Vaccines: The Week in Review
22 November 2010
Center for Vaccine Ethics & Policy
http://centerforvaccineethicsandpolicy.wordpress.com/

A program of
- Center for Bioethics, University of Pennsylvania
  http://www.bioethics.upenn.edu/
- The Wistar Institute Vaccine Center
  http://www.wistar.org/vaccinecenter/default.html
- Children’s Hospital of Philadelphia, Vaccine Education Center
  http://www.chop.edu/consumer/lsp/microsite/microsite.jsp

This weekly summary targets news and events in the global vaccines field gathered from key governmental, NGO and company announcements, key journals and events. This summary provides support for ongoing initiatives of the Center for Vaccine Ethics & Policy, and is not intended to be exhaustive in its coverage.

Vaccines: The Week in Review is now also posted in a blog format at http://centerforvaccineethicsandpolicy.wordpress.com/. Each item is treated as an individual post on the blog, allowing for more effective retrospective searching. Given email system conventions and formats, you may find this alternative more effective. This blog also allows for RSS feeds, etc.

Comments and suggestions should be directed to
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WHO: Cholera in Haiti - update 3
17 November 2010 -- On 16 November, the Haitian Ministry of Public Health and Population (MSPP) reported that as of 14 November, 17,418 cumulative number of hospitalized admissions and 1,065 deaths were reported from seven Departments in the country. The departments reporting cases include Artibonite, Centre, Nord, Nord-Ouest, Nord Est, Ouest, and Sud. In metropolitan Port-au-Prince, communes reporting increases in cases include Carrefour, Cite Soleil, Delmas, Kenscoff, Petion Ville, and Tabarre. The rise in the number of cases in Cite Soleil is particularly concerning, due to its crowded living conditions, poor sanitation, and lack of access to potable water.

On 16 November, Dominican Republic registered its first case of cholera in a 32-year-old male returning from Haiti...

Recommendation
WHO does not recommend restrictions to international travel or trade due to the cholera outbreak in Haiti. For further information, please refer to the "WHO statement relating to international travel and trade to and from countries experiencing outbreaks of cholera" below.


WHO released the “Global report on antimalarial drug efficacy and drug resistance: 2000–2010,” and called on malaria-endemic countries "to be
increasingly vigilant in monitoring antimalarial drug efficacy in order to allow for early detection of artemisinin resistance." WHO said the report is based on 1,100 studies conducted by national malaria control programs and research institutes over the ten-year period. The report estimates that only 34% of malaria-endemic countries are complying with WHO recommendations to routinely monitor the efficacy of first- and second-line antimalarial medicines. Dr Pascal Ringwald of the Drug Resistance and Containment Unit, within WHO's Global Malaria Programme and one of the report authors, said, "A greater political commitment to support and sustain national monitoring of the efficacy of antimalarial medicines is critical to prevent a wider emergence of artemisinin resistance."

Dr Robert Newman, Director of WHO's Global Malaria Programme, commented, "The emergence of artemisinin resistance on the Cambodia-Thailand border has been a wake-up call to the world to prevent its spread, increase monitoring, and preserve ACTs as the only effective treatment we have for falciparum malaria. Prompt action will be critical to sustain progress in malaria control and achieve the health-related Millennium Development Goals."


WHO: Global report on antimalarial efficacy and drug resistance: 2000-2010

Merck announced that the U.S. Food and Drug Administration’s (FDA) Vaccines and Related Biological Products Advisory Committee "has advised that the data presented support an indication for GARDASIL [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] for the prevention of anal cancer and anal intraepithelial neoplasia (AIN) in both males and females 9 through 26 years of age.” The Committee's input will be considered by the FDA in its review of the supplemental Biologics License Application (sBLA) that Merck submitted for GARDASIL in early 2010. The FDA is not bound by the Committee's guidance, but takes its advice into consideration when reviewing vaccines.


