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Infection Control

Current Awareness Newsletter

Spring 2017

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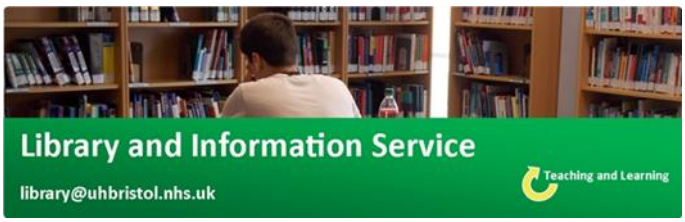

Lunchtime Drop-in Sessions

All sessions last one hour

April	(12.00)
Thurs 6th	**Literature Searching**
Mon 10th	**Critical Appraisal**
Tues 18th	**Interpreting Statistics**
Thurs 27th	**Literature Searching**
May	**(13.00)**
Mon 8th	**Critical Appraisal**
Mon 15th	**Literature Searching**
Fri 26th	**Interpreting Statistics**
Wed 31st	**Critical Appraisal**

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Contents

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Updates

NICE National Institute for Health and Care Excellence

Integrated multiplex PCR tests for identifying gastrointestinal pathogens in people with suspected gastroenteritis (xTAG Gastrointestinal Pathogen Panel, FilmArray GI Panel and Faecal Pathogens B assay) (DG26)

Evidence-based recommendations on integrated multiplex polymerase chain tests for identifying gastrointestinal pathogens in suspected gastroenteritis

Diagnostics guidance Published January 2017

Bronchiolitis in children

This interactive flowchart covers the diagnosis and management of bronchiolitis in children, and includes recommendations on when to refer and admit a child to hospital.Bronchiolitis can be caused by many respiratory viruses. It is most commonly

NICE Pathway Published June 2015 Last updated February 2017

Successful implementation of NICE SSI guidance and quality standard

...2017 Surgical site infection...challenges for surgical patients. Surgical Site Infection Surveillance (SSIS...Surgical siteinfections: prevention...prospective surgical site infection surveillance...of avoidable infections and work is...highlighted below: Surgical specialty 2009...

Shared learning Published January 2017

Cochrane Library

Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S. **Interventions to improve antibiotic prescribing practices for hospital inpatients**. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003543.pub4/full

Nelson RL, Suda KJ, Evans CT. **Antibiotic treatment for *Clostridium difficile*-associated diarrhoea in adults**. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD004610. DOI: 10.1002/14651858.CD004610.pub5.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004610.pub5/full

Alsharif U, Al-Moraissi E, Alabed S. **Systemic antibiotic prophylaxis for preventing infectious complications in maxillofacial trauma surgery (Protocol**). Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD012603. DOI: 10.1002/14651858.CD012603.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012603/full

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Clostridium difficile infection: Prevention and control

Authors: L Clifford McDonald, MD; Preeta K Kutty, MD, MPH; Section Editors: Stephen B Calderwood, MD; Sheldon L Kaplan, MD; Deputy Editor: Elinor L Baron, MD, DTMH

Literature review current through: Mar 2017. | This topic last updated: Mar 09, 2017.

https://www.uptodate.com/contents/clostridium-difficile-infection-prevention-and-control?source=related_link

Norovirus

Authors:David O Matson, MD, PhD; Miguel G O'Ryan, MD; Neil R Blacklow, MD; Section Editor: Martin S Hirsch, MD; Deputy Editor:Elinor L Baron, MD, DTMH

Literature review current through: Mar 2017. | This topic last updated: Mar 27, 2017.

https://www.uptodate.com/contents/norovirus?source=related_link

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: Mar 2017. | This topic last updated: Feb 23, 2017.

https://www.uptodate.com/contents/bronchiolitis-in-infants-and-children-treatment-outcome-and-prevention?source=related_link

Seasonal influenza in children: Prevention and treatment with antiviral drugs

Author: Flor M Munoz, MD, MSc; Section Editors: George B Mallory, MD; Morven S Edwards, MD

Deputy Editor:Mary M Torchia, MD

Literature review current through: Mar 2017. | This topic last updated: Feb 23, 2017.

https://www.uptodate.com/contents/seasonal-influenza-in-children-prevention-and-treatment-with-antiviral-drugs?source=related_link

Seasonal influenza in children: Prevention with vaccines

Author: Flor M Munoz, MD, MSc; Section Editors:George B Mallory, MD; Morven S Edwards, MD

Deputy Editor:Mary M Torchia, MD

Literature review current through: Mar 2017. | This topic last updated: Mar 13, 2017.

https://www.uptodate.com/contents/seasonal-influenza-in-children-prevention-with-vaccines?source=see_link

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: Mar 2017. | This topic last updated: Mar 21, 2017.

https://www.uptodate.com/contents/seasonal-influenza-vaccination-in-adults?source=see_link

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".)

Antimicrobial prophylaxis for prevention of surgical site infection in adults

Authors: Deverick J Anderson, MD, MPH; Daniel J Sexton, MD; Section Editor:Anthony Harris, MD, MPH

Deputy Editor:Elinor L Baron, MD, DTMH

Literature review current through: Mar 2017. | This topic last updated: Mar 31, 2017.

https://www.uptodate.com/contents/antimicrobial-prophylaxis-for-prevention-of-surgical-site-infection-in-adults?source=related_link

Antimicrobial prophylaxis for prevention of SSI will be reviewed here. Issues related to epidemiology and adjunctive measures for prevention of SSI are discussed separately. (See "Adjunctive measures for prevention of surgical site infection in adults" and "Epidemiology of surgical site infection in adults".)

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Current Awareness Database Articles

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

- **C Diff**
- **Norovirus**
- **Bronchiolitis**
- **RSV**
- **Flu**
- **Surgical Site Infection**

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

1. Clostridium difficile infection in inflammatory bowel disease: challenges in diagnosis and treatment.

Author(s): Tang, Ying M; Stone, Christian D

Source: Clinical journal of gastroenterology; Apr 2017; vol. 10 (no. 2); p. 112-123

Publication Type(s): Journal Article Review

Abstract: The problem of Clostridium difficile infection (CDI) has reached epidemic proportions, particularly in industrialized nations. The pathophysiology, disease course and the potential complications are well appreciated in the general hospitalized patient. However, when CDI occurs in the setting of inflammatory bowel disease (IBD), a number of distinct differences in the diagnosis and clinical management of the infection in this population should be appreciated by gastroenterologists, hospitalists and other care providers. This review highlights the unique aspects of CDI when it occurs in IBD patients with an emphasis on the challenge of distinguishing persistent infection from exacerbation of underlying chronic colitis. An understanding of how CDI may differ in presentation and how management should be altered can prevent serious and life-threatening complications.

2. Antibiotic treatment for Clostridium difficile-associated diarrhoea in adults.

Author(s): Nelson, Richard L; Suda, Katie J; Evans, Charlesnika T

Source: The Cochrane database of systematic reviews; Mar 2017; vol. 3 ; p. CD004610

Publication Type(s): Journal Article Review

Available in full text at Cochrane Library, The - from John Wiley and Sons

Abstract:BACKGROUNDClostridium difficile (C. difficile) is recognized as a frequent cause of antibiotic-associated diarrhoea and colitis. This review is an update of a previously published Cochrane review.OBJECTIVESThe aim of this review is to investigate the efficacy and safety of

antibiotic therapy for C. difficile-associated diarrhoea (CDAD), or C. difficile infection (CDI), being synonymous terms.SEARCH METHODSWe searched MEDLINE, EMBASE, CENTRAL and the Cochrane IBD Group Specialized Trials Register from inception to 26 January 2017…. [abstract truncated, full text freely available]

3. Clostridium difficile disease: Diagnosis, pathogenesis, and treatment update.

Author(s): Napolitano, Lena M; Edmiston, Charles E

Source: Surgery; Mar 2017

Publication Type(s): Journal Article Review

Abstract: Clostridium difficile infections are the leading cause of health care-associated infectious diarrhea, posing a significant risk for both medical and surgical patients. Because of the significant morbidity and mortality associated with C difficile infections, knowledge of the epidemiology of C difficile in combination with a high index of suspicion and susceptible patient populations (including surgical, postcolectomy, and inflammatory bowel disease patients) is warranted. C difficile infections present with a wide spectrum of disease, ranging from mild diarrhea to fulminant colitis or small bowel enteritis and recurrent C difficile infections. Early implementation of medical and operative treatment strategies for C difficile infections is imperative for optimal patient outcomes. National and international guidelines recommend early operative consultation and total abdominal colectomy with end ileostomy and preservation of rectum. Diverting loop ileostomy and colonic lavage followed by intravenous metronidazole and intracolonic vancomycin administered via the efferent limb of the ileostomy should be considered as an alternative to total colectomy in selected patients. New and emerging strategies for C difficile infection treatment include monoclonal antibodies, vaccines, probiotics, biotherapeutics, and new antibiotics. A successful C difficile prevention and eradication program requires a multidisciplinary approach that includes early disease recognition, implementation of guidelines for monitoring adherence to environmental control, judicious hand hygiene, evidence-based treatment and management strategies, and a focused antibiotic stewardship program. Surgeons are an important part of the clinical team in the management of C difficile infection prevention and treatment.

4. Dissemination of Clostridium difficile in food and the environment: Significant sources of C. difficile community-acquired infection?

Author(s): Warriner, K; Xu, C; Habash, M; Sultan, S; Weese, S J

Source: Journal of applied microbiology; Mar 2017; vol. 122 (no. 3); p. 542-553

Publication Type(s): Journal Article Review

Abstract: Clostridium difficile is a significant pathogen with over 300 000 cases reported in North America annually. Previously, it was thought that C. difficile was primarily a clinically associated infection. However, through the use of whole genome sequencing it has been revealed that the majority of cases are community acquired. The source of community-acquired C. difficile infections (CDI) is open to debate with foodborne being one route considered. Clostridium difficile fits the criteria of a foodborne pathogen with respect to being commonly encountered in a diverse range of foods that includes meat, seafood and fresh produce. However, no foodborne illness outbreaks have been directly linked to C. difficile there is also no conclusive evidence that its spores can germinate in food matrices. This does not exclude food as a potential vehicle but it is likely that the pathogen is also acquired through zoonosis and the environment. The most significant factor that defines susceptibility to CDI is the host microbiome and functioning immune system. In this respect, effective control can be exercised by reducing the environmental burden of C. difficile along with boosting the host defences against the virulent enteric pathogen.

5. A Review of Experimental and Off-Label Therapies for Clostridium difficile Infection.

Author(s): Fehér, Csaba; Soriano, Alex; Mensa, Josep

Source: Infectious diseases and therapy; Mar 2017; vol. 6 (no. 1); p. 1-35

Publication Type(s): Journal Article Review

Abstract: In spite of increased awareness and the efforts taken to optimize Clostridium difficile infection (CDI) management, with the limited number of currently available antibiotics for C. difficile the halt of this increasing epidemic remains out of reach. There are, however, close to 80 alternative treatment methods with controversial anti-clostridial efficacy or in experimental phase today. Indeed, some of these therapies are expected to become acknowledged members of the recommended anti-CDI arsenal within the next few years. None of these alternative treatment methods can respond in itself to all the major challenges of CDI management, which are primary prophylaxis in the susceptible population, clinical cure of severe cases, prevention of recurrences, and forestallment of asymptomatic C. difficile carriage and in-hospital spread. Yet, the greater the variety of treatment choices on hand, the better combination strategies can be developed to reach these goals in the future. The aim of this article is to provide a comprehensive summary of these experimental and currently off-label therapeutic options.

6. Insights into drug resistance mechanisms in Clostridium difficile.

Author(s): Harnvoravongchai, Phurt; Pipatthana, Methinee; Chankhamhaengdecha, Surang; Janvilisri, Tavan

Source: Essays in biochemistry; Feb 2017; vol. 61 (no. 1); p. 81-89

Publication Type(s): Journal Article Review

Abstract: The incidence of Clostridium difficile infection has been elevated and becoming common in hospitals worldwide. Although antibiotics usually serve as the primary treatment for bacterial infection including C. difficile infection, limitations and failures have been evident due to drug resistance. Antibiotic resistance in C. difficile has been recognized as one of the most important factors to promote the infection and increase the level of severity and the recurrence rate. Several outbreaks in many countries have been linked to the emergence of hypervirulent drug-resistant strains. This pathogen harbours various mechanisms against the actions of antibiotics. The present study highlights three main drug-resistant strategies in C. difficile including drug inactivation, target modification and efflux pump. Other mechanisms that potentially contribute to drug-resistant traits in this organism are also discussed.

7. Systematic review with meta-analysis: the impact of Clostridium difficile infection on the short and long-term risks of colectomy in inflammatory bowel disease.

Author(s): Law, C C Y; Tariq, R; Khanna, S; Murthy, S; McCurdy, J D

Source: Alimentary pharmacology & therapeutics; Feb 2017

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDClostridium difficile infection (CDI) is associated with increased mortality in inflammatory bowel disease (IBD), but the risk of colectomy is variable and has not been adequately studied.AIMTo perform a systematic review and meta-analysis to assess the impact of CDI on colectomy risk in IBD.METHODSMultiple databases were searched systematically for observational studies reporting colectomy risk in IBD, stratified by the presence of CDI, and the duration of follow-up (short term 3 months, and long term at least 1 year). Weighted summary estimates were

calculated using generalised inverse variance with random-effects model. Study quality was assessed using the Newcastle-Ottawa scale.RESULTSTwelve observational studies were identified and included 35 057 IBD patients with CDI, and 929 259 without CDI. CDI did not increase the short-term colectomy risk in IBD patients overall (10 studies) (OR: 1.35; 95% CI: 0.68-2.67), or in patients with ulcerative colitis (nine studies) (OR: 1.20; 95% CI: 0.39-3.76). In contrast, CDI was associated with higher long-term colectomy risk in patients with IBD overall (five studies) (OR: 2.23; 95% CI: 1.18-4.21), and in patients with ulcerative colitis (four studies) (OR: 2.96; 95% CI: 1.19-7.34). The results were stable in subgroups stratified by recruitment period, hospitalisation status and geographical location. All studies were at least of moderate quality. The results were limited in the ability to compare IBD severity and the type of anti-microbial therapy.CONCLUSIONBased on 12 observational studies with at least moderate quality, Clostridium difficile infection appears to increase colectomy risk in IBD in the long but not short term.

8. The efficacy of fidaxomicin in the treatment of Clostridium difficile infection in a real-world clinical setting: a Spanish multi-centre retrospective cohort.

Author(s): Fehér, C; Múñez Rubio, E; Merino Amador, P; Delgado-Iribarren Garcia-Campero, A; Salavert, M; Merino, E; Maseda Garrido, E; Díaz-Brito, V; Álvarez, M J; Mensa, J

Source: European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology; Feb 2017; vol. 36 (no. 2); p. 295-303

Publication Type(s): Clinical Study Multicenter Study Journal Article

Abstract: The objective of this study was to evaluate the efficacy and safety of fidaxomicin in the real-life clinical setting. This was a retrospective cohort of patients with Clostridium difficile infection (CDI) treated with fidaxomicin in 20 Spanish hospitals between July 2013 and July 2014. Clinical cure, 30-day recurrence, 30-day mortality, sustained cure, and factors associated with the failure to achieve sustained cure were analyzed. Of the 72 patients in the cohort 41 (56.9 %) had a fatal underlying disease. There were 44 (61.1 %) recurrent episodes and 26 cases (36.1 %) with a history of multiple recurrences. Most episodes were severe (26, 36 %) or severe-complicated (14, 19.4 %). Clinical cure rate was 90.3 %, recurrence rate was 16.7 % and three patients (4.2 %) died during the follow-up period. Sustained cure was achieved in 52 cases (72.2 %). Adverse events were reported in five cases (6.9 %). Factors associated with the lack of sustained cure were cardiovascular comorbidity (OR 11.4; 95 %CI 1.9-67.8), acute kidney failure (OR 7.4; 95 %CI 1.3-43.1), concomitant systemic antibiotic treatment (OR 6.2; 95 %CI 1.1-36.8), and C-reactive protein value at diagnosis (OR 1.2 for each 1 mg/dl increase; 95 %CI 1.03-1.3). Fidaxomicin is an effective and well tolerable treatment for severe CDI and for cases with elevated recurrence risk.

9. Management of Clostridium difficile Infection in Inflammatory Bowel Disease: Expert Review from the Clinical Practice Updates Committee of the AGA Institute.

Author(s): Khanna, Sahil; Shin, Andrea; Kelly, Ciarán P

Source: Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association; Feb 2017; vol. 15 (no. 2); p. 166-174

Publication Type(s): Journal Article Review

Abstract: The purpose of this expert review is to synthesize the existing evidence on the management of Clostridium difficile infection in patients with underlying inflammatory bowel disease. The evidence reviewed in this article is a summation of relevant scientific publications, expert opinion statements, and current practice guidelines. This review is a summary of expert opinion in the field without a formal systematic review of evidence. Best Practice Advice 1: Clinicians should test patients who present with a flare of underlying inflammatory bowel disease for

Clostridium difficile infection. Best Practice Advice 2: Clinicians should screen for recurrent C difficile infection if diarrhea or other symptoms of colitis persist or return after antibiotic treatment for C difficile infection. Best Practice Advice 3: Clinicians should consider treating C difficile infection in inflammatory bowel disease patients with vancomycin instead of metronidazole. Best Practice Advice 4: Clinicians strongly should consider hospitalization for close monitoring and aggressive management for inflammatory bowel disease patients with C difficile infection who have profuse diarrhea, severe abdominal pain, a markedly increased peripheral blood leukocyte count, or other evidence of sepsis. Best Practice Advice 5: Clinicians may postpone escalation of steroids and other immunosuppression agents during acute C difficile infection until therapy for C difficile infection has been initiated. However, the decision to withhold or continue immunosuppression in inflammatory bowel disease patients with C difficile infection should be individualized because there is insufficient existing robust literature on which to develop firm recommendations. Best Practice Advice 6: Clinicians should offer a referral for fecal microbiota transplantation to inflammatory bowel disease patients with recurrent C difficile infection.

10. Bezlotoxumab for Prevention of Recurrent Clostridium difficile Infection.

Author(s): Wilcox, Mark H; Gerding, Dale N; Poxton, Ian R; Kelly, Ciaran; Nathan, Richard; Birch, Thomas; Cornely, Oliver A; Rahav, Galia; Bouza, Emilio; Lee, Christine; Jenkin, Grant; Jensen, Werner; Kim, You-Sun; Yoshida, Junichi; Gabryelski, Lori; Pedley, Alison; Eves, Karen; Tipping, Robert; Guris, Dalya; Kartsonis, Nicholas; Dorr, Mary-Beth; MODIFY I and MODIFY II Investigators

Source: The New England journal of medicine; Jan 2017; vol. 376 (no. 4); p. 305-317

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Journal Article Clinical Trial, Phase Iii

Abstract: Background Clostridium difficile is the most common cause of infectious diarrhea in hospitalized patients. Recurrences are common after antibiotic therapy. Actoxumab and bezlotoxumab are human monoclonal antibodies against C. difficile toxins A and B, respectively. Methods We conducted two double-blind, randomized, placebo-controlled, phase 3 trials, MODIFY I and MODIFY II, involving 2655 adults receiving oral standard-of-care antibiotics for primary or recurrent C. difficile infection. Participants received an infusion of bezlotoxumab (10 mg per kilogram of body weight), actoxumab plus bezlotoxumab (10 mg per kilogram each), or placebo; actoxumab alone (10 mg per kilogram) was given in MODIFY I but discontinued after a planned interim analysis. The primary end point was recurrent infection (new episode after initial clinical cure) within 12 weeks after infusion in the modified intention-to-treat population. Results In both trials, the rate of recurrent C. difficile infection was significantly lower with bezlotoxumab alone than with placebo (MODIFY I: 17% [67 of 386] vs. 28% [109 of 395]; adjusted difference, -10.1 percentage points; 95% confidence interval [CI], -15.9 to -4.3; P<0.001; MODIFY II: 16% [62 of 395] vs. 26% [97 of 378]; adjusted difference, -9.9 percentage points; 95% CI, -15.5 to -4.3; P<0.001) and was significantly lower with actoxumab plus bezlotoxumab than with placebo (MODIFY I: 16% [61 of 383] vs. 28% [109 of 395]; adjusted difference, -11.6 percentage points; 95% CI, -17.4 to -5.9; P<0.001; MODIFY II: 15% [58 of 390] vs. 26% [97 of 378]; adjusted difference, -10.7 percentage points; 95% CI, -16.4 to -5.1; P<0.001). In prespecified subgroup analyses (combined data set), rates of recurrent infection were lower in both groups that received bezlotoxumab than in the placebo group in subpopulations at high risk for recurrent infection or for an adverse outcome. The rates of initial clinical cure were 80% with bezlotoxumab alone, 73% with actoxumab plus bezlotoxumab, and 80% with placebo; the rates of sustained cure (initial clinical cure without recurrent infection in 12 weeks) were 64%, 58%, and 54%, respectively. The rates of adverse events were similar among these groups; the most common events were diarrhea and nausea. Conclusions Among participants receiving antibiotic treatment for primary or recurrent C. difficile infection, bezlotoxumab was

associated with a substantially lower rate of recurrent infection than placebo and had a safety profile similar to that of placebo. The addition of actoxumab did not improve efficacy. (Funded by Merck; MODIFY I and MODIFY II ClinicalTrials.gov numbers, NCT01241552 and NCT01513239 .).

