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Infection Control

Current Awareness Newsletter

December 2016

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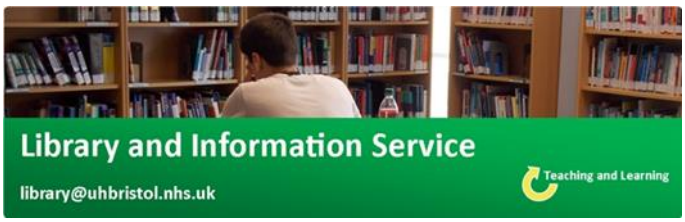

Lunchtime Drop-in Sessions

All sessions last one hour

January (13.00)

Tues 10th	**Literature Searching**
Wed 18th	**Critical Appraisal**
Thur 26th	**Statistics**

February (12.00)

Fri 3rd	**Literature Searching**
Mon 6th	**Critical Appraisal**
Tue 14th	**Statistics**
Wed 22nd	**Literature Searching**

March (13.00)

Thurs 2nd	**Critical Appraisal**
Fri 10th	**Statistics**
Mon 13th	**Literature Searching**
Tues 21st	**Critical Appraisal**
Weds 29th	**Statistics**

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New Additions to NICE, the Cochrane Library and UptoDate

NICE National Institute for Health and Care Excellence

Bronchiolitis in children. Quality standard [QS122]. Published date: June 2016

Why this quality standard is needed….Bronchiolitis symptoms are usually mild and may only last for a few days, but in some cases the disease can cause severe illness. There are several individual and environmental factors that increase the risk of these severe illnesses in children with bronchiolitis. These include social deprivation, congenital heart disease, neuromuscular disorders, immunodeficiency and chronic lung disease. Approximately 1 in 3 infants will develop clinical bronchiolitis in the first year of life, and 2–3% of these will need hospitalisation. In 2014/15 in England there were approximately 39,400 hospital admissions of children aged 0–4 with a primary diagnosis of bronchiolitis. Of these, around 93% (36,600) were aged under 1 year and around 7% (2,800) were aged 1–4 years[1]. Bronchiolitis can usually be managed at home by parents and carers. In most children bronchiolitis is mild, and breathing and feeding usually get better within 5 days. The cough may take longer to go (usually around 3–4 weeks). The quality standard is expected to contribute to improvements in the following outcomes:

- antibiotic use
- parent and carer experience of primary and secondary care
- hospital admissions.

Cochrane Library

Robinson KA, Odelola OA, Saldanha IJ. Palivizumab for prophylaxis against respiratory syncytial virus infection in children with cystic fibrosis. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD007743. DOI: 10.1002/14651858.CD007743.pub6

Objectives: To determine the efficacy and safety of palivizumab (Synagis®) compared with placebo, no prophylaxis or other prophylaxis, in preventing hospitalisation and mortality from respiratory syncytial virus infection in children with cystic fibrosis.

Grande AJ, Reid H, Thomas EE, Nunan D, Foster C. Exercise prior to influenza vaccination for limiting influenza incidence and its related complications in adults. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD011857. DOI: 10.1002/14651858.CD011857.pub2

Objectives: To assess the efficacy and safety of short and long-term exercise prior to influenza vaccination in enhancing influenza prevention in adults.

UpToDate®

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Infection prevention: General principles

Authors: Deverick J Anderson, MD, MPH; N Deborah Friedman, MPH, MBBS, FRACP, MD

Section Editor: Daniel J Sexton, MD; Deputy Editor: Elinor L Baron, MD, DTMH

Literature review current through: Nov 2016. | **This topic last updated:** Nov 28, 2016.

INTRODUCTION — Infection prevention and control (hereafter "infection prevention") is grounded in quality improvement techniques and is critical for patient safety [1,2]. Infection prevention programs use protocols and interventions to decrease the risk of infection associated with exposure to healthcare settings. …. In general, infection prevention programs focus on two broad goals: decrease the risk of infection following exposure to healthcare settings (particularly from multidrug-resistant organisms) and decrease the risk of device- and procedure-related infections.

Issues related to general principles of infection control are reviewed here. Interventions to precautions for preventing transmission of infection are reviewed separately. (See "Infection prevention: Precautions for preventing transmission of infection".)

Infection prevention: Precautions for preventing transmission of infection

Author: Deverick J Anderson, MD, MPH; Section Editor: Anthony Harris, MD, MPH;

Deputy Editor: Elinor L Baron, MD, DTMH

Literature review current through: Nov 2016. | **This topic last updated:** Nov 28, 2016.

INTRODUCTION — The risk of transmission of pathogens and subsequent infection in healthcare facilities is substantial. Pathogens may be transmitted from other patients, the hospital personnel, and/or the hospital environment. The risk is variable and depends on a patient's immune status, the local prevalence of various pathogens, and the infection control practices and antimicrobial stewardship utilized during hospitalization.

Issues related to precautions devised to minimize risk for transmission of infection are reviewed here. Issues related to the prevention of specific infections, prophylaxis after exposure to bloodborne pathogens, and immunizations for healthcare workers are discussed in detail separately. (See related topics.)

Bronchiolitis in infants and children: Treatment; outcome; and prevention

Authors: Pedro A Piedra, MD; Ann R Stark, MD; Section Editors: George B Mallory, MD; Morven S Edwards, MD; Deputy Editor: Mary M Torchia, MD

Literature review current through: Nov 2016. | **This topic last updated:** Nov 08, 2016.

INTRODUCTION — Bronchiolitis, part of the spectrum of lower respiratory tract diseases, is a major cause of

illness and hospitalization in infants and children younger than two years. The treatment, outcome, and prevention of bronchiolitis will be reviewed here. The epidemiology, clinical features, and diagnosis of bronchiolitis and the treatment of recurrent virus-induced wheezing in young children are discussed separately. (See "Bronchiolitis in infants and children: Clinical features and diagnosis" and "Treatment of recurrent virus-induced wheezing in young children".)

Respiratory syncytial virus infection: Prevention

Authors: Frederick E Barr, MD; Barney S Graham, MD, PhD; Section Editors: Morven S Edwards, MD; George B Mallory, MD; Deputy Editor: Mary M Torchia, MD

Literature review current through: Nov 2016. | **This topic last updated:** Nov 07, 2016.

INTRODUCTION — Respiratory syncytial virus (RSV) causes acute respiratory tract illness in persons of all ages. Almost all children are infected by two years of age, and reinfection is common [1]. The clinical manifestations vary with age, health status, and whether the infection is primary or secondary. The prevention of respiratory syncytial virus infection will be discussed here. The epidemiology, microbiology, clinical manifestations, diagnosis, and treatment of RSV infection are discussed separately. (See "Respiratory syncytial virus infection: Clinical features and diagnosis" and "Respiratory syncytial virus infection: Treatment".)

Seasonal influenza vaccination in adults

Author: Patricia L Hibberd, MD, PhD; Section Editor: Martin S Hirsch, MD; Deputy Editor: Anna R Thorner, MD

Literature review current through: Nov 2016. | **This topic last updated:** Oct 26, 2016.

INTRODUCTION — Influenza is an acute respiratory illness caused by influenza A or B viruses. It occurs in epidemics nearly every year, mainly during the winter season in temperate climates. Influenza viruses change their antigenic characteristics frequently, and their subsequent spread depends upon the susceptibility of the population to viruses with novel antigens. Annual influenza vaccination is an important public health measure for preventing influenza infection [1-3]. The protection provided by influenza vaccines is based upon induction of virus-neutralizing antibodies, mainly against the viral hemagglutinin. The role of influenza vaccination in the prevention of seasonal influenza will be reviewed here. The use of influenza vaccine in immunocompromised hosts, pregnant women, patients with chronic liver disease, patients with end-stage renal disease, healthcare workers, and travelers is discussed separately. (See associated topic reviews.)

The clinical manifestations and diagnosis of influenza in adults, the role of antiviral agents for the prevention and treatment of seasonal influenza, and vaccines against the 2009 pandemic H1N1 influenza ("swine influenza") virus, H5N1 avian influenza, and H7N9 avian influenza are also reviewed elsewhere. Seasonal influenza vaccination in children is also presented separately. (See "Clinical manifestations of seasonal influenza in adults" and "Diagnosis of seasonal influenza in adults" and "Prevention of seasonal influenza with antiviral drugs in adults" and "Treatment of seasonal influenza in adults" and "Treatment and prevention of pandemic H1N1 influenza ('swine influenza')", section on 'Vaccination' and "Avian influenza vaccines" and "Avian influenza A H7N9: Treatment and prevention", section on 'Vaccine development' and "Seasonal influenza in children: Prevention with vaccines".)

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Current Awareness Database

Below is a selection of articles recently added to the healthcare databases, grouped in the following categories:

- **C Diff**
- **Novovirus**
- **Bronchiolitis**
- **RSV**
- **Flu**

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk

Clostridium difficile

Title: Using expert process to combat Clostridium difficile infections.

Author(s): Guerreiro, Isabelle; Achonu, Camille; Volkening, Grace; MacFarlane, Sam; McCreight, Liz; Egan, Cathy; Robertson, Jennifer; Garber, Gary

Source: American Journal of Infection Control; Dec 2016; vol. 44 (no. 12); p. 1451-1453

Abstract: In 2008, Clostridium difficile rates were increasing in Ontario, Canada, and in response, hospitals were mandated by the Ontario Ministry of Health to publicly report their C difficile infection (CDI) rates. In order to assist hospitals which had ongoing CDI outbreaks, a process of an external infection control resource team (ICRT) was introduced. This article describes the function and process of the ICRT, managed by Public Health Ontario, and reviews the lessons learned over the first 5 years of operation. These lessons may assist other hospitals in managing their own infection prevention and control outbreak.

Title: Effect of an antimicrobial stewardship intervention on outcomes for patients with Clostridium difficile infection.

Author(s): Welch, Hanna K.; Nagel, Jerod L.; Patel, Twisha S.; Gandhi, Tejal N.; Chen, Benrong; De Leon, John; Chenoweth, Carol E.; Washer, Laraine L.; Rao, Krishna; Eschenauer, Gregory A.

Source: American Journal of Infection Control; Dec 2016; vol. 44 (no. 12); p. 1539-1543

Abstract: Background Although antimicrobial stewardship programs (ASPs) are uniquely positioned to improve treatment of Clostridium difficile infection (CDI) through targeted interventions, studies to date have not rigorously evaluated the influence of ASP involvement on clinical outcomes attributed to CDI. Methods We performed a quasiexperimental study of adult patients with CDI

before (n = 307) and after (n = 285) a real-time ASP review was initiated. In the intervention group, an ASP pharmacist was notified of positive CDI results and consulted with the care team to initiate optimal therapy, minimize concomitant antibiotic and acid-suppressive therapy, and recommend surgical/infectious diseases consultation in complicated cases. The primary outcome was a composite of attributable 30-day mortality, intensive care unit admission, colectomy/ileostomy, and recurrence. Results A higher percentage of patients in the ASP intervention group had acid-suppressive therapy discontinued (30% vs 13%; P < .01). Among patients with severe CDI, more patients in the intervention group received an infectious diseases consultation (17% vs 10%; P = .04), received appropriate therapy with oral vancomycin (87% vs 59%; P < .01), and vancomycin was initiated earlier (mean, 1.1 vs 1.7 days; P < .01). Incidence of the composite outcome was not significantly different between the 2 groups (12.3% vs 14.7%; P = .40). Conclusions ASP review and intervention improved CDI process measures. A decrease in composite outcomes was not found, which may be due to low baseline rates of attributable complications in our institution.

Title: Reduced health care-associated infections in an acute care community hospital using a combination of self-disinfecting copper-impregnated composite hard surfaces and linens.

Author(s): Sifri, Costi D.; Burke, Gene H.; Enfield, Kyle B.

Source: American Journal of Infection Control; Dec 2016; vol. 44 (no. 12); p. 1565-1571

Abstract: Background The purpose of this study was to determine the effectiveness of copper-impregnated composite hard surfaces and linens in an acute care hospital to reduce health care-associated infections (HAIs). Methods We performed a quasiexperimental study with a control group, assessing development of HAIs due to multidrug resistant organisms (MDROs) and Clostridium difficile in the acute care units of a community hospital following the replacement of a 1970s-era clinical wing with a new wing outfitted with copper-impregnated composite hard surfaces and linens. Results The study was conducted over a 25.5-month time period that included a 3.5-month washout period. HAI rates obtained from the copper-containing new hospital wing (14,479 patient-days; 72 beds) and the unmodified hospital wing (19,177 patient-days) were compared with those from the baseline period (46,391 patient-days). The new wing had 78% (P = .023) fewer HAIs due to MDROs or C difficile , 83% (P = .048) fewer cases of C difficile infection, and 68% (P = .252) fewer infections due to MDROs relative to the baseline period. No changes in rates of HAI were observed in the unmodified hospital wing. Conclusions Copper-impregnated composite hard surfaces and linens may be useful technologies to prevent HAIs in acute care hospital settings. Additional studies are needed to determine whether reduced HAIs can be attributed to the use of copper-containing antimicrobial hard and soft surfaces.

Title: Cleaning the grey zones of hospitals: A prospective, crossover, interventional study.

Author(s): Semret, Makeda; Dyachenko, Alina; Ramman-Haddad, Leila; Belzile, Eric; McCusker, Jane

Source: American Journal of Infection Control; Dec 2016; vol. 44 (no. 12); p. 1582-1588

Abstract: Background Environmental cleaning is a fundamental principle of infection prevention in hospitals, but its role in reducing transmission of health care-acquired pathogens has been difficult to prove experimentally. In this study we analyze the influence of cleaning previously uncleaned patient care items, grey zones (GZ), on health care-acquired transmission rates. Methods The intervention consisted of specific GZ cleaning by an extra cleaner (in addition to routine cleaning) on 2 structurally different acute care medical wards for a period of 6 months each, in a crossover design. Data on health care-acquired transmissions of vancomycin-resistant enterococci (VRE), methicillin-resistant Staphylococcus aureus , and Clostridium difficile were collected during both periods. Adjusted incidence rate ratios (IRRs) using Poisson regression were calculated to compare transmission of pathogens between both periods on both wards. Results During the intervention

VRE transmission was significantly decreased (2-fold) on the ward where patients had fewer roommates; cleaning of GZ did not have any effect on the ward with multiple-occupancy rooms. There was no impact on methicillin-resistant S aureus transmission and only a nonsignificant decrease in transmission of C difficile . Conclusions Our data provide evidence that targeted cleaning interventions can reduce VRE transmission when rooming conditions are optimized; such interventions can be cost-effective when the burden of VRE is significant. Enhanced cleaning interventions are less beneficial in the context of room sharing where many other factors contribute to transmission of pathogens.

Title: Antimicrobial stewardship programs that target only high-cost, broad-spectrum antimicrobials miss opportunities to reduce Clostridium difficile infections.

Author(s): Bui, Christine; Zhu, Elizabeth; Donnelley, Monica A.; Wilson, Machelle D.; Morita, Margaret; Cohen, Stuart H.; Brown, Jennifer

Source: American Journal of Infection Control; Dec 2016; vol. 44 (no. 12); p. 1684-1686

Abstract: Antimicrobial stewardship programs are promoted as a strategy to reduce Clostridium difficile infections. We implemented an antimicrobial stewardship program comprised of formulary restriction plus prospective audit with feedback for high-cost and broad-spectrum antimicrobials. Subsequently, we reviewed all heath care facility–onset, health care facility–associated C difficile infections. We found that most of these infections were associated with the antecedent receipt of nonaudited, and often unnecessary, antimicrobials.

Title: New and emerging therapies for Clostridium difficile infection.

Author(s): Martin, Jessica; Wilcox, Mark

Source: Current Opinion in Infectious Diseases; Dec 2016; vol. 29 (no. 6); p. 546-554

Abstract: Purpose Of Review: Clostridium difficile infection has attained high prominence given its prevalence and impacts on patients and healthcare institutions. Multiple new approaches to the prevention and treatment of C. difficile infection (CDI) are undergoing clinical trials.Recent Findings: Bezlotoxumab is a monoclonal antibody against toxin B that has successfully completed phase III studies, demonstrating a significant reduction in recurrent CDI when given with standard of care antibiotics. Antibiotics under development include cadazolid and ridinilazole, whereas surotomycin has had disappointing phase III results. Multiple live biotherapeutics are being developed, including freeze thawed and encapsulated versions of faecal microbiota transplantation to improve the practicality of treating patients with recurrent CDI. Alternatives to faecal microbiota transplantation, that aim to improve safety, including a microbial suspension, RBX2660, and a complex spore formulation, SER-109, have progressed to phase II studies. A nontoxigenic C. difficile strain has also shown promise to prevent recurrent CDI. In addition, three C. difficile vaccines have progressed to phase II/III clinical trials.Summary: The diverse approaches to treating and preventing CDI offer substantial promise that new treatment options will soon emerge, particular ones that reduce the risk of recurrences.

Title: Inappropriate Clostridium difficile Testing and Consequent Overtreatment and Inaccurate Publicly Reported Metrics.