The GAVI Alliance announced a new, “unprecedented” Joint Financing Arrangement (JFA) today with the Government of Nepal to support the implementation of the Nepalese National Health Sector Programme. GAVI said the three year agreement, involving a US$14.5 million contribution from GAVI, “is aimed at providing more predictable funding to the Nepalese Government so that it can better plan health programmes. It is also expected that the JFA will help Nepal deliver health services more equitably and sustainably and to use resources more effectively and efficiently.” Under the JFA’s terms, Nepal’s leading aid donors - GAVI, DFID, AusAid, World Bank, USAID, UNFPA, WHO and UNICEF – “agree to channel their development assistance in support of the Government’s health programmes through one simplified management system that will sharply reduce the reporting that donors require from low-income countries such as Nepal.” Carole Presern, Managing Director, GAVI Special Projects, commented, “We are shifting countries’ administrative burden to Platform
development partners and are confident that a long term and fruitful partnership, as the one we have signed in Nepal, is the way forward for achieving better health outcomes - more services, more health workers, and functioning logistics systems.”

The Health Systems Funding Platform was “established in 2009 at the recommendation of the High Level Taskforce on Innovative International Financing for Health Systems. The initiative is being developed by the GAVI Alliance, the Global Fund to fight HIV/AIDS, TB and Malaria and the World Bank, facilitated by the World Health Organization, and in consultations with countries and other key stakeholders, including civil society and the private sector. The platform is part of a broad international effort to strengthen health systems and accelerate progress towards the Millennium Development Goals.”
http://www.gavialliance.org/media_centre/statements/nepal_hsfp.php

Niger national health authorities presented Dr. Marc LaForce, director of the Meningitis Vaccine Project (MVP), with the "Illustre Combattant de la Ménингite." MVP is a partnership between PATH and the World Health Organization that is funded by the Bill & Melinda Gates Foundation. The partnership fostered development of MenAfriVac, a vaccine against the epidemic meningitis that sweeps through sub-Saharan countries known as the meningitis belt during the dry season. Beginning in December, more than 20 million people in Niger, Mali, and Burkina Faso will receive MenAfriVac™ in the first nationwide vaccination campaigns using a meningitis vaccine developed specifically for Africa.

The American Society of Tropical Medicine and Hygiene (ASTMH) announced that Sabin President Dr. Peter Hotez has assumed his role of president of the Society, “a worldwide organization of scientists, clinicians and program professionals whose mission is to promote global health through the prevention and control of infectious and other diseases that disproportionately afflict the global poor.”

WHO released a newsletter which reports on its main achievements in immunization for 2008-09. WHO said it “covers a broad scope of activities, from global immunization policy; to research and development of vaccines and technologies; quality, safety and standards; access to immunization services; and communication, advocacy and media. It also describes the framework and priorities for the Strategic Plan 2010-2015 of the Department of Immunization, Vaccines and Biologicals.”
The Weekly Epidemiological Record (WER) for 19 November 2010, vol. 85, 47 (pp 461–472) includes Turkmenistan certified malaria-free; WHO Quantitative Immunization and Vaccine-Related Research meeting, October 2010 – summary; Yellow fever surveillance and outbreak response: revision of case definitions, October 2010 http://www.who.int/entity/wer/2010/wer8547.pdf

The MMWR for November 19, 2010 / Vol. 59 / No. 45 includes:
- Update: Cholera Outbreak --- Haiti, 2010
- Occupational Transmission of Neisseria meningitidis --- California, 2009

Events/Conference Watch
[Editor’s Note]
Vaccines: The Week in Review is now monitoring key events and conferences and will include summaries of key announcements and other content. Event Watch is not intended to be exhaustive, but indicative of themes and issues the Center is actively tracking. If you would like to suggest events and conferences for coverage, please write to David Curry at david.r.curry@centerforvaccineethicsandpolicy.org


Conference: The Second Inter-Ministerial Conference on Health and Environment in Africa
Place: Luanda, Angola  Date: 23–26 November 2010
The Second Inter-Ministerial Conference on Health and Environment in Africa “aims to enhance political commitment to sustainable development in the African region. Participants will review how far countries have implemented the Libreville Declaration of 2008 (where health and environment ministers resolved to reduce environmental threats to human health and well-being), identify country-level actions and decide health and environmental priorities for achieving Millennium Development Goals.” http://www.who.int/mediacentre/events/meetings/2010/health_environment_africa/en/index.html

