

**A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO
VACCINATIONS 2010 - WHAT'S OLD, WHAT'S NEW
AVAILABLE AS FULL-TEXT, SOME FREE & SOME REQUIRE PAYMENT**

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – Pneumococcal vaccination does not reduce acute myocardial infarction and stroke in men

Tseng HF, Slezak JM, Quinn VP, Sy LS, Van den Eeden SK, Jacobsen SJ. Pneumococcal vaccination and risk of acute myocardial infarction and stroke in men. JAMA. 2010 May 5;303(17):1699-706.

URL: <http://jama.ama-assn.org/cgi/content/full/303/17/1699> (full free text)

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ABSTRACT

CONTEXT: Multiple studies have shown that preventing influenza by vaccination reduces the risk of vascular events. However, the effect of pneumococcal polysaccharide vaccine on vascular events remains controversial. OBJECTIVE: To examine the association between pneumococcal vaccination and risk of acute myocardial infarction (MI) and stroke among men. DESIGN, SETTING, AND PARTICIPANTS: A prospective cohort study of Kaiser Permanente Northern and Southern California health plans with 84 170 participants aged 45 to 69 years from the California Men's Health Study who were recruited between January 2002 and December 2003, and followed up until December 31, 2007. The cohort was similar to the population of health plan members and men who responded to a general health survey in California on important demographic and clinical characteristics. Demographic and detailed lifestyle characteristics were collected from surveys. Vaccination records were obtained from the Kaiser Immunization Tracking System. MAIN OUTCOME MEASURE: Incidence of acute MI and stroke during the follow-up period in men who had no history of such conditions. RESULTS: During follow-up, there were 1211 first MIs in 112,837 vaccinated person-years (10.73 per 1000 person-years) compared with 1494 first MI events in 246,170 unvaccinated person-years (6.07 per 1000 person-years). For stroke, there were 651 events in 122,821 vaccinated person-years (5.30 per 1000 person-years) compared with 483 events in 254,541 unvaccinated person-years (1.90 per 1000 person-years). With propensity score adjustment, we found no evidence for an association between pneumococcal vaccination and reduced risk of acute MI (adjusted hazard ratio [HR], 1.09; 95% confidence interval [CI], 0.98-1.21) or stroke (adjusted HR, 1.14; 95% CI, 1.00-1.31). An inverse association was also not found in men of different age and risk groups. The results appeared to be consistent, because using more specific International Classification of Diseases, Ninth Revision codes for the outcome definition did not change the estimations. CONCLUSION: Among a cohort of men aged 45 years or older, receipt of pneumococcal vaccine was not associated with subsequent reduced risk of acute MI and stroke. PMID: 20442385 [PubMed - indexed for MEDLINE]

READING 2 – 23-valent pneumococcal polysaccharide vaccine prevented pneumococcal pneumonia in nursing home residents

Maruyama T, Taguchi O, Niederman MS, Morser J, Kobayashi H, Kobayashi T, D'Alessandro-Gabazza C, Nakayama S, Nishikubo K, Noguchi T, Takei Y, Gabazza EC. Efficacy of 23-valent pneumococcal vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial. BMJ. 2010 Mar 8;340:c1004. doi: 10.1136/bmj.c1004.

URL: <http://www.bmj.com/cgi/pmidlookup?view=long&pmid=20211953> (free full text)

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ABSTRACT

OBJECTIVE: To determine the efficacy of a 23-valent pneumococcal polysaccharide vaccine in people at high risk of pneumococcal pneumonia. **DESIGN:** Prospective, randomised, placebo controlled double blind study. **SETTING:** Nursing homes in Japan. **PARTICIPANTS:** 1006 nursing home residents. **INTERVENTIONS:** Participants were randomly allocated to either 23-valent pneumococcal polysaccharide vaccine (n=502) or placebo (n=504). **MAIN OUTCOME MEASURES:** The primary end points were the incidence of all cause pneumonia and pneumococcal pneumonia. Secondary end points were deaths from pneumococcal pneumonia, all cause pneumonia, and other causes. **RESULTS:** Pneumonia occurred in 63 (12.5%) participants in the vaccine group and 104 (20.6%) in the placebo group. Pneumococcal pneumonia was diagnosed in 14 (2.8%) participants in the vaccine group and 37 (7.3%) in the placebo group (P<0.001). All cause pneumonia and pneumococcal pneumonia were significantly more frequent in the placebo group than in the vaccine group: incidence per 1000 person years 55 v 91 (P<0.0006) and 12 v 32 (P<0.001), respectively. Death from pneumococcal pneumonia was significantly higher in the placebo group than in the vaccine group (35.1% (13/37) v 0% (0/14), P<0.01). The death rate from all cause pneumonia (vaccine group 20.6% (13/63) v placebo group 25.0% (26/104), P=0.5) and from other causes (vaccine group 17.7% (89/502) v placebo group (80/504) 15.9%, P=0.4) did not differ between the two study groups. **CONCLUSION:** The 23-valent pneumococcal polysaccharide vaccine prevented pneumococcal pneumonia and reduced mortality from pneumococcal pneumonia in nursing home residents. Trial registration Japan Medical Association Center for Clinical Trials JMA-IIA00024. PMID: PMC2834887 PMID: 20211953 [PubMed - indexed for MEDLINE]

