjugués. L'IAC déterminera si les vaccins proposés par les fabricants correspondent au TPP et peuvent être achetés par l'Alliance GAVI au moyen de fonds AMC.

Un TPP/AMC est un document officiel fixant les critères d'efficacité minimum acceptables pour les vaccins pouvant faire l'objet d'un AMC pour la durée de celui-ci. Il ne peut être modifié que dans des circonstances exceptionnelles. Le profil de produit cible du vaccin antipneumococcique a été élaboré par un comité d'experts ad hoc en s'appuyant sur les lignes directrices de l'OMS et sur des documents techniques inspirés du rapport sur le Projet mondial de cartographie de sérotypes.[6] Le SAGE a examiné le TPP proposé par le groupe d'experts ad hoc.

Le GSP estime l'incidence et la proportion des divers sérotypes de *Steptococcus pneumoniae* responsables de la morbidité et de la mortalité aux niveaux mondial et régional, et repose sur un examen approfondi des données publiées et non publiées. L'analyse fait apparaître des variations dans la répartition des sérotypes selon les différentes régions: en Amérique du Nord, 6-7 sérotypes sont responsables de 80% des cas de maladie invasive, tandis qu'en Asie 11 sérotypes sont responsables de 80% des cas. Toutefois, les 8 types les plus courants sont les mêmes en Asie et en Afrique. On a observé que les sérotypes 1, 5 et 14 étaient les plus répandus dans les pays répondant aux critères GAVI et que les 6 sérotypes les plus répandus sont les mêmes dans toutes les régions, mais pas forcément dans le même ordre. Une formulation vaccinale reposant sur 6 sérotypes seulement (1, 5, 6B, 14, 19F, 23F) conférerait en Afrique et en Asie une couverture qui ne serait que légèrement inférieure à celle conférée par les prochaines formulations dirigées contre 10 et 13 sérotypes. En outre, il apparaît que des formulations régionales utiles pourraient être mises au point au moyen de 3-5 sérotypes seulement.

Le profil de produit cible proposé est composé d'un tableau où sont énumérés les critères d'efficacité minimum acceptables pour être pris en considération en vue d'un AMC et d'un document d'information supplémentaire exposant les raisons scientifiques du choix des critères fixés et proposant des caractéristiques du produit plus contraignantes mais non obligatoires. Le TPP stipule que les vaccins répondant aux critères devraient couvrir au moins 60% des souches isolées correspondant à des pneumococcies invasives et comprendre les sérotypes 1, 5 et 14. L'immunogénicité devrait être établie selon les critères existants de l'OMS et le calendrier vaccinal, comporter au maximum 3 doses pendant la première année de vie. En outre, le vaccin devrait pouvoir être intégré aux calendriers vaccinaux nationaux. Le vaccin devrait se présenter en monodose ou multidoses (petit nombre de doses), et uniquement sous forme liquide. Le stockage, le conditionnement et l'étiquetage devraient être conformes aux directives OMS. Les vaccins devraient être présélectionnés par l'OMS et il faudrait exercer une surveillance postcommercialisation conforme aux exigences de l'OMS et à la réglementation nationale.

[5] Voir N° 1/2, 2007, pp.1-16.

[6] Voir http://www.preventpneumo.org/pdf/GSP%20Summary%20for%20SAGE%20Nov6-8%202007_Oct%2019-07.pdf

SAGE members agreed that the TPP takes careful account of vaccines currently in development, disease epidemiology and scientific opportunities. There were no significant issues identified in the TPP, although amendments were requested to be made particularly to the safety and reactogenicity section. SAGE's members approved the TPP, subject to amendment, for recommendation to WHO's Director-General.[7]

Poliomyelitis eradication

SAGE reviewed the intensified eradication effort, launched following the Director-General's urgent stakeholder consultation and outlined in *The case for completing polio eradication*[8] in May 2007. New studies in India and Nigeria showed that monovalent OPVs afford a 3-fold to 4-fold higher effectiveness per dose than trivalent OPV. An October 2007 report found countries were largely on track to achieve the new milestones for polio eradication as a result of the new tools (such as monovalent OPVs) and tactics that had been tailored to each remaining infected area. In endemic countries, the proportion of polio-infected districts fell by 51% compared with 2006 (type-1 infected districts fell by 75%); coverage in infected areas had improved, except in southern Afghanistan and northern Nigeria. Of the 13 countries reinfected in 2006, all but 3 had already stopped transmission. The fourth milestone remained unmet, with a funding gap of US$ 60 million remaining to the end of 2007.

SAGE affirmed that with the new tools, tactics and commitments, interruption of wild poliovirus transmission globally was possible in the near term. The highest priority is to rapidly reach the large proportion of non-immunized children (30%) in the 3 very-high-risk states in northern Nigeria. SAGE was alarmed at the financing gap for 2008–2009 (>US$ 500 million). To better assess and track progress, SAGE requested further details on the immunization status of cases relative to the general population and analyses of the contribution of recent outbreaks to the current low incidence of cases.

SAGE reviewed the outcomes of the United States National Institutes of Health (NIH) meeting held in September 2007 (known as "Polio immunization: moving forward"), which discussed challenges to eradication, the strengths and weaknesses of OPV and inactivated poliovirus vaccine (IPV), current research activities and future policy considerations. The NIH meeting found broad support for completing eradication, adding IPV to accelerate eradication in India, stopping routine use of OPV worldwide after wild poliovirus eradication and expanding the use of IPV to protect future populations from poliovirus re-emergence. Promising approaches were presented for enhancing the safety of IPV production using alternate seed strains, thereby facilitating production in low-income settings. Such production, combined with fractional dosing, the use of adjuvants and reduced-dose schedules, could substantially reduce IPV costs.

[7] See http://www.who.int/immunization/sage/target_product_profile.pdf

[8] *The case for completing polio eradication.* Geneva, WHO, 2007. (Available from http://www.polioeradication.org/content/general/TheCase_FINAL.pdf)

Les membres du SAGE ont reconnu que le TPP tenait pleinement compte des vaccins actuellement mis au point, de l'épidémiologie de la maladie et des possibilités scientifiques. Le document n'a pas soulevé de problèmes importants même si des amendements ont été demandés, en particulier dans la section concernant l'innocuité et la réactogénicité. Les membres du SAGE ont approuvé le TPP sous réserve d'amendements en vue de sa recommandation au Directeur général de l'OMS.[7]

Eradication de la poliomyélite

Le SAGE a examiné l'effort intensifié d'éradication annoncé suite à la consultation urgente des partenaires organisée par le Directeur général et exposé dans le document intitulé *Les arguments pour mener à son terme l'éradication de la poliomyélite*[8] (mai 2007). Les nouvelles études menées au Nigéria et en Inde ont montré que le VPO monovalent offrait une efficacité par dose supérieure de 3 à 4 fois à celle du VPO trivalent. Un rapport d'octobre 2007 a révélé que les pays étaient sur le point d'atteindre les nouveaux jalons fixés pour l'éradication de la poliomyélite grâce aux nouveaux outils (VPOm) et une nouvelle tactique adaptée à chaque zone d'endémie restante. Dans les pays concernés, le nombre de districts touchés a diminué de 51% par rapport à 2006 (le nombre de districts infectés par le poliovirus type 1 a chuté de 75%); la couverture des zones touchées s'est améliorée, à l'exception du sud de l'Afghanistan et du nord du Nigéria. Sur les 13 pays réinfectés en 2006, tous sauf 3 ont déjà stoppé la transmission. La quatrième étape n'est toujours pas franchie et le déficit de financement jusqu'à fin 2007 est de US$ 60 millions.

Le SAGE a affirmé que, grâce aux outils, à la tactique et aux engagements nouveaux, l'interruption de la transmission du poliovirus sauvage dans le monde était possible à court terme. La priorité des priorités est d'atteindre rapidement la forte proportion d'enfants non vaccinés (30%) dans les 3 Etats «à très haut risque» du nord du Nigéria. Le SAGE est inquiet du déficit de financement pour 2008-2009 (>US$ 500 millions). Afin de mieux évaluer et suivre les progrès, il a demandé des informations plus détaillées sur l'état vaccinal des cas par rapport à celui de la population générale ainsi que des analyses montrant la contribution des flambées récentes au faible taux d'incidence actuel.

Le SAGE a examiné les conclusions de la réunion des National Institutes of Health (réunion à laquelle on se réfère sous le nom de «Polio immunization: moving forward»), qui s'est tenue en septembre 2007 et qui portait sur les problèmes posés par l'éradication, les points forts et les points faibles du VPO et du vaccin antipoliomyélitique inactivé (VPI), les activités de recherche en cours et les considérations politiques futures. La réunion des NIH a constaté un large appui pour mener à son terme l'éradication, en ajoutant le VPI de façon à accélérer l'éradication en Inde, en cessant l'utilisation systématique de VPO dans le monde une fois le poliovirus sauvage éradiqué et en élargissant l'utilisation du VPI pour protéger les populations futures de la réémergence du poliovirus. Des approches prometteuses ont été présentées pour renforcer la sécurité de la production du VPI au moyen d'autres souches de semence, ce qui faciliterait la production dans des milieux à faible revenu. Cette production, alliée au fractionnement des doses, à des adjuvants et à des calendriers d'administration réduits, pourrait permettre de réduire substantiellement les coûts du VPI.

[7] Voir http://www.who.int/immunization/sage/target_product_profile.pdf

[8] *Les arguments pour mener à son terme l'éradication de la poliomyélite.* Genève, OMS, 2007. (Accessible sur http://www.polioeradication.org/content/publications/TheCase_French.pdf)

SAGE highlighted the importance of carefully assessing any policy changes to be made in polio-free countries, noting that a switch from OPV to IPV would actually increase susceptibility to polioviruses. SAGE reaffirmed the need to explore fully the long-term role of IPV in order to facilitate timely development of appropriate products and delivery strategies. SAGE stated that the licensing of new IPV products should be feasible in the medium term since accepted correlates of protection exist. SAGE welcomed the reconvening of the WHO Polio Research Committee and requested that a future SAGE meeting devote sufficient time to reviewing long-term polio risks, strategies for managing and mitigating those risks, and their programmatic implications and opportunity costs in low-income settings.

Typhoid fever vaccines

WHO's IVB ad hoc working group on typhoid immunization presented to SAGE information on the magnitude of the disease burden of typhoid fever and the 2 new-generation licensed vaccines (Vi polysaccharide and Ty21a). Both vaccines have extensive safety and efficacy records in large-scale pre-licensure clinical trials and post-licensure demonstration projects. A high prevalence of typhoid fever has been found in several Asian sites, especially urban slums. Typhoid fever inflicts a high economic burden on families as well as on the health sector. There has been a significant increase in and spread of antibiotic resistance, and there is population demand for typhoid vaccines. Also, data have confirmed the impact and cost-effectiveness of the 2 new-generation typhoid vaccines. The number of producers and supplies of these vaccines have grown dramatically since 2000, with a resultant reduction in prices.

SAGE endorsed the following recommendations for typhoid vaccine utilization in regions where the disease is highly endemic.

1. In view of the continued high burden of typhoid fever and increasing antibiotic resistance, and given the safety, efficacy, feasibility and affordability of 2 licensed vaccines (Vi polysaccharide and Ty21a), countries should consider the programmatic use of typhoid vaccines for controlling endemic disease.

2. In most countries, control of the disease will require vaccination targeted only at high-risk groups and populations.
3. Countries should decide on the selection of populations and age groups to target, and on the delivery strategy (e.g. school-based or community-based vaccination), which will depend on the local context (age pattern of the disease, school enrolment rates, etc.).
4. Countries should select typhoid vaccines depending on the capacity of the local Expanded Programme on Immunization and other logistic and cultural factors, and should utilize opportunities coupled with other public health interventions in the age groups referred to in paragraph 3.

Le SAGE a souligné l'importance qu'il y a à évaluer avec soin tout changement au niveau des politiques dans les pays exempts de poliomyélite à l'heure actuelle, notant qu'un passage du VPO au VPI augmenterait en fait la sensibilité aux poliovirus. Le SAGE a réaffirmé la nécessité d'explorer pleinement le rôle à long terme du VPI pour faciliter la mise au point en temps opportun de produits et de stratégies de distribution appropriés. Il a indiqué que l'homologation de nouveaux VPI devrait être réalisable à moyen terme puisqu'il existe des indicateurs de protection reconnus. Le SAGE s'est félicité que le Comité de Recherche sur la Poliomyélite ait été à nouveau convoqué et a demandé qu'une future réunion du SAGE consacre suffisamment de temps à l'examen des risques poliomyélitiques à long terme, des stratégies visant à gérer et atténuer ces risques, et de leurs répercussions programmatiques ainsi que des coûts d'opportunité dans les milieux à faible revenu.

Vaccins antityphoïdiques

Le groupe de travail ad hoc OMS/IVB sur la vaccination antityphoïdique a exposé au SAGE l'ampleur de la charge de morbidité due à la fièvre typhoïde, et lui a présenté 2 vaccins homologués de nouvelle génération, le vaccin polyosidique Vi et le Ty21a. Ces 2 vaccins ont largement fait la preuve de leur innocuité dans des essais cliniques avant homologation et des projets de démonstration d'introduction après homologation et conduits à grande échelle. Une prévalence élevée de la typhoïde a été constatée dans plusieurs sites d'Asie, notamment des taudis urbains; la maladie représente une charge économique considérable pour les familles ainsi que pour le secteur de la santé; la résistance aux antibiotiques augmente sensiblement et s'étend; et il existe une demande de vaccins antityphoïdiques dans la population. Par ailleurs, les données confirment l'impact et la rentabilité des 2 vaccins antityphoïdiques de nouvelle génération. Le nombre de producteurs et de fournisseurs de ces vaccins a augmenté de façon spectaculaire depuis 2000, et les prix ont diminué en conséquence.

Le SAGE a approuvé les recommandations suivantes concernant l'utilisation du vaccin contre la typhoïde dans les régions où la maladie est fortement endémique.

1. Compte tenu de la charge élevée que continue de représenter la fièvre typhoïde et de l'augmentation de la résistance aux antibiotiques, et étant donné l'innocuité, l'efficacité, la faisabilité et le coût abordable de 2 vaccins homologués (Vi polysaccharide et Ty21a), les pays devraient envisager d'inscrire dans leurs programmes les vaccins antityphoïdiques pour lutter contre cette maladie lorsqu'elle est endémique.
2. Dans la plupart des pays, il suffira pour lutter contre la maladie de vacciner les groupes et les populations à haut risque.

3. Les pays devraient choisir les populations et les groupes d'âge visés ainsi que la stratégie d'administration (vaccination en milieu scolaire ou communautaire, par exemple) qui dépendra du contexte local (répartition par âge de la maladie, taux de scolarisation, etc.).