Author(s): Kelly, Sean G.; Yarrington, Michael; Zembower, Teresa R.; Sutton, Sarah H.; Silkaitis, Christina; Postelnick, Michael; Mikolajczak, Anessa; Bolon, Maureen K.

Source: Infection Control & Hospital Epidemiology; Dec 2016; vol. 37 (no. 12); p. 1395-1400

Title: An Evaluation of Food as a Potential Source for Clostridium difficile Acquisition in Hospitalized Patients.

Author(s): Kwon, Jennie H.; Lanzas, Cristina; Reske, Kimberly A.; Hink, Tiffany; Seiler, Sondra M.; Bommarito, Kerry M.; Burnham, Carey-Ann D.; Dubberke, Erik R.

Source: Infection Control & Hospital Epidemiology; Dec 2016; vol. 37 (no. 12); p. 1401-1407

Title: Assessing the Risk of Hospital-Acquired Clostridium Difficile Infection With Proton Pump Inhibitor Use: A Meta-Analysis.

Author(s): Arriola, Vanessa; Tischendorf, Jessica; Musuuza, Jackson; Barker, Anna; Rozelle, Jeffrey W.; Safdar, Nasia

Source: Infection Control & Hospital Epidemiology; Dec 2016; vol. 37 (no. 12); p. 1408-1417

Title: Prevention of Infection Due to Clostridium difficile.

Author(s): Cooper, Christopher C; Jump, Robin L P; Chopra, Teena

Source: Infectious disease clinics of North America; Dec 2016; vol. 30 (no. 4); p. 999-1012

Abstract: Clostridium difficile is one of the foremost nosocomial pathogens. Preventing infection is particularly challenging. Effective prevention efforts typically require a multifaceted bundled approach. A variety of infection control procedures may be advantageous, including strict hand decontamination with soap and water, contact precautions, and using chlorine-containing decontamination agents. Additionally, risk factor reduction can help reduce the burden of disease. The risk factor modification is principally accomplished though antibiotic stewardship programs. Unfortunately, most of the current evidence for prevention is in acute care settings. This review focuses on preventative approaches to reduce the incidence of Clostridium difficile infection in healthcare settings.

Title: Health care worker hand contamination at critical moments in outpatient care settings.

Author(s): Bingham, James; Abell, Ginnie; Kienast, LeAnne; Lerner, Lorie; Matuschek, Brittney; Mullins, Wanda; Parker, Albert; Reynolds, Nancy; Salisbury, Diane; Seidel, Joan; Young, Elizabeth; Kirk, Jane

Source: American Journal of Infection Control; Nov 2016; vol. 44 (no. 11); p. 1198-1202

Abstract: Background The delivery of health care in outpatient settings has steadily increased over the past 40 years. The risk of infection in these settings is considered to be low. However, the increasing severity of illness and complexity of care in outpatient settings creates a need to reexamine the transmission of pathogens in this setting. Materials and Methods Seventeen health care workers from 4 wound care facilities were sampled during 46 patient care encounters to determine the presence of health care-associated pathogens (ie, methicillin-resistant Staphylococcus aureus , vancomycin-resistant Enterococcus , multidrug-resistant Acinetobacter species, and Clostridium difficile) on their hands at key moments of care. Results Health care workers acquired at least 1 pathogen on their hands during 28.3% of all patient care encounters. Hands sampled before a clean or aseptic procedure and hands sampled after body fluid exposure risk were each contaminated in 17.4% of instances. Hand contamination occurred in 19.6% of instances where health care workers wore gloves during care compared with 14.6% when health care workers were ungloved. Conclusions Contamination of health care workers' hands presents a significant risk of pathogen transmission in outpatient settings. Gloving education, hand hygiene solutions at the point of care, and hand hygiene surveillance are important solutions for reducing transmission of pathogenic organisms.

Title: The tipping point: patients predisposed to Clostridium difficile infection and a hospital antimicrobial stewardship programme.

Author(s): Stites, S.D.; Cooblall, C.A.; Aronovitz, J.; Singletary, S.B.; Micklow, K.; Sjeime, M.

Source: Journal of Hospital Infection; Nov 2016; vol. 94 (no. 3); p. 242-248

Abstract: Background: The incidence and severity of Clostridium difficile infection (CDI) have increased in recent years. Predictive models may help to identify at-risk patients before the onset of infection. Early identification of high-risk patients could help antimicrobial stewardship (AMS) programmes and other initiatives to better prevent C. difficile in these patients.Aim: To develop a predictive model that identifies patients at high risk for CDI at the time of hospitalization. This approach to early identification was evaluated to determine if it could improve upon a pre-existing AMS programme.Methods: Logistic regression and receiver operating characteristic (ROC) curve analyses were used to develop an analytic model to predict risk for CDI at the time of hospitalization in a retrospective cohort of inpatients. The model was validated in a prospective cohort. Concurrence between the model's risk predictions and a pre-existing AMS programme was assessed.Findings: The model identified 55% of patients who later tested positive as being at high risk for CDI at the time of admission. One in every 32 high-risk patients with potentially modifiable antimicrobial risk factors tested positive for CDI. Half (53%) tested positive before meeting the risk criteria for the hospital's AMS programme.Conclusion: Analytic models can identify most patients prospectively at the time of admission who later test positive for C. difficile. This approach to early identification may help AMS programmes to pursue susceptibility testing and modifications to antimicrobial therapies at an earlier stage in order to better prevent CDI.

Title: The housefly Musca domestica as a mechanical vector of Clostridium difficile.

Author(s): Davies, M.P.; Anderson, M.; Hilton, A.C.

Source: Journal of Hospital Infection; Nov 2016; vol. 94 (no. 3); p. 263-267

Abstract: Background: Clostridium difficile is a bacterial healthcare-associated infection that may be transferred by houseflies (Musca domestica) due to their close ecological association with humans and cosmopolitan nature.Aim: To determine the ability of M. domestica to transfer C. difficile both mechanically and following ingestion.Methods: M. domestica were exposed to independent suspensions of vegetative cells and spores of C. difficile, then sampled on to selective agar plates immediately postexposure and at 1-h intervals to assess the mechanical transfer of C. difficile. Fly excreta was cultured and alimentary canals were dissected to determine internalization of cells and spores.Findings: M. domestica exposed to vegetative cell suspensions and spore suspensions of C. difficile were able to transfer the bacteria mechanically for up to 4h upon subsequent contact with surfaces. The greatest numbers of colony-forming units (CFUs) per fly were transferred immediately following exposure (mean CFUs 123.8 +/- 66.9 for vegetative cell suspension and 288.2 +/- 83.2 for spore suspension). After 1h, this had reduced (21.2 +/- 11.4 for vegetative cell suspension and 19.9 +/- 9 for spores). Mean C. difficile CFUs isolated from the M. domestica alimentary canal was 35 +/- 6.5, and mean C. difficile CFUs per faecal spot was 1.04 +/- 0.58. C. difficile could be recovered from fly excreta for up to 96h.Conclusion: This study describes the potential for M. domestica to contribute to environmental persistence and spread of C. difficile in hospitals, highlighting flies as realistic vectors of this micro-organism in clinical areas.

Title: An evaluation of the effectiveness of an algorithm intervention in reducing inappropriate faecal samples sent for Clostridium difficile testing.

Author(s): Thompson, Irene; Lavelle, Colin; Leonard, Laurence

Source: Journal of Infection Prevention; Nov 2016; vol. 17 (no. 6); p. 278-286

Title: An Increase in Healthcare-Associated Clostridium difficile Infection Associated with Use of a Defective Peracetic Acid-Based Surface Disinfectant.

Author(s): Cadnum, Jennifer L; Jencson, Annette L; O'Donnell, Marguerite C; Flannery, Elizabeth R; Nerandzic, Michelle M; Donskey, Curtis J

Source: Infection control and hospital epidemiology; Nov 2016 ; p. 1-6

Abstract:BACKGROUND We investigated an increase in the incidence of healthcare-associated Clostridium difficile infection (CDI) that occurred following a change from a bleach disinfectant to a peracetic acid-based disinfectant. OBJECTIVE To evaluate the efficacy of the peracetic acid-based disinfectant. DESIGN Laboratory-based product evaluation. METHODS The commercial peracetic acid-based product is activated on site by mixing a small volume of concentrated hydrogen peroxide and peracetic acid present in a "SmartCap" reservoir with the remaining contents of the container. We measured concentrations of peracetic acid in newly activated and in-use product and determined the stability of nonactivated and activated product. We tested the efficacy of the product against C. difficile spores using the American Society for Testing and Materials standard quantitative carrier disk test method. RESULTS Measured concentrations of peracetic acid (50-800 parts per million [ppm]) were significantly lower than the level stated on the product label (1,500 ppm), and similar results were obtained for containers from multiple lot numbers and from another hospital. Product with peracetic acid levels below 600 ppm had significantly reduced activity against C. difficile spores. Peracetic acid concentrations were reduced markedly after storage of either activated or nonactivated product for several weeks. The Environmental Protection Agency confirmed the finding of low disinfectant levels and ordered discontinuation of sale of the product. CONCLUSION Use of a defective peracetic acid-based surface disinfectant may have contributed to an increase in healthcare-associated CDI. Our findings highlight the importance of evaluating the efficacy of liquid disinfectants in healthcare settings.

Title: Reduction in Clostridium difficile infection associated with the introduction of hydrogen peroxide vapour automated room disinfection

Author(s): McCord, J.; Prewitt, M.; Dyakova, E.; Mookerjee, S.; Otter, J.A.

Source: Journal of Hospital Infection; Oct 2016; vol. 94 (no. 2); p. 185-187

Abstract: The clinical impact of implementing hydrogen peroxide vapour (HPV) disinfection of rooms vacated by patients with Clostridium difficile infection (CDI) was evaluated. Breakpoint time series analysis indicated a significant reduction ($P<0.001$) in the CDI rate at the time when HPV disinfection was implemented, resulting in a reduction in the CDI rate from 1.0 to 0.4 cases per 1000 patient-days in the 24 months before HPV usage compared with the first 24 months of HPV usage. HPV should be considered to augment the terminal disinfection of rooms vacated by patients with CDI.

Title: Fecal microbiota transplant in patients with Clostridium difficile infection: A systematic review.

Author(s): Chapman, Brandon C.; Moore, Hunter B.; Overbey, Douglas M.; Morton, Alex P.; Harnke, Ben; Gerich, Mark E.; Vogel, Jon D.

Source: Journal of Trauma & Acute Care Surgery; Oct 2016; vol. 81 (no. 4); p. 756-764

Abstract: Background: Fecal microbiota transplantation (FMT) restores a diverse bacterial profile to the gastrointestinal tract and may effectively treat patients with Clostridium difficile infection (CDI). The objective of this systematic review was to evaluate the effectiveness of FMT in the treatment of CDI.Methods: Ovid MEDLINE, EMBASE, Web of Science, and Cochrane database were used. The authors searched studies with 10 or more patients examining the resolution of symptoms after FMT

in patients with CDI. Reviews, letters to the editors, and abstracts were excluded. Participants were patients with CDI. Intervention used was FMT. Quality assessment was performed using the Cochrane risk of bias assessment tool. Results were synthesized using a narrative approach.Results: Retrospective and uncontrolled prospective cohort studies suggest that FMT is a highly effective therapy for recurrent/refractory CDI, with clinical success rates ranging from 83% to 100%, which is similar to rates published by two randomized controlled trials. Fecal microbiota transplantation may be effectively administered via antegrade (upper gastrointestinal) or retrograde (lower gastrointestinal) routes of delivery. Fecal microbiota transplantation rarely results in major adverse events. However, diarrhea, cramping, and bloating commonly occur and are typically self-limited. Most studies were uncontrolled retrospective studies.Conclusion: Fecal microbiota transplantation should be considered in patients with recurrent episodes of mild to moderate CDI who have failed conventional antimicrobial therapy. There is insufficient evidence to recommend FMT for the treatment of severe CDI.Level Of Evidence: Systematic review, level III.

Title: The Cost-efficiency and Care Effectiveness of Probiotic Administration with Antibiotics to Prevent Hospital-Acquired Clostridium difficile Infection.

Author(s): Starn, Emily S.; Hampe, Holly; Cline, Thomas

Source: Quality Management in Health Care; Oct 2016; vol. 25 (no. 4); p. 238-243

Title: Probiotics as adjunctive therapy for preventing Clostridium difficile infection - What are we waiting for?

Author(s): Spinler, Jennifer K; Ross, Caná L; Savidge, Tor C

Source: Anaerobe; Oct 2016; vol. 41 ; p. 51-57

Abstract: With the end of the golden era of antibiotic discovery, the emergence of a new post-antibiotic age threatens to thrust global health and modern medicine back to the pre-antibiotic era. Antibiotic overuse has resulted in the natural evolution and selection of multi-drug resistant bacteria. One major public health threat, Clostridium difficile, is now the single leading cause of hospital-acquired bacterial infections and is by far the most deadly enteric pathogen for the U.S. Due to the high morbidity and mortality and increasing incidence that coincides with antibiotic use, non-traditional therapeutics are ideal alternatives to current treatment methods and also provide an avenue towards prevention. Despite the need for alternative therapies to antibiotics and the safety of most probiotics on the market, researchers are inundated with regulatory issues that hinder the translational science required to push these therapies forward. This review discusses the regulatory challenges of probiotic research, expert opinion regarding the application of probiotics to C. difficile infection and the efficacy of probiotics in preventing this disease

Title: Evolution of an audit and monitoring tool into an infection prevention and control process

Author(s): Denton, A.; Topping, A.; Humphreys, P.

Source: Journal of Hospital Infection; Sep 2016; vol. 94 (no. 1); p. 32-40

Abstract: Background: In 2010, an infection prevention and control team in an acute hospital trust integrated an audit and monitoring tool (AMT) into the management regime for patients with Clostridium difficile infection (CDI). Aim: To examine the mechanisms through which the implementation of an AMT influenced the care and management of patients with CDI. Methods: A constructivist grounded theory approach was used, employing semi-structured interviews with ward staff (N = 8), infection prevention and control practitioners (IPCPs) (N = 7) and matrons (N = 8), and subsequently a theoretical sample of senior managers (N = 4). All interviews were transcribed

verbatim and analysed using a constant comparison approach until explanatory categories emerged. Findings: The AMT evolved into a daily review process (DRP) that became an essential aspect of the management of all patients with CDI. Participants recognized that the DRP had positively influenced the care received by patients with CDI. Two main explanatory themes emerged to offer a framework for understanding the influence of the DRP on care management: education and learning, and the development and maintenance of relationships. Conclusion: The use of auditing and monitoring tools as part of a daily review process may enable ward staff, matrons, and IPCPs to improve patient outcomes and achieve the required levels of environmental hygiene if they act as a focal point for interaction, education, and collaboration. The findings offer insights into the behavioural changes and improved patient outcomes that ensue from the implementation of a DRP. References

Title: Cost-Effectiveness Analysis of the Use of Probiotics for the Prevention of Clostridium difficile–Associated Diarrhea in a Provincial Healthcare System.

Author(s): Leal, Jenine R.; Heitman, Steven J.; Conly, John M.; Henderson, Elizabeth A.; Manns, Braden J.

Source: Infection Control & Hospital Epidemiology; Sep 2016; vol. 37 (no. 9); p. 1079-1086

Title: Clostridium difficile Infections in Children: Impact of the Diagnostic Method on Infection Rates.

Author(s): AlGhounaim, Mohammad; Longtin, Yves; Gonzales, Milagros; Merckx, Joanna; Winters, Nicholas; Quach, Caroline

Source: Infection Control & Hospital Epidemiology; Sep 2016; vol. 37 (no. 9); p. 1087-1093

Norovirus

Title: Decrease of Rotavirus Gastroenteritis to a Low Level Without Resurgence for Five Years After Universal RotaTeq Vaccination in Finland.

Author(s): Hemming-Harlo, Maria; Markkula, Jukka; Huhti, Leena; Salminen, Marjo; Vesikari, Timo

Source: The Pediatric infectious disease journal; Dec 2016; vol. 35 (no. 12); p. 1304-1308

Abstract: Universal rotavirus (RV) vaccination with RotaTeq was introduced into National Immunization Programme (NIP) of Finland in September 2009. We have previously reported the reduction of RV gastroenteritis (GE) cases in the first 2 years after RV vaccination in NIP in Finland. In Tampere University Hospital, a 2-year survey of acute GE (AGE) in children was conducted before NIP in the years 2006 to 2008. This was followed by a similar prospective survey in years 2009 to 2011 and now extended to years 2012 to 2014. Stool samples from children examined in the hospital for AGE were analyzed by real-time polymerase chain reaction assays for RV and norovirus, and positive samples were typed by sequencing. The proportion of RVGE of all AGE cases decreased from 52% (421 of 809 cases) in pre-NIP years to 26% (86 of 330 cases) in post-NIP years 2009 to 2011 falling to 12% (40 of 347 cases) in 2012 and 2014. The hospitalizations for RVGE were reduced by 90% and the outpatient clinic visits also by 90% in 2012 to 2014, compared with pre-NIP year; all AGE cases were reduced by 59%. Norovirus was a major causative agent of AGE in the post-NIP period, accounting for 34% of the cases in 2009 to 2011 and 29% in 2012 to 2014. RV vaccination in NIP has led to a major reduction of RVGE cases seen in hospital with no resurgence in 5 years after NIP. A high coverage of RV vaccination will maintain RV activity at a low level but not eliminate wild-type RV circulation.