READING 3 – 7-valent pneumococcal conjugate vaccine protected HIV-infected adults from recurrent pneumococcal infection caused by vaccine serotypes or serotype 6A

French N, Gordon SB, Mwalukomo T, White SA, Mwafulirwa G, Longwe H, Mwaiponya M, Zijlstra EE, Molyneux ME, Gilks CF. A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults. N Engl J Med. 2010 Mar 4;362(9):812-22.

URL: <http://content.nejm.org/cgi/content/full/362/9/812> (payment required)

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ABSTRACT

BACKGROUND: Streptococcus pneumoniae is a leading and serious coinfection in adults with human immunodeficiency virus (HIV) infection, particularly in Africa. Prevention of this disease by vaccination with the current 23-valent polysaccharide vaccine is suboptimal. Protein conjugate vaccines offer a further option for protection, but data on their clinical efficacy in adults are needed. **METHODS:** In this double-blind, randomized, placebo-controlled clinical efficacy trial, we studied the efficacy of a 7-valent conjugate pneumococcal vaccine in predominantly HIV-infected Malawian adolescents and adults who had recovered from documented invasive pneumococcal disease. Two doses of vaccine were given 4 weeks apart. The primary end point was a further episode of pneumococcal infection caused by vaccine serotypes or serotype 6A. **RESULTS:** From February 2003 through October 2007, we followed 496 patients (of whom 44% were male and 88% were HIV-seropositive) for 798 person-years of observation. There were 67 episodes of pneumococcal disease in 52 patients, all in the HIV-infected subgroup. In 24 patients, there were 19 episodes that were caused by vaccine serotypes and 5 episodes that were caused by the 6A serotype. Of these episodes, 5 occurred in the vaccine group and 19 in the placebo group, for a vaccine efficacy of 74% (95% confidence interval [CI], 30 to 90). There were 73 deaths from any cause in the vaccine group and 63 in the placebo group (hazard ratio in the vaccine group, 1.18; 95% CI, 0.84 to 1.66). The number of serious adverse events within 14 days after vaccination was significantly lower in the vaccine group than in the placebo group (3 vs. 17, P=0.002), and the number of minor adverse events was significantly higher in the vaccine group (41 vs. 13, P=0.003). **CONCLUSIONS:** The 7-valent pneumococcal conjugate vaccine protected HIV-infected adults from recurrent pneumococcal infection caused by vaccine serotypes or serotype 6A. (Current Controlled Trials number, ISRCTN54494731.) 2010 Massachusetts Medical Society PMID: 20200385 [PubMed - indexed for MEDLINE]

READING 4 – Herpes zoster vaccine in older, immunocompetent persons is well tolerated

Simberkoff MS et al. Safety of herpes zoster vaccine in the shingles prevention study: a randomized trial. *Ann Intern Med.* 2010 May 4;152(9):545-54.

URL: <http://www.annals.org/content/152/9/545.long> (full free text)