11. Role of cephalosporins in the era of Clostridium difficile infection.

Author(s): Wilcox, Mark H; Chalmers, James D; Nord, Carl E; Freeman, Jane; Bouza, Emilio

Source: The Journal of antimicrobial chemotherapy; Jan 2017; vol. 72 (no. 1); p. 1-18

Publication Type(s): Journal Article Review

Abstract: The incidence of Clostridium difficile infection (CDI) in Europe has increased markedly since 2000. Previous meta-analyses have suggested a strong association between cephalosporin use and CDI, and many national programmes on CDI control have focused on reducing cephalosporin usage. Despite reductions in cephalosporin use, however, rates of CDI have continued to rise. This review examines the potential association of CDI with cephalosporins, and considers other factors that influence CDI risk. EUCLID (the EUropean, multicentre, prospective biannual point prevalence study of CLostridium difficile Infection in hospitalized patients with Diarrhoea) reported an increase in the annual incidence of CDI from 6.6 to 7.3 cases per 10 000 patient bed-days from 2011-12 to 2012-13, respectively. While CDI incidence and cephalosporin usage varied widely across countries studied, there was no clear association between overall cephalosporin prescribing (or the use of any particular cephalosporin) and CDI incidence. Moreover, variations in the pharmacokinetic and pharmacodynamic properties of cephalosporins of the same generation make categorization by generation insufficient for predicting impact on gut microbiota. A multitude of additional factors can affect the risk of CDI. Antibiotic choice is an important consideration; however, CDI risk is associated with a range of antibiotic classes. Prescription of multiple antibiotics and a long duration of treatment are key risk factors for CDI, and risk also differs across patient populations. We propose that all of these are factors that should be taken into account when selecting an antibiotic, rather than focusing on the exclusion of individual drug classes.

12. Characteristics of the Clostridium difficile cell envelope and its importance in therapeutics.

Author(s): Kirk, Joseph A; Banerji, Oishik; Fagan, Robert P

Source: Microbial biotechnology; Jan 2017; vol. 10 (no. 1); p. 76-90

Publication Type(s): Journal Article Review

Abstract: Clostridium difficile infection (CDI) is a challenging threat to human health. Infections occur after disruption of the normal microbiota, most commonly through the use of antibiotics. Current treatment for CDI largely relies on the broad-spectrum antibiotics vancomycin and metronidazole that further disrupt the microbiota resulting in frequent recurrence, highlighting the need for C. difficile-specific antimicrobials. The cell surface of C. difficile represents a promising target for the development of new drugs. C. difficile possesses a highly deacetylated peptidoglycan cell wall containing unique secondary cell wall polymers. Bound to the cell wall is an essential S-layer, formed of SlpA and decorated with an additional 28 related proteins. In addition to the S-layer, many other cell surface proteins have been identified, including several with roles in host colonization. This review aims to summarize our current understanding of these different C. difficile cell surface components and their viability as therapeutic targets.

13. Conventional and alternative treatment approaches for Clostridium difficile infection.

Author(s): Aljarallah, Khalid M

Source: International journal of health sciences; 2017; vol. 11 (no. 1); p. 1-10

Publication Type(s): Journal Article Review

Abstract: Clostridium difficile-associated disease continues to be one of the leading health concerns worldwide. C. difficile is considered as a causative agent of nosocomial diarrhea that causes serious infection, which may result in death. The incidences of C. difficile infection (CDI) in developed countries have become increasingly high which may be attributed to the emergence of newer epidemic strains, extensive use of antibiotics, and limited alternative therapies. The available treatment options against CDI are expensive and promote resistance. Therefore, there is urgent need for new approaches to meet these challenges. This review discusses the current understanding of CDI, the existing clinical treatment strategies and future potential options as antidifficile agents based on the available published works.

14. Clostridium difficile infection: Updates in management.

Author(s): Tariq, Raseen; Khanna, Sahil

Source: Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology; Jan 2017; vol. 36 (no. 1); p. 3-10

Publication Type(s): Journal Article Review

Abstract: Clostridium difficile was first identified in 1978 as a diarrhea-causing bacterium in humans. In the last three decades, C. difficile infection (CDI) has reached an epidemic state, both in health care and community settings worldwide. There has been substantial progress in the field of CDI, including identification of novel risk factors, presence of CDI in individuals not considered at risk previously, and treatment options including new drugs, monoclonal antibodies, and fecal microbiota transplantation. This review discusses epidemiology, novel and traditional risk factors, and updates in management for CDI.

15. Clostridium difficile contamination of health care workers' hands and its potential contribution to the spread of infection: Review of the literature.

Author(s): Jullian-Desayes, Ingrid; Landelle, Caroline; Mallaret, Marie-Reine; Brun-Buisson, Christian; Barbut, Frédéric

Source: American journal of infection control; Jan 2017; vol. 45 (no. 1); p. 51-58

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDClostridium difficile infection (CDI) can be transmitted from patient to patient by the hands of health care workers (HCWs); however, the relative importance of this route in the spread of C difficile in the hospital is currently unknown. Our aim was to review studies examining HCWs' hand carriage and its potential role in CDI transmission.METHODSFirst, English-speaking references addressing HCWs' hand sampling obtained from the PubMed database were reviewed. Second, C difficile outbreaks definitely or probably implicating HCWs were retrieved from the Outbreak Database Web site (www.outbreak-database.com). Finally, cases of C difficile occurring in HCWs after contact with an infected patient were retrieved from PubMed.RESULTSA total of 11 studies dealing with HCWs' hand carriage were selected and reviewed. Between 0% and 59% of HCWs' hands were found contaminated with C difficile after caring for a patient with CDI. There were several differences between studies regarding site of hands sampling, timing after contact, and bacteriologic methods. Only 2 C difficile outbreaks implicating HCWs and 6 series of cases of transmission from patients to HCWs have been reported.CONCLUSIONSThis review shows that HCWs' hands could play an important role in the transmission of C difficile. Hand hygiene and reduction of environmental contamination are essential to control C difficile transmission.

16. Timely use of Probiotics in Hospitalized Adults Prevents Clostridium difficile Infection: a Systematic Review with Meta-Regression Analysis.

Author(s): Shen, Nicole T; Maw, Anna; Tmanova, Lyubov L; Pino, Alejandro; Ancy, Kayley; Crawford, Carl V; Simon, Matthew S; Evans, Arthur T

Source: Gastroenterology; Feb 2017

Publication Type(s): Journal Article

Abstract:BACKGROUND & AIMSSystematic reviews have provided evidence for the efficacy of probiotics in preventing Clostridium difficile infection (CDI), but guidelines do not recommend probiotic use for prevention of CDI. We performed an updated systematic review to help guide clinical practice.METHODSWe searched MEDLINE, EMBASE, International Journal of Probiotics and Prebiotics, and The Cochrane Library databases for randomized controlled trials evaluating use of probiotics and CDI in hospitalized adults taking antibiotics. Two reviewers independently extracted data and assessed risk of bias and overall quality of the evidence. Primary and secondary outcomes, respectively, were incidence of CDI and adverse events. Secondary analyses examined the effects of probiotic species, dose, timing, formulation, duration, and study quality.RESULTSWe analyzed data from 19 published studies, comprising 6261 subjects. The incidence of CDI in the probiotic cohort, 1.6% (54/3277), was lower than of controls, 3.9% (115/2984) (P<.001). The pooled relative risk of CDI in probiotic users was 0.42 (95% CI, 0.30-0.57; I2=0.0%). Meta-regression analysis demonstrated that probiotics were significantly more effective if given closer to the first antibiotic dose, with a decrement in efficacy for every day of delay in starting probiotics (P=.04); probiotics given within 2 days of antibiotic initiation produced a greater reduction of risk for CDI (relative risk, 0.32, 95% CI, 0.22-0.48; I2=0%) than later administration (relative risk 0.70, 95% CI, 0.40-1.23; I2=0%) (P=.02). There was no increased risk for adverse events among patients given probiotics. The overall quality of the evidence was high.CONCLUSIONSIn a systematic review with meta-regression analysis, we found evidence that administration of probiotics closer to the first dose of antibiotic reduces the risk of CDI by more than 50% in hospitalized adults. Future research should focus on optimal probiotic dose, species, and formulation. Systematic Review Registration: PROSPERO CRD42015016395.

17. Clostridium difficile Infection in Older Adults: Systematic Review of Efforts to Reduce Occurrence and Improve Outcomes.

Author(s): Marshall, Leisa L; Peasah, Samuel; Stevens, Gregg A

Source: The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists; Jan 2017; vol. 32 (no. 1); p. 24-41

Publication Type(s): Journal Article

Abstract:OBJECTIVEProvide a systematic review of the primary literature on efforts to reduce Clostridium difficile infection (CDI) occurrence and improve outcomes in older adults.DATA SOURCES, STUDY SELECTION, DATA EXTRACTIONPubMed and CINAHL databases were searched for research studies using search terms CDI, CDI prevention, reduction, control, management, geriatric, elderly, adults 65 years of age and older. The MeSH categories Aged and Aged, 80 and older, were used. A second search of PubMed, CINAHL, National Guideline Clearinghouse, and TRIP databases was conducted for primary, secondary, and tertiary literature for CDI epidemiology, burden, and management in adults of all ages, and prevention and management guidelines. Of the 2,263 articles located, 105 were selected for full review: 55 primary and 50 secondary, tertiary. Primary literature selected for full review included studies of interventions to prevent, reduce occurrence, control, manage, or improve outcomes in adults 65 years of age and older. Patient settings included the community, assisted living, nursing facility, subacute care, or hospital.DATA SYNTHESISThe main outcome measures for research studies were whether the studied intervention prevented, reduced occurrence, controlled, managed, or improved outcomes. Studies were conducted in acute or long-

term hospitals, with a few in nursing facilities. Interventions that prevented or reduced CDI included antibiotic policy changes, education, procedure changes, infection control, and multi-intervention approaches. There were few management studies for adults 65 years of age and older or for all adults with results stratified by age. Treatments studied included efficacy of fidaxomicin, metronidazole, vancomycin, and fecal microbiota transplant. Though clinical outcomes were slightly less robust in those 65 years of age and older, age was not an independent predictor of success or failure. The current prevention and management guidelines for adults of all ages, as well as special considerations in skilled nursing facilities, extracted from the secondary/tertiary literature selected, are summarized.CONCLUSIONThere are a limited number of studies designed for older adults. Our findings suggest that guideline recommendations for adults are adequate and appropriate for older adults. Exposure to antibiotics and Clostridium difficile remain the two major risk factors for CDI, reinforcing the importance of antibiotic stewardship and infection control.

18. Effectiveness of probiotics in reducing the incidence of Clostridium difficile-associated diarrhea in elderly patients: a systematic review.

Author(s): Vernaya, Marina; McAdam, Jennifer; Hampton, Michelle DeCoux

Source: JBI database of systematic reviews and implementation reports; Jan 2017; vol. 15 (no. 1); p. 140-164

Publication Type(s): Journal Article

Abstract:BACKGROUNDClostridium difficile bacteria are a leading cause of infectious diarrhea. This is an anaerobic, gram-positive and spore-forming rod responsible for significant morbidity and mortality, especially among elderly hospitalized patients. Standard management of C. difficile-associated diarrhea (CDAD) consists of discontinuing a causative antibiotic, correcting fluid-electrolytes imbalance and initiating an antibiotic treatment for CDAD. Alternative approaches for prevention of CDAD include probiotics. This systematic review will provide a comprehensive, unbiased summary of the available research on the effectiveness of probiotics in decreasing the incidence of infectious diarrhea in elderly hospitalized patients.OBJECTIVESTo conduct a systematic review to determine the best available evidence related to the effectiveness of probiotics in the prevention of CDAD in elderly hospitalized patients. The review question was: are probiotics effective in decreasing the incidence of CDAD in elderly hospitalized patients?INCLUSION CRITERIA TYPES OF PARTICIPANTSThe current review included studies of participants who were aged 60 years and more and who were residents of acute- and post-acute care facilities undergoing or planning to undergo antibiotic treatment for the management of any infectious conditions, except CDAD.TYPES OF INTERVENTION(S)The current review included studies that evaluated the effectiveness of probiotics for prevention of CDAD in elderly hospitalized patients in acute- and post-acute care settings compared to usual care.OUTCOMESThe current review included studies examining the following outcome measures: incidence or relapse of CDAD. Cases of CDAD were defined by presence of diarrhea and verified by positive results for stool enzyme immunoassay for toxins A and B.TYPES OF STUDIESThe current review included only experimental study designs including randomized controlled trials.SEARCH STRATEGYThe search strategy included studies published in English between 1978, when the first case of CDAD was reported, and 2015.ASSESSMENT OF METHODOLOGICAL QUALITYPapers selected for retrieval were assessed by two independent reviewers for methodological quality prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute (JBI).DATA EXTRACTIONData were extracted from papers included in the review using the standardized data extraction tool from the JBI Meta-Analysis of Statistics Assessment and Review Instrument. The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.DATA SYNTHESISQuantitative data were pooled using statistical meta-analysis. Effect sizes were expressed as odds ratios, and their 95% confidence intervals were

calculated to determine if probiotic treatment was superior to placebo in reducing CDAD incidence. Heterogeneity was assessed using the standard I statistic.RESULTSFive studies were included in the review. The individual study results were conflicting, including non-significant results for four studies and statistically significant results in one that demonstrated fewer cases of CDAD among patients receiving probiotics compared to placebo. The meta-analysis finding indicated that there was no statistically significant difference in CDAD incidence in elderly hospitalized patients taking probiotics when compared to a placebo.CONCLUSIONProbiotics were not found to be more effective than placebo for reducing CDAD incidence in elderly hospitalized patients. However, studies that demonstrate improved outcomes must be examined to determine future needs for research. Studies varied with regard to the dose, frequency, method of administration (probiotic drinks versus capsule), length of administration and the number of strains of bacteria administered. Further studies are needed to evaluate the effectiveness of probiotics for CDAD prevention in this population. Clinical trials with evidence-based administration methods and meta-analyses that pool the results of studies with congruent methodologies are needed to enable conclusions to be drawn on the effectiveness of probiotic administration for CDAD prevention.

19. Clostridium Difficile Infection in Acute Care Hospitals: Systematic Review and Best Practices for Prevention.

Author(s): Louh, Irene K; Greendyke, William G; Hermann, Emilia A; Davidson, Karina W; Falzon, Louise; Vawdrey, David K; Shaffer, Jonathan A; Calfee, David P; Furuya, E Yoko; Ting, Henry H

Source: Infection control and hospital epidemiology; Apr 2017; vol. 38 (no. 4); p. 476-482

Publication Type(s): Journal Article

Abstract:OBJECTIVE Prevention of Clostridium difficile infection (CDI) in acute-care hospitals is a priority for hospitals and clinicians. We performed a qualitative systematic review to update the evidence on interventions to prevent CDI published since 2009. DESIGN We searched Ovid, MEDLINE, EMBASE, The Cochrane Library, CINAHL, the ISI Web of Knowledge, and grey literature databases from January 1, 2009 to August 1, 2015. SETTING We included studies performed in acute-care hospitals. PATIENTS OR PARTICIPANTS We included studies conducted on hospitalized patients that investigated the impact of specific interventions on CDI rates. INTERVENTIONS We used the QI-Minimum Quality Criteria Set (QI-MQCS) to assess the quality of included studies. Interventions were grouped thematically: environmental disinfection, antimicrobial stewardship, hand hygiene, chlorhexidine bathing, probiotics, bundled approaches, and others. A meta-analysis was performed when possible. RESULTS Of 3,236 articles screened, 261 met the criteria for full-text review and 46 studies were ultimately included. The average quality rating was 82% according to the QI-MQCS. The most effective interventions, resulting in a 45% to 85% reduction in CDI, included daily to twice daily disinfection of high-touch surfaces (including bed rails) and terminal cleaning of patient rooms with chlorine-based products. Bundled interventions and antimicrobial stewardship showed promise for reducing CDI rates. Chlorhexidine bathing and intensified hand-hygiene practices were not effective for reducing CDI rates. CONCLUSIONS Daily and terminal cleaning of patient rooms using chlorine-based products were most effective in reducing CDI rates in hospitals. Further studies are needed to identify the components of bundled interventions that reduce CDI rates.

20. Clostridium difficile Infection and Risk of Colectomy in Patients with Inflammatory Bowel Disease: A Bias-adjusted Meta-analysis.

Author(s): Chen, Yingxi; Furuya-Kanamori, Luis; Doi, Suhail A; Ananthakrishnan, Ashwin N; Kirk, Martyn

Source: Inflammatory bowel diseases; Feb 2017; vol. 23 (no. 2); p. 200-207

Publication Type(s): Journal Article

Abstract:BACKGROUNDClostridium difficile infection (CDI) is a common complication of inflammatory bowel diseases (IBDs) and is associated with worse outcome. Variable rates of colectomy have been reported among IBD complicated by CDI. We conducted a systematic review and meta-analysis of studies to assess the association between CDI and colectomy among patients with IBD.METHODSThe literature was systematically searched using PubMed from inception through April 2016. Studies were limited to cohort, case-control, and cross-sectional studies reporting colectomy risk stratified by CDI in patients with IBD. We estimated summary ORs and 95% CIs using the quality-effects model. Study quality was assessed using an adaptation of the Newcastle-Ottawa scale.RESULTSSix studies were included in the meta-analysis, comprising 8 data sets. Results from meta-analysis showed that CDI was a significant risk factor for colectomy among patients with IBD, mainly patients with ulcerative colitis, almost doubling the odds (OR 1.90; 95% CI, 1.23-2.93). There was significant heterogeneity across studies (Q = 22.02, P < 0.001; I = 68%). Funnel plots were grossly asymmetrical. Results of sensitivity analysis restricting studies to those reporting ulcerative colitis only and studies using laboratory tests to confirm CDI were consistent with the result from the main analysis.CONCLUSIONSCDI is a significant risk factor for colectomy in patients with IBD. Further research is needed to investigate the attributable risks of surgery due to CDI among patients with Crohn's disease.

21. Management of a cluster of Clostridium difficile infections among patients with osteoarticular infections.

Author(s): Färber, Jacqueline; Illiger, Sebastian; Berger, Fabian; Gärtner, Barbara; von Müller, Lutz; Lohmann, Christoph H; Bauer, Katja; Grabau, Christina; Zibolka, Stefanie; Schlüter, Dirk; Geginat, Gernot

Source: Antimicrobial resistance and infection control; 2017; vol. 6 ; p. 22

Publication Type(s): Journal Article

Available in full text at Antimicrobial Resistance and Infection Control - from BioMed Central

Abstract:BACKGROUNDHere we describe a cluster of hospital-acquired Clostridium difficile infections (CDI) among 26 patients with osteoarticular infections. The aim of the study was to define the source of C. difficile and to evaluate the impact of general infection control measures and antibiotic stewardship on the incidence of CDI.METHODSEpidemiological analysis included typing of C. difficile strains and analysis of possible patient to patient transmission. Infection control measures comprised strict isolation of CDI patients, additional hand washings, and intensified environmental cleaning with sporicidal disinfection. In addition an antibiotic stewardship program was implemented in order to prevent the use of CDI high risk antimicrobials such as fluoroquinolones, clindamycin, and cephalosporins.RESULTSThe majority of CDI (n = 15) were caused by C. difficile ribotype 027 (RT027). Most RT027 isolates (n = 9) showed high minimal inhibitory concentrations (MIC) for levofloxacin, clindamycin, and remarkably to rifampicin, which were all used for the treatment of osteoarticular infections. Epidemiological analysis, however, revealed no closer genetic relationship among the majority of RT027 isolates. The incidence of CDI was reduced only when a significant reduction in the use of fluoroquinolones (p = 0.006), third generation cephalosporins (p = 0.015), and clindamycin (p = 0.001) was achieved after implementation of an intensified antibiotic stewardship program which included a systematic review of all antibiotic prescriptions.CONCLUSIONThe successful reduction of the CDI incidence demonstrates the importance of antibiotic stewardship programs focused on patients treated for osteoarticular infections.