4. Les pays devraient sélectionner les vaccins antityphoïdiques – Ty21a ou Vi – en fonction de la capacité du Programme élargi de vaccination local, d'autres facteurs logistiques et culturels, et en utilisant les possibilités offertes par d'autres interventions de santé publique dans ces groupes d'âge.

5. The availability of the above-mentioned licensed typhoid vaccines will be enhanced by pre-qualification by WHO of these products and by enhanced global awareness and commitment to reduce the burden of typhoid disease.
6. Due to the epidemic potential of typhoid, and observations on the effectiveness of vaccination in interrupting outbreaks, typhoid vaccination is recommended for outbreak control.

7. Typhoid vaccination programmes should be implemented in the context of other efforts to control the disease, including health education programmes, improvements in water quality and sanitation, and programmes to train health professionals in diagnosis and treatment.
8. Given the importance of information on disease incidence for targeting vaccination and assessing its impact, priority should be given to strengthening surveillance systems for typhoid fever, including sentinel site surveillance in pre-school (2–4 years old) children and school-aged children (5–15 years old). The development of reliable and appropriate diagnostics assays for use in developing countries is required.
9. Development and research on new typhoid vaccines (such as the Vi conjugate vaccine) are encouraged, particularly for use in infants and young children, but this should not limit the use of currently available vaccines for control of endemic disease.

SAGE emphasized the need for feedback from WHO's regional offices and countries to determine how countries could implement SAGE's recommendations. SAGE anticipates that these responses will be available within 12–18 months.

SAGE also recommended that WHO's position paper on typhoid vaccine should be updated to reflect new information (e.g. on incidence of disease and vaccine effectiveness in children aged <5 years, and on herd immunity effects) and give specific guidance to countries on issues such as the choice of vaccine and delivery strategy (school-based versus community-based), age groups to vaccinate, the number of vaccine doses to be delivered and at what intervals, and when to repeat courses of vaccination.

The need for advocacy and prioritization at the international level was emphasized in order to support the broader introduction of typhoid vaccines into endemic countries. This includes prioritizing WHO's prequalification for new-generation typhoid vaccines and the need for international financing mechanisms.

Categorization of vaccine-preventable diseases

The WHO Vaccine-Preventable Diseases Categorization Project aimed to categorize, by public health priority, diseases for which vaccines are currently available but not yet recommended for universal use or are likely to be available in the near-term (by 2012). The goal of the project is meant to represent the overall global picture. The objectives of the project are to help guide

5. L'offre des vaccins antityphoïdiques homologués susmentionnés sera renforcée par la présélection de ces produits par l'OMS et par une sensibilisation et un engagement accrus au niveau mondial en vue de réduire la charge de morbidité due à la maladie.
6. En raison du caractère potentiellement épidémique de la typhoïde et des observations relatives à l'efficacité de la vaccination pour interrompre les flambées, la vaccination antityphoïdique est recommandée pour maîtriser les flambées.
7. Les programmes de vaccination contre la typhoïde devraient être mis en œuvre dans le cadre d'autres efforts de lutte contre la maladie, y compris l'éducation sanitaire, l'amélioration de la qualité de l'eau et de l'assainissement, et la formation des professionnels de santé au diagnostic et au traitement.

8. Compte tenu de l'importance de l'information sur l'incidence de la maladie pour cibler la vaccination et évaluer l'impact, la priorité devrait aller au renforcement des systèmes de surveillance de la typhoïde, et notamment la surveillance par des sites sentinelles chez les enfants d'âge préscolaire (2-4 ans) et scolaire (5-15 ans). Il faudrait mettre au point des épreuves diagnostiques fiables et adaptées pour les pays en développement.
9. La recherche et le développement de nouveaux vaccins antityphoïdiques (tels que le vaccin conjugué Vi) sont encouragés, en particulier pour l'administration au nourrisson et au jeune enfant, mais cela ne devrait pas limiter l'utilisation des vaccins actuellement disponibles pour lutter contre la maladie endémique.

Le SAGE a souligné la nécessité d'une information en retour des bureaux régionaux de l'OMS et des pays afin de déterminer comment les pays pourraient mettre en œuvre ces recommandations. Il a prévu que ces réponses seraient disponibles dans les 12 à 18 mois.

Le SAGE a également recommandé que la prise de position de l'OMS sur le vaccin antityphoïdique soit actualisée pour tenir compte des informations nouvelles (par exemple concernant l'incidence et l'efficacité du vaccin chez les enfants de <5 ans, et l'immunité collective), et donner des indications spécifiques aux pays sur des questions telles que le choix du vaccin et la stratégie de distribution (scolaire ou communautaire), les groupes d'âge à vacciner, le nombre de doses de vaccin à administrer et à quels intervalles, et les rappels.

La nécessité d'une sensibilisation et de la détermination de priorités au niveau international a été soulignée, afin de favoriser une plus large adoption des vaccins antityphoïdiques par les pays d'endémie. Il faut pour cela donner la priorité à la préqualification par l'OMS des vaccins antityphoïdiques de nouvelle génération, et mettre en place des mécanismes de financement internationaux.

Catégorisation des maladies à prévention vaccinale

Le projet OMS de catégorisation des maladies à prévention vaccinale vise à classer par catégories, selon leur degré de priorité pour la santé publique, les maladies pour lesquelles il existe actuellement des vaccins, mais dont l'usage universel n'est pas encore recommandé, ou pour lesquelles des vaccins devraient être disponibles à court terme (d'ici 2012). Le but du projet est de présenter une perspective mondiale. Ses objectifs

the development of a healthy vaccine market, to assist countries and partners in determining which vaccine-preventable diseases are priorities at the global level, and to help guide the work of global funding agencies, such as the GAVI Alliance, in making decisions about which vaccines to support.

In undertaking the categorization project, an approach of "rational consensus" was taken, using structured techniques to elicit the opinions of the global immunization community and disease experts. After conducting a landscape analysis in which information on all vaccine-preventable diseases and candidate vaccines was collected, input was obtained in 3 phases. In the first phase, a widespread consultation was held (by e-mail) to determine which diseases should be included in the exercise, as well as which criteria should be used in making public health decisions about evaluating diseases. In 2 subsequent phases, 38 expert individuals and institutions (members of SAGE, Chairs of regional technical advisory groups, WHO's regional advisers, and core immunization partners) were contacted.

Preliminary results in ranking the 10 criteria to be used to evaluate diseases in decreasing relative importance are as follows: mortality, epidemic or pandemic potential, economic impact, case-fatality rate, disease incidence in regions with the highest burden, long-term sequelae, morbidity, inequity (greater impact on the economically disadvantaged), lack of other alternative treatment or prevention measures, and severity of symptoms.

In this preliminary ranking, diseases were clustered into 3 groups: malaria and pneumococcal disease were ranked as "very high priorities"; HPV infections, cholera, dengue, Japanese encephalitis, meningococcal meningitis A, C, W135 and Y, rabies, rotavirus infections, seasonal influenza, typhoid fever, and yellow fever were ranked as "high priorities"; and hepatitis A, hepatitis E, meningococcal meningitis B, mumps, rubella and varicella were ranked as "medium priorities".

SAGE welcomed the effort to try to lead and guide public health priorities through careful analysis of the data and the use of a consultative process. SAGE's members acknowledged the fact that the methods used have general validity and have been used in similar prioritization exercises elsewhere, but urged that some reanalysis be considered because of the short timeframe in which respondents were expected to reply; the study should also be conducted on a regional basis.

SAGE concluded that the results should be considered preliminary and recommended that steps be taken to validate and complete the prioritization exercise. A second stage of this exercise should be undertaken to look at longer-term priorities for developing vaccines, taking a 10–20 year time horizon.

The Executive Secretary of the GAVI Alliance indicated that the process and results were potentially useful in the Alliance's considerations in developing a vaccine-investment strategy. Accordingly, the Chair of SAGE

consistent à aider à développer un marché sain pour les vaccins, à aider les pays et les partenaires à déterminer quelles maladies à prévention vaccinale sont prioritaires au niveau mondial et à guider l'action des organismes de financement mondiaux tels que l'Alliance GAVI, qui doivent prendre des décisions quant aux vaccins à financer.

En entreprenant le projet de catégorisation de ces maladies, on a adopté une approche fondée sur le «consensus rationnel», en utilisant des techniques structurées pour solliciter l'opinion des spécialistes mondiaux de la vaccination et des maladies. Après une analyse générale de la situation, au cours de laquelle des informations sur toutes les maladies évitables par la vaccination et tous les vaccins expérimentaux ont été recueillies, les données ont été réunies en 3 phases. Lors de la première phase, une consultation élargie a été organisée (par courrier électronique) sur les maladies à faire figurer dans l'exercice, ainsi que sur les critères à prendre en compte dans les décisions de santé publique concernant l'évaluation des maladies. Lors des 2 phases suivantes, 38 experts/institutions (membres du SAGE, Présidents des Groupes consultatifs techniques régionaux, conseillers régionaux de l'OMS et principaux partenaires de la vaccination) ont été contactés.

Les résultats préliminaires du classement des 10 critères par ordre d'importance relative décroissante sont les suivants: mortalité, potentiel épidémique/pandémique, impact économique, taux de létalité, incidence de la maladie dans les régions à plus forte charge de morbidité, séquelles à long terme, morbidité, inégalité (impact plus important sur les personnes économiquement désavantagées), absence d'autres traitements ou mesures de prévention, et gravité des symptômes.

Dans ce classement préliminaire, les maladies ont été regroupées en 3 catégories: le paludisme et les maladies pneumococciques, classées comme «priorités élevées»; les infections à papillomavirus, le choléra, la dengue, l'encéphalite japonaise, la méningite ACWY, la rage, les infections à rotavirus, la grippe saisonnière, la fièvre typhoïde et la fièvre jaune, classés comme «priorités élevées», et l'hépatite A, l'hépatite E, la méningite B, les oreillons, la rubéole et la varicelle, classés comme «priorités moyennes».

Le SAGE a salué les efforts visant à diriger et orienter les priorités de santé publique à travers une analyse soigneuse des données disponibles et un processus de consultation. Les membres du SAGE ont reconnu que les méthodes utilisées étaient généralement valables et avaient été utilisées lors d'exercices analogues de détermination des priorités dans d'autres domaines, mais a invité instamment à envisager une nouvelle analyse, en raison du délai très court qui avait été laissé aux personnes consultées pour répondre; l'étude devrait également être conduite sur une base régionale.

Le SAGE a conclu que les résultats actuels devaient être considérés comme préliminaires et recommandé des étapes afin de valider et parachever l'exercice de détermination des priorités. Une deuxième étape de cet exercice devrait consister à examiner les priorités à plus long terme pour la mise au point de vaccins, à l'horizon de 10 à 20 ans.

Le Secrétaire exécutif de l'Alliance GAVI a indiqué que la démarche suivie et les résultats pouvaient être utiles à l'Alliance pour élaborer une stratégie d'investissement en matière de vaccins. Aussi le Président du SAGE a-t-il présenté ces résultats

presented these preliminary results to the November 2007 meeting of the GAVI Alliance's Board, and a refined version, taking into account SAGE's recommendations above, will be made available by the April 2008 SAGE meeting.

Potential uses of WHO H5N1 vaccine stockpile and H5N1 vaccine

In May 2007, the World Health Assembly requested that WHO develop a stockpile of influenza A (H5N1) vaccine. Plans by WHO to develop this stockpile have been supported by a pledge of 50 million vaccine doses made by GlaxoSmithKline Biologicals, which is under negotiation, and pledges of unspecified amounts of vaccine by 3 other companies. Several other H5N1 vaccines are under development by additional companies, and the regulatory approval of some H5N1 vaccines is anticipated in the near future. In 2 separate WHO consultations held in October 2007, safety and immunogenicity data were reviewed as were the critical technical parameters of this stockpile.

The establishment of an H5N1 vaccine stockpile by WHO provides an important new opportunity for mitigating the impact of an H5N1 pandemic. However, from the outset, it has been clear that WHO's stockpile will not be sufficient to meet most national needs for vaccine if an H5N1 pandemic occurs. Therefore, countries must develop and continue to update comprehensive, operational pandemic preparedness plans and, if vaccines are considered to be a national priority in those plans, explore other additional avenues for accessing H5N1 vaccines. In this regard, WHO's work with manufacturers to increase the production capacity and supplies of H5N1 vaccines at affordable prices is urgent. Although the stockpile will increase access by countries to H5N1 vaccine, the supplies should not be considered a substitute for pandemic preparedness plans.

SAGE reviewed current evidence on H5N1 vaccines with regard to safety and immunogenicity. Based on this review, SAGE found no data indicating undue safety concerns related to these vaccines over seasonal influenza vaccines but noted that larger studies are needed to assess the incidence of rare reactions. Data on vaccination in children are needed. Data were reassuring about cross-reactivity against heterologous strains; long-term studies on immune responses to boosting will be important. Agreement on standard immunological criteria and standard reagents for assessing H5N1 vaccine immunogenicity are needed to improve comparisons of clinical trials of different vaccines.

SAGE made the following recommendations.

1. WHO should continue to urgently develop the H5N1 vaccine stockpile and develop associated procurement, management, governance, regulatory and distribution procedures, as well as procuring necessary ancillary supplies such as syringes and needles. In doing so, WHO should also address the logistic aspects and long-term sustainability of the stockpile.

préliminaires au Conseil de l'Alliance en novembre 2007, et une version révisée tenant compte des recommandations susmentionnées du SAGE sera mise à disposition par celui-ci lors de sa réunion d'avril 2008.

Utilisations potentielles du stock de vaccin anti-H5N1 de l'OMS et du vaccin anti-H5N1

En mai 2007, l'Assemblée mondiale de la Santé a demandé que l'OMS constitue un stock de vaccin contre la grippe A (H5N1). La constitution de ce stock par l'OMS s'est appuyée sur une promesse de GlaxoSmithKline Biologicals de fournir 50 millions de doses de vaccin (en cours de négociation), et sur la fourniture annoncée de quantités non précisées de vaccin par 3 autres sociétés. D'autres laboratoires sont en train de mettre au point plusieurs autres vaccins anti-H5N1 et l'on prévoit que certains vaccins anti-H5N1 seront approuvés prochainement. Lors de 2 consultations distinctes de l'OMS tenues en octobre 2007, les données disponibles quant à l'innocuité et à l'immunogénicité, ainsi que les paramètres techniques essentiels de ce stock ont été passés en revue.