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ABSTRACT

BACKGROUND: The herpes zoster vaccine is effective in preventing herpes zoster and postherpetic neuralgia in immunocompetent older adults. However, its safety has not been described in depth. **OBJECTIVE:** To describe local adverse effects and short- and long-term safety profiles of herpes zoster vaccine in immunocompetent older adults. **DESIGN:** Randomized, placebo-controlled trial with enrollment from November 1998 to September 2001 and follow-up through April 2004 (mean, 3.4 years). A Veterans Affairs Coordinating Center generated the permuted block randomization scheme, which was stratified by site and age. Participants and follow-up study personnel were blinded to treatment assignments. (ClinicalTrials.gov registration number: NCT00007501) **SETTING:** 22 U.S. academic centers. **PARTICIPANTS:** 38 546 immunocompetent adults 60 years or older, including 6616 who participated in an adverse events substudy. **INTERVENTION:** Single dose of herpes zoster vaccine or placebo. **MEASUREMENTS:** Serious adverse events and rashes in all participants and inoculation-site events in substudy participants during the first 42 days after inoculation. Thereafter, vaccination-related serious adverse events and deaths were monitored in all participants, and hospitalizations were monitored in substudy participants. **RESULTS:** After inoculation, 255 (1.4%) vaccine recipients and 254 (1.4%) placebo recipients reported serious adverse events. Local inoculation-site side effects were reported by 1604 (48%) vaccine recipients and 539 (16%) placebo recipients in the substudy. A total of 977 (56.6%) of the vaccine recipients reporting local side effects were aged 60 to 69 years, and 627 (39.2%) were older than 70 years. After inoculation, herpes zoster occurred in 7 vaccine recipients versus 24 placebo recipients. Long-term follow-up (mean, 3.39 years) showed that rates of hospitalization or death did not differ between vaccine and placebo recipients. **LIMITATIONS:** Participants in the substudy were not randomly selected. Confirmation of reported serious adverse events with medical record data was not always obtained. **CONCLUSION:** Herpes zoster vaccine is well tolerated in older, immunocompetent adults. **PRIMARY FUNDING SOURCE:** Cooperative Studies Program, Department of Veterans Affairs, Office of Research and Development; grants from Merck to the Veterans Affairs Cooperative Studies Program; and the James R. and Jesse V. Scott Fund for Shingles Research. PMID: 20439572 [PubMed - in process]

READING 5 – Pregnant women had disproportionately high risk in Pandemic 2009 influenza (H1N1) virus illness

Siston AM et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA.* 2010 Apr 21;303(15):1517-25.

URL: <http://jama.ama-assn.org/cgi/content/full/303/15/1517> (full free text)

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ABSTRACT

CONTEXT: Early data on pandemic 2009 influenza A(H1N1) suggest pregnant women are at increased risk of hospitalization and death. **OBJECTIVE:** To describe the severity of 2009 influenza A(H1N1) illness and the association with early antiviral treatment among pregnant women in the United States. **DESIGN, SETTING, AND PATIENTS:** Surveillance of 2009 influenza A(H1N1) in pregnant women reported to the Centers for Disease Control and Prevention (CDC) with symptom onset from April through December 2009. **MAIN OUTCOME MEASURES:** Severity of illness (hospitalizations, intensive care unit [ICU] admissions, and deaths) due to 2009

influenza A(H1N1) among pregnant women, stratified by timing of antiviral treatment and pregnancy trimester at symptom onset. RESULTS: We received reports on 788 pregnant women in the United States with 2009 influenza A(H1N1) with symptom onset from April through August 2009. Among those, 30 died (5% of all reported 2009 influenza A(H1N1) influenza deaths in this period). Among 509 hospitalized women, 115 (22.6%) were admitted to an ICU. Pregnant women with treatment more than 4 days after symptom onset were more likely to be admitted to an ICU (56.9% vs 9.4%; relative risk [RR], 6.0; 95% confidence interval [CI], 3.5-10.6) than those treated within 2 days after symptom onset. Only 1 death occurred in a patient who received treatment within 2 days of symptom onset. Updating these data with the CDC's continued surveillance of ICU admissions and deaths among pregnant women with symptom onset through December 31, 2009, identified an additional 165 women for a total of 280 women who were admitted to ICUs, 56 of whom died. Among the deaths, 4 occurred in the first trimester (7.1%), 15 in the second (26.8%), and 36 in the third (64.3%); CONCLUSIONS: Pregnant women had a disproportionately high risk of mortality due to 2009 influenza A(H1N1). Among pregnant women with 2009 influenza A(H1N1) influenza reported to the CDC, early antiviral treatment appeared to be associated with fewer admissions to an ICU and fewer deaths. PMID: 20407061 [PubMed - indexed for MEDLINE]

READING 6 – 2009 pandemic H1N1 ten times more than estimated from clinical surveillance

Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet. 2010 Mar 27;375(9720):1100-8. Epub 2010 Jan 21.