Norovirus

1. Detection and differentiation of norovirus genogroups I and II from clinical stool specimens using real-time PCR.

Author(s): Ramanan, Poornima; Espy, M J; Khare, Reeti; Binnicker, M J

Source: Diagnostic microbiology and infectious disease; Apr 2017; vol. 87 (no. 4); p. 325-327

Publication Type(s): Journal Article

Abstract:A real-time RT-PCR assay was designed to detect and differentiate norovirus genogroups I (GI) and II (GII), with primers and probes targeting the nonstructural polyprotein gene. Stool samples (n = 100) submitted for routine testing by the BioFire FilmArray® GI panel were also tested by the norovirus GI/GII real-time PCR assays. When compared to the FilmArray GI panel, the norovirus real-time PCR assay demonstrated a sensitivity of 77.5% (62/80) and specificity of 95% (19/20). Specimens yielding discordant results (n = 19) were tested at two outside laboratories for adjudication. Following discordant resolution, the adjusted sensitivity and specificity of the norovirus real-time PCR assays were 96.9% (63/65) and 100% (35/35), respectively. These results suggest that the real-time PCR assays are able to accurately detect and differentiate norovirus GI/GII from clinical stool specimens. Furthermore, our report highlights a potential issue with the specificity of the BioFire FilmArray® norovirus assay, which warrants additional investigation.

2. Evaluation of real-time RT-PCR assays for detection and quantification of norovirus genogroups I and II.

Author(s): Rupprom, Kitwadee; Chavalitshewinkoon-Petmitr, Porntip; Diraphat, Pornphan; Kittigul, Leera

Source: Virologica Sinica; Feb 2017

Publication Type(s): Journal Article

Abstract: Noroviruses are the leading cause of acute gastroenteritis in humans. Real-time reverse transcription-polymerase chain reaction (real-time RT-PCR) is a promising molecular method for the detection of noroviruses. In this study, the performance of three TaqMan real-time RT-PCR assays was assessed, which were one commercially available real-time RT-PCR kit (assay A: Norovirus Real Time RT-PCR kit) and two in-house real-time RT-PCR assays (assay B: LightCycler RNA Master Hybprobe and assay C: RealTime ready RNA Virus Master). Assays A and B showed higher sensitivity than assay C for norovirus GI, while they all had the same sensitivity (103 DNA copies/mL) for GII DNA standard controls. Assay B had the highest efficiency for both genogroups. No cross-reactivity was observed among GI and GII noroviruses, rotavirus, hepatitis A virus, and poliovirus. The detection rates of these assays in GI and GII norovirus-positive fecal samples were not significantly different. However, the mean quantification cycle (Cq) value of assay B for GII was lower than assays A and C with statistical significance (P-value, 0.000). All three real-time RT-PCR assays could detect a variety of noroviruses including GI.2, GII.2, GII.3, GII.4, GII.6, GII.12, GII.17, and GII.21. This study suggests assay B as a suitable assay for the detection and quantification of noroviruses GI and GII due to good analytical sensitivity and higher performance to amplify norovirus on DNA standard controls and clinical samples.

3. Infection of exposed patients during norovirus outbreaks: are there predictive parameters?

Author(s): Kampmeier, S; Pillukat, M H; Kossow, A; Pettke, A; Mellmann, A

Source: The Journal of hospital infection; Feb 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDNorovirus outbreak management comprises isolation and cohorting of patients. In this context, exposed patients are preferably cohorted separately from symptomatic and unexposed asymptomatic patients, since they potentially develop symptoms of norovirus gastroenteritis. Whether routinely examined clinical or laboratory parameters can help to predict occurrence of gastroenteritis symptoms in those patients has not yet been examined.AIMTo evaluate routinely examined clinical and laboratory parameters as predictive values for the development of norovirus symptoms in exposed patients during outbreaks.METHODSExposed patients during norovirus outbreaks were observed throughout a two-year period in the university hospital of Muenster. The development of laboratory confirmed norovirus gastroenteritis symptoms was examined in exposed patients, and clinical as well as laboratory parameters prior to onset of the outbreak were compared in exposed symptomatic and asymptomatic patients.FINDINGSWe detected 42 exposed patients within 10 outbreaks. Of these, 33 remained asymptomatic, whereas nine patients developed norovirus gastroenteritis. Exposed symptomatic patients were significantly older (50±10.51 vs 28±4.68 years), had significantly higher blood sodium concentration (142.5±1.48 vs 138.8±0.47mmol/L) and higher systolic blood pressure (119.3±3.84 vs 108.5±2.41mmHg). Development of symptoms among exposed patients was significantly associated with blood type O (75% vs 20%).CONCLUSIONIn order to minimize patient-to-patient transmission within norovirus outbreaks in hospital, risk stratification of exposed patients is helpful. To achieve this, routinely detected clinical and laboratory parameters can be useful to predict development of symptoms in these patients.

4. Multicenter evaluation of the revised RIDA® QUICK test (N1402) for rapid detection of norovirus in a diagnostic laboratory setting.

Author(s): Jonckheere, Stijn; Botteldoorn, Nadine; Vandecandelaere, Patricia; Frans, Johan; Laffut, Wim; Coppens, Guy; Vankeerberghen, Anne; De Beenhouwer, Hans

Source: Diagnostic microbiology and infectious disease; Feb 2017

Publication Type(s): Journal Article

Abstract: The updated RIDA® QUICK (N1402) immunochromatographic assay (R-Biopharm) for detection of norovirus was evaluated during a prospective, multicenter study using 771 stool samples from patients with gastroenteritis. Compared to real-time reverse transcriptase polymerase chain reaction (RT-rtPCR) as gold standard, the RIDA® QUICK had an overall sensitivity of 72.8% (91/125) and a specificity of 99.5% (640/643). Genotype analysis of the polymerase (ORF1) and capsid (ORF2) region of the genome indicated that the RIDA® QUICK assay could detect a broad range of genotypes including new variants (15 of 125 positive samples) which were detected by an in-house SYBR®Green RT-rtPCR, but not by the RIDA® GENE PCR PG1415 (R-Biopharm) and mostly not by the RIDA® GENE PCR PG1405 and the Xpert® Norovirus assay (Cepheid). The RIDA® QUICK can be used to reliably confirm norovirus in stool samples, but a negative result does not definitively exclude the presence of norovirus.

5. Re-assessing the total burden of norovirus circulating in the United Kingdom population.

Author(s): Harris, John P; Iturriza-Gomara, Miren; O'Brien, Sarah J

Source: Vaccine; Feb 2017; vol. 35 (no. 6); p. 853-855

Publication Type(s): Journal Article

Abstract: The second Infectious Intestinal Diseases study (IID2) estimated the incidence of norovirus in the UK at 47/1000 population (three million cases annually). Clinically significant norovirus was defined using a cycle threshold (ct) value of <30; a more stringent cut-off than used in diagnostic laboratories. The low infectious dose of norovirus means asymptomatic individuals potentially

contribute to ongoing transmission. Using a less stringent but diagnostically relevant threshold increases the estimation of the population burden of norovirus infection by around 26% to 59/1000 person years (95% CI 52.32-64.98), equating to 3.7 million norovirus infections annually (3.3-4.1 million). With possible vaccines on the horizon for norovirus, having a good estimate of the total burden of norovirus infection, as well as symptomatic disease will be useful in helping to guide vaccination policy when candidate vaccines become available.

6. Evaluation of various real-time reverse transcription quantitative PCR assays for norovirus detection.

Author(s): Yoo, Ju Eun; Lee, Cheonghoon; Park, SungJun; Ko, GwangPyo

Source: Journal of microbiology and biotechnology; Feb 2017

Publication Type(s): Journal Article

Abstract: Human noroviruses are widespread and contagious viruses causing nonbacterial gastroenteritis. Real-time reverse transcription quantitative PCR (real-time RT-qPCR) is currently the gold standard for sensitive and accurate detection for these pathogens and serves as a critical tool in outbreak prevention and control. Different surveillance teams, however, may use different assays and variability in specimen conditions may lead to disagreement in results. Furthermore, the norovirus genome is highly variable and continuously evolving. These issues necessitate the re-examination of the real-time RT-qPCR's robustness in the context of accurate detection as well as the investigation of practical strategies to enhance assay performance. Four widely referenced real-time RT-qPCR assays (Assay A-D) were simultaneously performed to evaluate characteristics such as PCR efficiency, detection limit, as well as sensitivity and specificity with RT-PCR, and to assess the most accurate method for detecting norovirus genogroups I and II. Overall, Assay D was evaluated to be the most precise and accurate assay in this study. A Zen internal quencher, which decreases nonspecific fluorescence during the PCR reaction, was added to Assay D's probe which further improved assay performance. This study compared several detection assays for noroviruses and an improvement strategy based on such comparisons provided useful characterizations of a highly optimized real-time RT-qPCR assay for norovirus detection.

7. Environmental indicators for human norovirus outbreaks.

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

Source: International journal of environmental health research; Feb 2017; vol. 27 (no. 1); p. 40-51

Publication Type(s): Journal Article Review

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.

8. Capturing norovirus transmission.

Author(s): de Graaf, Miranda; Villabruna, Nele; Koopmans, Marion Pg

Source: Current opinion in virology; Feb 2017; vol. 22 ; p. 64-70

Publication Type(s): Journal Article Review

Abstract: Human norovirus is a leading cause of gastroenteritis and is efficiently transmitted between humans and around the globe. The burden of norovirus infections in the global community and in health-care settings warrant the availability of outbreak prevention strategies and control measures that are tailored to the pathogen, outbreak setting and population at risk. A better understanding of viral and host determinants of transmission would aid in developing and fine-tuning such efforts. Here, we describe mechanisms of transmission, available model systems for studying norovirus transmission and their strengths and weaknesses as well as future research strategies.

9. Comparison of Xpert Norovirus and RidaGene Norovirus assays for the detection of noroviruses in clinical fecal specimens.

Author(s): Aho-Laukkanen, E; Hirvonen, J J; Saha, K

Source: European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology; Jan 2017

Publication Type(s): Journal Article

Abstract: The purpose of this study was to investigate the usability and performance of the Xpert Norovirus and RidaGene Norovirus assays for the detection of noroviruses in fecal specimens. Of the 186 stool specimens, 53 (28.5%) were considered true-positive for norovirus (NoV). Of the true-positive specimens, Xpert detected 53 and RidaGene detected 52. The respective sensitivity and specificity were 100% and 94.7% [95% confidence interval (CI), 91.0-98.5%] for the Xpert assay, and 98.1% (95% CI, 94.4-100%) and 97.0% (95% CI, 94.1-99.9%) for the RidaGene assay. Positive and negative predictive values (PPVs and NPVs) were 88.3% and 100% for the Xpert assay, and 92.9% and 99.2% for the RidaGene assay, respectively. Based on this study, it can be concluded that there were no significant differences (p-value > 0.5) between the results of the Xpert and RidaGene Norovirus assays. We found that both assays are useful for the detection of noroviruses in clinical stool samples.

10. Influence of School Year on Seasonality of Norovirus Outbreaks in Developed Countries.

Author(s): Kraut, Roni Y; Snedeker, Kate G; Babenko, Oksana; Honish, Lance

Source: The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale; 2017; vol. 2017 ; p. 9258140

Publication Type(s): Journal Article

Abstract: Factors affecting the seasonal distribution of norovirus outbreaks are not well understood. This study examined whether grade school settings at the start of the school year may be a factor. We searched Ovid Medline from January 2002 to June 2014 for studies that provided all reported

norovirus outbreaks in a developed country by month for a minimum of three years. Historical school years were obtained from verifiable sources. The start of the norovirus seasonal outbreak peak and peak outbreak month were determined for each study and compared to the start month of school. Northern hemisphere and southern hemisphere countries had a different norovirus seasonality and different school year structures (traditional compared to year round). In the two studies that provided outbreaks by age, outbreaks among children started several months before outbreaks in the adult population. The median number of months between school start and start of the seasonal outbreak peak was two months (interquartile range [IQR] = 2.0-3.0), while the median number of months between school start and peak outbreak month was four months (IQR = 3.0-4.0). These findings suggest the possibility the school setting at the start of the school year may be a factor in the seasonality of norovirus.

11. Static and Evolving Norovirus Genotypes: Implications for Epidemiology and Immunity.

Author(s): Parra, Gabriel I; Squires, R Burke; Karangwa, Consolee K; Johnson, Jordan A; Lepore, Cara J; Sosnovtsev, Stanislav V; Green, Kim Y

Source: PLoS pathogens; Jan 2017; vol. 13 (no. 1); p. e1006136

Publication Type(s): Journal Article

Available in full text at PLoS Pathogens - from ProQuest

Available in full text at PLoS Pathogens - from National Library of Medicine

Abstract: Noroviruses are major pathogens associated with acute gastroenteritis worldwide. Their RNA genomes are diverse, with two major genogroups (GI and GII) comprised of at least 28 genotypes associated with human disease. To elucidate mechanisms underlying norovirus diversity and evolution, we used a large-scale genomics approach to analyze human norovirus sequences. Comparison of over 2000 nearly full-length ORF2 sequences representing most of the known GI and GII genotypes infecting humans showed a limited number (≤5) of distinct intra-genotypic variants within each genotype, with the exception of GII.4. The non-GII.4 genotypes were comprised of one or more intra-genotypic variants, with each variant containing strains that differed by only a few residues over several decades (remaining "static") and that have co-circulated with no clear epidemiologic pattern. In contrast, the GII.4 genotype presented the largest number of variants (>10) that have evolved over time with a clear pattern of periodic variant replacement. To expand our understanding of these two patterns of diversification ("static" versus "evolving"), we analyzed using NGS the nearly full-length norovirus genome in healthy individuals infected with GII.4, GII.6 or GII.17 viruses in different outbreak settings. The GII.4 viruses accumulated mutations rapidly within and between hosts, while the GII.6 and GII.17 viruses remained relatively stable, consistent with their diversification patterns. Further analysis of genetic relationships and natural history patterns identified groupings of certain genotypes into larger related clusters designated here as "immunotypes". We propose that "immunotypes" and their evolutionary patterns influence the prevalence of a particular norovirus genotype in the human population.

12. Efficacy of a disinfectant containing silver dihydrogen citrate against GI.6 and GII.4 human norovirus.

Author(s): Manuel, C S; Moore, M D; Jaykus, L-A

Source: Journal of applied microbiology; Jan 2017; vol. 122 (no. 1); p. 78-86

Publication Type(s): Journal Article

Abstract:AIMSHuman 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.METHODS AND RESULTSPure® 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, sodium dodecyl sulphate-polyacrylamide gel electrophoresis/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 2·0-3·0 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 histo-blood group antigen receptor-binding ability.CONCLUSIONSOur results suggest that SDC acts exclusively on the viral capsid, and shows efficacy against HuNoV when used on precleaned surfaces.SIGNIFICANCE AND IMPACT OF THE STUDYThis study sheds light on the mechanisms and efficacy of a novel antimicrobial against HuNoV. Our results suggest: (i) silver ions exclusively target the viral capsid, and not the RNA genome; (ii) citrate is not crucial for HuNoV capsid deformation.

13. 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; Jan 2017; vol. 38 (no. 1); p. 96-102

Publication Type(s): Journal Article

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.

Bronchiolitis

1. Diagnosis, prevention, and management of bronchiolitis in children: review of current controversies.

Author(s): House, Samantha A; Ralston, Shawn L

Source: Minerva pediatrica; Apr 2017; vol. 69 (no. 2); p. 141-155

Publication Type(s): Journal Article

Abstract: Viral bronchiolitis is a common and costly condition among young children worldwide, contributing to high medical expenditures in industrialized countries and significant mortality in low-income countries. Much research has focused on therapy for this disease entity, though the standard of care remains merely supportive. Current areas of active research include the nuances of defining bronchiolitis, a deeper exploration of causative viruses, the role and development of preventive strategies, and associated long-term outcomes. This review aims to explore relevant recent literature, and particularly to focus on active areas of uncertainty and controversy.

2. Clinical Outcomes of Bronchiolitis After Implementation of a General Ward High Flow Nasal Cannula Guideline.

Author(s): Riese, Jeffrey; Porter, Timothy; Fierce, Jamie; Riese, Alison; Richardson, Troy; Alverson, Brian K

Source: Hospital pediatrics; Mar 2017

Publication Type(s): Journal Article

Available in full text at Hospital Pediatrics - from Highwire Press

Abstract:OBJECTIVEThe goal of this study was to assess the association of the introduction of a ward's high-flow nasal cannula (HFNC) guideline with clinical outcomes of infants with bronchiolitis.METHODSWe conducted a retrospective, pre-post intervention study with an interrupted time series analysis of infants admitted with bronchiolitis between 2010 and 2014 at an urban, tertiary care children's hospital. Patients admitted in the 24 months before and after initiation of a guideline for HFNC use on the general wards were compared. The primary outcome was length of hospital stay. Secondary outcomes were PICU transfer rate and length of stay, intubation rate, and 30-day readmission, adjusted for season.RESULTSA total of 1937 patients met inclusion criteria; 936 were admitted before and 1001 admitted after the introduction of HFNC use on the general wards. Comparing the 2 groups, the hospital-wide rate of HFNC use in bronchiolitis treatment increased after HFNC became available on the wards (23.9% vs 35.2%; P < .001). The ward's HFNC guideline was not associated with a change in preintervention trajectory of total hospital length of stay (P = .48), PICU length of stay (P = .06), or rate of PICU transfer (P = .97). There was also no difference in intubation rate or 30-day readmission between the 2 groups.CONCLUSIONSInitiating a guideline for HFNC use on the general pediatric wards was associated with an increase in the use of the intervention with no significant change in total hospital length of stay, PICU length of stay and transfer rate, intubation rate, or 30-day readmission for patients with bronchiolitis.

3. Intravenous magnesium sulfate for bronchiolitis: A randomized trial.

Author(s): Alansari, Khalid; Sayyed, Rafah; Davidson, Bruce L; Al Jawala, Shahaza; Ghadier, Mohamed

Source: Chest; Mar 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDTo determine if intravenous magnesium, useful for severe pediatric asthma, reduces time to medical readiness for discharge in bronchiolitis patients when added to supportive care METHODS: We compared a single dose of 100 mg/kg intravenous magnesium sulfate versus placebo for acute bronchiolitis. Patients received bronchodilator therapy, nebulized hypertonic saline, and 5 days of dexamethasone if there was eczema and/or a family history of asthma. Time to medical readiness for discharge was the primary efficacy outcome. Bronchiolitis severity scores and need for infirmary or hospital admission and for clinic revisits within 2 wk were secondary outcomes.

Cardiorespiratory instability onset was the safety outcome.RESULTS162 previously healthy infants diagnosed with bronchiolitis aged 22 days to 17.6 months, median 3.7 months, were enrolled. About half had eczema and/or a family history of asthma. 86.4% had positive nasopharyngeal virus swabs. Geometric mean time until medical readiness for discharge was 24.1h (95% CI, 20.0-29.1) for the 78 magnesium patients and 25.3h (95% CI, 20.3-31.5) for the 82 placebo patients (ratio 0.95; 95% CI,0.52-1.80, p=0.91). Mean bronchiolitis severity scores over time were similar for the two groups. The frequency of clinic visits in the subsequent 2 wk, 33.8% and 27.2%, respectively, was also similar. Fifteen (19.5%) magnesium versus 5 (6.2%) placebo patients were readmitted to infirmary or hospital within 2 wk (p= 0.016). No acute cardiorespiratory side effects were reported.CONCLUSIONSIntravenous magnesium did not provide benefit for patients with acute bronchiolitis and may be harmful.

4. High-flow warm humidified oxygen versus standard low-flow nasal cannula oxygen for moderate bronchiolitis (HFWHO RCT): an open, phase 4, randomised controlled trial.