Title: No! When the immunologist becomes a virologist: Norovirus - an emerging infection in immune deficiency diseases.

Author(s): Hartono, Stella; Bhagia, Amrita; Joshi, Avni Y

Source: Current opinion in allergy and clinical immunology; Dec 2016; vol. 16 (no. 6); p. 557-564

Abstract: Norovirus infection is an emerging chronic infection in immunocompromised hosts. The aim of this review is to discuss the pathophysiology of Norovirus infection and explore mechanistic models for chronic infection/shedder state, especially in patients with immune deficiency diseases. Chronic Norovirus infection is increasingly associated with enteropathy associated with both primary and secondary immune deficiency diseases. There is an ongoing debate in the immune deficiency community whether it is truly a causative agent for the enteropathy or it is an innocent bystander.We describe the historic aspects of Norovirus infection, its immunology and viral structure and the basis for preventive and vaccination strategies.We also postulate in this review a disease model in immune deficiency subjects which creates a milieu for it to become a chronic and explore newer frontiers for disease modification and prevention. Norovirus is the most common cause of acute gastroenteritis in general population but the factors that lead to its persistence in patients with immune deficiency need further holistic studies. This should include host assessment, microbiome signatures, and viral pathogenic factors assessment.

Title: Environmental indicators for human norovirus outbreaks.

Author(s): Shamkhali Chenar, Shima; Deng, Zhiqiang

Source: International journal of environmental health research; Nov 2016 ; p. 1-12

Abstract: Norovirus is the most common cause of outbreaks of non-bacterial gastroenteritis in human. While the winter seasonality of norovirus outbreaks has been widely reported, the association between norovirus outbreak epidemics and environmental factors remains not fully understood. This literature review is intended to improve understanding of environmental factors governing norovirus outbreaks and how the factors affect norovirus transmission. To that end, a large number of studies (67) from countries around the world were critically reviewed and discussed. Results of the literature review show that temperature, humidity, and rainfall are the most important environmental variables governing the norovirus epidemic cycle. It was found that low temperature between -6.6 and 20 °C, relative humidity between 10 and 66 %, and rainfall from 1 day to 3 months before an outbreak are effective ranges of the environmental factors, which favor the prevalence of norovirus. Some other environmental factors might have an association with the cycle of norovirus epidemics. However, further investigations are needed to understand effects of the other factors on norovirus incidence. The findings of this literature review improve our understanding of the relationship between norovirus outbreaks and environmental factors and provide the direction for future research on norovirus outbreaks.

Title: Incidence of Hospital Norovirus Outbreaks and Infections Using 2 Surveillance Methods in Sweden.

Author(s): Fraenkel, Carl-Johan; Inghammar, Malin; Johansson, P J Hugo; Böttiger, Blenda

Source: Infection control and hospital epidemiology; Nov 2016 ; p. 1-7

Abstract: OBJECTIVE To evaluate 2 different methods of surveillance and to estimate the incidence of norovirus (NoV) outbreaks in hospitals. DESIGN Prospective observational study. SETTING All 194 hospital wards in southern Sweden during 2 winter seasons (2010-2012). METHODS Clinical surveillance based on outbreak reports of 2 or more clinical cases, with symptom onset within 5

days, was compared with laboratory surveillance based on positive NoV results among inpatients. At least 2 NoV positive patients sampled within 5 days at a ward defined a cluster. Outbreak reports including at least 1 NoV positive case and clusters including at least 1 NoV positive patient with 5 or more days from ward admission to sampling were defined as NoV outbreaks. RESULTS During the study periods 135 NoV outbreaks were identified; 74 were identified by both clinical and laboratory surveillance, 18 were identified only by outbreak reports, and 43 were identified only by laboratory surveillance. The outbreak incidence was 1.0 (95% CI, 0.8-1.2) and 0.5 (95% CI, 0.3-0.6) per 1,000 admissions for the 2 different seasons, respectively. To correctly identify NoV outbreaks, the sensitivity and positive predictive value of the clinical surveillance were 68% and 88% and of the laboratory surveillance were 86% and 81%, respectively. CONCLUSION The addition of laboratory surveillance significantly improves outbreak surveillance and provides a more complete estimate of NoV outbreaks in hospitals. Laboratory surveillance can be recommended for evaluation of clinical surveillance.

Title: Efficacy of a Disinfectant Containing Silver Dihydrogen Citrate Against GI.6 and GII.4 Human Norovirus.

Author(s): Manuel, Clyde; Moore, Matthew; Jaykus, Lee-Ann

Source: Journal of applied microbiology; Oct 2016

Abstract: Human norovirus is a major public health burden and is resistant to numerous sanitizers and disinfectants. In this study, we tested the efficacy of an antimicrobial product containing a blend of silver ions and citric acid (silver dihydrogen citrate; SDC) against GI.6 and GII.4 HuNoV. Pure(®) hard surface disinfectant (Pure Bioscience, El Cajon, CA) was evaluated using ASTM International virucidal suspension and stainless steel carrier assays. The effect of SDC (or citrate alone) exposure on viral integrity was evaluated using RT-qPCR, transmission electron microscopy, SDS-PAGE/Western blot analysis, and a receptor-binding assay. Suspension assays showed a 4.0 log10 reduction in RNA copy number within 5 min, while carrier assays showed a 2.0 to 3.0 log10 reduction in 30 min. Incorporating a simulated soil load into the sample matrix significantly reduced product efficacy. Treated particles displayed deformation and aggregation, a 50% reduction in viral capsid protein band intensity, and an 80% reduction in HBGA receptor binding ability. Our results suggest SDC to act exclusively on the viral capsid, and shows efficacy against HuNoV when used on pre-cleaned surfaces. This study sheds light on the mechanisms and efficacy of a novel antimicrobial against HuNoV. Our results suggest: 1) silver ions exclusively target the viral capsid, and not the RNA genome; 2) citrate is not crucial for HuNoV capsid deformation.

Title: Targeting pediatric versus elderly populations for norovirus vaccines: a model-based analysis of mass vaccination options.

Author(s): Steele, Molly K; Remais, Justin V; Gambhir, Manoj; Glasser, John W; Handel, Andreas; Parashar, Umesh D; Lopman, Benjamin A

Source: Epidemics; Oct 2016; vol. 17 ; p. 42-49

Abstract: Noroviruses are the leading cause of acute gastroenteritis and foodborne diarrheal disease in the United States. Norovirus vaccine development has progressed in recent years, but critical questions remain regarding which age groups should be vaccinated to maximize population impact. We developed a deterministic, age-structured compartmental model of norovirus transmission and immunity in the U.S. The model was fit to age-specific monthly U.S. hospitalizations between 1996 and 2007. We simulated mass immunization of both pediatric and elderly populations assuming realistic coverages of 90% and 65%, respectively. We considered two mechanism of vaccine action, resulting in lower vaccine efficacy (lVE) between 22% and 43% and higher VE (hVE) of 50%.

Pediatric vaccination was predicted to avert 33% (95% CI: 27%, 40%) and 60% (95% CI: 49%, 71%) of norovirus episodes among children under five years for lVE and hVE, respectively. Vaccinating the elderly averted 17% (95% CI: 12%, 20%) and 38% (95% CI: 34%, 42%) of cases in 65+ year olds for lVE and hVE, respectively. At a population level, pediatric vaccination was predicted to avert 18-21 times more cases and twice as many deaths per vaccinee compared to elderly vaccination. The potential benefits are likely greater for a pediatric program, both via direct protection of vaccinated children and indirect protection of unvaccinated individuals, including adults and the elderly. These findings argue for a clinical development plan that will deliver a vaccine with a safety and efficacy profile suitable for use in children.

Title: Curcumin Shows Antiviral Properties against Norovirus.

Author(s): Yang, Minji; Lee, GilJae; Si, Jiyeon; Lee, Sung-Joon; You, Hyun Ju; Ko, GwangPyo

Source: Molecules (Basel, Switzerland); Oct 2016; vol. 21 (no. 10)

Abstract: Phytochemicals provide environmentally friendly and relatively inexpensive natural products, which could potentially benefit public health by controlling human norovirus (HuNoV) infection. In this study, 18 different phytochemicals were evaluated for antiviral effects against norovirus using murine norovirus (MNV) as a model for norovirus biology. Among these phytochemicals, curcumin (CCM) was the most potent anti-noroviral phytochemical, followed by resveratrol (RVT). In a cell culture infection model, exposure to CCM or RVT for 3 days reduced infectivity of norovirus by 91% and 80%, respectively. To confirm the antiviral capability of CCM, we further evaluated its antiviral efficacy at various doses (0.25, 0.5, 0.75, 1, and 2 mg/mL) and durations (short-term: 10, 30, 60, and 120 min; long-term: 1, 3, 7, and 14 days). The anti-noroviral effect of CCM was verified to occur in a dose-dependent manner. Additionally, we evaluated the inhibitory effect of each phytochemical on the replication of HuNoV using a HuNoV replicon-bearing cell line (HG23). Neither CCM nor RVT had a strong inhibitory effect on HuNoV replication, which suggests that their antiviral mechanism may involve viral entry or other life cycle stages rather than the replication of viral RNA. Our results demonstrated that CCM may be a promising candidate for development as an anti-noroviral agent to prevent outbreaks of foodborne illness.

Title: Rotavirus and Norovirus in Pediatric Healthcare-Associated Gastroenteritis.

Author(s): Yi, Jumi; Sederdahl, Bethany K; Wahl, Kelly; Jerris, Robert R; Kraft, Colleen S; McCracken, Courtney; Gillespie, Scott; Kirby, Amy E; Shane, Andi L; Moe, Christine L; Anderson, Evan J

Source: Open forum infectious diseases; Oct 2016; vol. 3 (no. 4); p. ofw181

Available in full text at Open Forum Infectious Diseases - from Highwire Press

Abstract: Rotavirus and norovirus are important etiologies of gastroenteritis among hospitalized children. During 2012-2013, we tested 207 residual stool specimens from children with healthcare-associated vomiting and/or diarrhea for rotavirus and norovirus. Twenty (10%) were rotavirus positive, and 3 (3%) were norovirus positive, stressing the importance of these pathogens in hospitalized children.

Title: Norovirus as the cause of medically attended gastroenteritis: a hospital-based experience.

Author(s): Gastañaduy, A S; Zabaleta, J; Li, L; Bégué, R E

Source: Epidemiology and infection; Oct 2016; vol. 144 (no. 13); p. 2773-2779

Available in full text at Epidemiology and Infection - from ProQuest

Abstract: Gastroenteritis remains an important cause of morbidity and mortality worldwide. With the introduction of vaccines against rotavirus, interest has shifted to understanding the epidemiology of norovirus (NoV). While the importance of NoV in gastroenteritis outbreaks is well established, its role in sporadic gastroenteritis is less known. To better define the role of NoV as a cause of sporadic gastroenteritis we investigated its prevalence in the patients seen in our paediatric hospital with special emphasis on its seasonal and age distribution. Over a 12-month period discarded stool specimens submitted to our paediatric hospital for testing of an infectious aetiology were retrieved and additionally tested for NoV by real-time reverse transcriptase-polymerase chain reaction; demographical and clinical information were also obtained. Overall, NoV was the single most commonly identified pathogen and found in 68/892 (7·6%) total specimens or 68/258 (26%) of pathogen-positive specimens. The highest rates of NoV were detected in children aged 6 months to 4 years (50/332, 15·1%) and presenting between October and January (46/314, 14·7%). NoV has become the main cause of gastroenteritis in our paediatric population.

Title: Norovirus infections in a tertiary care centre - individual cases do not necessarily lead to an outbreak.

Author(s): Kampmeier, Stefanie; Pettke, Aleksandra; Kossow, Annelene; Willems, Stefanie; Mellmann, Alexander

Source: Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology; Sep 2016; vol. 84 ; p. 39-41

Abstract: Norovirus is responsible for the majority of gastroenteritis outbreaks within healthcare settings. Routes of spread include foodborne-, waterborne- and especially person-to-person transmissions. We investigated the overall attack rate of norovirus, within and outside outbreak situations, transmitted via patient-to-patient contact in a tertiary care centre from January 2012 to March 2015. We monitored exposed asymptomatic patients next to infectious patients for the development of symptoms of acute gastroenteritis following exposure. We detected 102 patients with contact to 94 infectious patients. Of these only 11 patients developed typical norovirus symptoms after exposure while 91 patients remained asymptomatic. Total secondary attack rate was only 10.8%. Patient-to-patient transmission of norovirus is potentially overestimated within clinical settings. Future prevention strategies should consider personal risk factors of exposed patients.

Title: Usability of an Alcohol Disinfectant Containing Organic Acids and Metal Salt for Environmental Surfaces.

Author(s): Okunishi, Junji; Nagahara, Hironori; Tsujitani, Kumiko; Matsuse, Hitoshi; Kugawa, Kazuyuki; Soga, Manabu

Source: Yakugaku zasshi : Journal of the Pharmaceutical Society of Japan; Sep 2016; vol. 136 (no. 9); p. 1233-1242

Abstract: Environmental cleaning and disinfection plays an important role as a part of the standard precautions to prevent healthcare-associated infections, whereas hand hygiene is one of the most important strategies for breaking the chain of transmission. Cleaning and disinfection of high-touch areas in a health-care facility is emphasized. And wiping with an alcohol-saturated cloth which has features such as low corrosion and a wide range of antimicrobial activity is performed commonly for this purpose. Although alcohol provides immediate activity against enveloped viruses, its virucidal activity against certain non-enveloped viruses, including norovirus, is insufficient. We created a novel alcohol-based hand rub, MR06B7, which is safe for the skin, and is active against an extended spectrum of microorganisms including non-enveloped viruses. For environmental surface

disinfection, a novel disinfectant MR13B15, which is based on MR06B7, has been developed. In vitro antimicrobial activity against a variety of pathogens, material compatibility, and simulated surface disinfection and decontamination efficacy of MR13B15 were investigated. According to the results, MR13B15 demonstrated potent bactericidal, fungicidal, mycobactericidal, and virucidal activity within a short contact time in addition to superior efficacy against non-enveloped viruses compared to ethanol for disinfection. Moreover, MR13B15 showed better material compatibility. Two simulation tests conducted for evaluating the disinfection and decontamination potency on environmental surfaces against feline calicivirus, a surrogate for norovirus, indicated that MR13B15 had superior efficacy for surface treatment compared to ethanol. These findings suggest that MR13B15, which satisfies most requirements of an environmental surface disinfectant, may contribute to accomplishing advanced standard precautions in preventing infections.

Title: Epidemiology of Norovirus Infection Among Immunocompromised Patients at a Tertiary Care Research Hospital, 2010-2013.

Author(s): Bok, Karin; Prevots, D Rebecca; Binder, Alison M; Parra, Gabriel I; Strollo, Sara; Fahle, Gary A; Behrle-Yardley, Allison; Johnson, Jordan A; Levenson, Eric A; Sosnovtsev, Stanislav V; Holland, Steven M; Palmore, Tara N; Green, Kim Y

Source: Open forum infectious diseases; Sep 2016; vol. 3 (no. 3); p. ofw169

Available in full text at Open Forum Infectious Diseases - from Highwire Press

Abstract: Background. Noroviruses are a major cause of infectious gastroenteritis worldwide, and viruses can establish persistent infection in immunocompromised individuals. Risk factors and transmission in this population are not fully understood. Methods. From 2010 through 2013, we conducted a retrospective review among immunocompromised patients (n = 268) enrolled in research studies at the National Institutes of Health Clinical Center and identified a subset of norovirus-positive patients (n = 18) who provided stool specimens for norovirus genotyping analysis. Results. Norovirus genome was identified by reverse-transcription quantitative polymerase chain reaction in stools of 35 (13%) of the 268 immunocompromised patients tested, and infection prevalence was 21% (11 of 53) in persons with primary immune deficiencies and 12% (20 of 166) among persons with solid tumors or hematologic malignancies. Among 18 patients with norovirus genotyping information, norovirus GII.4 was the most prevalent genotype (14 of 18, 78%). Persistent norovirus infection (≥6 months) was documented in 8 of 18 (44%) individuals. Phylogenetic analysis of the GII.4 capsid protein sequences identified at least 5 now-displaced GII.4 variant lineages, with no evidence of their nosocomial transmission in the Clinical Center. Conclusions. Norovirus was a leading enteric pathogen identified in this immunocompromised population. Both acute and chronic norovirus infections were observed, and these were likely community-acquired. Continued investigation will further define the role of noroviruses in these patients and inform efforts toward prevention and treatment.

Bronchiolitis

Title: Bronchiolitis: Analysis of 10 consecutive epidemic seasons.