URL: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)62126-7/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62126-7/fulltext) (payment required)

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ABSTRACT

BACKGROUND: Knowledge of the age-specific prevalence of immunity from, and incidence of infection with, 2009 pandemic influenza A H1N1 virus is essential for modelling the future burden of disease and the effectiveness of interventions such as vaccination. **METHODS:** In this cross-sectional serological survey, we obtained 1403 serum samples taken in 2008 (before the first wave of H1N1 infection) and 1954 serum samples taken in August and September, 2009 (after the first wave of infection) as part of the annual collection for the Health Protection Agency seroepidemiology programme from patients accessing health care in England. Antibody titres were measured by use of haemagglutination inhibition and microneutralisation assays. We calculated the proportion of samples with antibodies to pandemic H1N1 virus in 2008 by age group and compared the proportion of samples with haemagglutination inhibition titre 1:32 or more (deemed a protective response) before the first wave of infection with the proportion after the first wave. **FINDINGS:** In the baseline serum samples from 2008, haemagglutination inhibition and microneutralisation antibody titres increased significantly with age (F test $p < 0.0001$). The proportion of samples with haemagglutination inhibition titre 1:32 or more ranged from 1.8% (three of 171; 95% CI 0.6-5.0) in children aged 0-4 years to 31.3% (52 of 166; 24.8-38.7) in adults aged 80 years or older. In London and the West Midlands, the difference in the proportion of samples with haemagglutination inhibition titre equal to or above 1:32 between baseline and September, 2009, was 21.3% (95% CI 8.8-40.3) for children younger than 5 years of age, 42.0% (26.3-58.2) for 5-14-year-olds, and 20.6% (1.6-42.4) for 15-24-year-olds, with no difference between baseline and September in older age groups. In other regions, only children younger than 15 years showed a significant increase from baseline (6.3%, 1.8-12.9). **INTERPRETATION:** Around one child in every three was infected with 2009 pandemic H1N1 in the first wave of infection in regions with a high incidence, ten times more than estimated from clinical surveillance. Pre-existing antibody in older age groups protects against infection. Children have an important role in transmission of influenza and would be a key target group for vaccination both for their protection and for the protection of others through herd immunity. **FUNDING:** National Institute for Health Research Health Technology Assessment Programme. Copyright 2010 Elsevier Ltd. All rights reserved. PMID: 20096450 [PubMed - indexed for MEDLINE]

READING 7 – Influenza vaccination of children reduces infection rates in rural communities

Loeb M, Russell ML, Moss L, Fonseca K, Fox J, Earn DJ, Aoki F, Horsman G, Van Caesele P, Chokani K, Vooght M, Babiuk L, Webby R, Walter SD. Effect of influenza vaccination of children on infection rates in Hutterite communities: a randomized trial. JAMA. 2010 Mar 10;303(10):943-50.

URL: <http://jama.ama-assn.org/cgi/pmidlookup?view=long&pmid=20215608> (full free text)

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ABSTRACT

CONTEXT: Children and adolescents appear to play an important role in the transmission of influenza. Selectively vaccinating youngsters against influenza may interrupt virus transmission and protect those not immunized. **OBJECTIVE:** To assess whether vaccinating children and adolescents with inactivated influenza vaccine could prevent influenza in other community members. **DESIGN, SETTING, AND PARTICIPANTS:** A cluster randomized trial involving 947 Canadian children and adolescents aged 36 months to 15 years who received study vaccine and 2326 community members who did not receive the study vaccine in 49 Hutterite colonies in Alberta, Saskatchewan, and Manitoba. Follow-up began December 28, 2008, and ended June 23, 2009. **INTERVENTION:** Children were randomly assigned according to community and in a blinded manner to receive standard dosing of either inactivated trivalent influenza vaccine or hepatitis A vaccine, which was used as a control. **MAIN OUTCOME MEASURES:** Confirmed influenza A and B infection using a real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay and by measuring serum hemagglutination inhibition titers. **RESULTS:** The mean rate of study vaccine coverage among eligible participants was 83% (range, 53%-100%) for the influenza vaccine colonies and 79% (range, 50%-100%) for the hepatitis A vaccine colonies. Among nonrecipients, 39 of 1271 (3.1%) in the influenza vaccine colonies and 80 of 1055 (7.6%) in the hepatitis A vaccine colonies had influenza illness confirmed by RT-PCR, for a protective effectiveness of 61% (95% confidence interval [CI], 8%-83%; $P = .03$). Among all study participants (those who were and those who were not vaccinated), 80 of 1773 (4.5%) in the influenza vaccine colonies and 159 of 1500 (10.6%) in the hepatitis A vaccine colonies had influenza illness confirmed by RT-PCR for an overall protective effectiveness of 59% (95% CI, 5%-82%; $P = .04$). No serious vaccine adverse events were observed. **CONCLUSION:** Immunizing children and adolescents with inactivated influenza vaccine significantly protected unimmunized residents of rural communities against influenza. **TRIAL REGISTRATION:** clinicaltrials.gov Identifier: NCT00877396. PMID: 20215608 [PubMed - indexed for MEDLINE]

READING 8 – Cholera - recommendations for prevention in travellers

Aust Fam Physician. 2010 Apr;39(4):220-6. Neilson AA, Mayer CA. Cholera - recommendations for prevention in travellers.