Author(s): Kepreotes, Elizabeth; Whitehead, Bruce; Attia, John; Oldmeadow, Christopher; Collison, Adam; Searles, Andrew; Goddard, Bernadette; Hilton, Jodi; Lee, Mark; Mattes, Joerg

Source: Lancet (London, England); Mar 2017; vol. 389 (no. 10072); p. 930-939

Publication Type(s): Journal Article

Abstract:BACKGROUNDBronchiolitis is the most common lung infection in infants and treatment focuses on management of respiratory distress and hypoxia. High-flow warm humidified oxygen (HFWHO) is increasingly used, but has not been rigorously studied in randomised trials. We aimed to examine whether HFWHO provided enhanced respiratory support, thereby shortening time to weaning off oxygen.METHODSIn this open, phase 4, randomised controlled trial, we recruited children aged less than 24 months with moderate bronchiolitis attending the emergency department of the John Hunter Hospital or the medical unit of the John Hunter Children's Hospital in New South Wales, Australia. Patients were randomly allocated (1:1) via opaque sealed envelopes to HFWHO (maximum flow of 1 L/kg per min to a limit of 20 L/min using 1:1 air-oxygen ratio, resulting in a maximum FiO2 of 0·6) or standard therapy (cold wall oxygen 100% via infant nasal cannulae at low flow to a maximum of 2 L/min) using a block size of four and stratifying for gestational age at birth. The primary outcome was time from randomisation to last use of oxygen therapy. All randomised children were included in the primary and secondary safety analyses. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12612000685819.FINDINGSFrom July 16, 2012, to May 1, 2015, we randomly assigned 202 children to either HFWHO (101 children) or standard therapy (101 children). Median time to weaning was 24 h (95% CI 18-28) for standard therapy and 20 h (95% CI 17-34) for HFWHO (hazard ratio [HR] for difference in survival distributions 0·9 [95% CI 0·7-1·2]; log rank p=0·61). Fewer children experienced treatment failure on HFWHO (14 [14%]) compared with standard therapy (33 [33%]; p=0·0016); of these children, those on HFWHO were supported for longer than were those on standard therapy before treatment failure (HR 0·3; 95% CI 0·2-0·6; p<0·0001). 20 (61%) of 33 children who experienced treatment failure on standard therapy were rescued with HFWHO. 12 (12%) of children on standard therapy required transfer to the intensive care unit compared with 14 (14%) of those on HFWHO (difference -1%; 95% CI -7 to 16; p=0·41). Four adverse events occurred (oxygen desaturation and condensation inhalation in the HFWHO group, and two incidences of oxygen tubing disconnection in the standard therapy group); none resulted in withdrawal from the trial. No oxygen-related serious adverse events occurred. Secondary effectiveness outcomes are reported in the Results section.INTERPRETATIONHFWHO did not significantly reduce time on oxygen compared with standard therapy, suggesting that early use of HFWHO does not modify the underlying disease process in moderately severe bronchiolitis. HFWHO might have a role as a rescue therapy to reduce the proportion of children requiring high-

cost intensive care.FUNDINGHunter Children's Research Foundation, John Hunter Hospital Charitable Trust, and the University of Newcastle Priority Research Centre GrowUpWell.

5. Association of Bronchiolitis Clinical Pathway Adherence With Length of Stay and Costs.

Author(s): Bryan, Mersine A; Desai, Arti D; Wilson, Lauren; Wright, Davene R; Mangione-Smith, Rita

Source: Pediatrics; Mar 2017; vol. 139 (no. 3)

Publication Type(s): Journal Article

Available in full text at Pediatrics - from Highwire Press ; Notes: Username: library5 Password: library5

Available in full text at Pediatrics - from Highwire Press

Abstract:OBJECTIVESTo examine the associations between the level of adherence to bronchiolitis clinical pathway recommendations, health care use, and costs.METHODSWe conducted a retrospective cohort study of 267 patients ≤24 months old diagnosed with bronchiolitis from 12/2009 to 7/2012. Clinical pathway adherence was assessed by using a standardized scoring system (0-100) for 18 quality measures obtained by medical record review. Level of adherence was categorized into low, middle, and high tertiles. Generalized linear models were used to examine relationships between adherence tertile and (1) length of stay (LOS) and (2) costs. Logistic regression was used to examine the associations between adherence tertile and probability of inpatient admission and 7-day readmissions.RESULTSMean adherence scores were: ED, 78.8 (SD, 18.1; n = 264), inpatient, 95.0 (SD, 6.3; n = 216), and combined ED/inpatient, 89.1 (SD, 8.1; n = 213). LOS was significantly shorter for cases in the highest versus the lowest adherence tertile (ED, 90 vs 140 minutes, adjusted difference, -51 [95% confidence interval (CI), -73 to -29; P <.05]; inpatient, 3.1 vs 3.8 days, adjusted difference, -0.7 [95% CI, -1.4 to 0.0; P <.05]). Costs were less for cases in the highest adherence tertile (ED, -$84, [95% CI, -$7 to -$161; P <.05], total, -$1296 [95% CI, -126.43 to -2466.03; P <.05]). ED cases in the highest tertile had a lower odds of admission (odds ratio, 0.38 [95% CI, 0.15-0.97; P < .05]). Readmissions did not differ by tertile.CONCLUSIONSHigh adherence to bronchiolitis clinical pathway recommendations across care settings was associated with shorter LOS and lower cost.

6. What Works to Reduce Unnecessary Care for Bronchiolitis? A Qualitative Analysis of a National Collaborative.

Author(s): Ralston, Shawn L; Atwood, Emily Carson; Garber, Matthew D; Holmes, Alison Volpe

Source: Academic pediatrics; Mar 2017; vol. 17 (no. 2); p. 198-204

Publication Type(s): Journal Article

Abstract:OBJECTIVEUnnecessary care is well established as a quality problem affecting acute viral bronchiolitis, one of the most common pediatric illnesses. Although there is an extensive quality improvement literature on the disease, published work primarily reflects the experience of freestanding children's hospitals. We sought to better understand the specific barriers and drivers for successful quality improvement in community and nonfreestanding children's facilities.METHODSWe undertook a mixed methods study to identify correlates of success in a bronchiolitis quality improvement collaborative of community hospitals and children's hospitals within adult hospitals. We assessed site demographic characteristics, compliance with project interventions, and team engagement for association with end of project performance. We then used performance quartiles on a composite assessment of project measures (use of bronchodilators and steroids) to design a purposive sample of sites approached for qualitative interviews.RESULTSTeam engagement was the only factor quantitatively associated with better performance in the overall

cohort. Fifteen sites, from the total cohort of 21, completed qualitative interviews. Qualitative themes around team engagement, including the presence of buy-in for successful sites and the inability to engage colleagues at unsuccessful sites, were important differentiating factors between top and bottom performance quartiles. Regardless of performance quartile, most programs cited intrainstitutional competition for limited resources to do quality improvement work as a specific barrier for pediatrics. The ability to overcome such barriers and specifically garner information technology (IT) resources also differentiated the top and bottom performance quartiles.CONCLUSIONSTeam engagement showed a consistent association with success across our quantitative and qualitative evaluations. Competition for limited resources in this cohort of nonfreestanding children's programs, particularly those in hospital IT, was a key qualitative theme.

7. Systematic review of instruments aimed at evaluating the severity of bronchiolitis.

Author(s): Rodriguez-Martinez, Carlos E; Sossa-Briceño, Monica P; Nino, Gustavo

Source: Paediatric respiratory reviews; Feb 2017

Publication Type(s): Journal Article Review

Abstract:OBJECTIVENo recent studies have performed a systematic review of all available instruments aimed at evaluating the severity of bronchiolitis. The objective of the present study was to perform a systematic review of instruments aimed at evaluating the severity of bronchiolitis and to evaluate their measurement properties.METHODSA systematic search of the literature was performed in order to identify studies in which an instrument for evaluating the severity of bronchiolitis was described. Instruments were evaluated based on their reliability, validity, utility, endorsement frequency, restrictions in range, comprehension, and lack of ambiguity.RESULTSA total of 77 articles, describing a total of 32 different instruments were included in the review. The number of items included in the instruments ranged from 2 to 26. Upon analyzing their content, respiratory rate turned out to be the most frequently used item (in 26/32, 81.3% of the instruments), followed by wheezing (in 25/32, 78.1% of the instruments). In 18 (56.3%) instruments, there was a report of at least one of their measurement properties, mainly reliability and utility. Taking into consideration the information contained in the instruments, as well as their measurement properties, one was considered to be the best one available.CONCLUSIONSAmong the 32 instruments aimed at evaluating the severity of bronchiolitis that were identified and systematically examined, one was considered to be the best one available. However, there is an urgent need to develop better instruments and to validate them in a more comprehensive and proper way.

8. Non-invasive ventilation improves respiratory distress in children with acute viral bronchiolitis: a systematic review.

Author(s): Combret, Yann; Prieur, Guillaume; LE Roux, Pascal; Médrinal, Clément

Source: Minerva anestesiologica; Feb 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDNon-invasive ventilation (NIV) is a common treatment for bronchiolitis. However, consensus concerning its efficacy is lacking. The aim of this systematic review was to assess NIV effectiveness to reduce respiratory distress. Secondary objectives were to summarize the effects of NIV, identify predictive factors for failure and describe settings and applications.METHODSSearches were conducted in MEDLINE Pubmed, PEDro, COCHRANE, EMBASE, CINAHL, Web of Science, Up-todate and Sudoc from 1990 to April 2015. Randomized controlled trials, controlled non-randomized trials and prospective studies of NIV (CPAP: continuous positive airway pressure, biPAP: bi-level CPAP, or NAVA: neurally adjusted ventilator assist) for bronchiolitis in infants younger than 2 years were included.RESULTSFourteen studies were included (total 379

children). Three hundred fifty-seven children were treated with NIV as first intention. Respiratory distress, heart rate, respiratory rate and respiratory effort improved (p<0.05). Results were inconclusive regarding prevention of endotracheal intubation. Few adverse events were reported. NIV reduced carbon dioxide pressure PCO2 in 10 studies. Two randomized controlled studies reported a decrease of 7 mmHg in PCO2 (p<0.05). Predictive factors of NIV failure were apneas, high PCO2, young age, low weight, elevated heart rate and high pediatric risk of mortality score. NIV is mostly administered through a nasal mask, nasal cannula or helmet, with an initial expiratory positive airway pressure of 7 cmH2O.CONCLUSIONSNIV shows promising results for the reduction of respiratory distress in acute viral bronchiolitis, as shown in several recent studies. However, there is a lack of robust studies to confirm this.

9. The Utility of Bedside Lung Ultrasound Findings in Bronchiolitis.

Author(s): Cohen, Joanna S; Hughes, Naomi; Tat, Sonny; Chamberlain, James M; Teach, Stephen J; Boniface, Keith

Source: Pediatric emergency care; Feb 2017; vol. 33 (no. 2); p. 97-100

Publication Type(s): Journal Article

Abstract:OBJECTIVESRecent literature suggests that bedside lung ultrasound may have a role in the evaluation of infants with bronchiolitis. B lines, which are multiple and diffuse vertical artifacts spreading from the lung pleural interface to the edge of the ultrasound screen, have been associated with thickened interlobular septa, extravascular lung water, and diffuse parenchymal disease. The aims of this study were (1) to describe the prevalence of B lines in children younger than 24 months presenting to the emergency department with wheezing, (2) to determine the interrater reliability of lung ultrasound findings in this setting, and (3) to determine the association of B lines with atopy and other clinical findings.METHODSThis was a pilot, prospective, observational study of a convenience sample of patients younger than 2 years presenting with wheezing to a large academic pediatric hospital emergency department. Investigators performed lung ultrasound examinations, and a second provider reviewed the ultrasound examinations to determine interrater reliability. We performed univariate analyses to test for associations between ultrasound findings and atopy, acute illness severity, age, and treatment response.RESULTSStudies were obtained on 29 patients (mean [SD] age, 291 [187] days; 62% male). Twenty-one patients (72%) had compact B lines. B lines were significantly associated with older age and an absence of atopic features. There was poor correlation of lung ultrasound examination interpretation among enrolling providers.CONCLUSIONSIn this small sample of patients with bronchiolitis, B lines were associated with older age and an absence of atopic features. Lung ultrasound interpretation had poor interrater reliability.

10. Quality assessment of acute viral bronchiolitis clinical practice guidelines.

Author(s): Rodriguez-Martinez, Carlos E; Sossa-Briceño, Monica P; Acuña-Cordero, Ranniery

Source: Journal of evaluation in clinical practice; Feb 2017; vol. 23 (no. 1); p. 37-43

Publication Type(s): Journal Article

Abstract:RATIONALE, AIMS AND OBJECTIVESRecently, in an attempt to reduce variability in clinical practice and produce better results for patients, several clinical practice guidelines (CPGs) for the appropriate diagnosis and management of bronchiolitis in infants have been developed. However, the quality of available CPGs for bronchiolitis management has not yet been systematically evaluated. The aim of this study was to assess the quality of acute viral bronchiolitis CPGs.METHODWe performed a systematic and exhaustive search of CPGs on bronchiolitis published from 2000 to 2014. Three independent appraisers assessed the quality of the CPGs using the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument. A standardized score was

calculated for each of the six domains, and the CPGS were rated as recommended, recommended with modifications, or not recommended.RESULTSSix CPGs published between the years 2000 and 2014 were selected from a total of 111 citations. There was substantial agreement among reviewers (ICC: 0.75; 95% CI, 0.61-0.89). The domains that scored the highest were 'scope and purpose', with a mean value of 92.1% (range: 77.8-100%), and 'clarity of presentation' [83.3% (69.4-91.7%)]. Those that scored the lowest were 'applicability' [44.3% (8.3-77.1%)], and 'stakeholder involvement' [66.7% (47.2-94.4%)]. Three CPGS were evaluated as being recommended with modifications, and only two were recommended for use in clinical practice.CONCLUSIONSAvailable bronchiolitis CPGs vary in quality, and the findings of the present study are useful for identifying aspects or domains where there is room for improvement in future CPGs.

11. A systematic review of the psychometric properties of bronchiolitis assessment tools.

Author(s): Davies, Clare J; Waters, Donna; Marshall, Andrea

Source: Journal of advanced nursing; Feb 2017; vol. 73 (no. 2); p. 286-301

Publication Type(s): Journal Article Review

Abstract:AIMThe aim of this study was to assess the psychometric properties of tools developed for the purpose of assessing infants with bronchiolitis.BACKGROUNDBronchiolitis is the leading cause of hospitalization in infants under the age of 1 year. Several bronchiolitis assessment tools have been developed primarily for use in randomized control trials of medical treatments for infants with bronchiolitis, however, the reliability and validity of many of these tools is not well reported.DESIGNSystematic review.DATA SOURCESCINAHL, MEDLINE, EMBASE and PubMed electronic databases were searched between January 1960-December 2015 using the key words 'bronchiolitis' and 'assessment' or 'screen' or 'tool' or 'scale' or 'score'.REVIEW METHODSA systematic review of the psychometric properties of bronchiolitis assessment tools was undertaken using the COSMIN checklist.RESULTSFourteen studies meeting the inclusion criteria were reviewed and the methodological quality of the studies and reported psychometric properties of 11 instruments were assessed. Overall, the reliability and validity of bronchiolitis assessment tools was poorly established. Although several studies reported that their tools had good inter-rater reliability, the methodological quality of these studies was generally poor. Only one study underwent psychometric testing that was assessed as being of excellent quality. The Respiratory Distress Assessment Index was deemed to have undergone the most rigorous psychometric testing but had poor to moderate construct validity and considerable test-retest error.CONCLUSIONCurrent bronchiolitis assessment tools lack clearly established reliability and validity and may not be sensitive to clinically meaningful outcomes for patients.

12. High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study).

Author(s): Milési, Christophe; Essouri, Sandrine; Pouyau, Robin; Liet, Jean-Michel; Afanetti, Mickael; Portefaix, Aurélie; Baleine, Julien; Durand, Sabine; Combes, Clémentine; Douillard, Aymeric; Cambonie, Gilles; Groupe Francophone de Réanimation et d'Urgences Pédiatriques (GFRUP)

Source: Intensive care medicine; Feb 2017; vol. 43 (no. 2); p. 209-216

Publication Type(s): Journal Article

Abstract:PURPOSENasal continuous positive airway pressure (nCPAP) is currently the gold standard for respiratory support for moderate to severe acute viral bronchiolitis (AVB). Although oxygen delivery via high flow nasal cannula (HFNC) is increasingly used, evidence of its efficacy and safety is lacking in infants.METHODSA randomized controlled trial was performed in five pediatric intensive

care units (PICUs) to compare 7 cmH2O nCPAP with 2 L/kg/min oxygen therapy administered with HFNC in infants up to 6 months old with moderate to severe AVB. The primary endpoint was the percentage of failure within 24 h of randomization using prespecified criteria. To satisfy noninferiority, the failure rate of HFNC had to lie within 15% of the failure rate of nCPAP. Secondary outcomes included success rate after crossover, intubation rate, length of stay, and serious adverse events.RESULTSFrom November 2014 to March 2015, 142 infants were included and equally distributed into groups. The risk difference of -19% (95% CI -35 to -3%) did not allow the conclusion of HFNC noninferiority (p = 0.707). Superiority analysis suggested a relative risk of success 1.63 (95% CI 1.02-2.63) higher with nCPAP. The success rate with the alternative respiratory support, intubation rate, durations of noninvasive and invasive ventilation, skin lesions, and length of PICU stay were comparable between groups. No patient had air leak syndrome or died.CONCLUSIONIn young infants with moderate to severe AVB, initial management with HFNC did not have a failure rate similar to that of nCPAP. This clinical trial was recorded in the National Library of Medicine registry (NCT 02457013).

13. Non-invasive respiratory support for infants with bronchiolitis: a national survey of practice.

Author(s): Turnham, H; Agbeko, R S; Furness, J; Pappachan, J; Sutcliffe, A G; Ramnarayan, P

Source: BMC pediatrics; Jan 2017; vol. 17 (no. 1); p. 20

Publication Type(s): Journal Article

Available in full text at BMC Pediatrics - from ProQuest

Available in full text at BMC Pediatrics - from BioMed Central

Available in full text at BMC Pediatrics - from National Library of Medicine

Abstract:BACKGROUNDBronchiolitis is a common respiratory illness of early childhood. For most children it is a mild self-limiting disease but a small number of children develop respiratory failure. Nasal continuous positive airway pressure (nCPAP) has traditionally been used to provide non-invasive respiratory support in these children, but there is little clinical trial evidence to support its use. More recently, high-flow nasal cannula therapy (HFNC) has emerged as a novel respiratory support modality. Our study aims to describe current national practice and clinician preferences relating to use of non-invasive respiratory support (nCPAP and HFNC) in the management of infants (<12 months old) with acute bronchiolitis.METHODSWe performed a cross-sectional web-based survey of hospitals with inpatient paediatric facilities in England and Wales. Responses were elicited from one senior doctor and one senior nurse at each hospital. We analysed the proportion of hospitals using HFNC and nCPAP; clinical thresholds for their initiation; and clinician preferences regarding first-line support modality and future research.RESULTSThe survey was distributed to 117 of 171 eligible hospitals; 97 hospitals provided responses (response rate: 83%). The majority of hospitals were able to provide nCPAP (89/97, 91.7%) or HFNC (71/97, 73.2%); both were available at 65 hospitals (67%). nCPAP was more likely to be delivered in a ward setting in a general hospital, and in a high dependency setting in a tertiary centre. There were differences in the oxygenation and acidosis thresholds, and clinical triggers such as recurrent apnoeas or work of breathing that influenced clinical decisions, regarding when to start nCPAP or HFNC. More individual respondents with access to both modalities (74/106, 69.8%) would choose HFNC over nCPAP as their first-line treatment option in a deteriorating child with bronchiolitis.CONCLUSIONSDespite lack of randomised trial evidence, nCPAP and HFNC are commonly used in British hospitals to support infants with acute bronchiolitis. HFNC appears to be currently the preferred first-line modality for non-invasive respiratory support due to perceived ease of use.

14. Viral bronchiolitis.

Author(s): Florin, Todd A; Plint, Amy C; Zorc, Joseph J

Source: Lancet (London, England); Jan 2017; vol. 389 (no. 10065); p. 211-224

Publication Type(s): Research Support, N.i.h., Extramural Journal Article Review

Abstract: Viral bronchiolitis is a common clinical syndrome affecting infants and young children. Concern about its associated morbidity and cost has led to a large body of research that has been summarised in systematic reviews and integrated into clinical practice guidelines in several countries. The evidence and guideline recommendations consistently support a clinical diagnosis with the limited role for diagnostic testing for children presenting with the typical clinical syndrome of viral upper respiratory infection progressing to the lower respiratory tract. Management is largely supportive, focusing on maintaining oxygenation and hydration of the patient. Evidence suggests no benefit from bronchodilator or corticosteroid use in infants with a first episode of bronchiolitis. Evidence for other treatments such as hypertonic saline is evolving but not clearly defined yet. For infants with severe disease, the insufficient available data suggest a role for high-flow nasal cannula and continuous positive airway pressure use in a monitored setting to prevent respiratory failure.

15. The interdependencies of viral load, the innate immune response, and clinical outcome in children presenting to the emergency department with respiratory syncytial virus-associated bronchiolitis.