Author(s): Cangiano, Giulia; Nenna, Raffaella; Frassanito, Antonella; Evangelisti, Melania; Nicolai, Ambra; Scagnolari, Carolina; Pierangeli, Alessandra; Antonelli, Guido; Papoff, Paola; Petrarca, Laura; Capocaccia, Paolo; Moretti, Corrado; Midulla, Fabio

Source: Pediatric pulmonology; Dec 2016; vol. 51 (no. 12); p. 1330-1335

Abstract: Bronchiolitis is the leading cause of hospitalization in infants under 12 months. Our aims were to analyze epidemiological characteristics of infants with bronchiolitis over 10 consecutive

seasons and to evaluate whether there are any clinical differences between infants hospitalized for bronchiolitis during epidemic peak months and infants in non-peak months. We enrolled consecutive enrolled 723 previously healthy term infants hospitalized at the Paediatric Emergency Department, "Sapienza" University of Rome over the period 2004-2014. Fourteen respiratory viruses were detected from nasopharyngeal aspirates by molecular methods. Clinical and demographic data were extracted from clinical charts. Viruses were detected in 351 infants (48.5%): RSV in 234 (32.4%), RV in 44 (6.1%), hBoV in 11 (1.5%), hMPV in 12 (1.6%), co-infections in 39 (5.4%), and other viruses in 11 (1.5%). Analyzing the 10 epidemic seasons, we found higher incidence for bronchiolitis every 4 years with a peak during the months December-January. Infants hospitalized during peak months had lower family history for asthma (P = 0.003), more smoking mothers during pregnancy (P = 0.036), were slightly higher breastfed (0.056), had lower number of blood eosinophils (P = 0.015) and had a higher clinical severity score (P = 0.017). RSV was detected mostly during peak months, while RV was equally distributed during the seasons. We found some variations in bronchiolitis incidence during epidemics, and discriminative characteristics in infants hospitalized for bronchiolitis during peak months and in non-peak months, that might reflect two different populations of children.

Title: Exposure to vehicular traffic is associated to a higher risk of hospitalization for bronchiolitis during the first year of life.

Author(s): Lanari, Marcello; Vandini, Silvia; Prinelli, Federica; Adorni, Fulvio; DI Santo, Simona; Silvestri, Michela; Musicco, Massimo; Study Group of Italian Society of Neonatology on Risk Factors for RSV Hospitalization

Source: Minerva pediatrica; Dec 2016; vol. 68 (no. 6); p. 391-397

Abstract: The most common cause of hospitalization for children younger than age one is bronchiolitis. Several prenatal and environmental risk factors may affect the incidence of hospitalization for bronchiolitis. The aim of this study was to investigate the relation between exposure to vehicular traffic and the incidence of hospitalization for bronchiolitis in children during their first year of life in Italy. A multicenter prospective birth cohort study, where equal numbers of newborns of 33-34, 35-37 and ≥38 wGA were recruited at birth (1814 children) in 30 Italian neonatology units. Two interviewer-administered questionnaires were used to collect data. The first interview was carried out at the end of the Italian epidemic season. The second interview was carried out when the child was one year old. Data on possible prenatal, perinatal, and postnatal/environmental risk factors and on vehicular traffic density in the zone of residence were collected. On each interview, parents were also asked about any hospitalizations of the child. The outcome measure was the hospitalization for bronchiolitis (International Health Service ICD-9 code 466). Univariate analysis demonstrated that exposure to air pollution due to vehicular traffic, was significantly associated with an increased risk of hospitalization for bronchiolitis. The adjusted risk from logistic regression model confirmed that children exposed to air pollution due to vehicular traffic were at increased risk of hospitalization for bronchiolitis. Exposure to air pollution due to vehicular traffic may increase the risk of hospitalization for bronchiolitis in the first year of life.

Title: A regional cohort study of the treatment of critically ill children with bronchiolitis.

Author(s): Carroll, Christopher L; Faustino, Edward Vincent S; Pinto, Matthew G; Sala, Kathleen A; Canarie, Michael F; Li, Simon; Giuliano, John S; The Northeast Pediatric Critical Care Research Consortium

Source: The Journal of asthma : official journal of the Association for the Care of Asthma; Dec 2016; vol. 53 (no. 10); p. 1006-1011

Abstract: To describe the treatment practices in critically ill children with RSV bronchiolitis across four regional PICUs in the northeastern United States, and to determine the factors associated with increased ICU length of stay in this population. We conducted a retrospective cohort study of children who were admitted with RSV bronchiolitis between July 2009 and July 2011 to the PICUs of Connecticut Children's Medical Center, Yale-New Haven Children's Hospital, Maria Fareri Children's Hospital, and Baystate Children's Hospital. Data were collected regarding clinical characteristics and intensive care course among these hospitals. During the study period, 323 children were admitted to one of the four ICUs with RSV bronchiolitis. Despite similar mortality risk scores among ICUs, there was considerable variation in the use of therapies, particularly intubation and mechanical ventilation, in which there was greater than a 3.5-fold increased risk of intubation between sites with the highest and lowest frequency of intubation (odds ratio: 3.8; 95% confidence interval: 2.2-6.4). Albuterol was the most commonly used respiratory treatment, followed by chest physiotherapy, high-flow nasal cannula, and hypertonic saline. Longer stays in the ICU were associated with more frequent use of therapies, specifically invasive mechanical ventilation, inhaled corticosteroids, intrapulmonary percussive ventilation, and chest physiotherapy. Even within a close geographic region, there is significant variation in the treatment provided to critically ill children with RSV bronchiolitis. None of these treatments were associated with shorter durations of hospitalization in this population and some, such as mechanical ventilation, were associated with longer ICU lengths of stay.

Title: Rhinopharyngeal Retrograde Clearance Induces Less Respiratory Effort and Fewer Adverse Effects in Comparison With Nasopharyngeal Aspiration in Infants With Acute Viral Bronchiolitis.

Author(s): Gomes, Gabriela R; Calvete, Fernanda Pg; Rosito, Gabriela F; Donadio, Márcio Vf

Source: Respiratory care; Dec 2016; vol. 61 (no. 12); p. 1613-1619

Abstract: Acute viral bronchiolitis is an inflammatory disease of the lower respiratory tract. This study aimed to compare the immediate effects of retrograde rhinopharyngeal clearance with nasopharyngeal aspiration in children admitted with acute viral bronchiolitis. This was a randomized controlled clinical trial with children admitted for acute viral bronchiolitis up to 12 months old. Subjects were divided into a nasopharyngeal aspiration group and a clearance group, submitted to retrograde rhinopharyngeal clearance with physiological solution (0.9%) instillation. In both groups, there were 3 evaluations on the same day (data collections 1, 2, and 3), including cardiorespiratory parameters, clinical score of respiratory dysfunction, and adverse effects. One hundred children were included, with no statistical differences between groups regarding the characteristics of the sample. There was a significant reduction ($P < .05$) in heart rate in data collections 1 and 2 after 10 and 30 min. The number of episodes of nasal bleeding (28 vs 1) and vomiting (11 vs 7) was higher in the aspiration group compared with the clearance group. Children classified as moderate showed a significant reduction of retractions (100% vs 84.6%) and nasal bleeding (44.8% vs 0%). An increase of 6.7 and 19.5% in wheezing and retractions, respectively, was shown for the aspiration group, whereas the clearance group showed only 4.6% for both parameters. The use of retrograde rhinopharyngeal clearance in the management of infants with acute viral bronchiolitis can be an alternative for the clearance of the upper airways, since it showed immediate positive effects on the occurrence of complications and signs of respiratory effort compared with nasopharyngeal aspiration. Children classified with a moderate clinical score appear to benefit the most. (ClinicalTrials.gov registration NCT02460614.).

Title: High-flow oxygen therapy is more cost-effective for bronchiolitis than standard treatment-A decision-tree analysis.

Author(s): Heikkilä, Paula; Forma, Leena; Korppi, Matti

Source: Pediatric pulmonology; Dec 2016; vol. 51 (no. 12); p. 1393-1402

Abstract: We evaluated the cost-effectiveness of high-flow nasal cannula (HFNC) to provide additional oxygen for infants with bronchiolitis, compared to standard low-flow therapy. The cost-effectiveness was evaluated by decision analyses, using decision tree modeling, and was based on real costs from our recently published retrospective case-control study. The data on the effectiveness of HFNC treatment were collected from earlier published retrospective studies, using admission rates to pediatric intensive care units (PICU). The analyses in the study showed that the expected treatment costs of each episode of infant bronchiolitis varied between €1,312-2,644 ($1,786-3,600) in the HFNC group and €1,598-3,764 ($2,175-5,125) in the standard treatment group. The PICU admission rates and consequential costs were lower for HFNC than for standard treatment. HFNC treatment proved more cost-effective than standard treatment in all the baseline analyses and was also more cost-effective in the sensitivity analyses, except for in the worst-case scenario analysis. In conclusion, our modeling demonstrated that HFNC was strongly cost-effective for infant bronchiolitis, compared to standard treatment because it was both more effective and less expensive. Thus, if children hospitalized for bronchiolitis need oxygen, it should be delivered as HFNC treatment.

Title: Association of nasopharyngeal microbiota profiles with bronchiolitis severity in infants hospitalised for bronchiolitis.

Author(s): Hasegawa, Kohei; Mansbach, Jonathan M; Ajami, Nadim J; Espinola, Janice A; Henke, David M; Petrosino, Joseph F; Piedra, Pedro A; Shaw, Chad A; Sullivan, Ashley F; Camargo, Carlos A; on behalf of the MARC-35 Investigators

Source: The European respiratory journal; Nov 2016; vol. 48 (no. 5); p. 1329-1339

Available in full text at European Respiratory Journal - from Highwire Press

Abstract: Little is known about the relationship between the specific airway microbiota composition and severity of bronchiolitis. We aimed to identify nasopharyngeal microbiota profiles and link these profiles to acute severity in infants hospitalised for bronchiolitis.We conducted a multicentre prospective cohort study of 1005 infants (age <1 year) hospitalised for bronchiolitis over three winters, 2011-2014. By applying a 16S rRNA gene sequence and clustering approach to the nasopharyngeal aspirates collected within 24 h of hospitalisation, we determined nasopharyngeal microbiota profiles and their association with bronchiolitis severity. The primary outcome was intensive care use, i.e. admission to an intensive care unit or use of mechanical ventilation.We identified four nasopharyngeal microbiota profiles: three profiles were dominated by one of Haemophilus, Moraxella or Streptococcus, while the fourth profile had the highest bacterial richness. The rate of intensive care use was highest in infants with a Haemophilus-dominant profile and lowest in those with a Moraxella-dominant profile (20.2% versus 12.3%; unadjusted OR 1.81, 95% CI 1.07-3.11, p=0.03). After adjusting for 11 patient-level confounders, the rate remained significantly higher in infants with Haemophilus-dominant profiles (OR 1.98, 95% CI 1.08-3.62, p=0.03). These findings were externally validated in a separate cohort of 307 children hospitalised for bronchiolitis.

Title: Management of Bronchiolitis in Community Hospitals in Ontario: a Multicentre Cohort Study.

Author(s): Plint, Amy C; Taljaard, Monica; McGahern, Candice; Scott, Shannon D; Grimshaw, Jeremy M; Klassen, Terry P; Johnson, David W

Source: CJEM; Nov 2016; vol. 18 (no. 6); p. 443-452

Abstract: Bronchiolitis is the leading cause of hospital admission for infants, but few studies have examined management of this condition in community hospital settings. We reviewed the management of children with bronchiolitis presenting to community hospitals in Ontario. We retrospectively reviewed a consecutive cohort of infants less than 12 months old with bronchiolitis who presented to 28 Ontario community hospitals over a two-year period. Bronchiolitis was defined as first episode of wheezing associated with signs of an upper respiratory tract infection during respiratory syncytial virus season. Of 543 eligible children, 161 (29.7%, 95% Confidence Interval (CI) 22.3 to 37.0%) were admitted to hospital. Hospital admission rates varied widely (Interquartile Range 0%-40.3%). Bronchodilator use was widespread in the emergency department (ED) (79.7% of patients, 95% CI 75.0 to 84.5%) and on the inpatient wards (94.4% of patients, 95% CI 90.2 to 98.6%). Salbutamol was the most commonly used bronchodilator. At ED discharge 44.7% (95% CI 37.5 to 51.9%) of patients were prescribed a bronchodilator medication. Approximately one-third of ED patients (30.8%, 95% CI 22.7 to 38.8%), 50.3% (95% CI 37.7 to 63.0%) of inpatients, and 23.5% (95% CI 14.4 to 32.7) of patients discharged from the ED were treated with corticosteroids. The most common investigation obtained was a chest x-ray (60.2% of all children; 95% CI 51.9 to 68.5%). Infants with bronchiolitis receive medications and investigations for which there is little evidence of benefit. This suggests a need for knowledge translation strategies directed to community hospitals.

Title: Viral Bronchiolitis is Associated With Altered Cytokine Gene Expression and Lymphocyte Activation Status.

Author(s): Leahy, T Ronan; McManus, Ross; Doherty, Derek G; Grealy, Robert; Carr, Michael J; Slattery, Dubhfeasa; Ryan, Thomas

Source: The Pediatric infectious disease journal; Nov 2016; vol. 35 (no. 11); p. e326

Abstract: Disease severity in viral bronchiolitis is often difficult to predict at onset, and may be related to the host immune response. Recognizing the particular immunologic features of infants who develop severe disease might offer an opportunity for developing diagnostic tools to facilitate early intervention and improve outcomes. We compared cytokine gene expression (by real-time reverse-transcriptase polymerase chain reaction), cytokine concentrations (by enzyme-linked immunosorbent assay) and the activation status of lymphocytes (by flow cytometry) in the peripheral blood of children hospitalized with moderate and severe viral bronchiolitis and a group of age-matched controls. Analysis was undertaken on 57 children with viral bronchiolitis and 33 controls. Interleukin-7 mRNA expression at enrollment in peripheral blood mononuclear cells differed significantly between those with moderate and severe bronchiolitis, and correlated with both the subsequent length of hospital stay and need for supplemental oxygen therapy. Serum interleukin-10 concentration also distinguished moderate from severe disease. Participants with viral bronchiolitis demonstrated a more activated γδ-T cell phenotype (Vδ1+), but a more naive TCR αβ-T cell compartment compared with controls. Viral bronchiolitis is characterized by a distinct pattern of cytokine expression and lymphocyte activation. These changes suggest an inadequate innate response in severe disease, and may offer potential as markers of disease severity.

Title: Impact of the implementation of an evidence-based guideline on diagnostic testing, management, and clinical outcomes for infants with bronchiolitis.

Author(s): Henao-Villada, Ricardo; Sossa-Briceño, Monica P; Rodríguez-Martínez, Carlos E

Source: Therapeutic advances in respiratory disease; Oct 2016; vol. 10 (no. 5); p. 425-434

Abstract: Although bronchiolitis poses a significant health problem in low- and middle-income countries (LMICs), to the best of our knowledge, to date it has not been determined whether evidence-based bronchiolitis clinical practice guidelines (CPGs) complemented by standardized

educational strategies reduce the use of unnecessary diagnostic tests and medications and improve clinically important outcomes in LMICs. In an uncontrolled before and after study, we assessed the impact of the implementation of an evidence-based bronchiolitis CPG on physician behavior and the care of infants with bronchiolitis by comparing pre-guideline (March to August 2014) and post-guideline (March to August 2015) use of diagnostic tests and medications through an electronic medical record review in a children's hospital in Bogota, Colombia. We also sought to assess the impact of the implementation of the CPG on clinically important outcomes such as lengths of stay, hospital admissions, intensive care admissions, and hospital readmissions. Data from 662 cases of bronchiolitis (pre-guideline period) were compared with the data from 703 cases (post-guideline period). On comparing the pre- and post-guideline periods, it was seen that there was a significant increase in the proportion of patients with an appropriate diagnosis and treatment of bronchiolitis (36.4% versus 44.5%, p = 0.003), and there were statistically significant decreases in the use of a hemogram (33.2% versus 26.6%, p=0.010), procalcitonin (3.9% versus 1.6%, p=0.018), nebulized beta-2 agonists (45.6% versus 3.4%, p < 0.001), nebulized anticholinergics (3.3% versus 1.4%, p= 0.029), and nebulized epinephrine (16.2% versus 7.8%, p < 0.001). Likewise, a significant increase in the use of nebulized hypertonic saline was seen (79.6% versus 91.7%, p < 0.001). However, implementation of the CPG for bronchiolitis was not associated with significant changes in clinically important outcomes. The development and implementation of a good quality bronchiolitis CPG is associated with a significant increase in the proportion of cases with an appropriate diagnosis and treatment of the disease in the context of a university-based hospital located in the capital of an LMIC. However, we could not demonstrate an improvement in clinically important outcomes such as any of the bronchiolitis severity parameters.

Title: Caffeine for the Treatment of Apnea in Bronchiolitis: A Randomized Trial.

