

**A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO  
ADULT VACCINATION AVAILABLE AS FULL-TEXT  
(SOME FREE, SOME REQUIRING PAYMENT)**  
Selection of readings made by A/Prof Goh Lee Gan

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## VACCINES AND TRAVEL

### Reading 1

Ahmed QA, Arabi YM, Memish ZA. Health risks at the Hajj. *Lancet*. 2006 Mar 25;367(9515):1008-15.

URL: <http://www.sciencedirect.com/> (payment required)

Medical University of South Carolina, Charleston, SC, USA.

#### ABSTRACT

Annually, millions of Muslims embark on a religious pilgrimage called the "Hajj" to Mecca in Saudi Arabia. The mass migration during the Hajj is unparalleled in scale, and pilgrims face numerous health hazards. The extreme congestion of people and vehicles during this time amplifies health risks, such as those from infectious diseases, that vary each year. Since the Hajj is dictated by the lunar calendar, which is shorter than the Gregorian calendar, it presents public-health policy planners with a moving target, demanding constant preparedness. We review the communicable and non-communicable hazards that pilgrims face. With the rise in global travel, preventing disease transmission has become paramount to avoid the spread of infectious diseases, including SARS (severe acute respiratory syndrome), avian influenza, and haemorrhagic fever. We examine the response of clinicians, the Saudi Ministry of Health, and Hajj authorities to these unique problems, and list health recommendations for prospective pilgrims.

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### Reading 2

Keystone JS. Travel-related hepatitis B: risk factors and prevention using an accelerated vaccination schedule. *Am J Med*. 2005 Oct;118 Suppl 10A:63S-68S.

URL: <http://www.sciencedirect.com/> (payment required)

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#### ABSTRACT

Rates of global travel and tourism are increasing dramatically, especially to regions with medium or high endemicity for hepatitis A and B, such as Asia, Africa, Latin America, and the Middle East. International travelers to these areas should be protected against both hepatitis A and B, regardless of their anticipated length of stay. However, many travelers depart within weeks of planning their trip (too late to complete the accelerated 0-, 1-, 2-month regimen for hepatitis B), and a majority of those traveling depart without being vaccinated. Although extended-stay travelers are at high risk for hepatitis B, short-stay travelers also are at risk. The most commonly encountered risk factors for travel-related hepatitis B are casual sexual activity with a new partner, medical and dental care abroad, and in the expatriate community, adoption of children who are hepatitis B carriers. Although efficacy studies of accelerated schedules for hepatitis B immunization have not been conducted, the results of immunogenicity studies in healthy volunteers who received an accelerated, 3-dose regimen on a 0-, 7-, and 21-day schedule suggest that excellent, rapid, and long-term protection will be conferred. More data are needed to assess the efficacy of accelerated schedules in persons aged >40 years and to determine whether a fourth dose of hepatitis B vaccine is needed in all age groups.

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**Reading 3**

Connor BA. Hepatitis A vaccine in the last-minute traveler. *Am J Med.* 2005 Oct;118 Suppl 10A:58S-62S.

URL: <http://www.sciencedirect.com/> (payment required)

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**ABSTRACT**

Current recommendations state that travelers should receive hepatitis A vaccine 2 to 4 weeks before departure. Such recommendations, however, may dissuade last-minute travelers from receiving the vaccine. A preponderance of evidence exists to support hepatitis A vaccination of the imminent-departure traveler and therefore suggests that these guidelines merit reconsideration. In examining this issue, one of the most important elements to determine is the amount of time required for seroconversion following vaccination. Clinical trials of hepatitis A vaccines measured antibody response at 2 and 4 weeks after vaccination. However, studies investigating early seroconversion found that the vast majority of vaccinees develop antibodies within 2 weeks of vaccination, some as early as 12 days after vaccination. This is relevant information, given that the hepatitis A virus has an average incubation period of 28 days. Seroconversion is predicated on achieving a "protective" antibody level. However, levels of antibody considered protective remain debatable. Evidence suggests that clinical disease does not occur at antibody levels lower than those currently accepted as protective. Furthermore, hepatitis A vaccine has been proved effective in controlling outbreaks worldwide. Research data show that a single dose of vaccine can halt outbreaks if an adequate number of susceptible individuals are vaccinated. Information from rapid-outbreak control studies and those assessing post-exposure administration of hepatitis A vaccine suggest that late vaccination provides a significant degree of protection. For these reasons, hepatitis A vaccine may be administered at any time before departure because it will still provide travelers with protection.