Journal Watch
[Editor’s Note]
Vaccines: The Week in Review continues its weekly scanning of key journals to identify and cite articles, commentary and editorials, books reviews and other content supporting our focus on vaccine ethics and policy. Journal Watch is not intended to
be exhaustive, but indicative of themes and issues the Center is actively tracking. We selectively provide full text of some editorial and comment articles that are specifically relevant to our work. Successful access to some of the links provided may require subscription or other access arrangement unique to the publisher. Our initial scan list includes the journals below. If you would like to suggest other titles, please write to David Curry at david.r.curry@centerforvaccineethicsandpolicy.org

Clinical Infectious Diseases
15 December 2010 Volume 51, Number 12
http://www.journals.uchicago.edu/toc/cid/current

**MAJOR ARTICLE**

Influenza Vaccine Given to Pregnant Women Reduces Hospitalization Due to Influenza in Their Infants
Isaac Benowitz,1 Daina B. Esposito,1 Kristina D. Gracey,1 Eugene D. Shapiro,1,2,3 and Marietta Vázquez1
Departments of 1Pediatrics and 2Investigative Medicine, and 3Public Health, Yale University School of Medicine, New Haven, Connecticut

Abstract

Background. Infants aged <12 months are at high risk of hospitalization for influenza. Influenza vaccine is recommended for pregnant women and for most children; however, no vaccine is approved for infants aged <6 months. Effective approaches are needed to protect this vulnerable population. Vaccination of women during pregnancy may protect the infant through transfer of antibodies from the mother. Few studies have examined the effectiveness of this strategy, and those studies produced mixed results.

Methods. In a matched case-control study, case patients were infants aged <12 months admitted to a large urban hospital in the northeastern United States because of laboratory-confirmed influenza from 2000 to 2009. For each case, we enrolled 1 or 2 control subjects who were infants who tested negative for influenza and matched cases by date of birth and date of hospitalization (within 4 weeks). Vaccine effectiveness was calculated on the basis of matched odds ratios and was adjusted for confounding.

Results. The mothers of 2 (2.2%) of 91 case subjects and 31 (19.9%) of 156 control subjects aged <6 months, and 1 (4.6%) of 22 case subjects and 2 (5.6%) of 36 control subjects aged ≥6 months, had received influenza vaccine during pregnancy. The effectiveness of influenza vaccine given to mothers during pregnancy in preventing hospitalization among their infants, adjusted for potential confounders, was 91.5% (95% confidence interval [CI], 61.7%–98.1%; P = .001) for infants aged <6 months. The unadjusted effectiveness was 90.7% (95% CI, 59.9%–97.8%; P = .001).

Conclusions. Influenza vaccine given to pregnant women is 91.5% effective in preventing hospitalization of their infants for influenza in the first 6 months of life.

**Editorial Commentary: How Did the 2008–2009 Seasonal Influenza Vaccine Affect the Pandemic?**
W. Paul Glezen
[Free full-text]

**VIEWPOINTS**

Pandemic Influenza’s 500th Anniversary
David M. Morens, Jeffery K. Taubenberger, Gregory K. Folkers, and Anthony S. Fauci
Abstract
It is impossible to know with certainty the first time that an influenza virus infected humans or when the first influenza pandemic occurred. However, many historians agree that the year 1510 a.d.—500 years ago—marks the first recognition of pandemic influenza. On this significant anniversary it is timely to ask: what were the circumstances surrounding the emergence of the 1510 pandemic, and what have we learned about this important disease over the subsequent five centuries? We conclude that in recent decades significant progress has been made in diagnosis, prevention, control, and treatment of influenza. It seems likely that, in the foreseeable future, we may be able to greatly reduce the burden of influenza pandemics with improved vaccines and other scientific and public health approaches.