Author(s): Alansari, Khalid; Toaimah, Fatihi Hassan; Khalafalla, Hany; El Tatawy, Lamiaa Awny; Davidson, Bruce L; Ahmed, Wessam

Source: The Journal of pediatrics; Oct 2016; vol. 177 ; p. 204

Abstract: To evaluate the efficacy and safety of caffeine citrate in the treatment of apnea in bronchiolitis. Eligible infants aged ≤4 months presenting to the main pediatric emergency service with apnea associated bronchiolitis were stratified by gestational age (<34 weeks or longer) and randomized to receive a single dose of intravenous 25 mg/kg caffeine citrate or saline placebo. The primary efficacy outcome was a 24-hour apnea-free period beginning after completion of the blinded study drug infusion. Secondary outcomes were frequency of apnea by 24, 48, and 72 hours after study medication, need for noninvasive/invasive ventilation, and length of stay in the hospital's pediatric intensive care/step-down unit. A total of 90 infants diagnosed with viral bronchiolitis associated with apnea (median age, 38 days) were enrolled. The rate of respiratory virus panel positivity was similar in the 2 groups (78% for the placebo group vs 84% for the caffeine group). The geometric mean duration to a 24-hour apnea-free period was 28.1 hours (95% CI, 25.6-32.3 hours) for the caffeine group and 29.1 hours (95% CI, 25.7-32.9 hours) for the placebo group (P = .88; OR, 0.99; 95% CI, 0.83-1.17). The frequency of apnea at 24 hours, 24-48 hours, and 48-72 hours after enrollment and the need for noninvasive and invasive ventilation were similar in the 2 groups. No safety issues were reported. A single dose of caffeine citrate did not significantly reduce apnea episodes associated with bronchiolitis. Clinicaltrials.gov: NCT01435486.

Title: Predictors of Airspace Disease on Chest X-ray in Emergency Department Patients With Clinical Bronchiolitis: A Systematic Review and Meta-analysis.

Author(s): Chao, Jennifer H; Lin, Raymond Chou-Jui; Marneni, Shashidhar; Pandya, Shreya; Alhajri, Sana; Sinert, Richard

Source: Academic emergency medicine : official journal of the Society for Academic Emergency Medicine; Oct 2016; vol. 23 (no. 10); p. 1107-1118

Abstract: An abnormal chest X-ray (CXR) inconsistent with simple bronchiolitis is found in 7%-23% of cases. Despite national guidelines stating "current evidence does not support routine radiography in children with bronchiolitis"; the use of CXR in these patients remains high. Inappropriate use of CXR not only exposes children to excess radiation, but also increases medical costs. The majority of the time, CXRs are obtained to diagnose or rule out pneumonia. We aim to provide an evidence-based approach defining the utility of CXR in bronchiolitis for the diagnosis and treatment of bacterial pneumonia. We performed a systematic review and meta-analysis to describe potential predictors of a CXR with airspace disease in patients with bronchiolitis. We searched the medical literature from 1965 to June 2015 in PubMed/EMBASE using the following PICO formulation of our clinical question, "What characteristic(s) of history/physical examination (H&P) and vital signs (VS) in a child with bronchiolitis should prompt the physician to order a CXR?": Patients-pediatric emergency department (ED) patients (<2 years) with clinical bronchiolitis; Intervention-H&P and VS; Comparator-a CXR positive for airspace disease (+CXR), defined as atelectasis versus infiltrate or infiltrate/consolidation; and Outcome-operating characteristics of H&P and VS predicting an +CXR were calculated: sensitivity, specificity, and likelihood ratios (LR+ or LR-). The methodologic quality of the studies was assessed using the quality assessment of studies of diagnostic accuracy tool (QUADAS-2). We created a test-treatment threshold model based on the operating characteristics of the CXR to accurately identify a child with bronchiolitis and a superimposed bacterial pneumonia while accounting for the risks of a CXR and risks of treating patients with and without a bacterial infection. We found five studies including 1,139 patients meeting our inclusion/exclusion criteria. Prevalence of a +CXR ranged from 7% to 23%. An oxygen saturation < 95% was the predictor with highest LR+ of 2.3 (95% confidence interval = 1.3 to 3.07) to predict a +CXR. None of the H&P and VS variables were found to have sufficiently low LR- to significantly decrease the pretest probability of finding a +CXR. Our test-treatment threshold model showed that hypoxia (O2 Sat < 95%) alone complicating bronchiolitis did not show a benefit to obtaining a CXR. Our model only suggested that a CXR maybe indicated for a child with hypoxia (O2 Sat < 95%) and respiratory failure requiring ventilatory support. No single predictor of a +CXR was of sufficient accuracy to either support or refute ordering a CXR in a child with clinical bronchiolitis. We provide a decision threshold model to estimate a test threshold for obtaining a CXR and a treatment threshold for administering antibiotics. Application of this model requires the clinician to approximate the empiric benefit of antibiotics based on the clinical situation, highlighting the importance of clinical assessment.

Respiratory Syncytial Virus

Title: The influence of birth weight amongst 33-35 weeks gestational age (wGA) infants on the risk of respiratory syncytial virus (RSV) hospitalisation: a pooled analysis.

Author(s): Carbonell-Estrany, Xavier; Fullarton, John R; Gooch, Katherine L; Gouyon, Jean-Bernard; Lanari, Marcello; Rodgers-Gray, Barry S; Thwaites, Richard J; Vo, Pamela G; Liese, Johannes G

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Jan 2017; vol. 30 (no. 2); p. 134-140

Abstract: To investigate the association between birth weight and respiratory syncytial virus (RSV) hospitalisation during the first year of life in 33°-35(6) weeks' gestational age (wGA) infants. Pooled analysis of data (n = 1218) from Spain, Germany, France and Italy. RSV hospitalised infants overall had a significantly higher birth weight than non-hospitalised infants (2.24 versus 2.14 kg; p < 0.001) for both males (2.25 versus 2.18 kg; p = 0.049) and females (2.22 versus 2.11 kg, p = 0.007). The effect was significant only in 34 wGA infants (33 wGA: hospitalised 1.95 kg versus

non-hospitalised 1.95 kg, p = 0.976; 34 wGA: 2.26 versus 2.14 kg, p = 0.007; 35 wGA: 2.37 versus 2.29 kg, p = 0.070), particularly female 34 wGA infants (female: 2.24 versus 2.08 kg, p = 0.019; male: 2.27 versus 2.20, p = 0.191). Birth weight was shown to be an independent risk factor for RSV hospitalisation. In 33-35 wGA infants, a higher birth weight appeared independently associated with an increased risk of RSV hospitalisation.

Title: Clinical characterization of influenza A and human respiratory syncytial virus among patients with influenza like illness.

Author(s): Saxena, Swati; Singh, Dharamveer; Zia, Amreen; Umrao, Jyoti; Srivastava, Naveen; Pandey, Ankita; Singh, Sushma; Bhattacharya, Piyali; Kumari, Reema; Kushwaha, Ramawadh; Dhole, T N

Source: Journal of medical virology; Jan 2017; vol. 89 (no. 1); p. 49-54

Abstract: Influenza A and Respiratory Syncytial Virus (RSV) has been recognized as a major cause of acute respiratory tract infection. H1N1 is one of the subtypes of influenza A, pandemic worldwide in July 2009, causing 18,449 deaths globally. To investigate the prevalence and clinical manifestation of the influenza A, H1N1pdm09, and RSV. Throat/nasal swab collected from the patients of all age group either outpatients/inpatients having respiratory illness from 2 to 5 days. The clinical data were recorded in a predesigned questionnaire. RNA was extracted and analyzed by real time PCR at a tertiary care center, 2009-2014. Total 4,352 samples tested for influenza A and H1N1. Out of 4,352, 32.2% (median positivity 21%; range 16-41% during 6 years) were positive for influenza A and 19% were H1N1 (median positivity 16.7%; range 8.7-23% during 6 years). Total 1653 samples were analyzed for RSV from 2011 to 2014, 12% were RSV positive (median positivity 11.35%; range 10-16.3% during 4 years). Pharyngitis, dyspnea were frequent symptoms in influenza A and H1N1 ($P < 0.005$) whereas bronchiolitis and pneumonia were commonly present in RSV ($P < 0.005$). The positivity of influenza A and H1N1 was higher in age-group 21-30, whereas RSV in infant and children. H1N1 and RSV were co-circulated and have common clinical symptoms particularly in lower age group. Therefore, laboratory confirmation is necessary for further disease prognosis. Age was an important risk factor that affects the positivity of influenza A, H1N1, and RSV. Different clinical manifestation of H1N1 and RSV will be helpful for early and accurate diagnosis.

Title: Respiratory Syncytial Virus: Infection, Detection, and New Options for Prevention and Treatment.

Author(s): Griffiths, Cameron; Drews, Steven J; Marchant, David J

Source: Clinical microbiology reviews; Jan 2017; vol. 30 (no. 1); p. 277-319

Abstract: Respiratory syncytial virus (RSV) infection is a significant cause of hospitalization of children in North America and one of the leading causes of death of infants less than 1 year of age worldwide, second only to malaria. Despite its global impact on human health, there are relatively few therapeutic options available to prevent or treat RSV infection. Paradoxically, there is a very large volume of information that is constantly being refined on RSV replication, the mechanisms of RSV-induced pathology, and community transmission. Compounding the burden of acute RSV infections is the exacerbation of preexisting chronic airway diseases and the chronic sequelae of RSV infection. A mechanistic link is even starting to emerge between asthma and those who suffer severe RSV infection early in childhood. In this article, we discuss developments in the understanding of RSV replication, pathogenesis, diagnostics, and therapeutics. We attempt to reconcile the large body of information on RSV and why after many clinical trials there is still no efficacious RSV vaccine and few therapeutics.

Title: Factors predicting life-threatening infections with respiratory syncytial virus in adult patients.

Author(s): Park, Se Yoon; Kim, Taeeun; Jang, Young Rock; Kim, Min-Chul; Chong, Yong Pil; Lee, Sang-Oh; Choi, Sang-Ho; Kim, Yang Soo; Woo, Jun Hee; Kim, Sung-Han

Source: Infectious diseases (London, England); Dec 2016 ; p. 1-8

Abstract: Respiratory syncytial virus (RSV) is a significant cause of acute respiratory illness with a clinical spectrum ranging from self-limiting upper respiratory infection to severe lower respiratory infection in elderly persons as well as young children. However, there are limited data on risk factors for life-threatening infections that could guide the appropriate use of antiviral agents in adult patients with RSV. We conducted a retrospective cohort study from October 2013 to September 2015. Adult patients with RSV who visited the emergency department were enrolled. Primary outcome was life-threatening infection (admission to intensive care unit, need for ventilator care or in-hospital death). A total of 227 patients were analysed. Thirty-four (15%) were classified as having life-threatening infections. By logistic regression, lower respiratory infection, chronic lung disease and bacterial co-infection were independent predictors of life-threatening infections. We developed a simple clinical scoring system using these variables (lower respiratory tract infection = score 4, chronic respiratory disease = score 3, bacterial co-infection = score 3 and fever ≥38 °C = score 2) to predict life-threatening infection. A score of >5 differentiated life-threatening RSV from non-life-threatening RSV with 82% sensitivity (95% CI, 66-93) and 72% specificity (95% CI, 65-78). The use of a clinical scoring system based on lower respiratory infection, chronic respiratory disease, bacterial co-infection and fever appears to be useful for outcome prediction and risk stratification in order to select patients who may need early antiviral therapy.

Title: Defining the Risk and Associated Morbidity and Mortality of Severe Respiratory Syncytial Virus Infection Among Infants with Chronic Lung Disease.

Author(s): Paes, Bosco; Fauroux, Brigitte; Figueras-Aloy, Josep; Bont, Louis; Checchia, Paul A; Simões, Eric A F; Manzoni, Paolo; Carbonell-Estrany, Xavier

Source: Infectious diseases and therapy; Dec 2016; vol. 5 (no. 4); p. 453-471

Abstract: The REGAL (RSV evidence-a geographical archive of the literature) series provide a comprehensive review of the published evidence in the field of respiratory syncytial virus (RSV) in Western countries over the last 20 years. This third publication covers the risk and burden of RSV infection in infants with chronic lung disease (CLD), formerly called bronchopulmonary dysplasia (BPD). A systematic review was undertaken of publications between January 1, 1995 and December 31, 2015 across PubMed, Embase, The Cochrane Library, and Clinicaltrials.gov. Studies reporting data for hospital visits/admissions for RSV infection among infants with CLD/BPD who were not prophylaxed, as well as studies reporting RSV-associated morbidity, mortality, and healthcare costs, were included. Burdens of disease data were compared with preterm infants without CLD/BPD, other high-risk groups and term infants. Study quality and strength of evidence (SOE) were graded using recognized criteria. A total of 1837 studies were identified and 39 were included. CLD/BPD is a significant independent risk factor for RSV hospitalization [RSVH (odds ratio 2.2-7.2); high SOE]. Infants and young children with CLD/BPD had high RSVH rates which were generally similar in Europe, the United States, and Canada, mostly varying between 12 and 21%. Infants with CLD also had a longer length of hospital stay than other high-risk groups and term infants (high SOE). On average, infants spent 4-11 days in hospital (moderate SOE). Once hospitalized for RSV, affected children were at risk for a more severe course of disease than children with no RSVH (moderate SOE). Severe RSV infection in infants and young children with CLD/BPD poses a significant health burden in Western countries. Further studies focussing on the burden of RSV infection in this well-

recognized population at high risk for severe disease are needed to help improve outcomes and plan allocation of healthcare resources.

Title: Defining the Risk and Associated Morbidity and Mortality of Severe Respiratory Syncytial Virus Infection Among Preterm Infants Without Chronic Lung Disease or Congenital Heart Disease.

Author(s): Figueras-Aloy, Josep; Manzoni, Paolo; Paes, Bosco; Simões, Eric A F; Bont, Louis; Checchia, Paul A; Fauroux, Brigitte; Carbonell-Estrany, Xavier

Source: Infectious diseases and therapy; Dec 2016; vol. 5 (no. 4); p. 417-452

Abstract: The REGAL (RSV Evidence-a Geographical Archive of the Literature) series provide a comprehensive review of the published evidence in the field of respiratory syncytial virus (RSV) in Western countries over the last 20 years. This second publication covers the risk and burden of RSV infection in preterm infants born at 100 per 1000 children with the highest rates shown in the lowest gestational age infants (high SOE). Independent risk factors associated with RSVH include: proximity of birth to the RSV season, living with school-age siblings, smoking of mother during pregnancy or infant exposure to environmental smoking, reduced breast feeding, male sex, and familial atopy (asthma) (high SOE). Predictive models can identify 32/33-35 wGA infants at risk of RSVH (high SOE). RSV infection remains a major burden on Western healthcare systems and is associated with significant morbidity. Further studies focusing on the prevalence and burden of RSV in different gestational age cohorts, the changing risk of RSVH during the first year of life, and on RSV-related mortality in preterm infants are needed to determine the true burden of disease.

Title: Impact of the Updated Guidance for Palivizumab Prophylaxis against Respiratory Syncytial Virus Infection: A Single Center Experience.

Author(s): Rajah, Bavani; Sánchez, Pablo J; Garcia-Maurino, Cristina; Leber, Amy; Ramilo, Octavio; Mejias, Asuncion

Source: The Journal of pediatrics; Nov 2016

Abstract: To determine the differences in number of respiratory syncytial virus (RSV) hospitalizations and outcomes in infants 29(0/7)-34(6/7) weeks' gestational age (wGA) the season before (season 1 [S1]; 2013-2014) and after (season 2 [S2]; 2014-2015) implementation of the 2014 American Academy of Pediatrics revised guidance for palivizumab prophylaxis. Children <12 months of age hospitalized with RSV infection were identified by the International Classification of Diseases, Ninth Revision codes and virology reports. Clinical, outcome data, palivizumab eligibility, and hospital charges were compared among infants 29-34 wGA in S1 vs S2. Of 1063 RSV hospitalizations in infants <12 months old, 7.1% (34/482) in S1 and 9.8% (57/581) in S2 occurred in 29(0/7)-34(6/7) wGA infants. On the other hand, 29-34 wGA infants who were <6 months old constituted 3.5% (17/482) of RSV hospitalizations in S1 vs 7.1% (41/581) in S2 (P = .01). Among 29(0/7)-34(6/7) wGA healthy infants who were <3 months old, oxygen administration (40.0% vs 78.9%; P = .05), pediatric intensive care unit admission (30.0% vs 68.4%; P = .04), mechanical ventilation (10.0% vs 52.6%; P = .04), duration of hospitalization (1.8 vs 8.8 days; P = .04), and hospital charges ($19 686 vs $30 662; P = .03) significantly increased in S2 vs S1. No differences in morbidity were observed in premature infants who were 3 to <6 and 6 to <12 months between seasons. Palivizumab eligibility decreased from 32.3% in S1 to 1.8% in S2 (P < .001). One infant died in each season. In the year following implementation of the 2014 palivizumab prophylaxis guidance, there was an increase in RSV hospitalizations and associated morbidity among 29-34 wGA infants of younger chronological age.