**HUMAN PAPILLOMAVIRUS VACCINES****Reading 4**

Lowy DR, Schiller JT. Prophylactic human papillomavirus vaccines. *J Clin Invest.* 2006 May;116(5):1167-73.

URL: <http://www.jci.org/cgi/reprint/116/5/1167> (free full-text)

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**ABSTRACT**

Human papillomavirus (HPV) infection causes virtually all cases of cervical cancer, the second most common cause of death from cancer among women worldwide. This Review examines prophylactic HPV subunit vaccines based on the ability of the viral L1 capsid protein to form virus-like particles (VLPs) that induce high levels of neutralizing antibodies. Following preclinical research by laboratories in the nonprofit sector, Merck and GlaxoSmithKline are developing commercial versions of the vaccine. Both vaccines target HPV16 and HPV18, which account for approximately 70% of cervical cancer. The Merck vaccine also targets HPV6 and HPV11, which account for approximately 90% of external genital warts. The vaccines have an excellent safety profile, are highly immunogenic, and have conferred complete type-specific protection against persistent infection and associated lesions in fully vaccinated women. Unresolved issues include the most critical groups to vaccinate and when the vaccine's cost may be low enough for widespread implementation in the developing world, where 80% of cervical cancer occurs.

## INFLUENZA VACCINATIONS AND THE ELDERLY

### Reading 5

Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet*. 2005 Oct 1;366(9492):1165-74. Epub 2005 Sep 22.

URL: <http://www.sciencedirect.com/> (payment required)

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#### ABSTRACT

**BACKGROUND:** Influenza vaccination of elderly individuals is recommended worldwide. Our aim was to review the evidence of efficacy and effectiveness of influenza vaccines in individuals aged 65 years or older.

**METHODS:** We searched five electronic databases to December, 2004, in any language, for randomised (n=5), cohort (n=49), and case-control (n=10) studies, assessing efficacy against influenza (reduction in laboratory-confirmed cases) or effectiveness against influenza-like illness (reduction in symptomatic cases). We expressed vaccine efficacy or effectiveness as a proportion, using the formula  $VE=1-\text{relative risk (RR)}$  or  $VE^*=1-\text{odds ratio (OR)}$ . We analysed the following outcomes: influenza, influenza-like illness, hospital admissions, complications, and deaths.

**FINDINGS:** In homes for elderly individuals (with good vaccine match and high viral circulation) the effectiveness of vaccines against influenza-like illness was 23% (95% CI 6-36) and non-significant against influenza (RR 1.04, 0.43-2.51). Well matched vaccines prevented pneumonia (VE 46%, 30-58) and hospital admission (VE 45%, 16-64) for and deaths from influenza or pneumonia (VE 42%, 17-59), and reduced all-cause mortality (VE 60%, 23-79). In elderly individuals living in the community, vaccines were not significantly effective against influenza (RR 0.19, 0.02-2.01), influenza-like illness (RR 1.05, 0.58-1.89), or pneumonia (RR 0.88, 0.64-1.20). Well matched vaccines prevented hospital admission for influenza and pneumonia (VE 26%, 12-38) and all-cause mortality (VE 42%, 24-55). After adjustment for confounders, vaccine performance was improved for admissions to hospital for influenza or pneumonia (VE\* 27%, 21-33), respiratory diseases (VE\* 22%, 15-28), and cardiac disease (VE\* 24%, 18-30), and for all-cause mortality (VE\* 47%, 39-54).