Emerging Infectious Diseases
Volume 16, Number 11—November 2010
http://www.cdc.gov/ncidod/EID/index.htm
[Reviewed earlier]

Human Vaccines
Volume 6, Issue 11  November 2010
http://www.landesbioscience.com/journals/vaccines/toc/volume/6/issue/11/
[Reviewed earlier]

JAMA
Vol. 304 No. 19, pp. 2095-2194, November 17, 2010
http://jama.ama-assn.org/current.dtl
[No relevant content]

Journal of Infectious Diseases
15 December 2010  Volume 202, Number 12
http://www.journals.uchicago.edu/toc/jid/current
Major Articles/Brief Reports
Cervical Human Papillomavirus Prevalence in 5 Continents: Meta-Analysis of 1 Million Women with Normal Cytological Findings
Laia Bruni, Mireia Diaz, Xavier Castellsagué, Elena Ferrer, F. Xavier Bosch, and Silvia de Sanjosé
Abstract
Background. Baseline information on human papillomavirus (HPV) prevalence and type distribution is highly desirable to evaluate the impact of prophylactic HPV vaccines in the near future.
Methods. A meta-analysis was performed of studies published between 1995 and 2009 that used polymerase chain reaction or Hybrid Capture 2 for HPV detection in women with normal cytological findings.
Results. The analysis included 194 studies comprising 1,016,719 women with normal cytological findings. The estimated global HPV prevalence was 11.7% (95% confidence interval, 11.6%–11.7%). Sub-Saharan Africa (24.0%), Eastern Europe (21.4%), and Latin America (16.1%) showed the highest prevalences. Age-specific HPV distribution presented with a first peak at younger ages (<25 years) and, in the Americas and Africa, a rebound at older ages (≥45 years). Among the women with type-specific HPV data (n = 215,568), the 5 most common types worldwide were HPV-16 (3.2%), HPV-18 (1.4%), HPV-52 (0.9%), HPV-31 (0.8%), and HPV-58 (0.7%).

Conclusions. Although the prevalence of HPV in women with normal cytological findings is high and variable across world regions, HPV types 16, 18, 31, 52, and 58 are consistently found among the 10 most common types in all of them. These results represent the most comprehensive assessment of HPV burden among women with normal cytological findings in the pre–HPV vaccination era worldwide.

The Lancet
Nov 20, 2010 Volume 376 Number 9754 Pages 1711 – 1798
http://www.thelancet.com/journals/lancet/issue/current

Comment
Measles eradication: past is prologue
David L Heymann, Paul E Fine, Ulla K Griffiths, Andrew J Hall, Sandra Mounier-Jack

Preview
In 1969, David Morley emphasised the high mortality rates from measles in west Africa and other countries. He predicted an increase in speculation about the possibility of measles eradication, and concluded that eradication programmes were likely to be successful only if built on a foundation of effective child-care services that are available to the whole community.1,2 Speculation about measles eradication has continued, most recently at a WHO meeting on measles in which a concluding statement encouraged a 2020 target for measles eradication.

Articles
Adult and child malaria mortality in India: a nationally representative mortality survey
Neeraj Dhingra, Prabhat Jha, Vinod P Sharma, Alan A Cohen, Raju M Jotkar, Peter S Rodriguez, Diego G Bassani, Wilson Suraweera, Ramanan Laxminarayan, Richard Peto, for the Million Death Study Collaborators

Summary
Background
National malaria death rates are difficult to assess because reliably diagnosed malaria is likely to be cured, and deaths in the community from undiagnosed malaria could be misattributed in retrospective enquiries to other febrile causes of death, or vice-versa. We aimed to estimate plausible ranges of malaria mortality in India, the most populous country where the disease remains common.

Methods
Full-time non-medical field workers interviewed families or other respondents about each of 122,000 deaths during 2001—03 in 6671 randomly selected areas of India, obtaining a half-page narrative plus answers to specific questions about the severity and course of any fevers. Each field report was sent to two of 130 trained physicians, who
independently coded underlying causes, with discrepancies resolved either via anonymous reconciliation or adjudication.