Title: Vaccination strategies against respiratory syncytial virus.

Author(s): Yamin, Dan; Jones, Forrest K; DeVincenzo, John P; Gertler, Shai; Kobiler, Oren; Townsend, Jeffrey P; Galvani, Alison P

Source: Proceedings of the National Academy of Sciences of the United States of America; Nov 2016; vol. 113 (no. 46); p. 13239-13244

Abstract: Respiratory syncytial virus (RSV) is the most common cause of US infant hospitalization. Additionally, RSV is responsible for 10,000 deaths annually among the elderly across the United States, and accounts for nearly as many hospitalizations as influenza. Currently, several RSV vaccine candidates are under development to target different age groups. To evaluate the potential effectiveness of age-specific vaccination strategies in averting RSV incidence, we developed a transmission model that integrates data on daily infectious viral load and changes of behavior associated with RSV symptoms. Calibrating to RSV weekly incidence rates in Texas, California, Colorado, and Pennsylvania, we show that in all states considered, an infected child under 5 y of age is more than twice as likely as a person over 50 y of age to transmit the virus. Geographic variability in the effectiveness of a vaccination program across states arises from interplay between seasonality patterns, population demography, vaccination uptake, and vaccine mechanism of action. Regardless of these variabilities, our analysis showed that allocating vaccine to children under 5 y of age would be the most efficient strategy per dose to avert RSV in both children and adults. Furthermore, due to substantial indirect protection, the targeting of children is even predicted to reduce RSV in the elderly more than directly vaccinating the elderly themselves. Our results can help inform ongoing clinical trials and future recommendations on RSV vaccination.

Title: Characterizing the risk of respiratory syncytial virus in infants with older siblings: a population-based birth cohort study.

Author(s): Jacoby, P; Glass, K; Moore, H C

Source: Epidemiology and infection; Nov 2016 ; p. 1-6

Available in full text at Epidemiology and Infection - from ProQuest

Abstract: From a population-based birth cohort of 245 249 children born in Western Australia during 1996-2005, we used linkage of laboratory and birth record datasets to obtain data including all respiratory syncytial virus (RSV) detections during infancy from a subcohort of 87 981 singleton children born in the Perth metropolitan area from 2000 to 2004. Using log binomial regression, we found that the risk of infant RSV detection increases with the number of older siblings, with those having ⩾3 older siblings experiencing almost three times the risk (relative risk 2·83, 95% confidence interval 2·46-3·26) of firstborn children. We estimate that 45% of the RSV detections in our subcohort were attributable to infection from an older sibling. The sibling effect was significantly higher for those infants who were younger during the season of peak risk (winter) than those who were older. Although older siblings were present in our cohort, they had very few RSV detections which could be temporally linked to an infant's infection. We conclude that RSV infection in older children leads to less severe symptoms but is nevertheless an important source of infant infection. Our results lend support to a vaccination strategy which includes family members in order to provide maximum protection for newborn babies.

Title: Burden of Severe Respiratory Syncytial Virus Disease Among 33-35 Week Gestational Age Infants Born During Multiple Respiratory Syncytial Virus Seasons.

Author(s): Anderson, Evan J; Carbonell-Estrany, Xavier; Blanken, Maarten; Lanari, Marcello; Sheridan-Pereira, Margaret; Rodgers-Gray, Barry; Fullarton, John; Rouffiac, Elisabeth; Vo, Pamela; Notario, Gerard; Campbell, Fiona; Paes, Bosco

Source: The Pediatric infectious disease journal; Oct 2016

Abstract: Moderate-late preterm infants, 33-35 weeks' gestational age (wGA), are at increased risk for respiratory syncytial virus hospitalization (RSVH). To quantify the burden of RSVH in moderate-late preterm infants. A pooled analysis was conducted on RSVH from 7 prospective, observational studies in the Northern Hemisphere from 2000-2014. Infants' 33 -35 wGA without comorbidity born during the RSV season who did not receive RSV immunoprophylaxis were enrolled. Data for the first confirmed RSVH during the season (+1 month) were analyzed. Incidence and hospitalization rate/100 patient-seasons, intensive care unit (ICU) admission and length of stay (LOS), oxygen support, mechanical ventilation, and overall hospital LOS were assessed. The pooled analysis comprised 7,820 infants; 267 experienced a confirmed RSVH at a median age of 8.4 weeks. The crude pooled RSVH incidence rate was 3.41% and the rate/100 patient-seasons was 4.52. Median hospital LOS was 5.7 days. 22.2% of infants required ICU admission for a median LOS of 8.3 days. 70.4% received supplemental oxygen support for a median of 4.9 days, and 12.7% required mechanical ventilation for a median of 4.8 days. The burden of RSVH in moderate-late, 33-35 weeks' wGA preterm infants without comorbidities born during the viral season in Northern Hemisphere countries is substantial. Severe cases required prolonged and invasive supportive therapy.

Title: Respiratory syncytial virus hospitalization and mortality: Systematic review and meta-analysis.

Author(s): Stein, Renato T; Bont, Louis J; Zar, Heather; Polack, Fernando P; Park, Caroline; Claxton, Ami; Borok, Gerald; Butylkova, Yekaterina; Wegzyn, Colleen

Source: Pediatric pulmonology; Oct 2016

Abstract: Respiratory syncytial virus (RSV) is a major public health burden worldwide. We aimed to review the current literature on the incidence and mortality of severe RSV in children globally. Systematic literature review and meta-analysis of published data from 2000 onwards, reporting on burden of acute respiratory infection (ARI) due to RSV in children. Main outcomes were hospitalization for severe RSV-ARI and death. Five thousand two hundred and seventy-four references were identified. Fifty-five studies were included from 32 countries. The global RSV-ARI hospitalization estimates, reported per 1,000 children per year (95% Credible Interval (CrI), were 4.37 (2.98, 6.42) among children <5 years, 19.19 (15.04, 24.48) among children <1 year, 20.01 (9.65, 41.31) among children <6 months and 63.85 (37.52, 109.70) among premature children <1 year. The RSV-ARI global case-fatality estimates, reported per 1,000 children, (95% CrI) were 6.21 (2.64, 13.73) among children <5 years, 6.60 (1.85, 16.93) for children <1 year, and 1.04 (0.17, 12.06) among preterm children <1 year. A substantial proportion of RSV-associated morbidity occurs in the first year of life, especially in children born prematurely. These data affirm the importance of RSV disease in the causation of hospitalization and as a significant contributor to pediatric mortality and further demonstrate gestational age as a critical determinant of disease severity. An important limitation of case-fatality ratios is the absence of individual patient characteristics of non-surviving patients. Moreover, case-fatality ratios cannot be translated to population-based mortality.

Title: Clinical and Socioeconomic Burden of Respiratory Syncytial Virus Infection in Children.

Author(s): Heikkinen, Terho; Ojala, Emilia; Waris, Matti

Source: The Journal of infectious diseases; Oct 2016

Abstract: Vaccines and antivirals against respiratory syncytial virus (RSV) are being developed, but there are scarce data on the full impact of RSV infection on outpatient children. We analyzed the burden of RSV illness in a prospective cohort study of children aged ≤13 years during 2 consecutive respiratory seasons in Turku, Finland (2231 child-seasons of follow-up). We examined the children and obtained nasal swabs for the detection of RSV during each respiratory illness. The parents filled

out daily symptom diaries throughout the study. Of 6001 medically attended respiratory infections, 302 (5%) were caused by RSV. Per 1000 children, the average annual RSV infection incidence rates among children aged <3, 3-6, and 7-13 years were 275, 117, and 46 cases, respectively. In children aged <3 years, acute otitis media developed in 58%, and 66% of children in this age group received antibiotics. The mean duration of RSV illness was longest (13.0 days) and the rate of parental work absenteeism was highest (136 days per 100 children with RSV illness) in children aged <3 years. The burden of RSV is particularly great among outpatient children aged <3 years. Young children are an important target group for the development of RSV vaccines and antivirals.

Title: Performance evaluation of four rapid antigen tests for the detection of Respiratory syncytial virus.

Author(s): Jung, Bo Kyeung; Choi, Sung Hyuk; Lee, Jong Han; Lee, JungHwa; Lim, Chae Seung

Source: Journal of medical virology; Oct 2016; vol. 88 (no. 10); p. 1720-1724

Abstract: Rapid identification of Respiratory syncytial virus (RSV) is important in the management of infected patients. Rapid diagnostic tests (RDT) are widely used for this purpose. This study aimed to evaluate the clinical performance of four RSV antigen tests including the BinaxNow RSV Card test, SD Bioline RSV test, BD Veritor RSV test, and Humasis RSV antigen test in comparison with real-time RT-PCR as the reference method. Nasopharyngeal swabs were collected from 280 patients with symptoms of lower respiratory tract infection and stored at -80°C. All swabs were tested for RSV using four rapid antigen tests and real time RT-PCR. The sensitivity of the BinaxNow RSV Card test, SD Bioline RSV test, BD Veritor RSV test, and Humasis RSV Antigen tests were 62.5%, 61.3%, 65.0%, and 67.5% for RSV A, and 61.3%, 65.0%, 61.3%, and 67.5% for RSV B compared to real time RT-PCR, respectively. The specificity of BD Veritor RSV test was 95.8% and those of the other three RDTs was 100%. Commercial RSV antigen detection assays are useful tools for the rapid diagnosis of RSV infection. However, confirmatory testing is always recommended.

Title: A Randomized, Controlled, Observer-Blinded Phase 1 Study of the Safety and Immunogenicity of a Respiratory Syncytial Virus Vaccine With or Without Alum Adjuvant.

Author(s): Langley, Joanne M; Aggarwal, Naresh; Toma, Azhar; Halperin, Scott A; McNeil, Shelly A; Fissette, Laurence; Dewé, Walthere; Leyssen, Maarten; Toussaint, Jean-François; Dieussaert, Ilse

Source: The Journal of infectious diseases; Sep 2016

Abstract: Respiratory syncytial virus (RSV) is a leading cause of childhood bronchiolitis and pneumonia, particularly in early infancy. Immunization of pregnant women could boost preexisting immune responses, providing passive protection to newborns through placental transfer of anti-RSV antibody. In this first-in-humans clinical trial of a purified recombinant RSV protein F vaccine engineered to preferentially maintain prefusion conformation (RSV-PreF), 128 healthy men 18-44 years old were randomized to one dose of a RSV-PreF vaccine containing 10, 30, or 60 μg of RSV-PreF antigen, with or without alum adjuvant, or control, and followed for one year for safety and immunogenicity outcomes. Injection site pain was the most common adverse event, reported by up to 81.3% of participants. The highest RSV neutralizing antibody responses were in the 30 μg RSV-PreF/alum, 60 μg RSV-PreF/alum, and 60 μg RSV-PreF/nonadjuvant groups. Responses were evident on day 7, and 30 days after vaccination these participants had RSV-A neutralizing antibody titers of ≥1:512, and >70% had titers of 1:1024, with titers increasing by 3.2-4.9 fold. Responses remained high on day 60 but waned on days 180 and 360. The RSV-PreF vaccine elicited rapid RSV neutralizing antibody responses in healthy young men, with an acceptable adverse event profile.

Title: Development and clinical applications of novel antibodies for prevention and treatment of respiratory syncytial virus infection.

Author(s): Mejias, Asuncion; Garcia-Maurino, Cristina; Rodriguez-Fernandez, Rosa; Peeples, Mark E; Ramilo, Octavio

Source: Vaccine; Sep 2016

Available in full text at Vaccine - from ProQuest

Abstract: Respiratory syncytial virus (RSV) remains a significant cause of morbidity and mortality in infants and young children, immunocompromised patients and the elderly. Despite the high disease burden, an effective and safe vaccine is lacking, although several candidates are currently in development. Current treatment for RSV infection remains largely supportive and RSV-specific options for prophylaxis are limited to palivizumab. In the past few years, novel therapeutic options including nanobodies, polyclonal and monoclonal antibodies have emerged and there are several products in preclinical and Phase-I, -II or -III clinical trials. The major target for antiviral drug development is the surface fusion (F) glycoprotein, which is crucial for the infectivity and pathogenesis of the virus. Solving the structures of the two conformations of the RSV F protein, the prefusion and postfusion forms, has revolutionized RSV research. It is now known that prefusion F is highly superior in inducing neutralizing antibodies. In this section we will review the stages of development and availability of different antibodies directed against RSV for the prevention and also for treatment of acute RSV infections. Some of these newer anti-RSV agents have shown enhanced potency, are being explored through alternative routes of administration, have improved pharmacokinetic profiles with an extended half-life, and may reduce design and manufacturing costs. Management strategies will require targeting not only high-risk populations (including adults or immunocompromised patients), but also previously healthy children who, in fact, represent the majority of children hospitalized with RSV infection. Following treated patients longitudinally is essential for determining the impact of these strategies on the acute disease as well as their possible long-term benefits on lung morbidity.

Title: Defining the Epidemiology and Burden of Severe Respiratory Syncytial Virus Infection Among Infants and Children in Western Countries.

Author(s): Bont, Louis; Checchia, Paul A; Fauroux, Brigitte; Figueras-Aloy, Josep; Manzoni, Paolo; Paes, Bosco; Simões, Eric A F; Carbonell-Estrany, Xavier

Source: Infectious diseases and therapy; Sep 2016; vol. 5 (no. 3); p. 271-298

Abstract: The REGAL (RSV [respiratory syncytial virus] Evidence-a Geographical Archive of the Literature) series provides a comprehensive review of the published evidence in the field of RSV in Western countries over the last 20 years. This first of seven publications covers the epidemiology and burden of RSV infection. A systematic review was undertaken for articles published between Jan 1, 1995 and Dec 31, 2015 across PubMed, Embase, The Cochrane Library, and Clinicaltrials.gov. Studies reporting data for hospital visits/admissions for RSV infection among children (≤18 years of age), as well as studies reporting RSV-associated morbidity, mortality, and risk factors were included. Study quality and strength of evidence (SOE) were graded using recognized criteria. 2315 studies were identified of which 98 were included. RSV was associated with 12-63% of all acute respiratory infections (ARIs) and 19-81% of all viral ARIs causing hospitalizations in children (high SOE). Annual RSV hospitalization (RSVH) rates increased with decreasing age and varied by a factor of 2-3 across seasons (high SOE). Studies were conflicting on whether the incidence of RSVH has increased, decreased, or remained stable over the last 20 years (moderate SOE). Length of hospital stay ranged from 2 to 11 days, with 2-12% of cases requiring intensive care unit admission (moderate SOE). Case-fatality rates were <0.5% (moderate SOE). Risk factors associated with RSVH included: male sex; age <6 months; birth during the first half of the RSV season; crowding/siblings; and day-care exposure

(high SOE). RSV infection remains a major burden on Western healthcare systems and has been associated with significant morbidity. Further studies focusing on the epidemiology of RSV infection (particularly in the outpatient setting), the impact of co-infection, better estimates of case-fatality rates and associated risk factors (all currently moderate/low SOE) are needed to determine the true burden of disease.

Flu

Title: Influenza vaccine as a coronary intervention for prevention of myocardial infarction.

Author(s): MacIntyre, C Raina; Mahimbo, Abela; Moa, Aye M; Barnes, Michelle

Source: Heart (British Cardiac Society); Dec 2016; vol. 102 (no. 24); p. 1953-1956

Available in full text at Heart - from Highwire Press

Abstract: Cardiovascular disease (CVD) is the leading cause of morbidity and mortality globally. Influenza is one of the leading infectious causes of morbidity and mortality globally, and evidence is accumulating that it can precipitate acute myocardial infarction (AMI). This is thought to be due to a range of factors including inflammatory release of cytokines, disruption of atherosclerotic plaques and thrombogenesis, which may acutely occlude a coronary artery. There is a large body of observational and clinical trial evidence that shows that influenza vaccine protects against AMI. Estimates of the efficacy of influenza vaccine in preventing AMI range from 15% to 45%. This is a similar range of efficacy compared with the accepted routine coronary prevention measures such as smoking cessation (32-43%), statins (19-30%) and antihypertensive therapy (17-25%). Influenza vaccine should be considered as an integral part of CVD management and prevention. While it is recommended in many guidelines for patients with CVD, rates of vaccination in risk groups aged <65 years are very low, in the range of 30%. The incorporation of vaccination into routine CVD prevention in patient care requires a clinical practice paradigm change.

Title: A Systematic Review of the Comparative Epidemiology of Avian and Human Influenza A H5N1 and H7N9 - Lessons and Unanswered Questions.