URL: <http://www.racgp.org.au/afp/201004/201004neilson.pdf> (full free text)

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ABSTRACT

This article about cholera is part of our travel medicine series for 2010, providing a summary of prevention strategies and vaccination for infections that may be acquired by travellers. The series aims to provide practical strategies to assist general practitioners in giving travel advice, as a synthesis of multiple information sources which must otherwise be consulted. Cholera is a severe diarrhoeal disease associated with worldwide pandemics. It affects vulnerable populations who lack adequate quality drinking water and sanitation. Travellers are generally at low risk of contracting cholera, even in endemic areas. It is prevented with general water and food precautions (also advisable for prevention of traveller's diarrhoea). In some situations, the oral killed whole cell B subunit vaccine may be recommended for travellers considered at risk. PMID: 20372681 [PubMed - in process]

READING 9 – Revaccination with BCG in early childhood on mortality - no overall beneficial effect

Roth AE, Benn CS, Ravn H, Rodrigues A, Lisse IM, Yazdanbakhsh M, Whittle H, Aaby P. Effect of revaccination with BCG in early childhood on mortality: randomised trial in Guinea-Bissau. *BMJ*. 2010 Mar 15;340:c671. doi: 10.1136/bmj.c671.

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2839082> (full free text)

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ABSTRACT

OBJECTIVE: To determine whether BCG revaccination at 19 months of age reduces overall child mortality. **DESIGN:** Randomised trial, with follow-up to age 5. **SETTING:** A health project in Bissau, Guinea-Bissau, which maintains a health and demographic surveillance system in an urban area with 90 000 inhabitants. **PARTICIPANTS:** 2871 children aged 19 months to 5 years with low or no reactivity to tuberculin and who were not severely sick on the day of enrollment. **INTERVENTION:** BCG vaccination or no vaccination (control). **MAIN OUTCOME MEASURE:** Hazard ratios for mortality. **RESULTS:** 77 children died during follow-up. Compared with controls, the BCG revaccinated children had a hazard ratio of 1.20 (95% confidence interval 0.77 to 1.89). Two hundred and fifty children were admitted to hospital for the first time between enrollment and the end of the study, with an incidence rate ratio for BCG revaccinated children versus controls of 1.04 (0.81 to 1.33). The trial was stopped prematurely because of a cluster of deaths in the BCG arm of the study. This increase in mortality occurred at a time when many children had received missing vaccinations or vitamin A or iron supplementation; the hazard ratio for BCG revaccinated children compared with controls was 2.69 (1.05 to 6.88) in the period after these campaigns. Throughout the trial, the effect of BCG revaccination on mortality was significantly different ($P=0.006$) in children who had received diphtheria-tetanus-pertussis (DTP) booster vaccination before enrollment (hazard ratio 0.36, 0.13 to 0.99) and children who had not received the booster before enrollment (1.78, 1.04 to 3.04). **CONCLUSIONS:** There was no overall beneficial effect of being revaccinated with BCG. The effect of BCG revaccination on mortality might depend on other health interventions. Trial registration Clinical Trials ICA4-CT-2002-10053-REVAC. PMID: PMC2839082 PMID: 20231251 [PubMed - indexed for MEDLINE]

READING 10 – Poliomyelitis - prevention in travelers

Mayer CA, Neilson AA. Poliomyelitis--prevention in travellers. *Aust Fam Physician*. 2010 Mar;39(3):122-5.

URL: <http://www.racgp.org.au/afp/201003/201003mayer.pdf> (full free text)

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ABSTRACT

This article is the second in a series providing a summary of prevention strategies and vaccination for infections that may be acquired by travellers. The series aims to provide practical strategies to assist general practitioners in giving travel advice, as a synthesis of multiple information sources which must otherwise be consulted. Poliomyelitis is a potentially fatal viral illness, which may cause acute flaccid paralysis and permanent central nervous system damage. Ongoing global efforts to eradicate poliomyelitis have been under way since 1988. Travellers are at risk of infection in countries with endemic wild poliomyelitis virus or imported cases, and can spread the infection to areas where poliomyelitis has been eradicated. While all adults should be immune to poliomyelitis, it is important that at-risk travellers are vaccinated appropriately. Vaccine options and regions currently reporting poliomyelitis are presented from a number of sources, which may facilitate the process of giving travel advice in a general practice setting, although it is also important to seek up-to-date epidemiological information. PMID: 20369113 [PubMed - in process]