La constitution d'un stock OMS de vaccin anti-H5N1 représente une possibilité nouvelle importante d'atténuer l'impact d'une pandémie de grippe H5N1. Toutefois, depuis le départ, il est apparu clairement que le stock OMS ne serait pas suffisant pour répondre à la plupart des besoins nationaux en cas de pandémie. C'est pourquoi les pays doivent élaborer et continuer à mettre à jour des plans complets et opérationnels de préparation à une pandémie et, si les vaccins sont considérés comme une priorité nationale, à étudier des moyens supplémentaires de se procurer des vaccins anti-H5N1. A cet égard, il est urgent que l'OMS s'emploie avec les fabricants à accroître les capacités de production et la fourniture de vaccin anti-H5N1 à des prix abordables pour les pays. Même si le stock permettra d'accroître l'accès des pays au vaccin anti-H5N1, il ne doit pas être considéré comme un substitut à un plan de préparation à une pandémie.

Le SAGE a examiné les données disponibles sur les vaccins anti-H5N1 eu égard à leur innocuité et à leur immunogénicité. Sur la base de cet examen, il n'a trouvé aucune donnée indiquant que les vaccins anti H5N1 susciteraient davantage de préoccupations en termes de sécurité que les vaccins contre la grippe saisonnière, mais a noté que des études plus larges seraient nécessaires pour évaluer l'incidence des réactions rares. Des données concernant la vaccination chez l'enfant sont également nécessaires. Les données disponibles sont rassurantes au sujet de la protection croisée contre des souches hétérologues; des études à long terme sur les réponses immunitaires suscitées par les rappels seraient importantes. Il faudrait se mettre d'accord sur des critères immunologiques standard et sur des réactifs standard permettant d'évaluer l'immunogénicité du vaccin anti-H5N1 afin de pouvoir mieux comparer les essais cliniques des différents vaccins.

Le SAGE a formulé les recommandations suivantes:

1. L'OMS devrait continuer à constituer d'urgence un stock de vaccin anti-H5N1, en prévoyant notamment les procédures d'achat, de gestion, de gouvernance, de réglementation et de distribution, et continuer à se procurer les fournitures annexes nécessaires telles que seringues et aiguilles. Ce faisant, l'OMS devrait également se préoccuper des aspects logistiques et de la durabilité à long terme du stock.

2. National pandemic preparedness plans, many of which were developed before the availability of H5N1 vaccines, should be updated to enable countries to receive and efficiently deploy H5N1 vaccines from the stockpile.
3. There should be 2 uses of the stockpiled vaccine.

   - For the first use, up to 50 million vaccine doses, or enough to vaccinate up to 25 million people, should be maintained to complement other interventions used in any operation to try to contain the earliest detected outbreak of H5N1 virus infections in which sustained human-to-human transmission of the H5N1 virus is identified and which is considered by WHO and the affected country to have the potential to initiate an influenza pandemic. The containment protocol, which is updated periodically as concepts evolve and new developments appear, is available online.[9] The estimated maximum amount of vaccine required to support such an intervention has been based on preliminary and unpublished modelling work. However, SAGE recognizes that the actual amount needed may vary depending on specific circumstances, and estimates might change based on future information. The decision to release stockpiled vaccine should be made jointly by the country in which the outbreak is located and WHO. Any country is eligible to receive stockpiled vaccine for this purpose because a pandemic could start anywhere, and its containment or delay to spread is in the interest of the country and global community.
   - For the second use, SAGE recommends that WHO work towards stockpiling as many as 100 million additional doses of the H5N1 vaccine. If there were sustained human-to-human transmission of the H5N1 virus, this stockpiled vaccine and any other stockpiled vaccine that had not been used for containment should be equitably distributed to low-income and middle-income countries to help maintain those services considered most essential by them. The amount provided to each country should be proportional to the size of the country's population. The release of vaccine from the stockpile for this purpose should be made by WHO according to the International Health Regulations (2005) and based on an assessment of the circumstances that pertain at that time.

SAGE also considered other possible uses of H5N1 vaccine but recognized the limitations of current knowledge and did not make further recommendations. However, at a later date SAGE will review issues such as the use of H5N1 vaccines in non-pandemic periods for populations who might benefit. Meanwhile, SAGE encourages continued vigorous research on H5N1 and other candidate pandemic vaccines, including long-term studies on vaccine stability, and further work to better define the potential risks and benefits of the other possible uses of H5N1 vaccine. Finally, SAGE is aware there are long-term resource implications of these recommendations and

[9] See http://www.who.int/csr/disease/avian_influenza/guidelines/draftprotocol/en/index.html.

2. Les plans nationaux de préparation à une pandémie, dont beaucoup ont été élaborés avant l'existence des vaccins anti-H5N1, devraient être actualisés pour permettre aux pays de recevoir et de déployer efficacement les vaccins en provenance du stock.
3. Le vaccin stocké devrait être utilisé à 2 fins distinctes.

   - Premièrement, jusqu'à 50 millions de doses de vaccin, ou un nombre de doses suffisant pour vacciner jusqu'à 25 millions de personnes, devraient être conservées pour compléter d'autres interventions utilisées lors d'une opération visant à endiguer la première flambée décelée d'infections à virus H5N1 dans laquelle une transmission interhumaine soutenue du virus H5N1 est identifiée et qui est considérée par l'OMS et par le pays touché comme susceptible de déclencher une pandémie de grippe. Le protocole d'endiguement, actualisé périodiquement à mesure que les concepts évoluent et que des faits nouveaux apparaissent, est disponible en ligne.[9] La quantité maximale estimative de vaccin nécessaire pour soutenir une telle intervention repose sur des travaux de modélisation préliminaires non publiés. Toutefois, le SAGE reconnaît que la quantité réelle nécessaire pourra varier en fonction des circonstances et que les estimations pourront changer selon les informations dont on disposera à l'avenir. La décision de libérer les vaccins stockés devrait être prise conjointement par le pays dans lequel la flambée est apparue et l'OMS. Tout pays est éligible pour recevoir du vaccin stocké à cette fin, car une pandémie peut démarrer n'importe où et son endiguement ou le retard de sa propagation est dans l'intérêt non seulement du pays mais du monde entier.
   - En ce qui concerne le deuxième usage, le SAGE recommande que l'OMS s'efforce de stocker jusqu'à 100 millions de doses supplémentaires de vaccin anti-H5N1. S'il y avait transmission interhumaine soutenue du virus H5N1, ce stock de vaccin et tout autre stock de vaccin qui n'aurait pas été utilisé pour l'endiguement devraient être équitablement distribués aux pays à revenu faible et moyen pour les aider à maintenir les services qu'ils considèrent comme indispensables. Les quantités fournies à chaque pays devront être proportionnelles à sa population. La décision de libérer du vaccin du stock à cette fin devra être prise par l'OMS conformément au Règlement sanitaire international (2005) et reposer sur une évaluation de la situation prévalant à ce moment-là.

Le SAGE a également envisagé d'autres utilisations possibles du vaccin anti-H5N1, mais a reconnu les limites des connaissances actuelles et n'a pas fait d'autres recommandations pour le moment. Toutefois, il reverra ultérieurement des questions telles que l'utilisation des vaccins anti-H5N1 pendant les périodes non pandémiques dans des populations qui pourraient en bénéficier. En attendant, le SAGE encourage la poursuite de recherches intensives sur le vaccin anti-H5N1 et d'autres vaccins expérimentaux contre la grippe pandémique, y compris des études à long terme sur la stabilité du vaccin, et des travaux plus poussés visant à mieux définir les risques et avantages potentiels d'autres utilisations possibles du vaccin anti H5N1. Enfin, le

[9] Voir http://www.who.int/csr/disease/avian_influenza/guidelines/draftprotocol/en/index.html.

that countries and industry will need to support WHO to develop and maintain the WHO H5N1 vaccine stockpile.

Pneumococcal polysaccharide vaccine

A progress report on the status of the position paper on pneumococcal polysaccharide vaccine was presented. SAGE's input was solicited on the issues to be covered, particularly the awareness of unpublished data.

Future plans are to complete the paper in time for presentation to SAGE in April 2008.

Rabies vaccines

SAGE reviewed a draft of an updated position paper on rabies vaccines, which was preceded by presentations on rabies pathogenesis, the evidence for post-exposure and pre-exposure prophylaxis, and the rationale and evidence base for the safety and efficacy of pre-exposure and post-exposure intradermal immunization. The experience in Sri Lanka of a successful shift to intradermal administration of rabies vaccine, including use in rural areas, was noted SAGE endorsed the recommendation that the production and use of nerve tissue vaccines for human use be discontinued and replaced by modern cell culture vaccines as soon as possible.

SAGE noted that studies have demonstrated the feasibility, safety, immunogenicity and cost-savings of intradermal administration of cell culture vaccines. Consistent with the 2004 expert consultation on rabies,[10] use of the intradermal route for pre-exposure or post-exposure prophylaxis is an acceptable alternative where modern rabies vaccines are unaffordable or in short supply. Vaccine used in this context should comply with the recommendations for inactivated rabies vaccine for human use produced in cell substrates and embryonated eggs adopted at the 2005 Expert Committee on Biological Standardization meeting.[11]

These and other recommendations for pre-exposure and post-exposure prophylaxis are specified in the WHO position paper.[12]

Immunization safety: cross-departmental report

At its November 2005 meeting, SAGE had affirmed that it would ensure the continuous oversight of immunization safety.

The November 2007 session provided an update of recent activities, progress and constraints on immunization-related waste management and injection safety. SAGE was presented with: (i) a brief report on progress and challenges from each of WHO's regional offices (ii) an update on injection safety and integrated infection

SAGE est conscient que ces recommandations ont des incidences financières à long terme et qu'un appui des pays et de l'industrie sera nécessaire à l'OMS pour constituer et maintenir ce stock de vaccin anti-H5N1.

Vaccin antipneumococcique polyosidique

Un rapport de situation sur la prise de position concernant le vaccin antipneumococcique polyosidique a été présenté. L'avis du SAGE a été sollicité sur les questions à faire figurer dans la prise de position, en particulier la mise à disposition de données non publiées.

Il est prévu d'achever la rédaction du document à temps pour sa présentation au SAGE en avril 2008.

Vaccins antirabiques

Le SAGE a examiné un projet de prise de position actualisé sur les vaccins antirabiques précédé d'exposés sur la pathogénie de la rage, les données factuelles en faveur de la prophylaxie avant et après exposition, et les raisons ainsi que la base de connaissances justifiant de l'innocuité et de l'efficacité de la vaccination intradermique avant et après exposition. Il a pris note de l'expérience d'un passage avec succès à l'administration intradermique du vaccin antirabique au Sri Lanka, y compris en milieu rural. Le SAGE a approuvé la recommandation visant à faire cesser la production et l'utilisation de vaccins à usage humain préparés sur tissu nerveux et à les remplacer dès que possible par des vaccins modernes obtenus sur culture cellulaire.

Le SAGE a noté que des études avaient montré la faisabilité, l'innocuité, l'immunogénicité et le caractère économique de l'administration intradermique de vaccins obtenus sur culture cellulaire. Conformément aux recommandations de la consultation d'experts de la rage en 2004,[10] l'utilisation de la voie intradermique pour la prophylaxie avant ou après exposition est une alternative acceptable lorsque les vaccins antirabiques modernes ne sont pas d'un coût abordable et/ou quand leur offre est insuffisante. Le vaccin utilisé dans ce contexte devrait être conforme aux recommandations applicables au vaccin antirabique inactivé à usage humain produit sur substrats cellulaires et sur œufs embryonnés adoptées à la réunion du Comité d'experts de la Standardisation biologique de 2005.[11]

Ces recommandations ainsi que d'autres applicables à la prophylaxie avant et après exposition sont précisées dans la note d'information de l'OMS.[12]

Sécurité vaccinale: rapport interdépartemental

Lors de sa réunion de novembre 2005, le SAGE a affirmé qu'il assurerait un contrôle continu de la sécurité vaccinale.

La session de novembre 2007 a permis de faire le point sur les activités récentes, les progrès et les obstacles en matière de gestion des déchets liés à la vaccination et de sécurité des injections. Le SAGE a été saisi: 1) d'un bref rapport sur les progrès accomplis et les difficultés rencontrées dans chaque bureau régional de l'OMS; 2) d'une mise à jour sur la sécurité des injections et les stratégies

[10] *WHO expert consultation on rabies: first report.* Geneva, WHO, 2005 (WHO, Technical Report Series, No. 931). Also available at http://whqlibdoc.who.int/trs/WHO_TRS_931_eng.pdf

[11] See http://www.who.int/biologicals/expert_committee/en/

[12] See No. 49/50, 2007, pp. 425–435.

[10] *WHO expert consultation on rabies: first report.* Genève, OMS, 2005 (OMS, Série de Rapports techniques, No 931). Accessible (uniquement en anglais) sur http://whqlibdoc.who.int/trs/WHO_TRS_931_eng.pdf

[11] Voir http://www.who.int/biologicals/expert_committee/en/

[12] Voir N° 49/50, 2007, pp. 425-435.

control strategies in health-care settings delivered by the secretariat of the SIGN Alliance (the Safe Injection Global Network); and (iii) an update on health-care waste management from WHO's Public Health and Environment Department.

SAGE is concerned that resources continue to be scarce for injection safety and waste management. Although there has been progress towards the use of auto-disable syringes, further progress is needed. Despite continued support from partners, there is clearly no sustainable long-term funding for auto-disable syringes and disposal equipment for countries for whom injection safety support from the GAVI Alliance is ending.

Although the GAVI Alliance added a milestone on injection safety in its 2008–2010 roadmap, funding for injection safety is insufficient. One way for countries to secure the funds needed for injection safety and health-care waste management would be to use the "health-system strengthening" support available from both the GAVI Alliance and the Global Fund to Fight AIDS, Tuberculosis and Malaria. SAGE urged that clarification be made of which activities could be funded under health-system strengthening and supported the inclusion of injection safety and waste management, which should also include training and supervision activities.

Particular concern was expressed by WHO's Eastern Mediterranean Region, however, because much had been achieved from 2000 to 2005 but progress slowed during 2006–2007 due to managerial and financial constraints. This demonstrates the need for continued specific attention to be paid to immunization safety within an integrated and holistic approach to injection safety and waste management.

SAGE encourages the development of simple technological solutions to waste disposal with improved environmental characteristics, and encourages donors to support such work. ■

intégrées de lutte contre l'infection en milieu médicalisé effectuée par le secrétariat du réseau mondial sur la sécurité des injections (SIGN); et 3) d'un bilan de la gestion des déchets en milieu médicalisé effectué par le Département OMS Santé publique et environnement.