Author(s): Bui, C; Bethmont, A; Chughtai, A A; Gardner, L; Sarkar, S; Hassan, S; Seale, H; MacIntyre, C R

Source: Transboundary and emerging diseases; Dec 2016; vol. 63 (no. 6); p. 602-620

Abstract: The aim of this work was to explore the comparative epidemiology of influenza viruses, H5N1 and H7N9, in both bird and human populations. Specifically, the article examines similarities and differences between the two viruses in their genetic characteristics, distribution patterns in human and bird populations and postulated mechanisms of global spread. In summary, H5N1 is pathogenic in birds, while H7N9 is not. Yet both have caused sporadic human cases, without evidence of sustained, human-to-human spread. The number of H7N9 human cases in the first year following its emergence far exceeded that of H5N1 over the same time frame. Despite the higher incidence of H7N9, the spatial distribution of H5N1 within a comparable time frame is considerably greater than that of H7N9, both within China and globally. The pattern of spread of H5N1 in humans and birds around the world is consistent with spread through wild bird migration and poultry trade activities. In contrast, human cases of H7N9 and isolations of H7N9 in birds and the environment have largely occurred in a number of contiguous provinces in south-eastern China. Although rates of contact with birds appear to be similar in H5N1 and H7N9 cases, there is a predominance of incidental contact reported for H7N9 as opposed to close, high-risk contact for H5N1. Despite the high number of human cases of H7N9 and the assumed transmission being from birds, the corresponding level of H7N9 virus in birds in surveillance studies has been low, particularly in poultry

farms. H7N9 viruses are also diversifying at a much greater rate than H5N1 viruses. Analyses of certain H7N9 strains demonstrate similarities with engineered transmissible H5N1 viruses which make it more adaptable to the human respiratory tract. These differences in the human and bird epidemiology of H5N1 and H7N9 raise unanswered questions as to how H7N9 has spread, which should be investigated further.

Title: Bias in the measure of the effectiveness of seasonal influenza vaccination among diabetics.

Author(s): Casanova, Ludovic; Gobin, Nirvina; Villani, Patrick; Verger, Pierre

Source: Primary care diabetes; Dec 2016; vol. 10 (no. 6); p. 398-406

Abstract: The influenza virus is an important cause of morbidity and mortality for diabetics. The seasonal influenza vaccine's immunologic effectiveness is proven within the type 1 and type 2 diabetic populations, but the level of evidence is low. This article presents a systematic review for the bias in the measure of the effectiveness of seasonal influenza vaccination among diabetics. Using systematic review methods, we searched three electronic databases for published literature (MEDLINE, EMBASE and the Cochrane Library) and two grey literature (SIGLE and NHS EED) databases, to identify studies published between 1997 and 2013, examining the effect of seasonal influenza vaccination, among diabetics, on any measure for influenza morbidity or mortality. 725 records were identified from the three databases and screening, short-listing was undertaken independently by two reviewers. After de-duplication, all records were screened by title and then abstract, and 34 short-listed records were reviewed in full, with 7 studies included: 4 cohort studies and 3 case-control studies, conducted in 7 countries. The most common outcome of interest in studies (n=4) was all-cause mortality among elderly diabetics (>65 years), with individual studies reporting reductions in risk of between 33% [95%CI: 4%-54%] and 68% [95%CI: 58%-75%]. We found only two studies for working-age adult diabetics: one reporting that vaccination prevented hospitalizations due to pneumonia or influenza (vaccine effectiveness [VE] 43%, [95%CI: 28%-54%]) and all-cause hospitalizations (VE: 28% [95%CI: 24%-32%]); and, another reporting no significant decrease in all-cause mortality for working-age adult diabetics. We have identified three major biases: the use of indirect health outcomes, a risk of selection bias (health-seeking bias), and no adjustment for participant pneumococcal vaccination status. The most recent included article finds that morbimortality is still lower during off-season influenza in both vaccinated and non-vaccinated diabetics, indicating important residual confounding. To date, the strength of evidence supporting the routine use of seasonal influenza vaccination is low for diabetics older than 65, and very low for working-age diabetics.

Title: Maternal Influenza Immunization and Adverse Birth Outcomes: Using Data and Practice to Inform Theory and Research Design.

Author(s): Phadke, Varun K; Steinhoff, Mark C; Omer, Saad B; MacDonald, Noni E

Source: American journal of epidemiology; Dec 2016; vol. 184 (no. 11); p. 789-792

Abstract: Maternal influenza immunization can reduce influenza-attributable morbidity and mortality among pregnant women and infants who are too young to be vaccinated. Data from empirical studies also support the hypothesis that immunization can protect the fetus against adverse outcomes if the mother is exposed to influenza. In their theoretical analysis in the Journal, Hutcheon et al. (Am J Epidemiol 2016;184(3):227-232) critiqued the existing evidence of the fetal benefits of maternal influenza immunization by calculating the sample sizes needed to demonstrate hypothetical reductions in risk and concluded that the benefits observed in empirical studies are likely implausible. However, in their analysis, they did not take into account multiple fundamental characteristics of influenza epidemiology, including the time-variable effects of influenza illness and

vaccination during pregnancy, or well-known differences in disease epidemiology between seasons, populations, and geographic regions. Although these and other factors might affect the magnitude of fetal benefit conferred by maternal influenza immunization, studies in which investigators have accounted for influenza circulation have demonstrated a consistent protective effect against a variety of adverse birth outcomes; those studies include the only randomized controlled trial designed a priori and adequately powered to do so. Only a comprehensive and nuanced assessment of the evidence base will allow for effective translation of these data into a global immunization policy

Title: Influenza Vaccine Research funded by the European Commission FP7-Health-2013-Innovation-1 project.

Author(s): Liu, Heng; Frijlink, Henderik W; Huckriede, Anke; van Doorn, Eva; Schmidt, Ed; Leroy, Odile; Rimmelzwaan, Guus; McCullough, Keneth; Whelan, Mike; Hak, Eelko

Source: Vaccine; Nov 2016; vol. 34 (no. 48); p. 5845-5854

Abstract: Due to influenza viruses continuously displaying antigenic variation, current seasonal influenza vaccines must be updated annually to include the latest predicted strains. Despite all the efforts put into vaccine strain selection, vaccine production, testing, and administration, the protective efficacy of seasonal influenza vaccines is greatly reduced when predicted vaccine strains antigenically mismatch with the actual circulating strains. Moreover, preparing for a pandemic outbreak is a challenge, because it is unpredictable which strain will cause the next pandemic. The European Commission has funded five consortia on influenza vaccine development under the Seventh Framework Programme for Research and Technological Development (FP7) in 2013. The call of the EU aimed at developing broadly protective influenza vaccines. Here we review the scientific strategies used by the different consortia with respect to antigen selection, vaccine delivery system, and formulation. The issues related to the development of novel influenza vaccines are discussed.

Title: The serological evidence for maternal influenza as risk factor for psychosis in offspring is insufficient: critical review and meta-analysis.

Author(s): Selten, Jean-Paul; Termorshuizen, Fabian

Source: Schizophrenia research; Nov 2016

Abstract: Maternal influenza during pregnancy has been suggested to increase the psychosis risk for the offspring. This hypothesis has been tested using "ecological" studies, which examined the risk for individuals born after epidemics, and "serological" studies, based on serological evidence. A study of the latter type obtained an increased schizophrenia risk for individuals exposed during the first trimester. A second study found a relationship between influenza at any time during gestation and risk for bipolar disorder with psychotic features. The aims of this paper are to assess the validity of the serological studies and to evaluate the combined results of ecological and serological investigations using meta-analysis. The serological studies turned out to be of limited validity, because they utilized a single serum specimen. Since influenza antibodies can remain positive for years after infection, many mothers of cases may have been infected before pregnancy. For an adequate timing of exposure one needs an acute and a convalescent specimen, obtained 10-20days later. Meta-analysis with respect to schizophrenia: we pooled the results of the single serological investigation and 8 ecological studies related to the 1957 pandemic (with negative results) and found that the first investigation carried hardly any weight. Bipolar disorder: we pooled the results of the serological investigation and three other studies and obtained a mean, weighted odds ratio of 1.34 (95% CI 0.78-2.29) for individuals possibly exposed during prenatal life. The evidence for gestational influenza as psychosis risk factor is insufficient

Title: A systematic review of rapid diagnostic tests for influenza: considerations for the community pharmacist.

Author(s): Koski, Renee R; Klepser, Michael E

Source: Journal of the American Pharmacists Association : JAPhA; Nov 2016

Abstract: Rapid influenza diagnostic tests (RIDTs) have a potential role in community pharmacy to optimize influenza infection management. The U.S. Food and Drug Administration (FDA) proposed changes to the classification of RIDTs may affect their use in community pharmacy. We reviewed the performance and features of RIDTs likely to meet FDA-proposed reclassification requirements. PubMed and Medline database searches were performed using the terms "Sofia Influenza A and B Fluorescent Immunoassay," "BD Veritor System for Rapid Detection of Flu A and B", and "Alere i Influenza A and B." All studies involving the use of the BD Veritor System for Rapid Detection of Flu A+B (BD Veritor, Sparks, MD), the Sofia Influenza A+B Fluorescent Immunoassay (Sofia FIA, San Diego, CA), and Alere i Influenza A&B (Alere i, Scarborough, ME) containing sensitivities and specificities with confidence intervals were considered for inclusion. Patient demographics, specimen type collected, setting, sensitivities, specificities, true positives, true negatives, false positives, false negatives, positive predictive values, and negative predictive values were extracted. Of the 22 studies identified, 14 contained sufficient data to incorporate into this review. One study contained comparative data for BD Veritor and Sofia FIA, 1 study compared Alere i and Sofia FIA, 2 studies specifically included BD Veritor, 5 studies specifically included Sofia FIA, and 5 studies specifically included Alere i. Performance characteristics among the RIDTs varied; however, all 3 RIDTs consistently provided sensitivities and specificities >70%. BD Veritor, Sofia FIA, and Alere i RIDTs performed well compared with reverse transcriptase-polymerase chain reaction or viral culture. These RIDTs are likely to satisfy the proposed reclassification requirements. Pharmacists are considered the most accessible health care providers, and implementing RIDT services in community pharmacy may benefit health systems.

Title: Pattern recognition receptor immunomodulation of innate immunity as a strategy to limit the impact of influenza virus.

Author(s): Pizzolla, Angela; Smith, Jeffery M; Brooks, Andrew G; Reading, Patrick C

Source: Journal of leukocyte biology; Nov 2016

Abstract: Influenza remains a major global health issue and the effectiveness of current vaccines and antiviral drugs is limited by the continual evolution of influenza viruses. Therefore, identifying novel prophylactic or therapeutic treatments that induce appropriate innate immune responses to protect against influenza infection would represent an important advance in efforts to limit the impact of influenza. Cellular pattern recognition receptors (PRRs) recognize conserved structures expressed by pathogens to trigger intracellular signaling cascades, promoting expression of proinflammatory molecules and innate immunity. Therefore, a number of approaches have been developed to target specific PRRs in an effort to stimulate innate immunity and reduce disease in a variety of settings, including during influenza infections. Herein, we discuss progress in immunomodulation strategies designed to target cell-associated PRRs of the innate immune system, thereby, modifying innate responses to IAV infection and/or augmenting immune responses to influenza vaccines.

Title: Influenza pathogenicity during pregnancy in women and animal models.

Author(s): van Riel, Debby; Mittrücker, Hans-Willi; Engels, Geraldine; Klingel, Karin; Markert, Udo R; Gabriel, Gülsah

Source: Seminars in immunopathology; Nov 2016; vol. 38 (no. 6); p. 719-726

Abstract: Pregnant women are at the highest risk to develop severe and even fatal influenza. The high vulnerability of women against influenza A virus infections during pregnancy was repeatedly highlighted during influenza pandemics including the pandemic of this century. In 2009, mortality rates were particularly high among otherwise healthy pregnant women. However, our current understanding of the molecular mechanisms involved in severe disease development during pregnancy is still very limited. In this review, we summarize the knowledge on the clinical observations in influenza A virus-infected pregnant women. In addition, knowledge obtained from few existing experimental infections in pregnant animal models is discussed. Since clinical data do not provide in-depth information on the pathogenesis of severe influenza during pregnancy, adequate animal models are urgently required that mimic clinical findings. Studies in pregnant animal models will allow the dissection of involved molecular disease pathways that are key to improve patient management and care.

Title: A systematic review of factors affecting intended and actual adherence with antiviral medication as treatment or prophylaxis in seasonal and pandemic flu.

Author(s): Smith, Louise E; D'Antoni, Donatella; Jain, Vageesh; Pearce, Julia M; Weinman, John; Rubin, G James

Source: Influenza and other respiratory viruses; Nov 2016; vol. 10 (no. 6); p. 462-478

Abstract: The aim of this review was to identify factors predicting actual or intended adherence to antivirals as treatment or prophylaxis for influenza. Literature from inception to March 2015 was systematically reviewed to find studies reporting predictors of adherence to antivirals and self-reported reasons for non-adherence to antivirals. Twenty-six studies were included in the review; twenty identified through the literature search and six through other means. Of these studies, 18 assessed predictors of actual adherence to antivirals, whereas eight assessed predictors of intended adherence. The most commonly found predictor of, and self-reported reason for, non-adherence was the occurrence of side effects. Other predictors include perceptions surrounding self-efficacy, response efficacy and perceived personal consequences as well as social influences of others' experiences of taking antivirals. Predictors identified in this review can be used to help inform communications to increase adherence to antivirals in both seasonal and pandemic influenza

Title: Effect of two-step hygiene management on the prevention of nosocomial influenza in a season with high influenza activity

Author(s): Ambrosch, A.; Rockmann, F.

Source: Journal of Hospital Infection; Oct 2016; vol. 94 (no. 2); p. 143-149

Abstract: Background: Rapid identification of patients infected with influenza virus, precise case definition and strict hygiene measures are important for the prevention of nosocomial transmission. Aim: To prove the usefulness of a case definition for rapid identification of patients with influenza and to investigate the effect of two-step hygiene management, including the continuous use of surgical masks by hospital staff, on the rate of nosocomial infections. Methods: All patients hospitalized between January and March 2015 with suspected influenza were enrolled. Real-time polymerase chain reaction testing for influenza was performed. Infected patients were managed according to the national hygiene guidelines, including the use of surgical masks by hospital staff during close contact with infected patients. When influenza activity increased, the continuous use of surgical masks by hospital staff was implemented as an add-on measure. Findings: Most patients enrolled in this study were elderly (N=212, mean age 75 years). Frequency of cough was the only clinical parameter of respiratory infection that differed between influenza-negative and influenza-positive patients. Compared with the targeted use of surgical masks during close contact with

infected patients, the continuous use of surgical masks for the entire working shift resulted in a reduction of nosocomial infections from 31% to 16%, respectively (P<0.01). Conclusion: Discrimination between influenza A and other respiratory infections in elderly hospitalized patients was not possible based on clinical characteristics. With regard to hygiene management, the continuous use of surgical masks by hospital staff seems to be effective for the prevention of nosocomial infections.

Title: Increasing the coverage of influenza vaccination in healthcare workers: review of challenges and solutions

Author(s): To, K.W.; Lai, A.; Lee, K.C.K.; Koh, D.; Lee, S.S.

Source: Journal of Hospital Infection; Oct 2016; vol. 94 (no. 2); p. 133-142

Abstract: Seasonal influenza vaccine uptake rate of healthcare workers (HCWs) varies widely from 90% worldwide. Perception of vaccine efficacy and side-effects are conventional factors affecting the uptake rates. These factors may operate on a personal and social level, impacting the attitudes and behaviours of HCWs. Vaccination rates were also under the influence of the occurrence of other non-seasonal influenza pandemics such as avian influenza. Different strategies have been implemented to improve vaccine uptake, with important ones including the enforcement of the local authority's recommendations, promulgation of practice guidelines, and mandatory vaccination polices. Practised in some regions in North America, mandatory policies have led to higher vaccination rate, but are not problem-free. The effects of conventional educational programmes and campaigns are in general of modest impact only. Availability of convenient vaccination facilities, such as mobile vaccination cart, and role models of senior HCWs receiving vaccination are among some strategies which have been observed to improve vaccination uptake rate. A multi-faceted approach is thus necessary to persuade HCWs to participate in a vaccination programme, especially in areas with low uptake rate.

Title: Nurses' knowledge, attitudes and practices regarding influenza vaccination: an integrative review

Author(s): Smith, Sarah; Sim, Jenny; Halcomb, Elizabeth

Source: Journal of Clinical Nursing; Oct 2016; vol. 25 (no. 19-20); p. 2730-2744

Abstract: Aims and objectives To critically analyse the literature describing nurses' knowledge, attitudes and practices regarding influenza vaccination. Background Influenza is a serious illness that has significant impacts on productivity, health outcomes and healthcare costs. Despite the recommendations for nurses to be vaccinated annually against influenza, the vaccination rates remain suboptimal. Design Integrative literature review. Methods An integrative review was conducted as described by Whittemore and Knafl (2005). A search of CINAHL, Cochrane Library, ProQuest Central, ClinicalKey, ScienceDirect, Wiley Online Library, and Informit was undertaken to identify relevant papers. Given the heterogeneity of included studies, a narrative approach was used to analyse the data. Results There was limited research available on this topic area, with only 10 papers identified as meeting the inclusion criteria. Five themes were identified: the relationship between knowledge and influenza vaccination, perception of risk, motivators for influenza vaccination, barriers to influenza vaccination and impact of demographics on vaccination. Conclusions Despite the evidence for the protective effects of influenza vaccination, rates of vaccination among nurses remain sub-optimal. Nurses' influenza vaccination practices likely relate to their level of knowledge and perception of risk; the greater nurses' knowledge regarding influenza and influenza vaccination the higher their perception of risk and the more likely they are to be vaccinated. This also translates to the advice that they give patients with vaccinated nurses more

inclined to recommend vaccination than those unvaccinated. Relevance to clinical practice The practices of nurses related to influenza vaccination may translate to the advice that they give their patients. Understanding the knowledge levels, practices and attitudes of nurses can assist in developing strategies to enhance education of nurses.