Author(s): Piedra, Felipe-Andrés; Mei, Minghua; Avadhanula, Vasanthi; Mehta, Reena; Aideyan, Letisha; Garofalo, Roberto P; Piedra, Pedro A

Source: PloS one; 2017; vol. 12 (no. 3); p. e0172953

Publication Type(s): Journal Article

Available in full text at PLoS ONE - from National Library of Medicine

Available in full text at PLoS One - from ProQuest

Abstract: Respiratory syncytial virus (RSV) causes significant infant morbidity and mortality. For decades severe RSV-induced disease was thought to result from an uncontrolled host response to viral replication, but recent work suggests that a strong innate immune response early in infection is protective. To shed light on host-virus interactions and the viral determinants of disease, copy numbers of five RSV genes (NS1, NS2, N, G, F) were measured by quantitative real-time polymerase chain reaction (qPCR) in nasal wash samples from children with RSV-associated bronchiolitis. Correlations were sought with host cytokines/chemokines and biomarkers. Associations with disposition from the emergency department (hospitalized or sent home) and pulse oximetry O2 saturation levels were also sought. Additionally, RNase P copy number was measured and used to normalize nasal wash data. RSV gene copy numbers were found to significantly correlate with both cytokine/chemokine and biomarker levels; and RNase P-normalized viral gene copy numbers (NS1, NS2, N and G) were significantly higher in infants with less severe disease. Moreover, three of the normalized viral gene copy numbers (NS1, NS2, and N) correlated significantly with arterial O2 saturation levels. The data support a model where a higher viral load early in infection can promote a robust innate immune response that protects against progression into hypoxic RSV-induced lower respiratory tract illness.

16. Complementary and alternative medicine for the treatment of bronchiolitis in infants: A systematic review.

Author(s): Kua, Kok Pim; Lee, Shaun Wen Huey

Source: PloS one; 2017; vol. 12 (no. 2); p. e0172289

Publication Type(s): Journal Article

Available in full text at PLoS ONE - from National Library of Medicine

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Abstract:BACKGROUNDBronchiolitis is a common cause of hospitalization among infants. The limited effectiveness of conventional medication has prompted the use of complementary and alternative medicine (CAM) as alternative or adjunctive therapy for the management of bronchiolitis.AIMSTo determine the effectiveness and safety of CAM for the treatment of bronchiolitis in infants aged less than 2 years.METHODSA systematic electronic search was performed in Medline, Embase, CINAHL, AMED, and Cochrane Central Register of Controlled Trials (CENTRAL) from their respective inception to June 30, 2016 for studies evaluating CAM as an intervention to treat bronchiolitis in infants (1 month to 2 years of age). The CAM could be any form of treatment defined by the National Center for Complementary and Integrative Health (NCCIH) and was utilized either as a single agent or adjunctive therapy. The predefined primary outcome was length of hospital stay. Secondary outcomes were time to resolution of bronchiolitis symptoms, adverse events, and all other clinical outcomes reported by the included studies.RESULTSThe review identified 11 studies (8 randomized controlled trials and 3 cohort studies) examining four herbal preparations and four supplements used either as adjunctive or alternative therapy for bronchiolitis in 904 infants. Most studies were of moderate quality. Among six studies reporting on length of stay, a significant benefit was found for Chinese herbal medicine compared to ribavirin in one cohort study (n = 66) and vitamin D compared to placebo in one randomized controlled trial (n = 89). Studies of Chinese herbal medicine (4 studies, n = 365), vitamin D (1 study, n = 89), N-acetylcysteine (1 study, n = 100), and magnesium (2 studies, n = 176) showed some benefits with respect to clinical severity scores, oxygen saturation, and other symptoms, although data were sparse for any single intervention and the outcomes assessed and reported varied across studies. Only five studies reported on adverse events; no serious adverse events were reported.CONCLUSIONSAmong 11 studies examining the effect of CAM on inpatients with bronchiolitis, six reported on the review's primary outcome of length of hospital stay. In general, findings did not show a significant benefit associated with the primary outcome. Preliminary evidence indicated that Chinese herbal medicine mixtures, vitamin D, N-acetylcysteine, and magnesium might be useful in managing the symptoms of bronchiolitis. However, the evidence was not sufficient or rigorous enough to formulate recommendations for the use of any CAM. Among studies that reported adverse events, no serious harms were noted.

Respiratory Syncytial Virus

1. 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); May 2017; vol. 49 (no. 5); p. 333-340

Publication Type(s): Journal Article

Abstract:BACKGROUNDRespiratory 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.METHODSWe 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).RESULTSA 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).CONCLUSIONSThe 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.

2. Sensitive detection of respiratory syncytial virus based on a dual signal amplified plasmonic enzyme-linked immunosorbent assay.

Author(s): Zhan, Lei; Wu, Wen Bi; Yang, Lin; Huang, Cheng Zhi

Source: Analytica chimica acta; Apr 2017; vol. 962 ; p. 73-79

Publication Type(s): Journal Article

Abstract: The timely detection of infectious pathogen is critical in clinical early diagnosis and treatment of infectious diseases. Plasmonic enzyme-linked immunosorbent assay (ELISA), by means of enzyme-mediated growth or aggregation of AuNPs, has received considerable attention because it allows a naked-eye detection of target in very low numbers. In this work, a dual-signal amplified plasmonic ELISA combined the high loading capacity of magnetic beads with the establishing stimulation effect of zinc ion has been developed to detect RSV as a model pathogen based on alkaline phosphatase-triggered dispersion of aggregated AuNPs. In ideal conditions, the proposed immunoassay can conveniently distinguish the concentration of RSV in a range of 0.1-30 pg/mL. In addition, the limit of detection of RSV of this immunoassay exceeds that of conventional ELISA by about 50 times. The high sensitivity makes this approach a good alternative to existing colorimetric immunoassays for pathogen detection.

3. Meeting report: WHO consultation on Respiratory Syncytial Virus (RSV) vaccine development, Geneva, 25-26 April 2016.

Author(s): Giersing, Birgitte K; Karron, Ruth A; Vekemans, Johan; Kaslow, David C; Moorthy, Vasee S

Source: Vaccine; Mar 2017

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) is a leading viral cause of respiratory morbidity and mortality in infants and young children worldwide. Low and middle income countries (LMICs) account for approximately 99% of the global mortality estimates in this population, with up to 200,000 RSV deaths per year. The vaccine product development pipeline is diverse with the most advanced clinical candidate currently in phase III efficacy testing in pregnant women. In addition, a long-acting RSV-neutralizing monoclonal antibody (mAb) to be administered at birth to prevent serious RSV-related respiratory disease is in late stage clinical development, as are additional conventional mAb for use in high-risk infants. Thus, there is a realistic possibility that an effective new intervention to prevent RSV disease will be available in the next 5-10year horizon. In anticipation of this outcome, the Strategic Advisory Group of Experts for Immunization (SAGE), WHO's vaccine policy recommendation body, reviewed the status of RSV vaccine and monoclonal antibody development in April 2016. Although substantial progress towards licensure has broadened the research agenda to consider intervention impact and cost effectiveness, significant gaps remain in the data that will be needed to inform and support a policy recommendation for implementation.

These aspects were the focus of WHO's second consultation on RSV vaccines and single dosage extended half-life mAb for prophylaxis.

4. Prevalence of co-infection between respiratory syncytial virus and influenza in children.

Author(s): Meskill, Sarah D; Revell, Paula A; Chandramohan, Lakshmi; Cruz, Andrea T

Source: The American journal of emergency medicine; Mar 2017; vol. 35 (no. 3); p. 495-498

Publication Type(s): Journal Article

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) and influenza have varying degree of seasonal overlap.OBJECTIVETo determine the prevalence of co-infection of RSV and influenza compared to the prevalence of those infections independently when both are in season.METHODSThis was a retrospective cross-sectional study of children evaluated between July 2010 and June 2013 for viral respiratory infection using multiplex PCR. Seasonality was defined retrospectively as weeks when >2% of the total annual positive tests were obtained and was calculated for influenza A, influenza B, and RSV independently. Periods of overlapping seasonality of RSV and influenza A and RSV and influenza B were identified. The expected incidences of co-infection were modeled as the product of the incidences of the individual viruses.RESULTS13,664 specimens were sent for PCR during the study period. Over all 3 seasons, RSV overlapped with influenza A and B for 22 and 18weeks, respectively; in 2011-12, RSV overlapped with neither influenza A nor B. Based on modeling, there were 6-7 fold fewer cases of RSV/influenza co-infection observed than expected: RSV/influenza A 77 vs. 12, ($p \leq 0.001$; RSV/influenza B 76 vs. 11 ($p \leq 0.001$).CONCLUSIONSThe observed incidence of co-infectivity of RSV and influenza was significantly less than the expected incidence even when both were co-circulating. In light of these data, it may be reasonable to forgo rapid influenza testing or empiric antiviral treatment for children whom rapid RSV testing is positive and who are at low risk of influenza-related complications, especially in times of antiviral therapy shortages.

5. Estimating the burden of respiratory syncytial virus (RSV) on respiratory hospital admissions in children less than five years of age in England, 2007-2012.

Author(s): Reeves, Rachel Melanie; Hardelid, Pia; Gilbert, Ruth; Warburton, Fiona; Ellis, Joanna; Pebody, Richard G

Source: Influenza and other respiratory viruses; Mar 2017; vol. 11 (no. 2); p. 122-129

Publication Type(s): Journal Article

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) is a leading cause of hospital admission in young children. With several RSV vaccines candidates undergoing clinical trials, recent estimates of RSV burden are required to provide a baseline for vaccine impact studies.OBJECTIVESTo estimate the number of RSV-associated hospital admissions in children aged <5 years in England over a 5-year period from 2007 using ecological time series modelling of national hospital administrative data.PATIENTS/METHODSMultiple linear regression modelling of weekly time series of laboratory surveillance data and Hospital Episode Statistics (HES) data was used to estimate the number of hospital admissions due to major respiratory pathogens including RSV in children <5 years of age in England from mid-2007 to mid-2012, stratified by age group (<6 months, 6-11 months, 1-4 years) and primary diagnosis: bronchiolitis, pneumonia, unspecified lower respiratory tract infection (LRTI), bronchitis and upper respiratory tract infection (URTI).RESULTSOn average, 33 561 (95% confidence interval 30 429-38 489) RSV-associated hospital admissions in children <5 years of age occurred annually from 2007 to 2012. Average annual admission rates were 35.1 (95% CI: 32.9-38.9) per 1000 children aged <1 year and 5.31 (95% CI: 4.5-6.6) per 1000 children aged 1-4 years. About 84% (95% CI: 81-91%) of RSV-associated admissions were for LRTI. The diagnosis-specific burden of RSV-

associated admissions differed significantly by age group.CONCLUSIONSRSV remains a significant cause of hospital admissions in young children in England. Individual-level analysis of RSV-associated admissions is required to fully describe the burden by age and risk group and identify optimal prevention strategies.

6. Population Pharmacokinetic Modeling of JNJ-53718678, a Novel Fusion Inhibitor for the Treatment of Respiratory Syncytial Virus: Results from a Phase I, Double-Blind, Randomized, Placebo-Controlled First-in-Human Study in Healthy Adult Subjects.

Author(s): Huntjens, Dymphy R H; Ouwerkerk-Mahadevan, Sivi; Brochot, Anne; Rusch, Sarah; Stevens, Marita; Verloes, Rene

Source: Clinical pharmacokinetics; Feb 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDJNJ-53718678 is a potent small-molecule inhibitor of the F-glycoprotein-mediated complex membrane fusion process of the respiratory syncytial virus. Here, we report the pharmacokinetics, the population pharmacokinetic modeling, and the safety and tolerability of JNJ-53718678 from the first-in-human, double-blind, randomized, placebo-controlled phase I study.METHODSHealthy subjects were randomized (6:3) into five single-dose groups (25-1000 mg) or three multiple-dose groups [250 mg every 24 h (q24h), 500 mg q24h, 250 mg every 12 h; fed conditions for 8 days] to receive JNJ-53718678 or placebo. Blood and urine samples were collected at several timepoints up to 72 h after intake of JNJ-53718678 and analyzed using validated liquid chromatography-mass spectrometry methods. A population pharmacokinetic model was developed and validated.RESULTSPeak plasma concentrations of JNJ-53718678 increased with increasing single (159 ± 54.9 to 6702 ± 1733 ng/mL) and multiple (on day 8, 1528 ± 256 to 2655 ± 591 ng/mL) doses. Steady-state conditions were reached on day 2 of the 8-day dosing regimen. Less than 4% of JNJ-53718678 was excreted in urine across all dose groups. Mean exposure of JNJ-53718678 was 7% lower in the fed state compared with the fasted state at the same dose. A two-compartment model with first-order absorption with parallel linear and non-linear elimination best described the pharmacokinetics of JNJ-53718678. No covariate effects were observed.CONCLUSIONSA population pharmacokinetic model that describes the concentration data well with good precision of all parameter estimates was developed and validated. JNJ-53718678 was well tolerated at all single and multiple doses studied.

7. Aptamers for respiratory syncytial virus detection.

Author(s): Percze, Krisztina; Szakács, Zoltán; Scholz, Éva; András, Judit; Szeitner, Zsuzsanna; Kieboom, Corné H van den; Ferwerda, Gerben; Jonge, Marien I de; Gyurcsányi, Róbert E; Mészáros, Tamás

Source: Scientific reports; Feb 2017; vol. 7 ; p. 42794

Publication Type(s): Journal Article

Abstract: The identification of the infectious agents is pivotal for appropriate care of patients with viral diseases. Current viral diagnostics rely on selective detection of viral nucleic acid or protein components. In general, detection of proteins rather than nucleic acids is technically more suitable for rapid tests. However, protein-based virus identification methods depend on antibodies limiting the practical applicability of these approaches. Aptamers rival antibodies in target selectivity and binding affinity, and excel in terms of robustness and cost of synthesis. Although aptamers have been generated for virus identification in laboratory settings, their introduction into routine virus diagnostics has not been realized, yet. Here, we demonstrate that the rationally designed SELEX protocol can be applied on whole virus to select aptamers, which can potentially be applied for viral

diagnostics. This approach does not require purified virus protein or complicated virus purification. The presented data also illustrate that corroborating the functionality of aptamers with various approaches is essential to pinpoint the most appropriate aptamer amongst the panel of candidates obtained by the selection. Our protocol yielded aptamers capable of detecting respiratory syncytial virus (RSV), an important pathogen causing severe disease especially in young infants, at clinically relevant concentrations in complex matrices.

8. Development of TaqMan RT-qPCR for the detection of type A human respiratory syncytial virus.

Author(s): Abdel-Moneim, Ahmed S; Shehab, Gaber M; Alsulaimani, Adnan A; Al-Malky, Mater I R

Source: Molecular and cellular probes; Feb 2017

Publication Type(s): Journal Article

Abstract: The human respiratory syncytial virus is a common respiratory pathogen in children. Improved diagnosis of the virus is dependent on the development of tools for the rapid detection and estimation of the viral loads. In the current study, RT-qPCR using TaqMan hydrolysis probe based on the F gene detection was developed to identify and quantify hRSV in clinical samples. The assay was validated by comparing the results with a commercially available RT-qPCR kit. The newly developed assay was sensitive in detecting hRSV positive samples (59/126) which were equivalent to those detected by the commercial kit (57/126) with a detection limit of 1 × 102 copies/mL. A high correlation was found between the results of the newly developed assay and the commercial one. It was concluded that the newly developed RT-qPCR assay can be used as a sensitive detection tool for hRSV-A.

9. Potent single-domain antibodies that arrest respiratory syncytial virus fusion protein in its prefusion state.

Author(s): Rossey, Iebe; Gilman, Morgan S A; Kabeche, Stephanie C; Sedeyn, Koen; Wrapp, Daniel; Kanekiyo, Masaru; Chen, Man; Mas, Vicente; Spitaels, Jan; Melero, José A; Graham, Barney S; Schepens, Bert; McLellan, Jason S; Saelens, Xavier

Source: Nature communications; Feb 2017; vol. 8 ; p. 14158

Publication Type(s): Journal Article

Available in full text at Nature Communications - from ProQuest

Abstract: Human respiratory syncytial virus (RSV) is the main cause of lower respiratory tract infections in young children. The RSV fusion protein (F) is highly conserved and is the only viral membrane protein that is essential for infection. The prefusion conformation of RSV F is considered the most relevant target for antiviral strategies because it is the fusion-competent form of the protein and the primary target of neutralizing activity present in human serum. Here, we describe two llama-derived single-domain antibodies (VHHs) that have potent RSV-neutralizing activity and bind selectively to prefusion RSV F with picomolar affinity. Crystal structures of these VHHs in complex with prefusion F show that they recognize a conserved cavity formed by two F protomers. In addition, the VHHs prevent RSV replication and lung infiltration of inflammatory monocytes and T cells in RSV-challenged mice. These prefusion F-specific VHHs represent promising antiviral agents against RSV.

10. Rapid and sensitive real-time assay for the detection of respiratory syncytial virus using RT-SIBA®.

Author(s): Eboigbodin, Kevin E; Moilanen, Kirsi; Elf, Sonja; Hoser, Mark

Source: BMC infectious diseases; Feb 2017; vol. 17 (no. 1); p. 134

Publication Type(s): Journal Article

Available in full text at BMC Infectious Diseases - from BioMed Central

Available in full text at BMC Infectious Diseases - from National Library of Medicine

Available in full text at BMC Infectious Diseases - from ProQuest

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) is one of the most common causes of respiratory tract infections among young children and the elderly. Timely and accurate diagnosis of respiratory tract infections improves patient care and minimizes unnecessary prescriptions of antibiotics. We sought to develop a rapid nucleic acid tests for the detection of RSV within minutes, while retaining the high sensitivity achieved with RT-PCR.METHODSWe developed and evaluated a reverse transcription isothermal nucleic acid amplification method, reverse transcription strand invasion based amplification (RT-SIBA), for the rapid detection of RSV.RESULTSThe developed RT-SIBA assay showed good sensitivity by detecting as few as 10 copies of RSV RNA within 20 min compared with reverse transcription polymerase chain reaction, which took approximately 2 h. The performance of the RT-SIBA RSV assay was further investigated using nasopharyngeal swab specimens. The RT-SIBA assay had a sensitivity of 100% (25/25) and a specificity of 100% (15/15).CONCLUSIONRT-SIBA did not require highly purified RNA for the rapid detection of RSV and was therefore compatible with rapid specimen processing methods. This reduces the complexity of specimen preparation and further shortens the total amount of time needed to detect RSV in clinical specimens. The developed RT-SIBA assay for RSV could be a useful tool for prompt management of this infection.

11. 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; Feb 2017; vol. 181 ; p. 183

Publication Type(s): Journal Article

Abstract:OBJECTIVESTo determine the differences in number of respiratory syncytial virus (RSV) hospitalizations and outcomes in infants 290/7-346/7 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.STUDY DESIGNChildren <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.RESULTSOf 1063 RSV hospitalizations in infants <12 months old, 7.1% (34/482) in S1 and 9.8% (57/581) in S2 occurred in 290/7-346/7 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 290/7-346/7 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.CONCLUSIONSIn 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.

12. Age-Specific Profiles of Antibody Responses against Respiratory Syncytial Virus Infection.

Author(s): Jounai, Nao; Yoshioka, Megumi; Tozuka, Miyuki; Inoue, Kazue; Oka, Tatsuya; Miyaji, Kazuki; Ishida, Katsuyasu; Kawai, Naoki; Ikematsu, Hideyuki; Kawakami, Chiaki; Shimizu, Hiroyuki; Mori, Masaaki; Ishii, Ken J; Takeshita, Fumihiko

Source: EBioMedicine; Feb 2017; vol. 16 ; p. 124-135

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) is one of the most prevalent causative agents of lower respiratory tract infections worldwide, especially in infants around 3 to 4months old. Infants at such a young age have maternally-transferred passive antibodies against RSV but do not have active immune systems efficient enough for the control of RSV infection. In order to elucidate age-specific profiles of immune responses against RSV protection, antibody responses were examined by using blood samples in both acute and convalescent phases obtained from child patients and adult patients. In addition to the serum neutralization activity, antibody responses to the RSV fusion protein (F protein) were dissected by analyzing levels of total IgG, IgG subclasses, the binding stability, and the levels of antibody for the neutralization epitopes. It was suggested that children's antibody responses against RSV are matured over months and years in at least 5 stages based on 1) levels of the neutralization titer and IgG3 for F protein in the convalescent phase, 2) geometric mean ratios of the neutralization titers and levels of IgG1 and IgG2 for F protein in the convalescent phase compared to those levels in the acute phase, 3) the affinity maturation of IgG for F protein and the cross reactivity of IgG for RSV glycoproteins of groups A and B, 4) levels of neutralization epitope-specific IgG, and 5) augmentation of overall antibody responses due to repetitive RSV infection.