Le SAGE s'inquiète de ce que l'on continue de manquer de ressources dans les domaines de la sécurité des injections et de la gestion des déchets. Bien que des progrès aient été enregistrés en ce qui concerne l'utilisation des seringues autobloquantes, il reste encore des progrès à faire. Malgré un soutien non démenti des partenaires, le financement des seringues autobloquantes et du matériel d'élimination ne bénéficie manifestement pas d'un financement durable à long terme dans des pays pour lesquels l'appui de l'Alliance GAVI à la sécurité des injections arrive à son terme.

Bien que l'Alliance GAVI ait ajouté un jalon concernant la sécurité des injections à son plan de travail pour 2008-2010, le financement de ce domaine est insuffisant. Une manière pour les pays de s'assurer les fonds nécessaires à la sécurité des injections et à la gestion des déchets liés aux soins de santé consisterait à utiliser l'appui au «renforcement des systèmes de santé» disponible au titre à la fois de l'Alliance GAVI et du Fonds mondial. Le SAGE a invité instamment à préciser quelles activités pourraient être financées au titre du renforcement des systèmes de santé et s'est prononcé en faveur de l'inclusion de la sécurité des injections et de la gestion des déchets, et notamment d'activités de formation et de supervision.

Cependant, la Région de la Méditerranée orientale s'est dite particulièrement préoccupée car beaucoup a été fait entre 2000 et 2005 mais les progrès se sont ralentis en 2006-2007, en raison de problèmes gestionnaires et financiers. Cela montre bien la nécessité de continuer à accorder une attention particulière à la sécurité de la vaccination dans le cadre d'une approche intégrée et globale de la sécurité des injections et de la gestion des déchets.

Le SAGE encourage la mise au point de solutions techniques simples en matière d'élimination des déchets, dotées de caractéristiques écologiques améliorées, et encourage les donateurs à soutenir ces travaux. ■

CORRIGENDUM, TO No. 49/50, 2007

Rabies vaccines – WHO Position paper

Please read as follows (changes shown in ***bold italics***), pages 432–433, section on post-exposure prophylaxis. Please note that "licks on broken skin" should be moved from Category II to Category III exposures.

Post-exposure prophylaxis

The indication for post-exposure prophylaxis with or without RIG depends on the type of contact with the suspected rabid animal:

- Category I – touching or feeding animals, licks on the skin (i.e. no exposure);
- Category II – nibbling of uncovered skin, minor scratches or abrasions without bleeding;

RECTIFICATIF AU No 49/50, 2007

Vaccins antirabiques – Note d'information de l'OMS

Prière de lire comme suit (changements indiqués en ***gras italique***), pages 432-433, section sur la vaccination post-exposition. Merci de noter que «léchage sur peau érodée» passe de la catégorie II à la catégorie III.

Vaccination post-exposition

Les indications de la vaccination post-exposition, associée ou non à l'administration d'IGR, dépendent du type de contact avec l'animal qu'on suppose enragé. On distingue les types de contact suivants:

- catégorie I – contact ou alimentation de l'animal, léchage de la peau (par exemple aucune exposition);
- catégorie II – peau découverte mordillée, griffures bénignes ou excoriations sans saignement;

- Category III – single or multiple transdermal bites or scratches, ***licks on broken skin***, contamination of mucous membrane with saliva from licks, exposures to bats. ■

- catégorie III – morsures ou griffures, uniques ou multiples, ayant traversé le derme, ***léchage sur peau érodée***, contamination des muqueuses par la salive après léchage, exposition à des chauves-souris. ■

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The Value of Vaccination

David E. Bloom, David Canning & Mark Weston

Introduction

> "You let a doctor take a dainty, helpless baby, and put that stuff from a cow, which has been scratched and had dirt rubbed into her wound, into that child. Even, the Jennerians now admit that infant vaccination spreads disease among children. More mites die from vaccination than from the disease they are supposed to be inoculated against." (George Bernard Shaw, 1929)

The world has come a long way since George Bernard Shaw fulminated against vaccination in the 1920s. Vaccines are now widely regarded as an effective and cheap tool for improving health. Children in all countries are routinely immunized against major diseases, and the practice has become a central plank of global public health efforts.

Despite these advances, however, immunization coverage remains far from universal, and the developing world in particular remains vulnerable to vaccine-preventable illnesses. For example, global coverage for DTP—the vaccine for diphtheria, tetanus, and pertussis (whooping cough)—had reached 70 per cent in the 1990s, but in sub-Saharan Africa it stood at just 53 per cent. In Somalia, Nigeria, and Congo, moreover, coverage halved between 1990 and 2000.[1] Vaccination against measles also falls short; the

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[1] World Health Organization (2002): "State of the World's Vaccines and Immunization 2002", WHO, Geneva.

disease caused 660,000 deaths in 2002.[2] In all, 3 million people die each year from vaccine-preventable diseases.[3]

In the developed world, too, vaccination efforts face obstacles. The rise of a well-organized anti-vaccine movement has persuaded some parents not to immunize their children. Vaccines, the campaigners claim, cause more harm than good: in societies where vaccine-preventable disease prevalence is minimal (ironically as a result of past immunization efforts, although this is rarely acknowledged by campaigners), the side effects of vaccines pose a greater health threat than the diseases themselves. Why, they ask, should everyone be vaccinated in order to protect the relatively small number of people that might contract the disease in the absence of mass immunization?

It is not just populist activists who overlook the positive effects of vaccination. More scientific estimates of the effects of vaccines also tend to underplay the benefits, disregarding the broad economic impacts of immunization in favor of a predominant and narrow focus on the averted costs of medical treatment and health care. With other human capital investments, such as education, economic analysis of the impacts focuses on the effect on earnings. This has not occurred, however, with vaccination, and until recently it did not occur for health in general. Public health specialists generally perceive vaccination as a hugely beneficial investment as it is both cheap and very effective at a population level (the influential 1993 World Development Report, "Investing in Health", listed the World Health Organization's Expanded Program on Immunization as the first component of "the essential public health package"[4]). Because of the narrow view of its impacts taken by the rest of the policy-making community, however, policy emphasis on vaccination is weaker than it might be if the full range of benefits were taken into account.

Health economists have long used two well-established tools to evaluate health interventions in economic terms. Both types of analysis are

[2] World Health Organization (2004): "Measles Deaths Drop Dramatically as Vaccine Reaches World's Poorest Children", WHO/UNICEF Joint Press Release, 27 April.
[3] Center for Global Development (2005): "Making Markets for Vaccines: From Ideas to Action", CGD, Washington DC.
[4] World Bank (1993): "Investing in Health", World Development Report 1993, World Bank, Washington DC: 106. A survey of health professionals in New Zealand, moreover, found that 94% supported vaccinations, with 86% of those with children reporting having had them immunized (Tim Jelleyman and Andrew Ure (2004): "Attitudes to immunization: a survey of health professionals in the Rotorua District", *Journal of the New Zealand Medical Association*, 20 February, Vol 117 No 1189).

widely used and appropriately respected. Cost-effectiveness analysis (CEA) seeks to determine the cost of an intervention (e.g. vaccination) in relationship to a particular outcome. How much does it cost to save a certain number of lives, or to avert a certain number of illnesses, for example? Averted medical costs (at least those that would be incurred in the short run in the absence of vaccination) are also typically taken into account. Cost-benefit analysis (CBA), by contrast, makes a direct comparison between costs and benefits by monetizing the value of the latter. This technique facilitates the comparison of two or more interventions, particularly when there is a range of discrete outcomes.

There are several problems with both types of analysis, as they have been used to date. First, neither type typically takes account of the cost of averted infections that may occur years later. This is understandable, since such infections are hard to predict, but that does not make future cost savings any less important.

Second, both types of analysis take a narrow view of the benefits of vaccination that fails to take account of recent academic work on the effects of health on incomes. The experience of development over the past half-century shows that good health fuels economic growth, just as bad health strangles it. Healthy children perform better at school, and healthy adults are both more productive at work and better able to tend to the health and education of their children. Healthy families are also more likely to save for the future; since they tend to have fewer children, resources spent on them go further, thereby improving their life prospects. Finally, healthier societies may be a stronger magnet for foreign direct investment and tourism than those where disease poses a constant threat.

Third, neither type of analysis factors in the effects that improved health has on triggering lower fertility rates. The combination of lowered mortality rates and subsequently lowered fertility rates leads to a "baby boom" generation that, when it reaches working age, can help bring about a significant economic boom (as happened in East Asia). In the case of vaccination, the consequent boost to health can catalyze a change in the age structure of the population (via the lowered fertility rates) that can lead to significant economic benefits.

Our research looks at all CEA and CBA studies listed in Pub. Med. for 2004 and 2005. The wide range of published results emphasizes the difficulties inherent in such work. However, since all of these studies fail to

address the broader considerations described in the preceding two paragraphs, they all either overstate the cost of achieving a given beneficial outcome or underestimate the net benefits. It is this insight that spurs the current work.

With the spread of immunization having stalled in many parts of the world, a wider look at its benefits is timely. In this paper, we discuss the value of vaccination from a broad perspective. As well as the health benefits, we examine the cost of vaccine programs and their economic impacts. Vaccination has proved a cost-effective and remarkably efficient way of improving health, and has saved millions of lives. It has the potential, however, to be more effective still, and renewed efforts are needed if the momentum is to be regained.

Part 1 of the paper provides a brief summary of the history of vaccination and its impacts on human health. Part 2 looks at the state of play today and at the reasons why progress on vaccine delivery and development has slowed. Part 3 considers research-to-date and presents new research on the economic benefits of immunization. It begins with a review of both cost-effectiveness analysis and cost-benefit analysis, which indicates that a broader view of the long-term benefits of vaccination makes immunization programs much more worthwhile, in terms of their economic consequences, than has been thought in the past. It broadens the analysis by reviewing recent research showing the relationship between health and wealth (Part 3.2), estimating the rates of return to one of GAVI's prospective investments (Part 3.3), and presenting a study on immunization and cognitive development, which has been linked to higher earnings (also Part 3.3).

1. A glorious past

The theory behind vaccination was brought to the West from Asia. The Chinese had observed that certain illnesses could only be contracted once, so they experimented with giving healthy individuals doses of diseases such as smallpox that would be too small to make them ill but large enough to stimulate immunity. The process was known as variolation and, in the case of smallpox, usually involved injecting powder from smallpox scabs into the vein. Although some individuals fell ill or died during the process, smallpox rates among communities that had been variolated were significantly lower than elsewhere.

Variolation was introduced to Britain in the early 18th century by Lady Mary Wortley Montagu, who had observed the process in Turkey, where her husband was British ambassador. Several decades later, Edward Jenner, who had undergone variolation as a child, noticed that people who contracted cowpox after working with cows became immune to smallpox. To test this observation, he injected a small child with cowpox. The child fell ill with cowpox but, when later injected with smallpox, did not contract the latter disease. Jenner published his findings in 1798, and named the process "vaccination", from the Latin word for cowpox.[5]

In 1890, Emil von Behring and Shibasaburo Kitasato gave substance to Jenner's observation when they discovered antibodies. Injecting a small amount of a disease organism into an uninfected individual, they found, stimulated the production of antibodies, which fought off the initial attack and thereby prepared the body to fend off infection later in life. At around this time, vaccines for rabies, cholera, typhoid, and the plague were developed, although it was not until after the World War II that vaccines became a widespread tool for improving health. Today, 26 diseases are vaccine-preventable.

Since World War II, vaccination has had a major impact on global health, as the following list of successes shows:

- Smallpox, which had killed two million people per year until the late 1960s, was wiped out by 1979 after a massive worldwide immunization campaign.
- The number of polio cases fell from over 300,000 per year in the 1980s to just 2,000 in 2002.[6]
- Two-thirds of developing countries have eradicated neonatal tetanus.[7]
- Since the launch of the World Health Organization's Expanded Program on Immunization (EPI) in 1974, the number of reported measles deaths has dropped from 6 million to less than 1 million per year.
- Whooping cough cases have fallen from 3 million per year to less than a quarter of a million.
- Diphtheria cases have declined from 80,000 in 1975 to less than 10,000 today.[8]

[5] The Hutchinson Encyclopaedia (1999): Helicon, Oxford.
[6] The Global Alliance for Vaccines and Immunization website. www.vaccinealliance.org
[7] WHO (2002) op cit.
[8] Birmingham, M., Stein C (2003): "The Burden of Vaccine-Preventable Diseases", in Barry R. Bloom, Paul-Henri Lambert (eds) (2003): *The Vaccine Book*. Academic Press, San Diego: 26.

- The haemophilus influenzae B (Hib) vaccine has reduced the incidence of Hib meningitis in Europe by 90 per cent in ten years.[9]

The EPI includes six vaccines, covering diphtheria, tetanus, whooping cough, measles, polio, and tuberculosis. Before 1974, only 5 per cent of children were vaccinated against these diseases. Today over 70 per cent are vaccinated.[10] The program has reduced the share of the six diseases it tackles in the total burden of disease in young children from 23 per cent to less than 10 per cent since the mid-1970s.[11] It has been estimated that declines in diphtheria, measles, and whooping cough have averted well over a million deaths in developing countries.[12]

In 2000, in an effort to maintain the EPI momentum, the Global Alliance for Vaccines and Immunization (GAVI) was launched. GAVI comprises United Nations agencies, governments, donors, foundations, private companies, and academic institutions. It has six core strategic objectives:[13]

- Improve access to sustainable immunization services
- Expand the use of all existing safe and cost-effective vaccines, and promote delivery of other appropriate interventions at immunization contacts
- Support the national and international accelerated disease control targets for vaccine-preventable diseases
- Accelerate the development and introduction of new vaccines and technologies
- Accelerate research and development efforts for vaccines needed primarily in developing countries
- Make immunization coverage a centerpiece in international development efforts.

As we will see in part 2 of the paper, such an initiative is urgently needed.

[9] Jenifer Ehreth (2003): "The value of vaccination: a global perspective", *Vaccine*, 21: 4112.
[10] WHO (2002) op cit.
[11] World Bank (2001): Immunization at a glance. World Bank, November. Available at http://childrensvaccine.org/files/World_Bank_Immuniz_rev_11_01.pdf
[12] Birmingham & Stein (2003) op cit.
[13] GAVI website: available at http://www.vaccinealliance.org/General_Information/About_alliance/Background/objectives.php

2. A difficult present

2.1 Lost momentum

The rapid progress towards universal vaccination coverage in the 1970s and 1980s has slowed in recent years.