**INTERPRETATION:** In long-term care facilities, where vaccination is most effective against complications, the aims of the vaccination campaign are fulfilled, at least in part. However, according to reliable evidence the usefulness of vaccines in the community is modest.

## VACCINE SAFETY, ACCEPTANCE, AND EFFECTIVENESS

### Reading 6

Plescia M, Leach L, Meriwether R. Clinical inquiries: What illnesses contraindicate immunization? *J Fam Pract*. 2005 Jul;54(7):621-3; discussion 621.

URL: <http://www.jfponline.com/Pages.asp?AID=1991> (free full-text)

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#### SUMMARY

Vaccination is safe and efficacious in the following situations: during a mild illness (e.g., diarrhea, otitis media or other mild upper respiratory infection whether or not the patient has a fever), during antimicrobial therapy, during the convalescent phase of an acute illness, when breastfeeding, and after mild to moderate reactions to a previous dose of vaccine.

Live vaccines (varicella, MMR) should not be used for pregnant women or significantly immunocompromised patients, and may not be effective for patients receiving immunoglobulin therapy. They can be administered to HIV-positive patients who are asymptomatic or not severely immunosuppressed, as determined by age-specific CD4 counts.

## Reading 7

Salmon DA, Teret SP, MacIntyre CR, Salisbury D, Burgess MA, Halsey NA. Compulsory vaccination and conscientious or philosophical exemptions: past, present, and future. *Lancet*. 2006 Feb 4;367(9508):436-42.

URL: <http://www.sciencedirect.com/> (payment required)

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### ABSTRACT

Compulsory vaccination has contributed to the success of immunisation programmes in the USA and Australia, yet the benefits from compulsory vaccination are not universally recognised. Some people – experts and the public alike – believe that the benefits of compulsory vaccination are outweighed by the associated ethical problems. A review of vaccination legislation in the UK, Australia, and the USA raises four main points. First, compulsory vaccination may be effective in preventing disease outbreaks, reaching and sustaining high immunisation coverage rates, and expediting the introduction of new vaccines. Second, to be effective, compulsory programmes must have a reliable supply of safe and effective vaccines and most people must be willing to be vaccinated. Third, allowance of exemptions to compulsory vaccination may limit public backlash. Finally, compulsory vaccination may increase the burden on governments to ensure the safety of vaccines. Nevertheless, although compulsory immunisation can be very effective, it might not be acceptable in some countries where high coverage has been achieved through other approaches or efforts, such as in Sweden, Norway, Denmark, the Netherlands, and the UK. These factors should be considered when compulsory vaccinations are being introduced or immunisation laws refined. Lessons learned from compulsory vaccination could be useful to other public-health programmes.

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## Reading 8

Ocama P, Opio CK, Lee WM. Hepatitis B virus infection: current status. *Am J Med*. 2005 Dec;118(12):1413.

URL: <http://www.sciencedirect.com/> (payment required)

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### ABSTRACT

Hepatitis B virus currently infects more than 400 million people worldwide. Despite the availability of hepatitis B vaccine, the overall prevalence of hepatitis B virus infection has declined little in recent years. Hepatitis B virus causes liver injury by an immune response against the virus-infected liver cells and is not directly cytopathic, although immunosuppression appears to enhance replication and lead to direct cytotoxicity. The interplay of the host immune response and the virus's ability to replicate is a prime determinant of the likelihood of liver injury, its intensity, and progression to cirrhosis. A series of stages evolve in the life cycle of each patient's infection, with associated decreases in viral load at each successive stage. Viral mutations in the polymerase or the core gene affect replication and may enhance liver injury. Recently, genotypes have been identified that are linked to clinical outcomes, drug responses, and mutations. Four drugs (interferon alpha, lamivudine, adefovir, and entecavir) have been approved by the US Food and Drug Administration for treatment of hepatitis B virus; they effectively decrease replication and reduce inflammation and fibrosis. Treatment of hepatitis B virus in complex situations such as co-infection with human immunodeficiency virus or immunosuppressive therapy remains challenging. The use of hepatitis B vaccine has been shown to reduce the incidence of new infection in many regions. A decline in the prevalence of hepatitis B infection worldwide will require changes in high-risk behavior and the wider use of vaccination.