13. Structural basis for antibody cross-neutralization of respiratory syncytial virus and human metapneumovirus.

Author(s): Wen, Xiaolin; Mousa, Jarrod J; Bates, John T; Lamb, Robert A; Crowe, James E; Jardetzky, Theodore S

Source: Nature microbiology; Jan 2017; vol. 2 ; p. 16272

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) and human metapneumovirus (HMPV) are two closely related viruses that cause bronchiolitis and pneumonia in infants and the elderly1, with a significant health burden2-6. There are no licensed vaccines or small-molecule antiviral treatments specific to these two viruses at present. A humanized murine monoclonal antibody (palivizumab) is approved to treat high-risk infants for RSV infection7,8, but other treatments, as well as vaccines, for both viruses are still in development. Recent epidemiological modelling suggests that cross-immunity between RSV, HMPV and human parainfluenzaviruses may contribute to their periodic outbreaks9, suggesting that a deeper understanding of host immunity to these viruses may lead to enhanced strategies for their control. Cross-reactive neutralizing antibodies to the RSV and HMPV fusion (F) proteins have been identified10,11. Here, we examine the structural basis for cross-reactive antibody binding to RSV and HMPV F protein by two related, independently isolated antibodies, MPE8 and 25P13. We solved the structure of the MPE8 antibody bound to RSV F protein and identified the 25P13 antibody from an independent blood donor. Our results indicate that both antibodies use germline residues to interact with a conserved surface on F protein that could guide the emergence of cross-reactivity. The induction of similar cross-reactive neutralizing antibodies using structural vaccinology approaches could enhance intrinsic cross-immunity to these paramyxoviruses and approaches to controlling recurring outbreaks.

14. 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; Jan 2017; vol. 35 (no. 3); p. 496-502

Publication Type(s): Journal Article

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.

15. Evaluation of Alere™ i RSV for rapid detection of respiratory syncytial virus in children hospitalized with acute respiratory tract infection.

Author(s): Peters, Rebecca Marie; Schnee, Sarah Valerie; Tabatabai, Julia; Schnitzler, Paul; Pfeil, Johannes

Source: Journal of clinical microbiology; Jan 2017

Publication Type(s): Journal Article

Available in full text at Journal of Clinical Microbiology - from National Library of Medicine

Abstract: Alere™ i RSV is a novel rapid test which applies a nicking enzyme amplification reaction to detect respiratory syncytial virus in point-of-care settings. In this study, we evaluated the Alere™ i RSV assay by using frozen nasopharyngeal swab samples that were collected in viral transport medium from children hospitalized with acute respiratory tract infection during winter season 2015/2016. Alere™ i RSV assay test results were compared to Altona® RealStar RSV real-time reverse transcription PCR (RT-PCR). We found that the overall sensitivity and specificity of the Alere™ i RSV test assay was 100% (CI95 93% - 100%) and 97% (CI95 89% - 100%), respectively. Positive samples were identified within 5-7 minutes from sample collection. Overall, the Alere™ i RSV test assay performed well in comparison to the RT-PCR assay and has the potential to facilitate the detection of RSV in point-of-care settings.

16. Respiratory syncytial virus associated hospitalizations in preterm infants of 29 to 32 weeks gestational age using a risk score tool for palivizumab prophylaxis.

Author(s): Resch, B; Bramreiter, V S; Kurath-Koller, S; Freidl, T; Urlesberger, B

Source: European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology; Jan 2017

Publication Type(s): Journal Article

Abstract: To evaluate the efficacy of palivizumab in infants of 29 to 32 weeks of gestational age (GA) based on a risk score tool developed for Austria. Retrospective single-center cohort study including all preterm infants of 29 (+0) to 32 (+6) weeks of GA born between 2004 and 2012 at a tertiary care university hospital. Data on RSV-related hospitalizations over the first 2 years of life were analyzed and compared between those having received palivizumab and those without. The study population was comprised of 789 of 816 screened infants, of whom 262 (33%) had received palivizumab and 527 (67%) had not. Nine of 107 rehospitalizations (8.4%) in the palivizumab group compared to 32 of 156 rehospitalizations (20.5%) in the group without prophylaxis were tested RSV-positive (p = 0.004; OR 0.356 [CI 90% 0.184-0.689]). Proven and calculated RSV hospitalization rate was 3.1% (8/262) in the palivizumab group and 5.9% (31/527) in the group without (p = 0.042; OR 0.504 [CI 90% 0.259-0.981]). Increasing number of risk factors (up to three) increased the RSV hospitalization rate in infants with (6.1%) and without (9.0%) prophylaxis. RSV-associated hospitalizations did not differ between groups with regard to length of stay, severity of infection, age at hospitalization, demand of supplemental oxygen, need for mechanical ventilation, and admission rate to the ICU. A risk score tool developed for infants of 29 to 32 weeks of gestational age led to a reduction of RSV-associated hospitalizations without influencing the severity of disease.

17. Predicting the relative impacts of maternal and neonatal respiratory syncytial virus (RSV) vaccine target product profiles: A consensus modelling approach.

Author(s): Pan-Ngum, Wirichada; Kinyanjui, Timothy; Kiti, Moses; Taylor, Sylvia; Toussaint, Jean-François; Saralamba, Sompob; Van Effelterre, Thierry; Nokes, D James; White, Lisa J

Source: Vaccine; Jan 2017; vol. 35 (no. 2); p. 403-409

Publication Type(s): Journal Article

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) is the major viral cause of infant and childhood lower respiratory tract disease worldwide. Defining the optimal target product profile (TPP) is complicated due to a wide range of possible vaccine properties, modalities and an incomplete understanding of the mechanism of natural immunity. We report consensus population level impact projections based on two mathematical models applied to a low income setting.METHODTwo structurally distinct age-specific deterministic compartmental models reflecting uncertainty associated with the natural history of infection and the mechanism by which immunity is acquired and lost were constructed. A wide range of vaccine TPPs were explored including dosing regime and uptake, and effects in the vaccinated individual on infectiousness, susceptibility, duration of protection, disease severity and interaction with maternal antibodies and natural induced immunity. These were combined with a range of vaccine implementation strategies, targeting the highest priority age group and calibrated using hospitalization data from Kilifi County Hospital, Kenya.FINDINGSBoth models were able to reproduce the data. The impact predicted by the two models was qualitatively similar across the range of TPPs, although one model consistently predicted higher impact than the other. For a proposed realistic range of scenarios of TPP combinations, the models predicted up to 70% reduction in hospitalizations in children under five years old. Vaccine designs which reduced the duration and infectiousness of infection were predicted to have higher impacts. The models were sensitive to the coverage and rate of loss of

vaccine protection but not to the interaction between vaccine and maternal/naturally acquired immunity.CONCLUSIONThe results suggest that vaccine properties leading to reduced virus circulation by lessening the duration and infectiousness of infection upon challenge are of major importance in population RSV disease control. These features should be a focus for vaccine development.

18. Outcomes of Infants Receiving Palivizumab Prophylaxis for Respiratory Syncytial Virus in Canada and Italy: An International, Prospective Cohort Study.

Author(s): Manzoni, Paolo; Paes, Bosco; Lanctôt, Krista L; Dall'Agnola, Alberto; Mitchell, Ian; Calabrese, Sara; Maule, Milena; Girardi, Elisa; Harimoto, Tetsuhiro; Li, Abby

Source: The Pediatric infectious disease journal; Jan 2017; vol. 36 (no. 1); p. 2-8

Publication Type(s): Journal Article

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) infection frequently results in RSV-related hospitalization (RSVH) in young infants. We examined the outcomes of palivizumab recipients within the Canadian Registry (CARESS) and the Torino-Verona Italian Registry over the 2002-2014 RSV seasons.METHODSRSVHs were captured during the study seasons. Premature infants who received palivizumab (≤35 completed weeks' gestational age; group1) were compared with infants given palivizumab for underlying disorders regardless of gestational age (group 2). Variables and between-group incidences were analyzed. Risk factors associated with RSVH were assessed by logistic regression.RESULTSA total of 14,468 palivizumab-exposed infants were enrolled (group 1, n = 9093; group 2, n = 4856; miscellaneous, n = 519). RSVH was significantly more frequent in group 2 (211/4856, 4.34%) versus group 1 infants (216/9093, 2.37% [relative risk 1.93; 95% confidence interval (CI): 1.60-2.33; P < 0.0001]). Infants with neuromuscular disorders (7.88%), airway anomalies (5.95%), bronchopulmonary dysplasia (4.75%) and hemodynamically significant congenital heart disease (4.10%) had the highest RSVH incidences. After multivariable logistic regression, only neuromuscular disease [odds ratio [OR] 4.29; 95% CI: 2.30-8.00; P < 0.01], airway anomalies (OR 3.23; 95% CI: 1.92-5.43; P < 0.01), Down syndrome (OR 2.25; 95% CI: 1.31-3.89; P < 0.01), hemodynamically significant congenital heart disease (OR 2.24; 95% CI: 1.52-3.31; P < 0.001), prematurity ≤28 completed weeks' gestational age (OR 1.82; 95% CI: 1.29-2.58; P < 0.001) and bronchopulmonary dysplasia (OR 1.81; 95% CI: 1.31-2.50; P < 0.001) significantly predicted RSVH. No significant association was detected with the number of doses administered or the time elapsed after the previous dose.CONCLUSIONSRSVH rates are higher in infants given palivizumab for reasons other than prematurity. It is uncertain whether these findings relate to inadequate current palivizumab dosing protocols or to a specific increased RSVH risk inherent in infants with severe underlying comorbidities.

19. 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; Jan 2017; vol. 215 (no. 1); p. 24-33

Publication Type(s): Journal Article

Abstract:BACKGROUND 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.METHODS 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.RESULTS 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.CONCLUSIONS The RSV-PreF vaccine elicited rapid RSV neutralizing antibody responses in healthy young men, with an acceptable adverse event profile.

20. 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; Jan 2017; vol. 215 (no. 1); p. 17-23

Publication Type(s): Journal Article

Abstract:BACKGROUND 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.METHODS 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.RESULTS 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.CONCLUSIONS 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.

21. Respiratory syncytial virus immunoprophylaxis in high-risk infants and development of childhood asthma.

Author(s): Carroll, Kecia N; Gebretsadik, Tebeb; Escobar, Gabriel J; Wu, Pingsheng; Li, Sherian Xu; Walsh, Eileen M; Mitchel, Ed; Sloan, Chantel D; Dupont, William D; Hartert, Tina V

Source: The Journal of allergy and clinical immunology; Jan 2017; vol. 139 (no. 1); p. 66

Publication Type(s): Journal Article

Available in full text at Journal of Allergy and Clinical Immunology - from ProQuest

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) lower respiratory tract infection is implicated in asthma development. RSV immunoprophylaxis during infancy is efficacious in preventing RSV-related hospitalizations and has been associated with decreased wheezing in the first years of life.OBJECTIVEWe investigated whether greater adherence to immunoprophylaxis in infants at high risk for severe RSV would be associated with decreased childhood asthma.METHODSWe conducted a retrospective cohort investigation including children born from 1996-2003 who were enrolled in Kaiser Permanente Northern California or Tennessee Medicaid and eligible to receive RSV immunoprophylaxis. Asthma was defined at 4.5 to 6 years of age by using asthma-specific health care visits and medication fills. We classified children into immunoprophylaxis

eligibility groups and calculated adherence (percentage receipt of recommended doses). We used a set of statistical strategies (multivariable logistic regression and propensity score [PS]-adjusted and PS-matched analyses) to overcome confounding by medical complexity because infants with higher adherence (≥70%) have higher prevalence of chronic lung disease, lower birth weight, and longer nursery stays.RESULTSBy using multivariable logistic regression and PS-adjusted models in the combined group, higher adherence to RSV immunoprophylaxis was not associated with decreased asthma. However, in PS-matched analysis, treated children with 70% or greater adherence had decreased odds of asthma compared with those with 20% or less adherence (odds ratio, 0.62; 95% CI, 0.50-0.78).CONCLUSIONSThis investigation of RSV immunoprophylaxis in high-risk children primarily found nonsignificant associations on prevention of asthma in specific preterm groups. Our findings highlight the need for larger studies and prospective cohorts and provide estimates of potential preventive effect sizes in high-risk children.

22. The interdependencies of viral load, the innate immune response, and clinical outcome in children presenting to the emergency department with respiratory syncytial virus-associated bronchiolitis.

Author(s): Piedra, Felipe-Andrés; Mei, Minghua; Avadhanula, Vasanthi; Mehta, Reena; Aideyan, Letisha; Garofalo, Roberto P; Piedra, Pedro A

Source: PloS one; 2017; vol. 12 (no. 3); p. e0172953

Publication Type(s): Journal Article

Available in full text at PLoS ONE - from National Library of Medicine

Available in full text at PLoS One - from ProQuest

Abstract: Respiratory syncytial virus (RSV) causes significant infant morbidity and mortality. For decades severe RSV-induced disease was thought to result from an uncontrolled host response to viral replication, but recent work suggests that a strong innate immune response early in infection is protective. To shed light on host-virus interactions and the viral determinants of disease, copy numbers of five RSV genes (NS1, NS2, N, G, F) were measured by quantitative real-time polymerase chain reaction (qPCR) in nasal wash samples from children with RSV-associated bronchiolitis. Correlations were sought with host cytokines/chemokines and biomarkers. Associations with disposition from the emergency department (hospitalized or sent home) and pulse oximetry O2 saturation levels were also sought. Additionally, RNase P copy number was measured and used to normalize nasal wash data. RSV gene copy numbers were found to significantly correlate with both cytokine/chemokine and biomarker levels; and RNase P-normalized viral gene copy numbers (NS1, NS2, N and G) were significantly higher in infants with less severe disease. Moreover, three of the normalized viral gene copy numbers (NS1, NS2, and N) correlated significantly with arterial O2 saturation levels. The data support a model where a higher viral load early in infection can promote a robust innate immune response that protects against progression into hypoxic RSV-induced lower respiratory tract illness.

23. 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; Jan 2017; vol. 145 (no. 2); p. 266-271

Publication Type(s): Journal Article

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.

24. 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

Publication Type(s): Journal Article Review

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.

25. SENTINEL1: An Observational Study of Respiratory Syncytial Virus Hospitalizations among U.S. Infants Born at 29 to 35 Weeks' Gestational Age Not Receiving Immunoprophylaxis.

Author(s): Anderson, Evan J; Krilov, Leonard R; DeVincenzo, John P; Checchia, Paul A; Halasa, Natasha; Simões, Eric A F; Domachowske, Joseph B; Forbes, Michael L; Pannaraj, Pia S; McBride, Scott J; McLaurin, Kimmie K; Kumar, Veena R; Ambrose, Christopher S

Source: American journal of perinatology; Jan 2017; vol. 34 (no. 1); p. 51-61

Publication Type(s): Journal Article

Abstract: Objective SENTINEL1 characterized U.S. preterm infants 29 to 35 weeks' gestational age (wGA) < 12 months old hospitalized for laboratory-confirmed respiratory syncytial virus (RSV) disease and not receiving RSV immunoprophylaxis during the 2014 to 2015 RSV season. Study Design This is a noninterventional, observational, cohort study. Results A total of 702 infants were hospitalized with community-acquired RSV disease, of whom an estimated 42% were admitted to the intensive care unit (ICU) and 20% required invasive mechanical ventilation (IMV). Earlier gestational age and younger chronologic age were associated with an increased frequency of RSV-

confirmed hospitalization (RSVH), ICU admission, and IMV. Among infants 29 to 32 wGA and < 3 months of age, 68% required ICU admission and 44% required IMV. One death occurred of an infant 29 wGA. Among the 212 infants enrolled for in-depth analysis of health care resource utilization, mean and median RSVH charges were $55,551 and $27,461, respectively, which varied by intensity of care required. Outpatient visits were common, with 63% and 62% of infants requiring visits before and within 1 month following the RSVH, respectively. Conclusion Preterm infants 29 to 35 wGA are at high risk for severe RSV disease, which imposes a substantial health burden, particularly in the first months of life.

Flu

1. Facilitators and barriers of parental attitudes and beliefs toward school-located influenza vaccination in the United States: Systematic review.

Author(s): Kang, Gloria J; Culp, Rachel K; Abbas, Kaja M

Source: Vaccine; Mar 2017

Publication Type(s): Journal Article Review

Abstract: The study objective was to identify facilitators and barriers of parental attitudes and beliefs toward school-located influenza vaccination in the United States. In 2009, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention expanded their recommendations for influenza vaccination to include school-aged children. We conducted a systematic review of studies focused on facilitators and barriers of parental attitudes toward school-located influenza vaccination in the United States from 1990 to 2016. We reviewed 11 articles by use of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework. Facilitators were free/low cost vaccination; having belief in vaccine efficacy, influenza severity, and susceptibility; belief that vaccination is beneficial, important, and a social norm; perception of school setting advantages; trust; and parental presence. Barriers were cost; concerns regarding vaccine safety, efficacy, equipment sterility, and adverse effects; perception of school setting barriers; negative physician advice of contraindications; distrust in vaccines and school-located vaccination programs; and health information privacy concerns. We identified the facilitators and barriers of parental attitudes and beliefs toward school-located influenza vaccination to assist in the evidence-based design and implementation of influenza vaccination programs targeted for children in the United States and to improve influenza vaccination coverage for population-wide health benefits.

2. Effectiveness of 2009 pandemic influenza A(H1N1) vaccines: A systematic review and meta-analysis.

Author(s): Lansbury, Louise E; Smith, Sherie; Beyer, Walter; Karamehic, Emina; Pasic-Juhas, Eva; Sikira, Hana; Mateus, Ana; Oshitani, Hitoshi; Zhao, Hongxin; Beck, Charles R; Nguyen-Van-Tam, Jonathan S

Source: Vaccine; Mar 2017

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDThe clinical effectiveness of monovalent influenza A(H1N1)pdm09 vaccines has not been comprehensively summarised. We undertook a systematic review and meta-analysis to assess vaccine effectiveness (VE) for adjuvanted and unadjuvanted vaccines.METHODSWe searched healthcare databases and grey literature from 11 June 2009 to 12 November 2014. Two researchers independently assessed titles and abstracts to identify studies for full review. Random effects meta-analyses estimated the pooled effect size of vaccination compared to placebo or no vaccination for

crude and adjusted odds ratios (OR) to prevent laboratory confirmed influenza illness (LCI) and related hospitalization. VE was calculated as (1-pooled OR)∗100. Narrative synthesis was undertaken where meta-analysis was not possible.RESULTSWe identified 9229 studies of which 38 at moderate risk of bias met protocol eligibility criteria; 23 were suitable for meta-analysis. Pooled adjusted VE against LCI with adjuvanted and unadjuvanted vaccines both reached statistical significance (adjuvanted: VE=80%; 95% confidence interval [CI] 59-90%; unadjuvanted: VE=66%; 95% CI 47-78%); in planned secondary analyses, VE in adults often failed to reach statistical significance and pooled point estimates were lower than observed in children. Overall pooled adjusted VE against hospitalization was 61% (95% CI 14-82%); in planned secondary analyses, adjusted VE attained statistical significance in adults aged 18-64years and children for adjuvanted vaccines. Adjuvanted vaccines were significantly more effective in children compared to adults for both outcomes.CONCLUSIONSAdjuvanted and unadjuvanted monovalent influenza A(H1N1)pdm09 vaccines were both effective in preventing LCI. Overall, the vaccines were also effective against influenza-related hospitalization. For both outcomes adjuvanted vaccines were more effective in children than in adults.

3. Influenza.

Author(s): Paules, Catharine; Subbarao, Kanta

Source: Lancet (London, England); Mar 2017

Publication Type(s): Journal Article Review

Abstract: Influenza is an acute respiratory illness, caused by influenza A, B, and C viruses, that occurs in local outbreaks or seasonal epidemics. Clinical illness follows a short incubation period and presentation ranges from asymptomatic to fulminant, depending on the characteristics of both the virus and the individual host. Influenza A viruses can also cause sporadic infections or spread worldwide in a pandemic when novel strains emerge in the human population from an animal host. New approaches to influenza prevention and treatment for management of both seasonal influenza epidemics and pandemics are desirable. In this Seminar, we discuss the clinical presentation, transmission, diagnosis, management, and prevention of seasonal influenza infection. We also review the animal-human interface of influenza, with a focus on current pandemic threats.