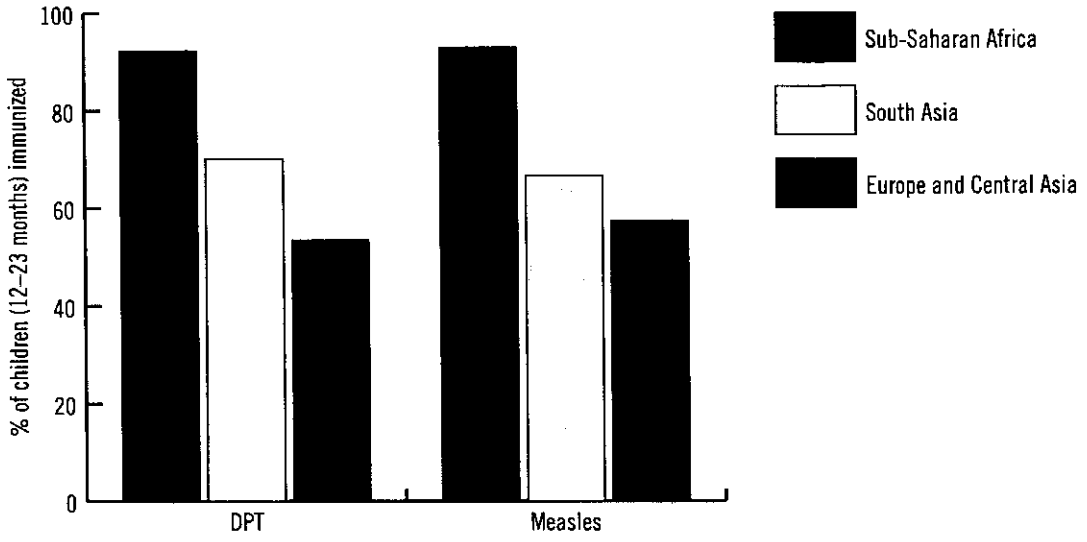
Declining funding for immunization has been mirrored in stagnating or falling coverage. UNICEF funding for vaccination fell from $182 million to $51.4 million between 1990 and 1998.[14] Global coverage of the diphtheria, tetanus, and pertussis (DTP3) vaccine has been stalled at around 74 per cent since 1990.[15] Fifty-seven developing countries have yet to eliminate neonatal tetanus, and 200,000 babies died of the disease in 2000.[16] Yellow fever has made a comeback, despite the availability of an effective vaccine; the number of outbreaks increased sharply after governments curtailed programs in the belief they had vanquished the disease.[17]

Developing countries lag behind the West in terms of vaccination coverage. Measles immunization rates are over 90 per cent in Europe but below 70 per cent in South Asia and below 60 per cent in sub-Saharan Africa (see Figure 1).[18] Ten developing countries reported cases of polio in June 2005, despite the massive (and largely successful) global effort to eradicate the virus.[19] Sixty-two per cent of countries, meanwhile, had still not achieved full routine immunization coverage in 2003, with GAVI estimating that at least 9.2 million additional infants need to be reached to achieve full coverage.[20]

There are several factors behind this loss of momentum. First, although dramatic progress has been made in increasing worldwide vaccination coverage from below 5 per cent to above 70 per cent, the task has inevitably become harder now that the easiest-to-reach populations have been vaccinated. Many of those whom campaigns have not yet reached are either living in inaccessible areas, out of range of clinics and health services, or reluctant to be vaccinated or to vaccinate their children. Because these

[14] Gauri, Varun & Khaleghian, Peyvand (2002): "Immunization in Developing Countries: Its Political and Organizational Determinants", World Development, Elsevier, vol. 30(12), pages 2109–32.
[15] GAVI (2003): "Progress towards immunization goals 2001: Summary presentation of key indicators", February.
[16] WHO (2002) op cit.
[17] GAVI (2001): "Global Market— Global Vaccines", Immunization Focus, June.
[18] World Bank (2004): "World Development Indicators 2004", World Bank, Washington DC.
[19] World Health Organization: Polio Eradication Website, Global Case Count. Available at: http://www.polioeradication.org/casecount.asp
[20] GAVI (2003) op cit.

Figure 1: Disparities in immunization rates



Source: World Bank, Washington DC (2004). Data are for 2002.

communities are more elusive, the average cost per vaccination has increased, and it may be that other apparently cheaper health interventions have become more attractive.

Second, there are many practical problems impeding vaccine delivery. Delivering vaccines to patients requires functioning freezers and refrigerators (which in turn require a constant supply of energy); good roads and reliable transport to move the vaccines from port to clinic; clinics with access to people who need to be immunized; parents who know the value of vaccination; trained medical staff to deliver the dose; and sterile syringes.

Many of the poor countries where vaccine coverage has stalled lack all or part of this infrastructure. In Burkina Faso and Niger for example, 23 per cent of refrigerators used for storing vaccines were found to be non-functioning.[21] Only 16 per cent of vaccine-importing countries could guarantee vaccine safety and quality,[22] while a further study of 19 developing countries found that at least half of injections were unsafe.[23]

[21] GAVI (2003) op cit.
[22] WHO (2002) op cit.
[23] Ibid.

The third factor behind the lack of progress in recent years is political. Political disruptions have affected coverage in some areas. In Somalia and Congo, for example, where vaccination rates have fallen rapidly in the past decade, war and social breakdown have impeded public health campaigns, despite "vaccination days" in Congo that temporarily halted fighting. Gauri *et al.* have found that the quality of institutions and governance are positively correlated with vaccination coverage.[24] Immunization campaigns do not operate in isolation—they are dependent on the prevailing political and social environment. As that environment is altered, immunization may be interrupted.

Politics in the developed world have also played a part. According to a report by the US Institute of Medicine, in 1982 the US vaccine industry was forced to stop offering low-price vaccines to developing countries following congressional hearings that "savaged" the industry for "allegedly subsidizing vaccines for the poor children of the world by charging high costs to US families and taxpayers".[25] As the Institute of Medicine points out, this move was based on a flawed premise, as the US vaccines would have been developed anyway to protect American children and travelers.

The fourth reason for the lost momentum relates to public perceptions of vaccination. As coverage spreads through a community, it reaches a point at which those who are unvaccinated are highly unlikely to catch a disease because herd immunity has set in. At this juncture, it may be more rational for an individual to refuse vaccination in order to avoid any risk of side effects. With the oral polio vaccine, for example, there is a one in a million chance of paralysis, and in societies where mass vaccination has eliminated the disease, the risk of paralysis is greater than that of catching polio itself. What had once been a public and private good is now a public good but a private risk. As more and more people choose to avoid this risk, of course, overall coverage rates decline, and the community is once again exposed to the threat of the disease.

Public perceptions have been influenced by vaccine scares. Controversy and the attendant bad publicity about the safety of vaccines has been abetted by incidents such as the withdrawal of half the US supply of flu vaccines in 2004 due to contamination at the manufacturer,

[24] Gauri *et al.* (2002) op cit.
[25] Institute of Medicine, National Academy of Sciences (1997): *America's Vital Interest in Global Health*. National Academy Press, Washington.

Chiron's UK plant[26], and by the swine flu vaccine, which led to deaths of some of those immunized (while the flu itself did not arrive).

In addition, alarms over the safety of vaccines such as that for measles, mumps and rubella (MMR), which some believe to cause autism, have further fanned the anti-vaccine movement's flames. In the US, disputes continue to rage about the scientific basis of such claims, but the preponderance of the evidence, according to the US Centers for Disease Control (CDC), says that the MMR vaccine is safe.[27] In the UK, physician Andrew Wakefield caused alarm over the MMR vaccine for the same reason. Rates of MMR coverage dropped in Britain and elsewhere in the wake of this scare, before Wakefield's case was to a large extent discredited and the journal that had published his research, *The Lancet*, partially retracted the study.

A survey of public reactions to Wakefield's findings showed that 53 per cent of people believed that, because media coverage gave roughly equal space to support and rejection of the autism theory, the scientific evidence base must be similarly balanced.[28] Only 25 per cent, moreover, were aware that no link between MMR and autism had been found in the overwhelming majority of studies.[29] A similar scare occurred over the hepatitis B vaccine, which in the mid-1990s was briefly believed to cause multiple sclerosis in some who received it. Subsequent cohort and case-control studies found no link between the two.[30]

Vaccine scares do not always lack foundation. The Rotashield vaccine for rotavirus, which was approved in the US in 1998, was withdrawn a year later after reports were received of acute intussusception (a potentially serious bowel condition) occurring shortly after delivery of the vaccine. A study later confirmed this relationship—between 1 in 5,000 and 1 in

[26] Los Angeles Times (2005): "Vaccine Delays Hit Chiron's Recovery", *LA Times*, Los Angeles, 16 July.
[27] Concerns are summarized in Robert Kennedy Junior (2005): "Autism, Mercury and Politics", *Boston Globe*, Boston MA, 1 July. In July 2005, the US Centers for Disease Control and Prevention (CDC) affirmed, in response to such stories, that, "the science states very clearly that vaccines save lives and protect our children." (New York Times (2005): "No Vaccine-Autism Link, Parents Are Told", New York Times, 20 July). At http://www.cdc.gov/nip/vacsafe/concerns/autism/default.htm, the CDC details the evidence concerning the absence of a connection between the MMR vaccine and autism and critiques the studies that show a link.
[28] Hargreaves, Ian, Justin Lewis and Tammy Speers (2003): *Towards a better map: Science, the public, and the media*, Economic And Social Research Council.
[29] Lewis, J. & Speers, T. (2003): "Misleading Media Reporting? The MMR story", Nature Reviews, *Immunology*, 3 (11) (2003) 913–18.
[30] Halsey, Neal A. (2003): "Vaccine Safety: Real and Perceived Issues" in Barry R Bloom, Paul-Henri Lambert (eds) (2003): *The Vaccine Book*. Academic Press, San Diego: 382.

10,000 infants developed intussusception within two weeks of vaccination.[31] Such events, as well as causing enormous financial losses to the company that developed the vaccine, can have negative effects on public trust in immunization. They also increase pressure on governments to tighten regulation of vaccines, thereby making their production even more costly.[32]

In response to these types of controversies in the US, the Institute of Medicine has called for independent oversight of vaccine safety studies to ensure the fairness and openness of the Vaccine Safety Datalink program, which is overseen by the CDC.[33]

2.2 Imperiled innovation

Like vaccine coverage, development of new vaccines has also stalled in recent years. The number of major western pharmaceutical companies making vaccines fell from 26 in 1967 to 5 today, although some of the slack has been taken up by developing-country manufacturers.[34] As profit margins for rich-world vaccines have outpaced those for vaccines needed by poor countries, drug developers have concentrated ever more on diseases of the developed world.

The profitability deficit for developing-world vaccines is huge. The developing-world vaccine market is estimated at just 10-15 per cent of the world total and less than 0.2 per cent of the entire global pharmaceutical market.[35] The total volume of all vaccine doses acquired by UNICEF and the Pan American Health Organization (PAHO) for distribution in the developing world, moreover, is 100 times greater than the number of doses of Prevnar (a vaccine for diseases caused by streptococcus pneumoniae) delivered in the US, but brings in less than half the revenue.

Rich and poor countries have different immunization needs. Parents in rich and poor countries alike are concerned with the safety of vaccine delivery; but governments in poor countries are concerned with its cost,

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[31] Mulholland, Edward Kim & Bjorvatn, Bjarne (2003): "Introduction of New Vaccines in the Healthcare System" in Bloom, Barry (eds) (2003) op cit: 401.

[32] A notable sidelight to this story is that GlaxoSmithKline has now developed Rotarix, a new rotavirus vaccine (which does not appear to have intussusception as a side effect), which has already been introduced in Mexico and will soon be introduced in other developing countries. See *Technology Review*, June 2005, available at http://www.technologyreview.com/articles/05/06/tri/tri_vaccine.asp?p=1.

[33] http://www4.nas.edu/news.nsf/6a3520dc2dbfc2ad85256ca8005c1381/e82b28891131e63e85256fab006fb1f3?OpenDocument

[34] Washington Times (2005): "Vaccine Vacillation", *Washington Times*, 13 June.

[35] Siwolop (2001): "Big steps for the vaccine industry", *New York Times*, 25 July.

too. Products have therefore begun to diverge, even when they tackle the same illness, and the new vaccines that respond to developed-world demands are often too expensive for poor countries. In the 1990s, for example, developed countries began to use the DTaP instead of DTwP vaccine. DTaP (which incorporates an acellular pertussis vaccine) is more expensive and no more effective than DTwP (which contains a whole-cell pertussis vaccine), but it has fewer side effects and has therefore proved more popular with developed-world consumers. Similarly, the oral polio vaccine has been replaced in countries such as the US by inactivated polio vaccine (IPV), which is delivered by injection. Unlike OPV, the IPV vaccine cannot cause paralysis.[36]

Pharmaceutical companies have found it difficult to persuade shareholders of the value of continuing to develop vaccines for poor countries. The pharmaceutical giant GlaxoSmithKline, for example, reported in 2001 that it was planning to allocate its freeze-drying capacity to the haemophilus influenzae B (Hib) vaccine rather than the less profitable meningitis A/C vaccine. Doses of the DTwP vaccine offered to UNICEF, moreover, declined from 600 million in 1998 to 150 million two years later.[37]

Intellectual property rights present a further challenge to vaccine development. Unlike many other drugs, people generally need only one dose of a vaccine or vaccine booster. Manufacturers therefore need to gain a return on their investment from a single use, rather than over a full course of treatment as in the case of antibiotics, or over a patient's entire lifetime as in the case of antiretroviral drugs for AIDS. Companies are thus particularly zealous about protecting vaccine patents—monopoly over production of a vaccine is, they believe, the best way to profit from it. Generic drug producers in poor countries, however, threaten these patents and increase the risk that vaccine developers will not gain a satisfactory return on their investment. Compulsory drug licensing, moreover, which some countries have introduced for antiretroviral treatment for AIDS, may deter future investment in drugs for the developing world. If pharmaceutical companies cannot guarantee a return on their research and development costs through to the end of the patent period, the attraction of vaccines for developing countries may weaken further.

[36] Batson *et al.* (2003) op cit.
[37] GAVI (2001) op cit.

There is a lively and important debate regarding the costs of drug development and how they should be assessed. The pharmaceutical industry has long claimed that the enormous costs of development are only sustainable by the prices charged for the subset of drugs that are finally approved. Critics have argued that the development costs are overstated, with Relman and Angell[38] pointedly stating that " ... research and development (R&D) constitutes a relatively small part of the budgets of the large drug companies. Their marketing and advertising expenditures are much greater than their investment in R&D". In addition, they argue that the pharmaceutical companies are not as innovative as generally assumed—and that much of the spending on truly new drugs is taxpayer-supported. DiMasi *et al.* respond to some of the drug industry's critics,[39] carefully critiquing their methodology, and offer new estimates of drug development costs.[40] (Relman and Angell also critique DiMasi *et al.*)

As Relman and Angell note, not all investment in vaccines comes from the private sector. Government research agencies and academic institutions are responsible for much investment in basic scientific research. A widely promoted means of filling the gap between the needs of developing countries and the demands of pharmaceutical firms' shareholders is for public organizations to step in and guarantee a market for vaccines once private companies have developed them. GAVI is currently coordinating this effort internationally but, as the downfall of an earlier initiative shows, encouraging diverse organizations to work together to achieve a common goal is a task riven with complexities.