Findings

Of all coded deaths at ages 1 month to 70 years, 2681 (3.6%) of 75,342 were attributed to malaria. Of these, 2419 (90%) were in rural areas and 2311 (86%) were not in any health-care facility. Death rates attributed to malaria correlated geographically with local malaria transmission rates derived independently from the Indian malaria control programme. The adjudicated results show 205,000 malaria deaths per year in India before age 70 years (55,000 in early childhood, 30,000 at ages 5—14 years, 120,000 at ages 15—69 years); 1.8% cumulative probability of death from malaria before age 70 years. Plausible lower and upper bounds (on the basis of only the initial coding) were 125,000—277,000. Malaria accounted for a substantial minority of about 1.3 million unattended rural fever deaths attributed to infectious diseases in people younger than 70 years.

Interpretation

Despite uncertainty as to which unattended febrile deaths are from malaria, even the lower bound greatly exceeds the WHO estimate of only 15,000 malaria deaths per year in India (5000 early childhood, 10,000 thereafter). This low estimate should be reconsidered, as should the low WHO estimate of adult malaria deaths worldwide.

The Lancet Infectious Disease
Nov 2010 Volume 10 Number 11 Pages 737 - 812
http://www.thelancet.com/journals/laninf/issue/current
[Reviewed earlier]

Nature
Volume 468 Number 7322 pp345-464 18 November 2010
http://www.nature.com/nature/current_issue.html
[No relevant content]

Nature Medicine
November 2010, Volume 16 No 11
http://www.nature.com/nm/index.html
[Reviewed earlier]

New England Journal of Medicine
November 18, 2010 Vol. 363 No. 21
http://content.nejm.org/current.shtml

Review Article
Current Concepts: Influenza Vaccines for the Future
L.C. Lambert, A.S. Fauci
[Free full text]
...Conclusions
Although the past decade has witnessed considerable improvements in our approach to the development of influenza vaccines, much still needs to be done. Although converting from egg-based to cell-based systems and adding adjuvants to enhance protective immune responses are important steps in the right direction, it is the new vaccine technologies that hold the promise of revolutionizing influenza vaccinology. Over the next decade, advances are anticipated that will substantially decrease vaccine production time, provide enhanced protection (especially in populations at greatest risk), and end mismatches between vaccine strains and circulating viruses. To fully reap the benefits as progress is made in developing new vaccines, we will need both clear regulatory guidance on pathways for their approval and a robust and agile infrastructure to ensure their timely production and equitable distribution.

The Pediatric Infectious Disease Journal
November 2010 - Volume 29 - Issue 11
http://journals.lww.com/pidj/pages/currenttoc.aspx
[Reviewed earlier]

Pediatrics
November 2010 / VOLUME 126 / ISSUE 5
http://pediatrics.aappublications.org/current.shtml
[Reviewed earlier]

PLoS Medicine
(Accessed 21 November 2010)
http://medicine.plosjournals.org/perlserv/?request=browse&issn=1549-1676&method=pubdate&search_fulltext=1&order=online_date&row_start=1&limit=10&document_count=1533&ct=1&SESSID=aac96924d41874935d8e1c2a2501181c#results
[No relevant content]

Science
19 November 2010 vol 330, issue 6007, pages 1009-1144
http://www.sciencemag.org/current.dtl
[No relevant content]

Science Translational Medicine
17 November 2010 vol 2, issue 58
http://stm.sciencemag.org/content/current
[No relevant content]

Vaccine
Volume 28, Issue 50 pp. 7825-8048 (23 November 2010)
**Regular papers**

**Dynamic model of rotavirus transmission and the impact of rotavirus vaccination in Kyrgyzstan**  Original Research Article
Pages 7923-7932
Birgitte Freiesleben de Blasio, Kaliya Kasymbekova, Elmira Flem

**Abstract**

New rotavirus vaccines show promise to reduce the burden of severe diarrhea among children in developing countries. We present an age-specific dynamic rotavirus model to assess the effect of rotavirus vaccination in Kyrgyzstan, a country in Central Asia that is eligible for funds from the GAVI Alliance. A routine rotavirus vaccination program at 95% coverage and 54% effectiveness against severe infection is estimated to lead to a 56% reduction in rotavirus-associated deaths and a 50% reduction in hospital admissions, while outpatient visits and homecare episodes would decrease by 52% compared to baseline levels after 5 years of intervention. A 10% reduction in vaccine efficacy due to incomplete 3-dose regimen is estimated to increase the numbers of severe cases by 6–8%. Herd immunity was found to account for 1% or less of averted cases of severe gastroenteritis, while an extra 7–8% of all rotavirus infections would be avoided due to reduced transmission. Conclusion: Rotavirus vaccines would reduce the burden of rotavirus disease substantially, but the results are sensitive to delay in age-appropriate vaccination.