4. Systematic review of the cost-effectiveness of influenza immunization programs.

Author(s): Ting, Eon E K; Sander, Beate; Ungar, Wendy J

Source: Vaccine; Mar 2017

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDSeasonal influenza immunization programs vary widely across jurisdictions. In Canada, some provinces offer universal programs while others target specific population groups. However, whether targeted or universal programs provide more benefit and value-for-money is unclear. The cost-effectiveness of influenza immunization programs was systematically reviewed to inform policy.METHODSCitation databases and the grey literature were searched for economic evaluations of influenza immunization programs. Eligible studies were appraised using the Scottish Intercollegiate Guidelines Network (SIGN) checklist with supplemental WHO vaccine-related questions. Data from high quality studies was extracted and the studies reviewed.RESULTSA total of 41influenza immunization studies were identified. Of these, 31 were high quality. For pregnant and postpartum women, vaccinating all versus only high risk women study results ranged from dominance (less costly and more effective) to $9773 per QALY gained (societal) and from dominance to $58,000 per QALY gained (healthcare system). Studies of vaccinating all versus only high risk children found vaccination to be dominant to $47,000 per QALY gained (societal), and dominant to

$18,000 per QALY gained (healthcare system). Vaccinating high risk adults was highly cost-effective and vaccinating health care workers resulted in $35,000 per QALY gained. Results for healthy working adults were mixed and sensitive to vaccine uptake, efficacy, and productivity loss.CONCLUSIONSFrom the societal perspective, vaccination was cost-effective for children, pregnant and postpartum women, high risk groups, and in some cases, healthy working age adults. Immunization programs using group administration are more cost-effective than programs using individual administration. The perspective, programmatic design, setting, and inclusion of herd immunity affects cost-effectiveness. In regions with targeted programs, re-evaluating "high risk" criteria and consideration of a universal program is warranted.

5. H5 influenza, a global update.

Author(s): Harfoot, Rhodri; Webby, Richard J

Source: Journal of microbiology (Seoul, Korea); Mar 2017; vol. 55 (no. 3); p. 196-203

Publication Type(s): Journal Article Review

Abstract:H5 influenza viruses have caused much alarm globally due to their high pathogenic potential. As yet we have not seen sustained spread of the virus amongst humans despite a high prevalence of the virus in avian populations. Nevertheless, isolated human cases of infection have demonstrated high mortality and there are substantial efforts being taken to monitor the evolution of the virus and to undertake preparedness activities. Here we review and discuss the evolution of the A/goose/Guangdong/1/96 (H5N1) virus with emphasis on recent events.

6. Pandemic and Avian Influenza A Viruses in Humans: Epidemiology, Virology, Clinical Characteristics, and Treatment Strategy.

Author(s): Li, Hui; Cao, Bin

Source: Clinics in chest medicine; Mar 2017; vol. 38 (no. 1); p. 59-70

Publication Type(s): Journal Article Review

Abstract: The intermittent outbreak of pandemic influenza and emergence of novel avian influenza A virus is worldwide threat. Although most patients present with mild symptoms, some deteriorate to severe pneumonia and even death. Great progress in the understanding of the mechanism of disease pathogenesis and a series of vaccines has been promoted worldwide; however, incidence, morbidity, and mortality remains high. To step up vigilance and improve pandemic preparedness, this article elucidates the virology, epidemiology, pathogenesis, clinical characteristics, and treatment of human infections by influenza A viruses, with an emphasis on the influenza A(H1N1)pdm09, H5N1, and H7N9 subtypes.

7. Universal influenza virus vaccines and therapeutic antibodies.

Author(s): Nachbagauer, R; Krammer, F

Source: Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases; Feb 2017

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDCurrent influenza virus vaccines are effective when well matched to the circulating strains. Unfortunately, antigenic drift and the high diversity of potential emerging zoonotic and pandemic viruses make it difficult to select the right strains for vaccine production. This problem causes vaccine mismatches, which lead to sharp drops in vaccine effectiveness and long

response times to manufacture matched vaccines in case of novel pandemic viruses.AIMSTo provide an overview of universal influenza virus vaccines and therapeutic antibodies in preclinical and clinical development.SOURCESPubMed and clinicaltrials.gov were used as sources for this review.CONTENTUniversal influenza virus vaccines that target conserved regions of the influenza virus including the haemagglutinin stalk domain, the ectodomain of the M2 ion channel or the internal matrix and nucleoproteins are in late preclinical and clinical development. These vaccines could confer broad protection against all influenza A and B viruses including drift variants and thereby abolish the need for annual re-formulation and re-administration of influenza virus vaccines. In addition, these novel vaccines would enhance preparedness against emerging influenza virus pandemics. Finally, novel therapeutic antibodies against the same conserved targets are in clinical development and could become valuable tools in the fight against influenza virus infection.IMPLICATIONSBoth universal influenza virus vaccines and therapeutic antibodies are potential future options for the control of human influenza infections.

8. Characteristics of patients with hospital-acquired influenza A (H1N1)pdm09 virus admitted to the intensive care unit.

Author(s): Álvarez-Lerma, F; Marín-Corral, J; Vilà, C; Masclans, J R; Loeches, I M; Barbadillo, S; González de Molina, F J; Rodríguez, A; H1N1 GETGAG/SEMICYUC Study Group

Source: The Journal of hospital infection; Feb 2017; vol. 95 (no. 2); p. 200-206

Publication Type(s): Multicenter Study Journal Article Observational Study

Abstract:BACKGROUNDInfluenza A (H1N1)pdm09 virus infection acquired in the hospital and in critically ill patients admitted to the intensive care unit (ICU) has been poorly characterized.AIMTo assess the clinical impact of hospital-acquired infection with influenza A (H1N1)pdm09 virus in critically ill patients.METHODSAnalysis of a prospective database of the Spanish registry (2009-2015) of patients with severe influenza A admitted to the ICU. Infection was defined as hospital-acquired when diagnosis and starting of treatment occurred from the seventh day of hospital stay with no suspicion on hospital admission, and community-acquired when diagnosis was established within the first 48 h of admission.FINDINGSOf 2421 patients with influenza A (H1N1)pdm09 infection, 224 (9.3%) were classified as hospital-acquired and 1103 (45.6%) as community-acquired (remaining cases unclassified). Intra-ICU mortality was higher in the hospital-acquired group (32.9% vs 18.8%, P < 0.001). Independent factors associated with mortality were hospital-acquired influenza A (H1N1)pdm09 infection (odds ratio: 1.63; 95% confidence interval: 1.37-1.99), APACHE II score on ICU admission (1.09; 1.06-1.11), underlying haematological disease (3.19; 1.78-5.73), and need of extrarenal depuration techniques (4.20; 2.61-6.77) and mechanical ventilation (4.34; 2.62-7.21).CONCLUSIONInfluenza A (H1N1)pdm09 infection acquired in the hospital is an independent factor for death in critically ill patients admitted to the ICU.

9. Immunization and treatment updates: 2016-2017 influenza season.

Author(s): de St Maurice, Annabelle; Halasa, Natasha

Source: Pediatric transplantation; Feb 2017; vol. 21 (no. 1)

Publication Type(s): Journal Article Review

Abstract: Influenza-associated infections cause significant morbidity and mortality worldwide, particularly among immunocompromised patients. Immunization is the primary mode of prevention of disease; however, efficacy in immunocompromised patients may be limited. Antiviral medications are important for treatment and prophylaxis of affected individuals. This article reviews treatment and prevention recommendations for the 2016-2017 influenza season in the Northern Hemisphere and Southern Hemisphere.

10. Influenza in Children.

Author(s): Kumar, Virendra

Source: Indian journal of pediatrics; Feb 2017; vol. 84 (no. 2); p. 139-143

Publication Type(s): Journal Article Review

Abstract: In children, influenza is one among the commonest causes of acute respiratory illness and loss of school days. Influenza A, B, and C are 3 types of viruses responsible for illness. Type A virus has many subtypes based on antigens but Type B and Type C viruses have no known subtypes. Currently, influenza A/H1N1, A/H3N2, and influenza type B viruses are circulating in humans. Transmission of influenza occurs through droplets from infected person or through direct contact with person or fomites. Clinically, influenza is characterized by acute onset fever, chills, running nose, cough, sore throat, headache and myalgia. Mostly, febrile illness lasts for 3-4 d with resolution of disease in 7-10 d. Confirmation of influenza can be done either by virus culture, RT-PCR or specific neutralizing antibodies in blood. Basic principles of management include prompt institution of infection control measures, early identification of children at higher risk, supportive care and antiviral drugs. Vaccine and chemoprophylaxis are two commonly used methods for prevention of influenza. Currently, inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV) are available for use with good efficacy. Cough etiquette, use of face masks and hand hygiene are the most important measures to reduce the risk of infection transmission from person to person.

11. Immune history and influenza virus susceptibility.

Author(s): Cobey, Sarah; Hensley, Scott E

Source: Current opinion in virology; Feb 2017; vol. 22 ; p. 105-111

Publication Type(s): Journal Article Review

Abstract: Antibody responses to influenza viruses are critical for protection, but the ways in which repeated viral exposures shape antibody evolution and effectiveness over time remain controversial. Early observations demonstrated that viral exposure history has a profound effect on the specificity and magnitude of antibody responses to a new viral strain, a phenomenon called 'original antigenic sin.' Although 'sin' might suppress some aspects of the immune response, so far there is little indication that hosts with pre-existing immunity are more susceptible to viral infections compared to naïve hosts. However, the tendency of the immune response to focus on previously recognized conserved epitopes when encountering new viral strains can create an opportunity cost when mutations arise in these conserved epitopes. Hosts with different exposure histories may continue to experience distinct patterns of infection over time, which may influence influenza viruses' continued antigenic evolution. Understanding the dynamics of B cell competition that underlie the development of antibody responses might help explain the low effectiveness of current influenza vaccines and lead to better vaccination strategies.

12. Pregnancy as a risk factor for severe outcomes from influenza virus infection: A systematic review and meta-analysis of observational studies.

Author(s): Mertz, Dominik; Geraci, Johanna; Winkup, Judi; Gessner, Bradford D; Ortiz, Justin R; Loeb, Mark

Source: Vaccine; Jan 2017; vol. 35 (no. 4); p. 521-528

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDPregnancy is considered to be an important risk factor for severe complications following influenza virus infection. As a consequence, WHO recommendations prioritize pregnant women over other risk groups for influenza vaccination. However, the risk associated with pregnancy has not been systematically quantified.PURPOSESystematic review and meta-analysis of observational studies that reported on pregnancy as a risk factor for severe outcomes from influenza virus infection.DATA SOURCEMEDLINE, EMBASE, CINAHL, and CENTRAL up to April 2014.DATA SELECTIONStudies reporting on outcomes in pregnant women with influenza in comparison to non-pregnant patients with influenza. Outcomes included community-acquired pneumonia, hospitalization, admission to intensive care units (ICU), ventilatory support, and death.DATA EXTRACTIONTwo reviewers conducted independent screening and data extraction. A random effects model was used to obtain risk estimates. Ecological studies were summarized descriptively.DATA SYNTHESISA total of 142 non-ecological and 10 ecological studies were included. The majority of studies (n=136, 95.8%) were conducted during the 2009 influenza A (pH1N1) pandemic. There was a higher risk for hospitalization in pregnant versus non-pregnant patients infected with influenza (odds ratio [OR] 2.44, 95% CI 1.22-4.87), but no significant difference in mortality (OR 1.04, 95% CI 0.81-1.33) or other outcomes. Ecologic studies confirmed the association between hospitalization risk and pregnancy and 4 of 7 studies reported higher mortality rates in pregnant women.LIMITATIONSNo studies were identified in which follow-up began prior to contact with the healthcare system and lack of adjustment for confounding factors.CONCLUSIONSWe found that influenza during pregnancy resulted in a higher risk of hospital admission than influenza infection in non-pregnant individuals, but that the risk of mortality following influenza was similar in both pregnant and non-pregnant individuals.

13. Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly: A systematic review and meta-analysis.

Author(s): Domnich, Alexander; Arata, Lucia; Amicizia, Daniela; Puig-Barberà, Joan; Gasparini, Roberto; Panatto, Donatella

Source: Vaccine; Jan 2017; vol. 35 (no. 4); p. 513-520

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDIn the elderly, traditional influenza inactivated vaccines are often only modestly immunogenic, owing to immunosenescence. Given that adjuvantation is a means of enhancing the immune response, the trivalent inactivated vaccine adjuvanted with MF59 (MF59-TIV) was specifically designed to overcome this problem. Considering that, for ethical reasons, the absolute effectiveness of an influenza vaccine in the elderly cannot be demonstrated in placebo-controlled studies, the present study aimed to assess the effectiveness of MF59-TIV in preventing influenza-related outcomes in the elderly.METHODSWe conducted a systematic review of observational studies aimed at evaluating the effectiveness of MF59-TIV against influenza-related outcomes. Results of single studies were pooled whenever possible.RESULTSOf the 1993 papers screened, 11 (6 case-control, 3 cohort and 2 prospective case-control) studies were identified. Hospitalization due to pneumonia/influenza and laboratory-confirmed influenza were reported in more than one study, while other outcomes (influenza-like illness, cardio- and cerebrovascular accidents) were investigated only by one study each. Pooled analysis of four case-control studies showed an adjusted MF59-TIV effectiveness of 51% (95% CI: 39-61%) against hospitalizations for pneumonia/influenza among community-dwelling seniors. Pooled results of the adjusted vaccine effectiveness against laboratory-confirmed influenza were also high (60.1%), although the 95% CI passed through zero (-1.3 to 84.3%). Other single community-based studies showed very high effectiveness of MF59-TIV in preventing hospitalizations for acute coronary [87% (95% CI: 35-97%)] and cerebrovascular [93% (95% CI: 52-99%)] events. MF59-TIV proved highly effective [94% (95% CI:

47-100%] in reducing influenza-like illness among institutionalized elderly. Furthermore, MF59-TIV displayed greater efficacy than non-adjuvanted vaccines in preventing hospitalizations due to pneumonia/influenza [adjusted risk ratio 0.75 (95% CI: 0.57-0.98)] and laboratory-confirmed influenza [adjusted odds ratio 0.37 (0.14-0.96)].CONCLUSIONSOur results suggest that MF59-TIV is effective in reducing several influenza-related outcomes among the elderly, especially hospitalizations due to influenza-related complications.

14. Do antibody responses to the influenza vaccine persist year-round in the elderly? A systematic review and meta-analysis.

Author(s): Young, Barnaby; Zhao, Xiahong; Cook, Alex R; Parry, Christopher M; Wilder-Smith, Annelies; I-Cheng, Mark Chen

Source: Vaccine; Jan 2017; vol. 35 (no. 2); p. 212-221

Publication Type(s): Journal Article Review

Available in full text at Vaccine - from ProQuest

Abstract:INTRODUCTIONThe influenza vaccine is less immunogenic in older than younger adults, and the duration of protection is unclear. Determining if protection persists beyond a typical seasonal epidemic is important for climates where influenza virus activity is year-round.METHODSA systematic review protocol was developed and registered with PROSPERO [CRD42015023847]. Electronic databases were searched systematically for studies reporting haemagglutination-inhibition (HI) titres 180-360days following vaccination with inactivated trivalent seasonal influenza vaccine, in adults aged ⩾65years. Geometric mean titre (GMT) and seroprotection (HI titre ⩾1:40) at each time point was extracted. A Bayesian model was developed of titre trajectories from pre-vaccination to Day 360. In the meta-analysis, studies were aggregated using a random-effects model to compare pre-vaccination with post-vaccination HI titres at Day 21-42 ('seroconversion'), Day 180 and Day 360. Potential sources of bias were systematically assessed, and heterogeneity explored.RESULTS2864 articles were identified in the literature search, of which nineteen met study inclusion/exclusion criteria. Sixteen studies contained analysable data from 2565 subjects. In the Bayesian model, the proportion of subjects seroprotected increased from 41-51% pre-vaccination to 75-78% at seroconversion. Seroprotection subsequently fell below 60% for all serotypes by Day 360: A/H1 42% (95% CI 38-46), A/H3 59% (54-63), B 47% (42-52). The Bayesian model of GMT trajectories revealed a similar pattern. By Day 360, titres were similar to pre-vaccination levels. In the meta-analysis, no significant difference in proportion of subjects seroprotected, 0 (-0.11, 0.11) or in log2GMT 0.30 (-0.02, 0.63) was identified by Day 360 compared with pre-vaccination. The quality of this evidence was limited to moderate on account of significant participant dropout.CONCLUSIONSThe review found consistent evidence that HI antibody responses following influenza vaccination do not reliably persist year-round in older adults. Alternative vaccination strategies could provide clinical benefits in regions where year-round protection is important.

Surgical Site Infection

1. Incidence of surgical site infection following caesarean section: a systematic review and meta-analysis protocol.

Author(s): Saeed, Khalid B M; Greene, Richard A; Corcoran, Paul; O'Neill, Sinéad M

Source: BMJ open; Jan 2017; vol. 7 (no. 1); p. e013037

Publication Type(s): Journal Article

Abstract:INTRODUCTIONCaesarean section (CS) rates have increased globally during the past three decades. Surgical site infection (SSI) following CS is a common cause of morbidity with reported rates of 3-15%. SSI represents a substantial burden to the health system including increased length of hospitalisation and costs of postdischarge care. The definition of SSI varies with the postoperative follow-up period among different health systems, resulting in differences in the reporting of SSI incidence. We propose to conduct the first systematic review and meta-analysis to determine the pooled estimate for the overall incidence of SSI following CS.METHODS AND ANALYSISWe will perform a comprehensive search to identify all potentially relevant published studies on the incidence of SSI following CS reported from 1992 in the English language. Electronic databases including PubMed, CINAHL, EMBASE and Scopus will be searched using a detailed search strategy. Following study selection, full-text paper retrieval, data extraction and synthesis, we will appraise study quality and risk of bias and assess heterogeneity. Incidence data will be combined where feasible in a meta-analysis using Stata software and fixed-effects or random-effects models as appropriate. This systematic review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.ETHICS AND DISSEMINATIONEthical approval is not required as this review will use published data. The review will evaluate the overall incidence of SSI following CS and will provide the first quantitative estimate of the magnitude of SSI. It will serve as a benchmark for future studies, identify research gaps and remaining challenges, and emphasise the need for appropriate prevention and control measures for SSI post-CS. A manuscript reporting the results of the systematic review and meta-analysis will be submitted to a peer-reviewed journal and presented at scientific conferences.TRIAL REGISTRATION NUMBERCRD42015024426.

2. Skin antisepsis with chlorhexidine versus iodine for the prevention of surgical site infection: A systematic review and meta-analysis.

Author(s): Privitera, Gaetano Pierpaolo; Costa, Anna Laura; Brusaferro, Silvio; Chirletti, Piero; Crosasso, Paola; Massimetti, Gabriele; Nespoli, Angelo; Petrosillo, Nicola; Pittiruti, Mauro; Scoppettuolo, Giancarlo; Tumietto, Fabio; Viale, Pierluigi

Source: American journal of infection control; Feb 2017; vol. 45 (no. 2); p. 180-189

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDSurgical site infection (SSI) is one of the most frequent health care-associated infections. One of the practices to reduce their incidence is preoperative skin antisepsis. Two of the most commonly active components used are chlorhexidine gluconate and povidone iodine. Of 3 reviews conducted between 2010 and 2012 comparing antiseptics, 2 were in favor of chlorhexidine; however, the latest was unable to draw conclusions.PURPOSETo verify whether recent evidence supports the hypothesis that chlorhexidine in preoperative antisepsis is more efficient than other antiseptics in reducing SSI rates.PROCEDURESWe conducted a systematic review from 2000-2014 in all languages. The primary end point was SSI incidence and secondary skin bacterial colonization.RESULTSNineteen studies were included. Meta-analysis were conducted for comparable studies for both outcomes. The results of the meta-analysis, including all of the studies in which chlorhexidine was compared with iodophor, were in favor of chlorhexidine for both SSI incidence (risk ratio [RR], 0.70; 95% confidence interval [CI], 0.52-0.92) and bacterial skin colonization (RR, 0.45; 95% CI, 0.36-0.55).CONCLUSIONSThere is moderate-quality evidence supporting the use of chlorhexidine for preoperative skin antisepsis and high-quality evidence that the use of chlorhexidine is associated with fewer positive skin cultures. Further rigorous trials will be welcomed to attain stronger evidence as to the best antiseptic to be used before surgery.