William Muraskin has detailed the demise of the Children's Vaccine Initiative (CVI), which was launched by the World Health Organization in 1990 in response to the slowdown in development of new vaccines and poor distribution of existing ones.[41] The CVI's efforts to bring together public and private sector scientists and organizations to work towards solutions were unsuccessful. As Muraskin explains, there was a "great gulf of distrust, often bordering on contempt," between public and private sectors.

[38] Relman, A. S., Angell, M. (2002): "America's other drug problem: how the drug industry distorts medicine and politics", *The New Republic* 16 December, 587(4): 27–41.
[39] DiMasi, Joseph A., Hansen, Ronald W. and Grabowski, Henry G. (2004): "Assessing Claims about the Cost of New Drug Development: A Critique of the Public Citizen and TB Alliance Reports". Available at http://csdd.tufts.edu/_documents/www/Doc_231_45_735.pdf
[40] DiMasi, J.A., Hansen, R.W., Grabowski, H.G. (2003): "The price of innovation: new estimates of drug development costs", *Journal of Health Economics* 22(2): 151–85.
[41] Muraskin (1998) op cit.

Public sector scientists saw their private sector counterparts as being purely driven by profit, while the latter saw the public sector as a wasteful and untrustworthy partner. The WHO closed down the CVI in 1999. Such experience reinvigorates the question of government's responsibility for ensuring the timely development and production of vaccines—both for old diseases and new. One alternative is that governments themselves could create greater vaccine development and production capacities. Another option is for governments to offer major financial incentives to pharmaceutical corporations in exchange for guaranteed increases in development efforts and actual construction of vaccine production facilities. Under this latter scenario, a government could promote competition among companies for contracts of this type. The case of avian flu, which could soon burst onto the world scene on a terrifying scale, brings this discussion into sharp focus: governments must assess whether they can rely on the private sector to take the initiative in guaranteeing public health when the steps needed to make such guarantees currently look unprofitable.

Developing and delivering vaccines, then, are by no means straightforward tasks. The progress in eliminating smallpox and drastically reducing cases of polio shows that, with will and effort, immunization campaigns can be successful, but the momentum for mass immunization has stalled in recent years. In the next section we examine the case for a renewed global effort to extend vaccination coverage, focusing on the economic impacts of vaccine programs.

3. An uncertain future

3.1 The narrow perspective

Assessment of the benefits of vaccines has traditionally focused on a specific range of health-related impacts: Cost-effectiveness and cost-benefit analyses of the numbers of averted illnesses; hospitalizations and deaths; disability-adjusted life years (DALYs) gained; and medical costs avoided are the most common assessment methods. Cost-effectiveness analysis looks at the cost of a health intervention per life saved (or per DALY gained, etc.); cost-benefit analysis takes into account the value of each life saved or the extra years of healthy life gained, and compares the total value of those benefits to the cost of the intervention.

The World Health Organization, for example, has estimated that polio eradication will save governments $1.5 billion per year in vaccine, treatment, and rehabilitation costs. The elimination of smallpox is thought to have saved $275 million per year in direct health care costs;[42] Barrett estimates that the $100 million invested in eradicating the disease in the ten years after 1967 "saved the world about $1.35 billion a year".[43] And the US Institute of Medicine reports that for every dollar spent on the MMR vaccine, $21 is saved.[44]

Other cost-effectiveness studies have also found that vaccination campaigns lead to substantial savings in medical costs,[45] but a recent review of 60 studies on the effectiveness, cost, and cost-effectiveness of immunization programs in developing countries concluded that the literature base on cost-effectiveness was flimsy. Only three of the studies addressed cost-effectiveness, and most studies were riddled with weaknesses. Few

[42] GAVI (2003) a: "The Impact of Immunization on Economic Development", Press information. Available at http://www.vaccinealliance.org/home/Media_Center/Background_Materials/press_econ.php.

[43] Barrett, Scott (2004): "Eradication versus control: the economics of global infectious disease policies", *Bulletin of the World Health Organization*, September 2004; 82: 683–8.

[44] Institute of Medicine, National Academy of Sciences (1997): "America's Vital Interest in Global Health", National Academy Press, Washington.

[45] See, for example, Coudeville, L. (1999): "The value of varicella vaccination in healthy children: cost-benefit analysis of the situation in France", *Vaccine*, Jan 17:2 142–51; Ekwueme, D. U. (2000): "Economic evaluation of use of diphtheria, tetanus, and acellular pertussis vaccine or diphtheria, tetanus, and whole-cell pertussis vaccine in the United States", 1997. *Arch Pediatr Adolesc Med* 2000 Aug 154:8 797–803; Pelletier, L. (1998): "A benefit-cost analysis of two-dose measles immunization in Canada", *Vaccine*, May–Jun 16:9-10 989–96; Tormans HIV/AIDS (1998): "Economic evaluation of pertussis prevention by whole-cell and acellular vaccine in Germany", *Eur J Pediatr*, May 157:5 395–401; Hussain, I. H. M. I., Syed Aljunid, Sofiah, A., Ong, L. C., Choo, K. E., Musa, M. N., Teh, K. H. & Ng, H. P. (1999): "Cost-Benefit Analysis Of Haemophilus Influenzae Vaccination Programme In Malaysia", *Buletin Kesihatan Masyarakat Jilid 5*; Ulla K. Griffiths, Lara J. Wolfson, Arshad Quddus, Mohammed Younus, Rehan A. Hafiz (2004): "Incremental cost-effectiveness of supplementary immunization activities to prevent neonatal tetanus in Pakistan", *Bulletin of the World Health Organization*, September 2004, 82(9); Uyl-de Groot, C. A., Vermorken, J. B., Hanna, M. G. Jr, Verboom, P., Groot, M. T., Bonsel, G. J., Meijer, C. J., Pinedo, H. M. (2005): "Immunotherapy with autologous tumor cell-BCG vaccine in patients with colon cancer: a prospective study of medical and economic benefits", *Vaccine*, 23(17-18):2379-87; Navas, E., Salleras, L., Gisbert, R., Dominguez, A., Timoner, E., Ibanez, D., Prat, A. (2005): "Cost-benefit and cost-effectiveness of the incorporation of the pneumococcal 7-valent conjugated vaccine in the routine vaccination schedule of Catalonia (Spain)", *Vaccine*, 23(17–18):2342–8; McIntosh, E. D., Conway, P., Willingham, J., Hollingsworth, R., Lloyd, A. (2005): "Pneumococcal pneumonia in the UK—how herd immunity affects the cost-effectiveness of 7-valent pneumococcal conjugate vaccine (PCV)", *Vaccine*, 23(14):1739–45; Jean-Jasmin, L. M., Lynette, S. P., Stefan, M., Kai, C. S., Chew, F. T., Wah, L.B. (2004): "Economic burden of varicella in Singapore—a cost benefit estimate of implementation of a routine varicella vaccination", *Southeast Asian J Trop Med Public Health*, 35(3):693–6; Uzicanin, A., Zhou, F., Eggers, R., Webb, E., Strebel, P. (2004): "Economic analysis of the 1996–1997 mass measles immunization campaigns in South Africa. *Vaccine*, 22(25–26):3419–26; Shepard, D. S., Suaya, J. A., Halstead, S. B., Nathan, M. B., Gubler, D. J., Mahoney, R. T., Wang, D. N., Meltzer, M. I. (2004): "Cost-effectiveness of a pediatric dengue vaccine", *Vaccine*, 22(9–10):1275–80. Two studies in developed countries, on the other hand, showed that programs were not cost-effective: Allsup, S., Haycox, A., Regan, M., Gosney, M. (2004): "Is influenza vaccination cost effective for healthy people between ages 65 and 74 years? A randomised controlled trial", *Vaccine*, 23(5):639–45; Melegaro, A., Edmunds, W. J. (2004): "The 23-valent pneumococcal polysaccharide vaccine. Part II. A cost-effectiveness analysis for invasive disease in the elderly in England and Wales", *Eur J Epidemiol*, 19(4):365–75.

provided confidence intervals for their findings, follow-up was limited, data sources were not clearly defined, and there was little discussion of confounding variables. Studies on costs, moreover, found wide variations depending on the setting in which a vaccine was being delivered, making estimates of cost-effectiveness difficult to generalize.[46]

The available literature on DALYs suggests immunization is a highly cost-effective intervention. The total cost of the EPI vaccine package is less than $1.[47] According to GAVI, most vaccination campaigns cost less than $50 per year of healthy life gained. By contrast, treatment for diseases such as hypertension in the US costs between $4,340 and $87,940 for each DALY gained.[48] Jamison *et al.* estimated that the EPI vaccine program costs $14-20 per year of healthy life gained in low-income countries.[49] Miller and McCann show a similar cost for the Hib vaccine in Africa, and that Hepatitis B immunization in low-income, high-prevalence countries costs just $8–11 per DALY gained.[50]

Although cost-effectiveness provides a robust demonstration of the extent to which vaccines reduce medical costs, it does not take account of the wider range of benefits that are covered by cost-benefit analysis. The latter also has the advantage of being comparable with investments that take place outside the health sector.

Many cost-benefit analyses of vaccination have shown positive effects. In South Africa, a study of the mass measles immunization campaign of 1996 and 1997 found a benefit–cost ratio of 2.27 in the province of Mpumalanga.[51] In Japan, the benefit–cost ratio of subsidized influenza vaccinations for the elderly was estimated at 22.9.[52] Purdy *et al.* found that most of the costs related to pertussis are due to lost productivity at work

[46] Pegurri, Elisabetta, Fox-Rushby, Julia A., Damian, Walker (2005): "The effects and costs of expanding the coverage of immunization services in developing countries: a systematic literature review", *Vaccine*, 23: 1624–1635.
[47] Gauri *et al.* (2002) op cit: 2124.
[48] GAVI (2003) a op cit; Ehreth (2003) op cit: 4113.
[49] Jamison, D. T., Mosley, W. H., Measham, A. R., Bobadilla, J. L. (1993): *Disease Control Priorities in Developing countries*. Oxford University Press.
[50] Miller, M. & McCann, L. (2000): "Policy analysis of the use of hepatitis B, Haemophilus influenzae type B, Streptococcus pneumoniae-conjugate and rotavirus vaccines in national immunization schedules", *Health Economics*, January.
[51] Uzicanin, A., Zhou, F., Eggers, R., Webb, E., Strebel, P. (2004): "Economic analysis of the 1996–1997 mass measles immunization campaigns in South Africa", *Vaccine*, 22(25–26): 3419–26
[52] Ohkusa, Y. (2005): "Policy evaluation for the subsidy for influenza vaccination in elderly", *Vaccine*, 23(17–18): 2256–60.

and that the benefit–cost ratio of the immunization of 10 to 19 year olds is strongly positive.[53]

Some studies, on the other hand, have shown higher costs than benefits. In the study of measles immunization in South Africa, the benefit–cost ratio in the Western Cape province was 0.89.[54] And a study to assess the incorporation of the pneumoccocal 7-valent conjugated vaccine into the routine immunization program in Spain found a benefit-cost ratio of only 0.59.[55]

3.2 A wider view

Neither cost-effectiveness nor cost-benefit analysis has so far taken full account of the broader economic impacts of immunization. These impacts stem from the fact that immunization protects individuals not only against getting an illness per se, but also against the long-term effects of that illness on their physical, emotional, and cognitive development. For example, by stunting physical growth, childhood diseases can curtail opportunities for carrying out manual labor during adulthood. In developing countries, where manual work is frequently the only option, physical handicaps are particularly damaging. Cognitive development may also be affected by vaccine-preventable disease. Measles, for example, can cause brain damage or impair learning abilities, with severe impacts on a child's life prospects.

The importance of these effects is borne out by recent work demonstrating the link from improved health to economic growth. This research has made clear the importance of health interventions for achieving growth and suggests that cost-effectiveness analyses, as currently conducted, are likely to underestimate the benefits of vaccination.

There are several channels through which health improves wealth. The first is through its impact on education. Healthy children are better able to attend school and to learn effectively while in class. Studies have found

[53] Purdy, K. W., Hay, J. W., Botteman, M. F., Ward, J. I. (2004): "Evaluation of strategies for use of acellular pertussis vaccine in adolescents and adults: a cost-benefit analysis", *Clin Infect Dis.*, 39(1): 20–8. See also Navas, E., Salleras, L., Gisbert, R., Dominguez, A., Bruguera, M., Rodriguez, G., Gali, N., Prat, A. (2005): "Efficiency of the incorporation of the hepatitis A vaccine as a combined A+B vaccine to the hepatitis B vaccination programme of preadolescents in schools", *Vaccine*, 23(17–18): 2185–9.

[54] Uzicanin *et al.* (2004) op cit.

[55] Navas, E., Salleras, L., Gisbert, R., Dominguez, A., Timoner, E., Ibanez, D., Prat, A. (2005): "Cost-benefit and cost-effectiveness of the incorporation of the pneumococcal 7-valent conjugated vaccine in the routine vaccination schedule of Catalonia (Spain)", *Vaccine*, 23(17-18): 2342–8.

that health interventions such as de-worming programs and iron supplementation reduce absenteeism from school.[56] Curing whipworm infection, meanwhile, has been found to lead to improved test scores.[57]

The second channel is through health's impact on productivity. Like schoolchildren, healthier workers have better attendance rates and are more energetic and mentally robust. Workers in healthy communities, moreover, need to take less time off to care for sick relatives. Body size, which is greatly influenced by one's health during childhood, has been found to have large impacts on long-term productivity.[58] Bloom *et al.* have calculated that a one-year increase in life expectancy improves labor productivity by 4 per cent.[59]

The third means by which health improves wealth is through its effect on savings and investment. Healthier people expect to live longer, so they have a greater incentive to save for retirement. They are also able to work productively for longer, giving them more time to save. Workers and entrepreneurs therefore have a larger capital base to draw on for investment, leading to greater job creation and higher incomes. The savings booms in the East Asian "tiger" economies in the last quarter of the 20th century were largely driven by rising life expectancy and greater savings for retirement.

Finally, health can boost economies via a demographic dividend. The transition from high to low rates of mortality in many developing countries has been rapid. Largely brought about by medical and dietary improvements, the transition has contributed to falls in fertility as parents realize they need fewer children to attain their ideal family size. The boom in young dependents that occurs when mortality falls is therefore followed by a decline in fertility. At this stage, parents can concentrate their

[56] Miguel, Edward, and Kremer, Michael (2004): "Worms: Identifying Impacts on Education and Health the Presence of Treatment Externalities", *Econometrica*, 72(1), 159–217; Bobonis, G. J., Miguel, E., and Sharma, C. P. (2004): "Iron Deficiency Anemia and School Participation", Poverty Action Lab Paper no. 7.