**Serologic testing to verify the immune status of internationally adopted children against vaccine preventable diseases**  Original Research Article
Pages 7947-7955
Mary Allen Staat, Laura Patricia Stadler, Stephanie Donauer, Indi Trehan, Marilyn Rice, Shelia Salisbury

**Abstract**

Definitive immunization guidelines for internationally adopted children are lacking. We examined whether these children had serologic evidence of protection against vaccine-preventable diseases. For children with ≥3 vaccine doses, overall protection was high for diphtheria (85%), tetanus (95%), polio (93%), hepatitis B (77%), and Hib (67%). For children ≥12 months of age with ≥1 dose of measles, mumps, or rubella vaccines, 95%, 72%, and 94% were immune, respectively. Children without immunization documentation had lower immunity. Serologic testing was useful in verifying the immunization status in internationally adopted children with and without documentation of immunizations.

**The impact of indirect benefits of vaccination on postlicensure vaccine effectiveness estimates: A scenario analysis**  Original Research Article
Pages 7987-7992
Manish M. Patel, Jacqueline Tate, Margaret Cortese, Daniel C. Payne, Greg Armstrong, Umesh D. Parashar, Ben Lopman

**Abstract**

Vaccine efficacy is measured in randomized, prelicensure clinical trials where vaccination typically affords only direct protection to the vaccinated individual. Vaccine effectiveness is measured in postlicensure observational studies where vaccination might provide indirect benefits to a population as a whole in addition to directly protecting the vaccinated individual. The potential discrepancy in effectiveness and efficacy estimates would depend on the postlicensure study design. We developed a mathematical model to assess the impact of indirect benefits on vaccine effectiveness as measured by the
common cohort study design under scenarios of homogenous and heterogenous vaccine allocation. We found that under the cohort design, effectiveness estimates equaled efficacy if either the indirect effects were assumed to be negligible or vaccine allocation in the community was homogenous. However, in presence of indirect benefits, effectiveness estimates would be biased upward compared with vaccine efficacy if one of the two sub-populations in the same study had a higher rate of vaccination. Because of indirect effects of vaccination, even in studies where other biases can be eliminated, the presence of distinct sub-populations with varying rates of vaccination can lead to discrepancies between effectiveness and efficacy estimates.

**Examining attitudes and knowledge about HPV and cervical cancer risk among female clinic attendees in Johannesburg, South Africa**


**Abstract**

Developing countries account for 85% of the nearly 500,000 yearly cases of cervical cancer worldwide with approximately 250,000 deaths occurring in Sub-Saharan Africa, South Asia, and Latin America. In South Africa, cervical cancer is the 3rd leading cause of death among women. Although cervical cancer can be screened for with regular Pap tests, access to preventive screenings may be nearly non-existent in resource poor settings that have limited public health infrastructure and where women may lack basic health education. Therefore, it is important to understand women's attitudes, knowledge, and beliefs about HPV, cervical cancer, and the HPV vaccine, and assess their access to preventive screening in order to mitigate their risk for developing the disease.

Eighty-six women, ages 18–44 with at least one child who presented at an antenatal clinic in a township in Johannesburg were recruited to complete a brief questionnaire. Using both descriptive and multivariate statistics, we assessed knowledge of cervical cancer, HPV, and the vaccine; assessed maternal-child communication about sex and STDs, assessed willingness to vaccinate child; and identified barriers to assessing medical care and the vaccine.

The majority of participants were unfamiliar with HPV and cervical cancer, were concerned about their child's and their own risk for HPV and cervical cancer, faced numerous barriers to accessing screening, and were willing to vaccinate their child. Our findings indicate that women in developing countries need increased access to screening and education about HPV and cervical cancer prevention.