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**Reading 9**

Laurence JC. Hepatitis A and B immunizations of individuals infected with human immunodeficiency virus. *Am J Med.* 2005 Oct;118 Suppl 10A:75S-83S.

URL: <http://www.sciencedirect.com/> (payment required)

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ABSTRACT

All persons at risk for infection with human immunodeficiency virus (HIV) types 1 and 2, including men who have sex with men, those with multiple heterosexual contacts, abusers of illegal injection drugs, and persons frequently exposed to blood and blood products, are also at high risk for hepatitis A virus (HAV) and acute and chronic hepatitis B virus (HBV) infections. HIV can prolong the duration and increase the level of HAV viremia and augment HAV-related liver abnormalities. HIV also magnifies HBV viremia and the risk of HBV reactivation, chronic active HBV infection, cirrhosis, and death. Because of these concerns, hepatitis A vaccination is recommended for all HIV-positive/HAV seronegative persons, with 2 standard doses given 6 to 12 months apart. Immune response to hepatitis A vaccines is excellent, even in moderately immune-suppressed individuals. Hepatitis B vaccination is also recommended for all HIV-positive persons lacking prior immunity. However, immune reactivity to hepatitis B vaccines is frequently suboptimal in terms of patients' rate of response, antibody titer, and durability. Relatively high CD4+ T-cell counts (> or =500/mm<sup>3</sup>) and low levels of HIV viremia (<1,000 RNA genome copies/mL plasma) are necessary to ensure adequate hepatitis B vaccine response. Higher hepatitis B vaccine doses, prolongation of the vaccination schedule, or both, as prescribed for many patients with non-HIV-related immune deficiencies, may be considered initially. Revaccination should be instituted if postvaccination titers of antibodies to hepatitis B surface antigen are <10 mIU/mL (<10 IU/L). Nonresponders may also react to a subsequent vaccine course if CD4+ T-cell counts rise to 500/mm<sup>3</sup> following institution of highly active antiretroviral therapy; vaccine adjuvant trials are under way. Universal, age-based immunization of all young and middle-aged adults appears to be the most comprehensive way of protecting all populations who are at high risk.

**Reading 10**

Tozzi AE, Celentano LP, Ciofi degli Atti ML, Salmaso S. Diagnosis and management of pertussis. *CMAJ.* 2005 Feb 15;172(4):509-15.

URL: <http://www.cmaj.ca.libproxy1.nus.edu.sg/cgi/content/full/172/4/509> (free full-text)

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ABSTRACT

Pertussis is increasing in frequency among children too young to be vaccinated and among adolescents and adults. This increase is due mainly to waning immunity among vaccinated individuals, who become susceptible during adolescence and adulthood and maintain the circulation of *Bordetella pertussis*. Infants are at highest risk of severe illness requiring hospital admission, complications and death. The clinical presentation in adolescents, adults and vaccinated individuals may be atypical, with paroxysmal cough of short duration or simply a persistent cough. Culture and polymerase chain reaction may be used to identify *B. pertussis* infection, but their sensitivity is high only in the early phase of the disease. Serologic tests are not standardized for the diagnosis of pertussis, and their clinical application is limited. Erythromycin is still considered in some countries to be the "gold standard" for therapy and prophylaxis; however, azithromycin and clarithromycin seem equally efficacious and are associated with fewer side effects.