[57] Nokes, C., Grantham-McGregor, S. M., Sawyer, A. W., Cooper, E. S., Robinson, B. A., Bundy, D. A. P. (1992): "Moderate-to-heavy infection of trichuris trichiura affect cognitive function in Jamaican school children", *Parasitology*, 104: 539–547.

[58] Fogel, R. W. (1991): "New Sources and New Techniques for the Study of Secular Trends in Nutritional Status, Health, Mortality and the Process of Aging." *National Bureau of Economic Research Working Paper Series on Historical Factors and Long Run Growth*, No. 26. Fogel, R. W. (1997): "New Findings on Secular Trends in Nutrition and Mortality: Some Implications for Population Theory," in M. R. Rosenzweig and O. Stark (eds.) *Handbook of Population and Family Economics*, Vol. 1a. Amsterdam: Elsevier Science, 433–481. Fogel, R. W. (2000): *The Fourth Great Awakening and the Future of Egalitarianism*. Chicago and London: The University of Chicago Press.

[59] Bloom, D. E., Canning, D., Sevilla, J. (2004): "The Effect of Health on Economic Growth: A Production Function Approach", *World Development*, Vol. 32, No. 1,1.

resources in nurturing fewer children, thus increasing the children's prospects of receiving a good education and effective health care. As the boom generation reaches working age, and provided it encounters a policy environment that is favorable to job creation, it can give a large boost to an economy by swelling the ratio of workers to dependents. It has been estimated that the demographic dividend accounted for as much as one third of East Asia's "economic miracle".[60]

A more thorough investigation of the impacts of vaccination, then, should look not just at direct medical cost savings and averted illness, but also at the effects on cognitive development, educational attainment, labor productivity, income, savings, investment, and fertility.

3.3 The benefits of vaccination—new evidence

The effect of GAVI (see Table 1)

We have carried out calculations for two vaccination campaigns, taking into account the broader economic impacts of immunization. The first study assesses GAVI's program to extend the use of the traditional basic childhood vaccination package; increase coverage of the under-used Hib, hepatitis B, and yellow fever vaccines; and help finance the introduction of anticipated vaccines covering pneumococcal disease, rotavirus, and meningococcal A/C conjugate. This program will operate in 75 low-income countries with a combined population of 3.8 billion from 2005–2020, and will cost $13 billion. We examine the likely effect of the program on worker productivity at the individual level. The second study covers efforts in the Philippines to immunize children with DTP, TB, polio, and measles vaccines. It measures vaccines' effects on children's cognitive development, an important determinant of adult earnings.

The countries involved in the GAVI immunization program suffer from high rates of child mortality. In countries that are not covered by the program, there are fewer than 10 child deaths per thousand live births. In the GAVI countries, there are over 65 deaths per thousand. GAVI estimates that its program will reduce child mortality by 4 deaths per thousand live births in 2005, and by 12 per thousand by 2020 as the campaign expands.

We used a life table to translate averted deaths into increased probability of adult survival (the proportion of 15 year olds who reach age 60), and

[60] Bloom, David E. & Williamson, Jeffrey G. (1998): "Demographic Transitions and Economic Miracles in Emerging Asia," *World Bank Economic Review*, Oxford University Press, vol. 12(3): 419–55.

Table 1: Projected costs and economic benefits of the expanded GAVI immunization program

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
1 Total cost ($million)	638	652	583	659	790	862	761	762	1,023	1,051	1,059	994	896	769	727	748
2 Deaths averted	732,673	855,998	923,529	993,247	1,052,696	1,125,275	1,229,883	1,349,584	1,608,999	1,741,284	1,913,958	1,955,902	1,973,229	1,990,757	2,002,458	2,014,390
3 Cost per death averted ($)	871	761	632	663	750	766	619	565	636	604	553	508	454	386	363	371
4 Reduction in under 5 mortality rate (per 1,000)	4.10	4.89	5.43	6.00	6.45	7.11	7.82	8.60	10.20	11.08	12.24	12.43	12.49	12.54	12.56	12.57
5 Total increase in adult survival rate (per 1,000)	6.61	7.87	8.74	9.64	10.37	11.43	12.56	13.81	16.38	17.80	19.65	19.97	20.06	20.14	20.17	20.19
6 Increase in life expectancy (years)	0.58	0.69	0.77	0.85	0.91	1.00	1.10	1.21	1.44	1.56	1.73	1.76	1.76	1.77	1.77	1.78
7 Average percentage increase in income for all children in that cohort	0.78	0.93	1.03	1.14	1.23	1.35	1.48	1.63	1.93	2.10	2.32	2.36	2.37	2.38	2.38	2.39
8 Increased annual earnings per child in the cohort	4.61	5.49	6.10	6.73	7.24	7.98	8.77	9.64	11.43	12.43	13.72	13.94	14.00	14.06	14.08	14.10
9 Increase in total cohort income per year, once earning starts ($million)	410	492	550	610	661	732	809	895	1068	1168	1297	1326	1340	1355	1365	1376
10 Internal rate of return (%)	12.4	13.2	14.4	14.3	13.8	13.8	15.0	15.5	14.9	15.2	15.8	16.2	16.9	17.8	18.2	18.0

found that the GAVI program will increase the adult survival rate by 5 per thousand initially and by 16 per thousand by 2020 (life expectancy will increase by half a year initially and by one and a half years by the end of the program).

To translate the latter into growth of wages and income per capita, we used estimates in the economics literature from Shastry and Weil (2003) and Weil (2005)[61] that show the link between health and wages in individuals.[62] This analysis shows that for a group of 1,000 adults, for each additional person surviving from age 15 to 60, average wages rise by 0.179 per cent. Based on the assumption that labor productivity and wages account for two-thirds of national income,[63] we calculate that each extra surviving adult in a group of 1,000 boosts income per capita by 0.119 per cent.

From this figure, we calculate that the average percentage increase in income for the children whose immunization coverage increases through the GAVI program will rise from 0.78 per cent in 2005 to 2.39 per cent by 2020. This equates to an increase in annual earnings per child of $14 by 2020 (see table 1). The total increase in income per year once the vaccinated cohort of children start earning will rise from $410 million in 2005 to $1.34 billion by 2020 (at a cost of $638 million in 2005 and $748 million in 2020).

We estimate the internal rate of return to the program by calculating the interest rate that would make the net present value of the flow of future benefits equal the initial costs. The rate of return amounts to 12.4 per cent in 2005, rising to 18 per cent in 2020 as vaccine costs decline. These are conservative estimates, since they do not take account of averted medical costs, the value of reduced pain and suffering among survivors, welfare benefits associated with averted deaths, or demographic dividend effects.

If these additional benefits of vaccination had been included, it is likely that the rate of return would be higher still, and possibly much higher, but

[61] Shastry, G. K. & Weil, D. N. (2002): "How Much of Cross-Country Income Variation is Explained by Health?" *Journal of the European Economic Association*, 1: 387-396. Weil, D.N. (2005): "Accounting for the Effect of Health on Economic Growth", *Mimeo*, Department of Economics, Brown University.

[62] This approach assumes that health is a uni-dimensional variable that is reflected in mortality and morbidity measures. Both microeconomic and macroeconomic studies of the effect of health on labor productivity use this approach, which enables a single measure to be used as an indicator of an individual's or a community's health. In our study, the health improvements generated by vaccination are therefore taken to have economic impacts similar to those of health improvements on average.

[63] See Hall, R. E., & Jones, C. I. (1999): "Why Do Some Countries Produce So Much More Output Per Worker Than Others? *Quarterly Journal of Economics* 114(1): 83–116.

even these conservative estimates compare favorably with the average rates of return to schooling. A review of 98 country studies from 1960 to 1997 showed that the average returns for primary, secondary and higher education were 19 per cent, 13 per cent and 11 per cent respectively.[64] This finding suggests that the benefits of vaccination have been greatly underestimated and amounts to a strong argument for increased immunization in developing countries.

Immunization and cognitive development—evidence from the Philippines

In the Philippines study, we examined the effect of immunization on productivity by looking at its impact on test scores that measure the cognitive ability of ten year olds. There is robust evidence that childhood illness can impair cognitive development, and that the latter affects adult productivity and earnings. Since our data cover children born in 1983–84 and thus do not offer information on wages, we take scores in cognitive tests at the age of ten as an indicator of likely productivity in adulthood.

Our study involves a sample of 1975 children from the Cebu Longitudinal Health and Nutrition Survey (CLHNS). CLHNS is part of a longitudinal survey of Filipino women and their children born in the year following 1 May 1983. The women lived in 33 districts of the metropolitan Cebu area. Bi-monthly interviews carried out over two years allow us to track immunization activities in the first two years of a child's life, while a follow-up study conducted between October 1994 and October 1995 provides us with scores on language, mathematics, and IQ tests.

We compared the test score results of children who had received the basic six vaccines (DTP, polio, measles, and TB) in the first two years of life with those who had received no vaccinations. It is important to recognize, of course, that children who are immunized have other advantages that make them more likely to succeed in cognitive tests. For example, they may receive a better education or hail from families that place a greater emphasis on health in general, meaning they would score well whether or not they were immunized. In order to eliminate these effects, we used a propensity score matching method that matches each child in the treatment group with a similar control group. We matched children on the probability that they would be vaccinated given their characteristics—

[64] Psacharopoulos, G. & Patrinos, H. (2002): "Returns to Investment in Education: A Further Update", World Bank Policy Research Working Paper 2881, September.

that is, their "propensity scores". Groups of children with a certain propensity score were matched with control groups whose propensity scores are close to their own, with the closest-matched groups given more weight.[65]

After controlling for these observed characteristics we found that immunization was associated with significantly improved scores in IQ, language, and mathematics tests. The effect was stronger (significant at the 5% confidence level) for IQ and language scores than for mathematics (where the effect was significant at the 10% level). Childhood vaccination appears to have positive and long-term health impacts that translate into increased cognitive ability in ten year olds, which in turn is associated with higher earnings in adulthood.

In both our studies, then, we found significant positive impacts of vaccination programs. As well as improving health, vaccines have long-term effects on the development of an individual. These individual effects, which are produced at a remarkably low cost, are likely to translate into lasting impacts on economies.

Summary

Clearly there is scope for more research to be conducted on the diverse benefits of vaccination. The Miller and McCann study cited above shows that rates of return differ by country and by income group. It is likely they also differ by the type of vaccine delivered. Further research is needed to calculate the value of vaccination for different countries and at different stages of development. However, immunization does appear to be an important tool for improving survival and strengthening economies. By boosting cognitive abilities, it improves children's prospects of success when reaching working age. And it does so in an extremely cost-beneficial way. Immunization provides a large return on a small investment—higher than most other health interventions, and at least as high as non-health development interventions such as education.

There is a strong case, therefore, for a renewed international commitment to vaccination. The impressive progress towards universal basic vaccine coverage in the 1970s and 1980s has stalled in the past decade, and several damaging childhood illnesses have begun to return as a result. A

[65] Full details of the methodology are available in Bloom, Canning, and Seiguer (2005): "Immunization as Human Capital", *Mimeo*, Harvard School of Public Health.

revived commitment to vaccination requires action on several fronts. First, the public health establishment must communicate clearer and more compelling messages about the value of vaccination. The targets of such communication should include governments in developed and developing countries, as well as donors that fund vaccination in the latter. Second, these messages should move beyond explanation of the effect of immunization on health and on medical costs to address the broader impacts on economies. Vaccination is not purely a health sector issue—it has resonance for wider economic planning and for long-term economic progress. Apprising finance ministries of its importance is vital for cementing its position in development policy.

The third area where renewed action is needed relates to leadership. At an international level, GAVI has begun to increase awareness of the value of vaccination and to push multiple partners toward expanding its breadth and scope. At the national level, politicians' commitment is important in driving immunization campaigns forward. Traditionally, individuals have submitted to state encouragement to vaccinate because they have trusted government to act in their best interests. Recent problems with vaccines, along with efforts (valid or not) of those who continue to argue that vaccines are unsafe, are weakening this trust. Politicians are not elected on vaccination platforms, so there is no pressure on them to champion vaccines once in power. However, the confusion caused by British Prime Minister Tony Blair's refusal to reveal whether his own son had received the MMR vaccine at the height of the MMR scare highlights the dangers of equivocal leadership on such sensitive issues. Blair's lack of clarity, which was the subject of extensive media coverage, may have increased uncertainty over the vaccine.[66] Public complacency, as measles outbreaks that have followed declines in vaccination coverage in the developed world show, can quickly imperil health, and governments and donors that recognize the benefits of immunization must continually hammer the point home.

Traditionally, governments and donors have only considered the health impacts of vaccine-preventable illnesses, and their effect on overall welfare has been underestimated. However, new evidence on the importance of health as a driver of economic development and poverty reduction

[66] Lewis and Speers (2003) op cit.

suggests the need for a re-think. Vaccines in particular, as the evidence presented in this paper shows, are an inexpensive and extremely effective means of improving health and overall welfare. Their impacts, moreover, are much greater than previously thought.

Making the push to complete worldwide vaccination coverage will be a difficult task, and finding ways of ensuring the continued development of effective vaccines in the future is potentially more complex still. Vaccines should be seen not as a cost that swells public health budget requirements, but as an investment with enduring and large-scale impacts. The benefits of a push for increased immunization are likely to heavily outweigh the costs, and policy makers who neglect immunization will be missing a great opportunity for promoting development.