Title: Passive immunization for influenza through antibody therapies, a review of the pipeline, challenges and potential applications.

Author(s): Sparrow, Erin; Friede, Martin; Sheikh, Mohamud; Torvaldsen, Siranda; Newall, Anthony T

Source: Vaccine; Oct 2016; vol. 34 (no. 45); p. 5442-5448

Available in full text at Vaccine - from ProQuest

Abstract: The Global Action Plan for influenza vaccines (GAP) aims to increase the production capacity of vaccines so that in the event of a pandemic there is an adequate supply to meet global needs. However, it has been estimated that even in the best case scenario there would be a considerable delay of at least five to six months for the first supplies of vaccine to become available after the isolation of the strain and availability of the candidate vaccine virus to vaccine manufacturers. By this time, the virus is likely to have already infected millions of people worldwide, causing significant mortality, morbidity and economic loss. Passive immunization through broadly neutralizing antibodies which bind to multiple, structurally diverse strains of influenza could be a promising solution to address the immediate health threat of an influenza pandemic while vaccines are being developed. These products may also have a role in seasonal influenza as an alternative to other options such as antivirals for the treatment of severe acute respiratory illness due to influenza. This article provides an overview of the current clinical pipeline of anti-influenza antibodies and discusses potential uses and the challenges to product development.

Title: Review of prescribing information for influenza vaccines for pregnant and lactating women.

Author(s): Proveaux, Tina; Lambach, Philipp; Ortiz, Justin R; Hombach, Joachim; Halsey, Neal A

Source: Vaccine; Oct 2016; vol. 34 (no. 45); p. 5406-5409

Available in full text at Vaccine - from ProQuest

Abstract: Information provided by most influenza vaccine manufacturers do not reflect the recommendations of WHO and/or national public health advisory groups with regard to the use of influenza vaccines in pregnant or lactating women. The majority of vaccines contain precautionary language which could discourage use in pregnant women and some include stronger language discouraging or contradicting use in pregnant or lactating women. Regulators and manufacturers should regularly assess the language of pregnancy and lactation sections in product information for vaccines and include information from national public health advisory groups regarding use by pregnant or lactating women and data from relevant studies

Title: **A global review of national influenza immunization policies: Analysis of the 2014 WHO/UNICEF Joint Reporting Form on immunization.**

Author(s): Ortiz, Justin R; Perut, Marc; Dumolard, Laure; Wijesinghe, Pushpa Ranjan; Jorgensen, Pernille; Ropero, Alba Maria; Danovaro-Holliday, M Carolina; Heffelfinger, James D; Tevi-Benissan, Carol; Teleb, Nadia A; Lambach, Philipp; Hombach, Joachim

Source: Vaccine; Oct 2016; vol. 34 (no. 45); p. 5400-5405

Available in full text at Vaccine - from ProQuest

Abstract: The WHO recommends annual influenza vaccination to prevent influenza illness in high-risk groups. Little is known about national influenza immunization policies globally. The 2014 WHO/UNICEF Joint Reporting Form (JRF) on Immunization was adapted to capture data on influenza immunization policies. We combined this dataset with additional JRF information on new vaccine introductions and strength of immunization programmes, as well as publicly available data on country economic status. Data from countries that did not complete the JRF were sought through additional sources. We described data on country influenza immunization policies and used bivariate analyses to identify factors associated with having such policies. Of 194 WHO Member States, 115 (59%) reported having a national influenza immunization policy in 2014. Among countries with a national policy, programmes target specific WHO-defined risk groups, including pregnant women (42%), young children (28%), adults with chronic illnesses (46%), the elderly (45%), and health care workers (47%). The Americas, Europe, and Western Pacific were the WHO regions that had the highest percentages of countries reporting that they had national influenza immunization policies. Compared to countries without policies, countries with policies were significantly more likely to have the following characteristics: to be high or upper middle income ($p<0.0001$); to have introduced birth dose hepatitis B virus vaccine ($p<0.0001$), pneumococcal conjugate vaccine ($p=0.032$), or human papilloma virus vaccine ($p=0.002$); to have achieved global goals for diphtheria-tetanus-pertussis vaccine coverage ($p<0.0001$); and to have a functioning National Immunization Technical Advisory Group ($p<0.0001$). The 2014 revision of the JRF permitted a global assessment of national influenza immunization policies. The 59% of countries reporting that they had policies are wealthier, use more new or under-utilized vaccines, and have stronger immunization systems. Addressing disparities in public health resources and strengthening immunization systems may facilitate influenza vaccine introduction and use.

Title: The inflammatory response triggered by Influenza virus: a two edged sword.

Author(s): Tavares, Luciana P; Teixeira, Mauro M; Garcia, Cristiana C

Source: Inflammation research : official journal of the European Histamine Research Society ... [et al.]; Oct 2016

Abstract: Influenza A virus (IAV) is a relevant respiratory tract pathogen leading to a great number of deaths and hospitalizations worldwide. Secondary bacterial infections are a very common cause of IAV associated morbidity and mortality. The robust inflammatory response that follows infection is important for the control of virus proliferation but is also associated with lung damage, morbidity and death. The role of the different components of immune response underlying protection or disease during IAV infection is not completely elucidated. Overall, in the context of IAV infection, inflammation is a 'double edge sword' necessary to control infection but causing disease. Therefore, a growing number of studies suggest that immunomodulatory strategies may improve disease outcome without affecting the ability of the host to deal with infection. This review summarizes recent aspects of the inflammatory responses triggered by IAV that are preferentially involved in causing severe pulmonary disease and the anti-inflammatory strategies that have been suggested to treat influenza induced immunopathology.

Title: Benefits of pharmacist-led flu vaccination services in community pharmacy.

Author(s): Kirkdale, C L; Nebout, G; Megerlin, F; Thornley, T

Source: Annales pharmaceutiques francaises; Oct 2016

Abstract: Seasonal influenza is a major cause of excess winter deaths and increased hospital admissions. There is a high level of economic burden associated with the infection. Although vaccination targets have been set to tackle this international issue, many countries struggle to reach

these coverage targets for their at-risk populations using traditional delivery methods. Traditional providers include family doctors and nurses; however, pharmacist-led influenza vaccination has become a more commonly utilised aid to support vaccination targets. Community pharmacies are convenient and widely accessible and evaluations consistently demonstrate that patients are satisfied with pharmacist-led vaccinations. Allowing community pharmacists to administer influenza vaccination as an alternative option for delivery helps to increase the coverage rate of vaccination. In addition, commissioning community pharmacists to provide this service has been shown to contribute to achieving targets for those at-risk. Pharmacist-led influenza vaccination services can create value for payors and reduce pressure on health systems. This review aims to demonstrate the success of pharmacy-led influenza vaccinations, and the impact it has had in driving up immunisation rates within other countries. Experiences of countries such as England, Portugal and the United States provide evidence to demonstrate the benefit to both the patient and the health system.

Title: Implementation of flu vaccination in community pharmacies: Understanding the barriers and enablers.

Author(s): Kirkdale, C L; Nebout, G; Taitel, M; Rubin, J; Jacinto, I; Horta, R; Megerlin, F; Thornley, T

Source: Annales pharmaceutiques francaises; Oct 2016

Abstract: Improving influenza vaccination coverage has been, and still remains a challenge internationally. There are now many examples where countries have pursued a pharmacist-led influenza vaccination service in order to enhance vaccination coverage of at-risk populations. England, Portugal and the United States are successful examples where their experience implementing this service can now be explored retrospectively and learnt from. This review aims to provide evidence to help overcome barriers to commissioning and implementation of such services in countries new to the experience. Implementation is influenced by differing regulatory frameworks underpinning the provision of pharmacist-led influenza vaccination, methods of remuneration, training, and operating procedures. Practical aspects such as the facilities required, how patient records are maintained and how patients and other healthcare professionals are engaged also have an impact. These examples illustrate how community pharmacists can be trained to deliver influenza vaccinations safely, and coupled with their accessibility and convenience, can provide a complementary service to that already provided by family doctors and nurses to deliver influenza vaccinations for the benefit of patients.

Title: Nurses' knowledge, attitudes and practices regarding influenza vaccination: an integrative review.

Author(s): Smith, Sarah; Sim, Jenny; Halcomb, Elizabeth

Source: Journal of clinical nursing; Oct 2016; vol. 25 (no. 19-20); p. 2730-2744

Abstract: To critically analyse the literature describing nurses' knowledge, attitudes and practices regarding influenza vaccination. Influenza is a serious illness that has significant impacts on productivity, health outcomes and healthcare costs. Despite the recommendations for nurses to be vaccinated annually against influenza, the vaccination rates remain suboptimal. Integrative literature review. An integrative review was conducted as described by Whittemore and Knafl (2005). A search of CINAHL, Cochrane Library, ProQuest Central, ClinicalKey, ScienceDirect, Wiley Online Library, and Informit was undertaken to identify relevant papers. Given the heterogeneity of included studies, a narrative approach was used to analyse the data. There was limited research available on this topic area, with only 10 papers identified as meeting the inclusion criteria. Five themes were identified: the relationship between knowledge and influenza vaccination, perception of risk, motivators for influenza vaccination, barriers to influenza vaccination and impact of demographics on vaccination.

Despite the evidence for the protective effects of influenza vaccination, rates of vaccination among nurses remain sub-optimal. Nurses' influenza vaccination practices likely relate to their level of knowledge and perception of risk; the greater nurses' knowledge regarding influenza and influenza vaccination the higher their perception of risk and the more likely they are to be vaccinated. This also translates to the advice that they give patients with vaccinated nurses more inclined to recommend vaccination than those unvaccinated. The practices of nurses related to influenza vaccination may translate to the advice that they give their patients. Understanding the knowledge levels, practices and attitudes of nurses can assist in developing strategies to enhance education of nurses.

Title: Australian general practice nurse's knowledge, attitudes and practices regarding influenza vaccination: a cross-sectional survey

Author(s): Smith, Sarah; Sim, Jenny; Halcomb, Elizabeth

Source: Journal of Clinical Nursing; Sep 2016; vol. 25 (no. 17-18); p. 2502-2510

Abstract: Aims and objectives: The aim of this study was to examine the knowledge, attitudes and practices of Australian general practice nurses (GPNs) regarding influenza vaccination. Background: Despite the evidence for the benefits of influenza vaccination, vaccination rates remain sub-optimal. The knowledge, attitudes and practices of nurses both affects vaccination rates and the advice given to consumers. Given their significant role in opportunistic and planned vaccinations, GPNs are in an optimal position to positively influence vaccination rates. Design: A descriptive cross-sectional survey was used. Methods: GPNs were recruited by email to complete an online survey. The survey tool comprised the King's College Nurses' Influenza Vaccination Questionnaire and adapted demographic items. Data analysis used descriptive and inferential statistics. Open-ended questions were analysed using thematic analysis. Results: Most of the 85 respondents had received the seasonal influenza vaccination in the last year (n = 67; 78·8%); fewer received the H1N1 vaccination (n = 54; 63·5%). Intention to receive vaccination was affected by previous vaccination. Those who had received the seasonal influenza vaccine in the last year had a higher total knowledge score. The seasonal and total influenza knowledge score was high, with lower scores on the H1N1 sub-scale. A positive correlation was identified between influenza knowledge and risk perception. Conclusions: This study highlighted the high level of knowledge amongst GPNs related to seasonal influenza, whilst identifying a knowledge deficit around the H1N1 items. It demonstrated that GPN's knowledge of seasonal influenza was related to vaccination status and risk perception. Further research is required to explore how this translates into the advice GPNs give to consumers. Relevance to clinical practice: Influenza vaccination should be considered as a key topic for GPNs ongoing professional development. The evidence for links between education and vaccination uptake should encourage employers to facilitate opportunities for this training. Future efforts to increase vaccination uptake in nurses should promote the benefits of vaccination in protecting the individual rather than as a professional responsibility.

Title: The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis.

Author(s): Klein, Eili Y; Monteforte, Bradley; Gupta, Alisha; Jiang, Wendi; May, Larissa; Hsieh, Yu-Hsiang; Dugas, Andrea

Source: Influenza and other respiratory viruses; Sep 2016; vol. 10 (no. 5); p. 394-403

Abstract: Coinfecting bacterial pathogens are a major cause of morbidity and mortality in influenza. However, there remains a paucity of literature on the magnitude of coinfection in influenza patients. A systematic search of MeSH, Cochrane Library, Web of Science, SCOPUS, EMBASE, and PubMed was performed. Studies of humans in which all individuals had laboratory confirmed influenza, and all

individuals were tested for an array of common bacterial species, met inclusion criteria. Twenty-seven studies including 3215 participants met all inclusion criteria. Common etiologies were defined from a subset of eight articles. There was high heterogeneity in the results (I(2) = 95%), with reported coinfection rates ranging from 2% to 65%. Although only a subset of papers were responsible for observed heterogeneity, subanalyses and meta-regression analysis found no study characteristic that was significantly associated with coinfection. The most common coinfecting species were Streptococcus pneumoniae and Staphylococcus aureus, which accounted for 35% (95% CI, 14%-56%) and 28% (95% CI, 16%-40%) of infections, respectively; a wide range of other pathogens caused the remaining infections. An assessment of bias suggested that lack of small-study publications may have biased the results. The frequency of coinfection in the published studies included in this review suggests that although providers should consider possible bacterial coinfection in all patients hospitalized with influenza, they should not assume all patients are coinfected and be sure to properly treat underlying viral processes. Further, high heterogeneity suggests additional large-scale studies are needed to better understand the etiology of influenza bacterial coinfection.

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Journal of Infection Prevention

November 2016, Volume 17, Issue 6

http://bji.sagepub.com/content/17/6.toc

Public Health England (Portal)

https://www.gov.uk/government/organisations/public-health-england

Exercise: Relative Risk

The relative risk is the ratio of probability of an event (a specified outcome) occurring in one group (i.e. those exposed to a particular intervention) compared to those in another group (i.e. those not exposed – a control group).

The relative risk can be interpreted using the following chart. First, you must determine whether the event (the outcome measure) is adverse or beneficial.

Relative Risk	Adverse outcome (e.g. death)	Beneficial outcome (e.g. recovery of limb function)
<1	Intervention better than control	Intervention worse than control
1	Intervention no better or worse than control	Intervention no better or worse than control
>1	Intervention worse than control	Intervention better than control

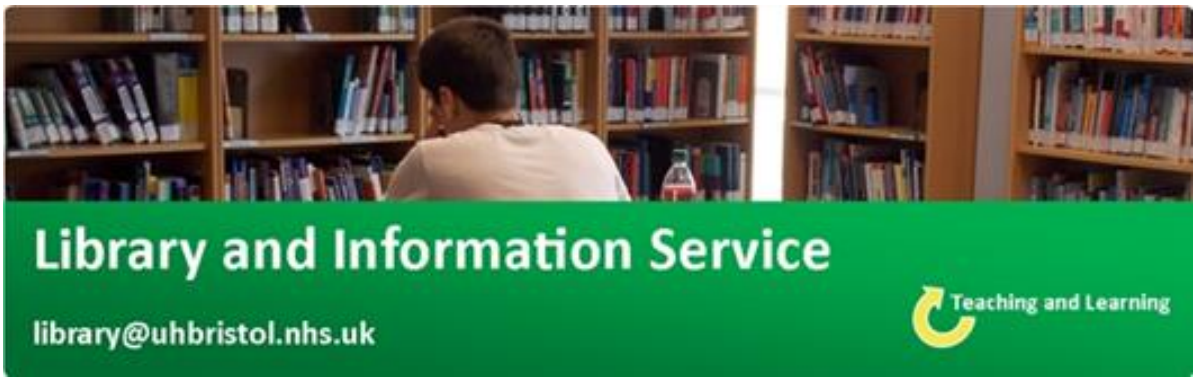
Have a go at interpreting the relative risks for these three studies using the chart above. Is the intervention better or worse than the control?

	Intervention	Population	Outcome measure (think: adverse or beneficial?)	Relative Risk
Study 1	Drug X	Adults at risk of a heart attack	Heart attack	1.2
Study 2	Therapy programme Y	Smokers	Smoking cessation	0.8
Study 3	Probiotic Z	Children on antibiotics	Diarrhoea	0.3

Find out more about relative risk in one of our Statistics training sessions.

For more details, email library@uhbristol.nhs.uk.

Answers: Study 1: worse; Study 2: worse; Study 3: better



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