3. Smoking and Risk of Surgical Site Infection after Spinal Surgery: A Systematic Review and Meta-Analysis.

Author(s): Kong, Lingde; Liu, Zhao; Meng, Fei; Shen, Yong

Source: Surgical infections; ; vol. 18 (no. 2); p. 206-214

Publication Type(s): Journal Article

Abstract:BACKGROUNDThe effect of smoking on the risk of surgical site infection (SSI) after spinal surgery remains controversial. Therefore, we conducted a meta-analysis to determine whether there is an association between smoking and the risk of SSI and to calculate the relative risk of infections attributable to smoking.METHODSWe performed a literature search of cohort and case-control studies in the MEDLINE, Embase, and ISI Web of Science databases. Sensitivity and subgroup analyses were performed to test the robustness of overall estimates of risk and to investigate potential sources of heterogeneity. We further calculated the population-attributable fraction (PAF) to evaluate the proportion of SSIs associated with smoking.RESULTSIn total, 26 independent observational studies involving 67,405 patients who underwent spinal surgery were analyzed. Smokers had a significantly higher risk of SSI than did nonsmokers (odds ratio [OR] 1.26; 95% confidence interval [CI] 1.05-1.51). Subgroup analysis according to the study design revealed an apparent association between smoking and SSI in the cohort subgroup (OR 1.40; 95% CI 1.17-1.66), but not in the case-control subgroup (OR 0.99; 95% CI 0.64-1.53). After evaluation of the PAF, the proportion of SSIs associated with smoking increased to 10.37%.CONCLUSIONSThis meta-analysis demonstrated that smoking increases the risk of SSI after spinal surgery. False-negative associations in other studies may have resulted from defects in the study design. However, because of the heterogeneity among the studies in the present meta-analysis, the results should be interpreted with caution.

4. Network meta-analysis of antibiotic prophylaxis for prevention of surgical-site infection after groin hernia surgery.

Author(s): Boonchan, T; Wilasrusmee, C; McEvoy, M; Attia, J; Thakkinstian, A

Source: The British journal of surgery; Jan 2017; vol. 104 (no. 2); p. e106

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDFirst-generation cephalosporins (such as cefazolin) are recommended as antibiotic prophylaxis in groin hernia repair, but other broad-spectrum antibiotics have also been prescribed in clinical practice. This was a systematic review and network meta-analysis to compare the efficacy of different antibiotic classes for prevention of surgical-site infection (SSI) after hernia repair.METHODSRCTs were identified that compared efficacy of antibiotic prophylaxis on SSI after inguinal or femoral hernia repair from PubMed and Scopus databases up to March 2016. Data were extracted independently by two reviewers. Network meta-analysis was applied to assess treatment efficacy. The probability of being the best antibiotic prophylaxis was estimated using surface under the cumulative ranking curve (SUCRA) analysis.RESULTSFifteen RCTs (5159 patients) met the inclusion criteria. Interventions were first-generation (7 RCTs, 1237 patients) and second-generation (2 RCTs, 532) cephalosporins, β-lactam/β-lactamase inhibitors (6 RCTs, 619) and fluoroquinolones (2 RCTs, 581), with placebo as the most common comparator (14 RCTs, 2190). A network meta-analysis showed that β-lactam/β-lactamase inhibitors and first-generation cephalosporins were significantly superior to placebo, with a pooled risk ratio of 0·44 (95 per cent c.i. 0·25 to 0·75) and 0·62 (0·42 to 0·92) respectively. However, none of the antibiotic classes was significantly different from the others. SUCRA results indicated that β-lactam/β-lactamase inhibitors and first-generation cephalosporins were ranked first and second respectively for best prophylaxis.CONCLUSIONβ-Lactam/β-lactamase inhibitors followed by first-generation cephalosporins ranked as the most effective SSI prophylaxis for adult patients undergoing groin hernia repair.

5. Allogeneic Blood Transfusion Is a Significant Risk Factor for Surgical-Site Infection Following Total Hip and Knee Arthroplasty: A Meta-Analysis.

Author(s): Kim, Jeong Lae; Park, Jong-Hoon; Han, Seung-Beom; Cho, Il Youp; Jang, Ki-Mo

Source: The Journal of arthroplasty; Jan 2017; vol. 32 (no. 1); p. 320-325

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDBlood loss occurs significantly more frequently during total hip and knee arthroplasty than among any other type of orthopedic operation, which can sometimes lead to requiring a blood transfusion. Although allogeneic blood transfusion has been identified as a risk factor for postoperative surgical-site infection following arthroplasty, results are inconclusive. The purpose of this study was to conduct a systematic meta-analysis to investigate whether having an allogeneic blood transfusion significantly increases the risk for surgical-site infection, particularly after total hip and knee arthroplasty.METHODSWe performed a systematic review and meta-analysis using random-effect models. Using an electronic database search, we selected 6 studies that included data on 21,770 patients and among these studies compared the postoperative infection rate between an allogeneic blood-transfusion exposure group and a nonexposure group. We calculated the pooled odds ratios and 95% confidence intervals for the groups.RESULTSThe prevalences of surgical-site infections in our pooled analyses were 2.88% and 1.74% for the transfusion and nontransfusion groups, respectively. The allogeneic blood transfusion group had a significantly higher frequency of surgical-site infections based on pooled analysis using a random-effect model (pooled odds ratio = 1.71, 95% confidence interval: 1.23-2.40, P = .002).CONCLUSIONAllogeneic blood transfusion is a significant risk factor for increasing the surgical-site infection rate after total hip and knee arthroplasty.

6. Albumin and surgical site infection risk in orthopaedics: a meta-analysis.

Author(s): Yuwen, Peizhi; Chen, Wei; Lv, Hongzhi; Feng, Chen; Li, Yansen; Zhang, Tao; Hu, Pan; Guo, Jialiang; Tian, Ye; Liu, Lei; Sun, Jiayuan; Zhang, Yingze

Source: BMC surgery; Jan 2017; vol. 17 (no. 1); p. 7

Publication Type(s): Meta-analysis Journal Article

Abstract:BACKGROUDSurigical site infection has been a challenge for surgeons for many years, the prevalence of serum albumin 3.5 was 2.39 (95 % CI 1.57 3.64), which was statistically significant (z = 4.06, P < 0.0001). Heterogeneity were found in the pooled MD of albumin and in the pooled RR for infection (P = 0.05, I2 = 61 % and P = 0.003, I2 = 68 %). No publication bias occurred based on two basically symmetrical funnel plots.CONCLUSIONOur meta-analysis demonstrated that an albumin level <3.5 g/dL had an almost 2.5 fold increased risk of SSI in orthopaedics, although this conclusion requires well-designed prospective cohort studies to be confirmed further.

7. Preoperative bathing of the surgical site with chlorhexidine for infection prevention: Systematic review with meta-analysis.

Author(s): Franco, Lúcia Maciel de Castro; Cota, Gláucia Fernandes; Pinto, Tatiana Saraiva; Ercole, Flávia Falci

Source: American journal of infection control; Jan 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDPreoperative bathing with 4% chlorhexidine is recommended as a measure to prevent surgical site infection (SSI) despite uncertainty regarding the effectiveness of the

intervention. This review aimed to assess the effect of bathing with 4% chlorhexidine on the prevention of SSIs in clean surgeries compared with bathing with placebo solution or soap.METHODSPreferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for systematic reviews and the Cochrane manual were followed. Sources were MEDLINE and Latin American and Caribbean Health Sciences Literature databases and manual search of references from evaluated studies. We included randomized studies evaluating clean surgical wounds and reporting SSIs after preoperative bathing with 4% chlorhexidine.RESULTSA total of 243 primary studies were identified and 8 were considered methodologically appropriate based on the Jadad Scale. Data were gathered from 10,655 patients. The global SSI rate was 7.2%. The SSI rate for chlorhexidine bathing, placebo, and soap without antiseptic groups was 7.1%, 9.1%, and 5.1%, respectively. A significant reduction in the infection rates was not found in the comparison between patients subjected to preoperative bathing with 4% chlorhexidine versus placebo solution (relative risk, 0.91; 95% confidence interval, 0.76-1.09). The same absence of benefit was observed comparing chlorhexidine bathing with soap (relative risk, 1.06; 95% confidence interval, 0.68-1.66).CONCLUSIONSControlled clinical trials are needed to assess the effect of preoperative chlorhexidine bathing on infection rates following clean surgery before the incorporation of this intervention in health care services.

8. Systematic review of risk prediction scores for surgical site infection or periprosthetic joint infection following joint arthroplasty.

Author(s): Kunutsor, S K; Whitehouse, M R; Blom, A W; Beswick, A D

Source: Epidemiology and infection; Mar 2017 ; p. 1-12

Publication Type(s): Journal Article

Available in full text at Epidemiology and Infection - from ProQuest

Abstract: Accurate identification of individuals at high risk of surgical site infections (SSIs) or periprosthetic joint infections (PJIs) influences clinical decisions and development of preventive strategies. We aimed to determine progress in the development and validation of risk prediction models for SSI or PJI using a systematic review. We searched for studies that have developed or validated a risk prediction tool for SSI or PJI following joint replacement in MEDLINE, EMBASE, Web of Science and Cochrane databases; trial registers and reference lists of studies up to September 2016. Nine studies describing 16 risk scores for SSI or PJI were identified. The number of component variables in a risk score ranged from 4 to 45. The C-index ranged from 0·56 to 0·74, with only three risk scores reporting a discriminative ability of >0·70. Five risk scores were validated internally. The National Healthcare Safety Network SSIs risk models for hip and knee arthroplasties (HPRO and KPRO) were the only scores to be externally validated. Except for HPRO which shows some promise for use in a clinical setting (based on predictive performance and external validation), none of the identified risk scores can be considered ready for use. Further research is urgently warranted within the field.

9. Surgical site infection after hand surgery outside the operating theatre: a systematic review.

Author(s): Jagodzinski, N A; Ibish, S; Furniss, D

Source: The Journal of hand surgery, European volume; Mar 2017; vol. 42 (no. 3); p. 289-294

Publication Type(s): Journal Article

Abstract: We carried out a systematic review to determine the incidence of infection for hand surgery done in settings other than the operating theatre. Databases were searched and a PRISMA chart created by three independent reviewers. From 1200 studies identified, 46 full text articles were reviewed and six were included (two Level 3 studies and four Level 4). In three studies there

were no infections after surgery in an office, procedure room or emergency department. Two studies with a combined number of 1962 procedures reviewed carpal tunnel decompressions and reported identical infection rates of 0.4%. Although the current evidence is of poor quality, it suggests that some types of hand surgery may be done outside the operating theatre without increasing the risk of infection.LEVEL OF EVIDENCEIV.

10. High inspired oxygen versus low inspired oxygen for reducing surgical site infection: a meta-analysis.

Author(s): Wang, Hongye; Hong, Shukun; Liu, Yuanyuan; Duan, Yan; Yin, Hongmei

Source: International wound journal; Feb 2017; vol. 14 (no. 1); p. 46-52

Publication Type(s): Journal Article

Abstract: To perform a meta-analysis of published literature to assess the role of high-concentration inspired oxygen in reducing the incidence of surgical site infections (SSIs) following all types of surgery, a comprehensive search for published randomized controlled trials (RCTs) comparing high- with low-concentration inspired oxygen for SSIs was performed. The related data were extracted by two independent authors. The fixed and random effects methods were used to combine data. Twelve RCTs involving 6750 patients were included. Our pooled result found that no significant difference in the incidence of SSIs was observed between the two groups, but there was high statistic heterogeneity across the studies [risk ratio (RR): 0·91; 95% confidence interval (CI): 0·72-1·14; P = 0·40; I2 = 54%]. The sensitivity analysis revealed the superiority of high-concentration oxygen in decreasing the SSI rate (RR: 0·86; 95% CI: 0·75-0·98; P = 0·02). Moreover, a subgroup analysis of studies with intestinal tract surgery showed that patients experienced less SSI when high-concentration inspired oxygen was administrated (RR: 0·53; 95% CI: 0·37-0·74; P = 0·0003). Our study provided no direct support for high-concentration inspired oxygen in reducing the incidence of SSIs in patients undergoing all types of surgery.

11. Meta-analysis of lower perioperative blood glucose target levels for reduction of surgical-site infection.

Author(s): de Vries, F E E; Gans, S L; Solomkin, J S; Allegranzi, B; Egger, M; Dellinger, E P; Boermeester, M A

Source: The British journal of surgery; Jan 2017; vol. 104 (no. 2); p. e95

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDThere is a clear association between hyperglycaemia and surgical-site infection (SSI). Intensive glucose control may involve a risk of hypoglycaemia, which in turn results in potentially severe complications. A systematic review was undertaken of studies comparing intensive versus conventional glucose control protocols in relation to reduction of SSI and other outcomes, including hypoglycaemia, mortality and stroke.METHODSPubMed, Embase, CENTRAL, CINAHL and WHO databases from 1 January 1990 to 1 August 2015 were searched. Inclusion criteria were RCTs comparing intensive with conventional glucose control protocols, and reporting on the incidence of SSI. Meta-analyses were performed with a random-effects model, and meta-regression was subsequently undertaken. Targeted blood glucose levels, achieved blood glucose levels, and important adverse events were summarized.RESULTSFifteen RCTs were included. The summary estimate showed a significant benefit for an intensive compared with a conventional glucose control protocol in reducing SSI (odds ratio (OR) 0·43, 95 per cent c.i. 0·29 to 0·64; P < 0·001). A significantly higher risk of hypoglycaemic events was found for the intensive group compared with the conventional group (OR 5·55, 2·58 to 11·96), with no increased risk of death (OR 0·74, 0·45 to 1·23) or stroke (OR 1·37, 0·26 to 7·20). These results were consistent both in patients with and those

without diabetes, and in studies with moderately strict and very strict glucose control.CONCLUSIONStricter and lower blood glucose target levels of less than 150 mg/dl (8·3 mmol/l), using an intensive protocol in the perioperative period, reduce SSI with an inherent risk of hypoglycaemic events but without a significant increase in serious adverse events.

12. Patient Self-Assessment of Surgical Site Infection is Inaccurate.

Author(s): Richter, Vered; Cohen, Matan J; Benenson, Shmuel; Almogy, Gideon; Brezis, Mayer

Source: World journal of surgery; Mar 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDAvailability of surgical site infection (SSI) surveillance rates challenges clinicians, healthcare administrators and leaders and the public. The purpose of this report is to demonstrate the consequences patient self-assessment strategies have on SSI reporting rates.METHODSWe performed SSI surveillance among patients undergoing general surgery procedures, including telephone follow-up 30 days after surgery. Additionally we undertook a separate validation study in which we compared patient self-assessments of SSI with surgeon assessment. Finally, we performed a meta-analysis of similar validation studies of patient self-assessment strategies.RESULTSThere were 22/266 in-hospital SSIs diagnosed (8.3%), and additional 16 cases were detected through the 30-day follow-up. In total, the SSI rate was 16.8% (95% CI 10.1-18.5). In the validation survey, we found patient telephone surveillance to have a sensitivity of 66% (95% CI 40-93%) and a specificity of 90% (95% CI 86-94%). The meta-analysis included five additional studies. The overall sensitivity was 83.3% (95% CI 79-88%), and the overall specificity was 97.4% (95% CI 97-98%). Simulation of the meta-analysis results divulged that when the true infection rate is 1%, reported rates would be 4%; a true rate of 50%, the reported rates would be 43%.CONCLUSIONPatient self-assessment strategies in order to fulfill 30-day SSI surveillance misestimate SSI rates and lead to an erroneous overall appreciation of inter-institutional variation. Self-assessment strategies overestimate SSIs rate of institutions with high-quality performance and underestimate rates of poor performance. We propose such strategies be abandoned. Alternative strategies of patient follow-up strategies should be evaluated in order to provide valid and reliable information regarding institutional performance in preventing patient harm.

13. Meta-analysis and trial sequential analysis of triclosan-coated sutures for the prevention of surgical-site infection.

Author(s): de Jonge, S W; Atema, J J; Solomkin, J S; Boermeester, M A

Source: The British journal of surgery; Jan 2017; vol. 104 (no. 2); p. e118

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDTriclosan-coated sutures (TCS) were developed to reduce the risk of surgical-site infection (SSI). Level 1A evidence of effectiveness has been presented in various recent meta-analyses, yet well designed RCTs have not been able to reproduce these favourable results. The aim of this study was to evaluate all available evidence critically with comprehensive analysis to seek a more reliable answer regarding the effectiveness of TCS in the prevention of SSI.METHODSPubMed, MEDLINE, Embase and Cochrane Library databases were searched from 1990 to November 2015 for RCTs that compared TCS with sutures that were exactly the same, but uncoated, in the prevention of SSI. Pooled relative risks (RRs) with corresponding 95 per cent confidence intervals were estimated using a random-effects model. Metaregression was used to substantiate subgroup effects, trial sequential analysis was employed to assess the risk of random error, and quality of evidence was determined using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.RESULTSTwenty-one RCTs including 6462 patients were included. Risk of bias was

serious. Pooled effects showed a RR of 0·72 (95 per cent c.i. 0·60 to 0·86; P < 0·001) for all publications. At a risk of 138 SSIs per 1000 procedures, the use of TCS reduced this by 39 (95 per cent c.i. 19, 55). Trial sequential analysis confirmed a RR reduction of 15 per cent for the use of TCS.CONCLUSIONGRADE assessment shows moderate-quality evidence that TCS are effective in reducing SSI. Trial sequential analysis indicates that the effect was robust, and additional data are unlikely to alter the summary effect.

14. The role of oral antibiotics prophylaxis in prevention of surgical site infection in colorectal surgery.

Author(s): Koullouros, Michalis; Khan, Nadir; Aly, Emad H

Source: International journal of colorectal disease; Jan 2017; vol. 32 (no. 1); p. 1-18

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDSurgical site infection (SSI) continues to be a challenge in colorectal surgery. Over the years, various modalities have been used in an attempt to reduce SSI risk in elective colorectal surgery, which include mechanical bowel preparation before surgery, oral antibiotics and intravenous antibiotic prophylaxis at induction of surgery. Even though IV antibiotics have become standard practice, there has been a debate on the exact role of oral antibiotics.AIMThe primary aim was to identify the role of oral antibiotics in reduction of SSI in elective colorectal surgery. The secondary aim was to explore any potential benefit in the use of mechanical bowel preparation (MBP) in relation to SSI in elective colorectal surgery.METHODSMedline, Embase and the Cochrane Library were searched. Any randomised controlled trials (RCTs) or cohort studies after 1980, which investigated the effectiveness of oral antibiotic prophylaxis and/or MBP in preventing SSIs in elective colorectal surgery were included.RESULTSTwenty-three RCTs and eight cohorts were included. The results indicate a statistically significant advantage in preventing SSIs with the combined usage of oral and systemic antibiotic prophylaxis. Furthermore, our analysis of the cohort studies shows no benefits in the use of MBP in prevention of SSIs.CONCLUSIONSThe addition of oral antibiotics to systemic antibiotics could potentially reduce the risk of SSIs in elective colorectal surgery. Additionally, MBP does not seem to provide a clear benefit with regard to SSI prevention.

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Exercise

Confounding Bias in Research Methodology

A confounder is a factor that is:

- *Linked to the outcome of interest, independent of the exposure*
- *Linked to the exposure but not the consequence of the exposure*

What is the confounding factor in the following relationships:

- People who carry matches are more likely to develop lung cancer
- People who eat ice-cream are more likely to drown
- Training in anaesthesia is more likely to make doctors commit suicide

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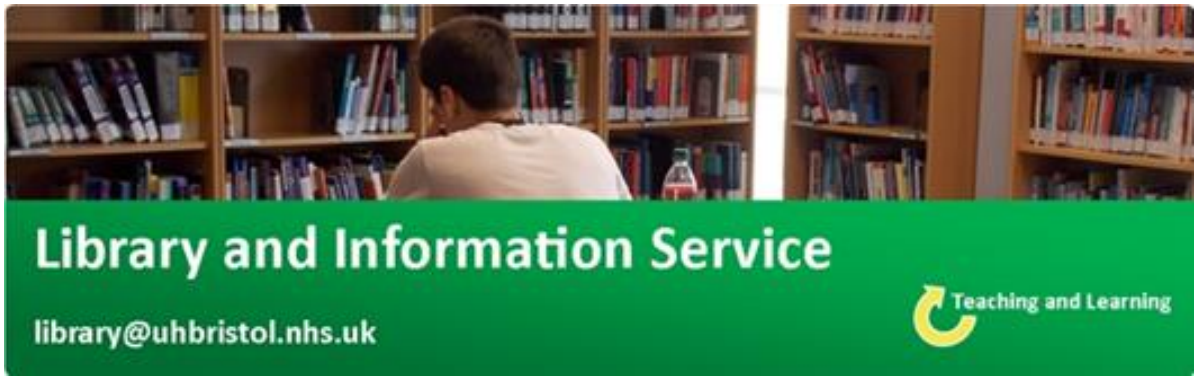

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