肺炎鏈球菌及疫苗資訊

1. 疫苗接種計劃的重要性

1.1 基層健康是醫護系統的基石，對生活質素和社會的醫護開支都有十分重要的影響。

1.2 疫苗接種計劃應是基層健康的重要環節。國際研究顯示：疫苗接種計劃有極佳的經濟效益。

1.3 兒童全民疫苗接種計劃是政府的責任。把醫護開支投資在兒童身上，可減少因貧富懸殊引起的跨代不公義、可以帶來最大的長遠經濟收益、亦可減少兒童作爲帶菌者所產生的疾病連鎖影響。

2. 香港兒童防疫計劃落後廿年

2.1 香港自 1960 年代開始推行兒童全民疫苗接種計劃，除 1986 年加入乙型肝炎疫苗後，20 年來鮮有重大革新，人均的政府疫苗計劃開支處於低水平。

2.2 香港兒童免疫接種計劃目前包括九個種類，與其他歐美國家相比，香港所提供的種類明顯較少、較落後 (見表一)。

表一: 各國幼兒疫苗接種計劃一覽

國家/城市 / 疾病	香港	澳門	新加坡	盧森堡	英國	美國
卡介苗	x	x	x			
白喉、 百日咳、破傷風	x	x	x	x	x	x
流行性感冒嗜血桿菌疫苗		x		x	x	x
甲型肝炎疫苗						x
乙型肝炎疫苗	x	x	x	x		x
流行性感冒						x (只提供於高危幼兒)

國家/城市 疾病	香港	澳門	新加坡	盧森堡	英國	美國
麻疹、腮腺炎、德國麻疹	x	x	x	x	x	x
流行性腦脊髓膜炎				x	x	x
肺炎鏈球菌疫苗				x	x	x
小兒麻痺	x	x	x	x	x	x
水痘		x				x

截止 2007 年 12 月

本資料單張旨在提供有關肺炎鏈球菌及其預防疫苗的相關資訊，以供各界考慮應否將預防肺炎鏈球菌疫苗納入香港兒童免疫接種計劃。

3. 肺炎鏈球菌危害香港兒童的健康

3.1 肺炎鏈球菌有高度傳染性

肺炎鏈球菌是一種非常普遍但可以致命的細菌。感染肺炎鏈球菌的早期徵狀與一般小兒常患的傷風感冒相似，極易被家長忽略。健康的人在沒有任何病徵的情況下亦可成爲帶菌者。每個帶菌者可透過打噴嚏及咳嗽散佈的飛沫，或直接接觸帶菌者口或鼻中的呼吸道分泌物將疾病傳播給無數朋友及家人，甚至所有曾接觸過的人。

3.2 肺炎鏈球菌會引致嚴重併發症

一旦受感染，除了細菌性肺炎、急性中耳炎(中耳感染)、鼻竇炎(鼻竇感染)外，更可引起嚴重和非常危險的入侵性肺炎鏈球菌疾病，包括：菌血性肺炎(肺部感染)、腦膜炎(大腦及脊髓神經薄膜細菌感染)、敗血症等。其中腦膜炎者的死亡率更可高達 20-50%[1]。而感染腦膜炎的幼兒，在康復後也會出現永久性腦神經受損，如失聰、學習障礙及行爲問題。敗血症的死亡率則高達 50% [2]。

3.3 肺炎鏈球菌疾病是可用疫苗預防的致命疾病

世界衛生組織資料顯示，肺炎鏈球菌疾病排名於引致死亡而又能以疫苗預防

[1] PneumoADIP/Meningitis website, 2006

[2] PneumoADIP/Sepsis website 2006

的疾病的比率首位，較白喉、破傷風、百日咳、小兒麻痺及麻疹還要高。

3.4 感染肺炎鏈球菌

- 每年全球約有 100 萬名 5 歲以下的兒童因感染肺炎鏈球菌而死亡[3]。
- 根據 2004 年世界衞生組織報告，17%的幼兒死亡個案是由肺炎鏈球菌疾病引起的[4]。
- 在歐洲及美國，由肺炎鏈球菌引起的肺炎最少佔所有社區感染肺炎留醫個案的 30%[5]。
- 在工業國家，2 歲以下幼兒的入侵性肺炎鏈球菌疾病每年發病率高達每 10 萬名 160 宗[5]。
- 65 歲或以上的長者發病率爲每 10 萬名 5,500 宗至 9,200 宗，死亡率佔 10-30%[5]。

3.5 香港的發病率較其他先進國家高

- 世界衞生組織指出，肺炎鏈球菌的問題在發展中國家一般較爲嚴重[6]。香港雖然未如一些發展中國家情況惡劣，但與其他先進國家比較，情況仍欠理想。
- 估計香港每年 5 歲或以下的幼兒入侵性肺炎鏈球菌疾病發病率爲每 10 萬名 16.1 宗，而 2 歲或以下發病率則高達每 10 萬名 23.7 宗[7]。發病率較某些歐洲國家更爲嚴重，例如德國(每十萬名有 8.9 宗)；瑞士(每十萬名有 7.6 宗)；英國及威爾斯(每十萬名有 14.5 宗)[7,8,9,10,11]。
- 而因肺炎鏈球菌而感染腦膜炎的比例則爲，5 歲或以下每十萬名 1.1

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[3] *Streptococcus Pneumoniae*, Initiative for Vaccine Research, World Health Organization

[4] WHO website, 2004

[5] WHO website, 2006

[6] WHO Weekly Epidemiological Record. 2007,82 93-104

[7] P L Ho, et al, Invasive Pneumococcocal Disease Burden in Hong Kong Children, *The Paediatric Infection Disease Journal*. May 2006, Vol 25 (5) 454-455

[8] Sleeman K et al. Invasive pneumococcal disease in English and Wales: vaccination implications Journal of Infection Disease 2001:183:239-246

[9] Madhi SA et al. The impact of a 9-valent pneumococcal conjugate vaccine on the public health burden of pneumonia in HIV-infected and uninfected children. Clinical Infection Disease. 2005; 40:1511-1518

[10] Ventez I et al, Paediatric, invasive pneumococcal disease in Switzerland, 1985-1994. Swiss Pneumococccal Study Group. International Journal of Epidermiology 1998;27:1101-1104

[11] Von Kries R et al Proportion of invasive pneumococcal infections in German children preventable by pneumococcal conjugate vaccines. *ClinInfect Dis*. 2000;31:482-287;

宗，2 歲或以下每十萬名 2.1 宗[7]。

- 一項在 2001 年進行的研究發現，香港小學生(6 至 12 歲)整體肺炎鏈球菌帶菌率爲 3.5%[12]。
- 另一項於同年在本港 79 間日間托兒所及幼稚園進行的研究，調查了肺炎鏈球菌在 2 至 6 歲幼兒間的普遍程度。結果顯示在 1,978 名幼兒中，383 名幼兒鼻腔中帶有肺炎鏈球菌，而年齡越小的幼兒帶菌率則越高[13](見表二)。

表二: 肺炎鏈球菌在 2 至 6 歲幼兒間的普遍程度

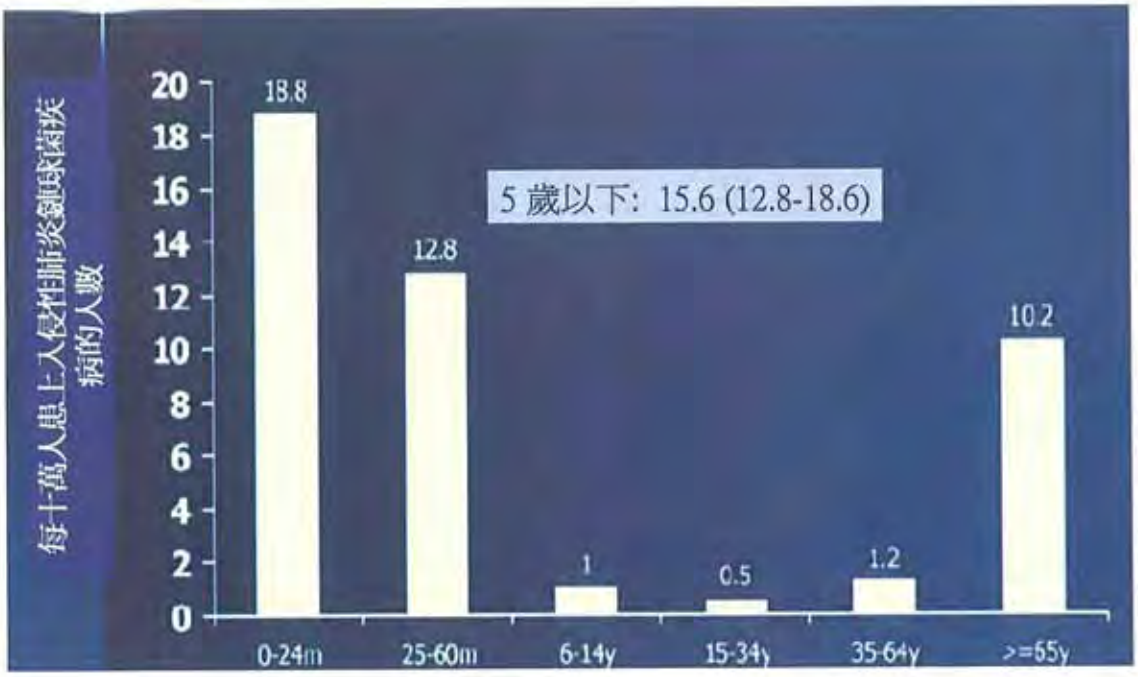
年齡	帶菌率
2-3	28.8%
4	32.6%
5	20.1%
6	15.2%

- 另一研究資料亦顯示，0-2 歲的幼兒是肺炎鏈球菌疾病高危群[12] (見表三)

表三: 1995-2004 年度患入侵性肺炎鏈球菌疾病的種菌結果(香港島數據)

[12] Boost MV et al, Prevalence of carriage of antimicrobial resistant strains of Streptococcus pneumoniae in primary school children in Hong Kong, *Epidemiology Infection*. 2001 Aug;127(1):49-55

[13] Chiu S. et al, Nasopharyngeal Carriage of Antimicrobial-Resistant Streptococcus pneumoniae among Young Children Attending 79 Kindergartens and Day Care Centers in Hong Kong, Antimicrobial Agents Chemotherapy. 2001 October; 45(10): 2765–2770.



入侵性肺炎鏈球菌疾病(IPD)是根據來自兩所主要醫院 (瑪麗醫院及東區尤德夫人那打素醫院) 所有陽性反應種菌結果 (包括血液、腦脊液、體液)，代表港島區1995至2004年全部個案的90% 。 用作計算的人口數據來自1996及2001年的人口普查。

何栢良教授,2006年

4. 頑強抗藥性難治肺炎鏈球菌

以上的數據反映肺炎鏈球菌問題嚴重，尤其在 2 歲以下的幼童中更爲普遍。另一方面，由於肺炎鏈球菌的堅固莢膜很難攻破，所以要倚靠身體自身免疫對抗這種細菌是非常困難的。因此，餘下來處理這個問題的方法主要有二:

4.1 抗生素治療方法

- 一般來說，盤尼西林可有效治療肺炎鏈球菌疾病。如果染上肺炎鏈球菌疾病的患者沒有即時接受治療或治療失敗，會引致失聰、癱瘓，甚至腦膜引致的死亡。可是在過去 30 年間，越來越多肺炎鏈球菌對盤尼西林及其它抗生素產生抗藥性，具抗藥性的菌株數目正在全球包括香港持續上升[14,18]。
- 根據研究資料顯示，在香港，肺炎鏈球菌對盤尼西林的抗藥性已從 18% (1993)上升至 69.1% (1999)；肺炎鏈球菌對紅霉素的抗藥性已從 10%

[14] Adam D, Global antibiotic resistance in Streptococcus pneumoniae. *J. Antimicrob. Chemother.*2002 50(Topic T1): 1-5;

(1993)上升至 78.5% (1999) [15]。此現象可能與香港醫生較常在幼兒入院前爲他們注射抗生素有關。

- 在香港幼兒身上引發 89.7%入侵性肺炎鏈球菌的 7 種肺炎鏈球菌血清型，都對抗菌藥有抗藥性[16]。
- 一項在 2001 年進行的研究發現，小學生(6 至 12 歲)整體肺炎鏈球菌帶菌率爲 3.5%，其中 49%學生對盤尼西林有抗藥性。在所有發病的患者中，只有一半可使用盤尼西林治療[17]。

5. 接種預防疫苗

5.1 世界衞生組織曾表示，「接種疫苗是預防肺炎鏈球菌疾病的唯一方法[18]。」其後更於 2007 年 3 月罕有地建議全球各國政府，將肺炎鏈球菌預防疫苗列入常規疫苗接種計劃中，爲 5 歲以下的兒童免費注射，有助大幅降低死亡率與發病率[6]。

事實上，多個國家已把肺炎鏈球菌接合疫苗列入在國家全民防疫注射計劃內(見表四)。

表四: 18 個國家已將肺炎鏈球菌接合疫苗列入國家全民防疫注射計劃內

澳洲	比利時	加拿大	法國
德國	希臘	盧森堡	墨西哥
荷蘭	挪威	卡達	瑞士
英國	美國	意大利	科威特
哥斯達黎加	新西蘭		

5.2 經濟效益考慮

- 數據顯示，肺炎鏈球菌接合疫苗能保障兩歲以下幼童預防多種常患的肺

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[15] Ho PL et al, Emergence of fluoroquinolone resistance among multiply resistant strains of Streptococcus pneumoniae in Hong Kong. *Antimicrob. Agents Chemother*. 43: 1310-1313

[16] Ho PL et al, Serotype distribution and antimicrobial resistance patterns of nasopharyngeal and invasive Streptococcus pneumoniae isolates in Hong Kong children, Vaccine 22 (2004) 3334-3339

[17] Boost MV et al, Prevalence of carriage of antimicrobial resistant strains of Streptococcus pneumoniae in primary school children in Hong Kong, *Epidemiology Infection*. 2001 Aug;127(1):49-55

[18] *WHO Weekly Epidemiological Record, .11 June 1999*

[27] P L Ho, et al, Pediatric hospitalisation for pneumococcal diseases preventable by 7-valent pneumococcal conjugate vaccine in Hong Kong *Vaccine 25(2007) 6837-6841.*

炎鏈球菌疾病。因此，全球超過 18 個國家已進行有關肺炎鏈球菌接合疫苗的經濟效益研究，肯定其成本效益，並將之納入兒童常規免疫接種計劃內。

- 在亞太區，很多國家政府對於納入肺炎鏈球菌疫苗於兒童疫苗接種計劃表現積極。最近在台灣亦舉行了一個「從全球疫苗發展趨勢看台灣疫苗政策」的國際研討會。出席的學者包括哈佛經濟學者 David E. Bloom 博士等人，會中 David E. Bloom 博士把疫苗比喻爲「經濟成長的引擎」，經濟發展及人民健康是息息相關，人民愈健康，國家經濟愈富強。David Bloom 博士更指出，預防接種是公共衛生工作中對於預防傳染病最具成本效益的投資，每 1 美元的疫苗支出，平均可節省 7 至 20 美元的後續醫療支出。

- 2007 年 8 月初**香港中文大學**藥劑學院副院長(外務)**李炯前教授**在香港發表的「利用藥物經濟學研究方法評估肺炎鏈球菌接合疫苗經濟效益」的研究報告，亦顯示肺炎鏈球菌接合疫苗合乎世衛所訂定的成本效益準則，故此亦建議應將疫苗納入本港兒童常規疫苗計劃，爲香港的未來棟樑提供必須的保障，達至長遠的人才保育目標，同時減低社會未來的醫療負擔。