University Hospitals Bristol NHS
NHS Foundation Trust

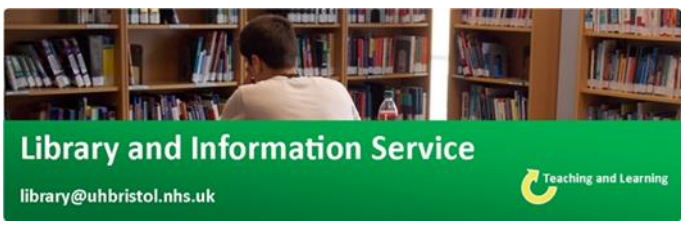
Infection Control

Evidence Update

Winter 2017/2018

(Quarterly)

Respecting everyone
Embracing change
Recognising success
Working together
Our hospitals.



Lunchtime Drop-in Sessions

All sessions last one hour

February (12.00-13.00)

1st (Thu)	**Literature Searching**
9th (Fri)	**Critical Appraisal**
12th (Mon)	**Statistics**
20th (Tue)	**Literature Searching**
28th (Wed)	**Critical Appraisal**

March (13.00-14.00)

8th (Thu)	**Statistics**
12th (Mon)	**Literature Searching**
20th (Tue)	**Critical Appraisal**
28th (Wed)	**Statistics**

Your Outreach Librarian – Sarah Barrett

Whatever your information needs, the library is here to help. Just email us at library@uhbristol.nhs.uk

Outreach: Your Outreach Librarian can help facilitate evidence-based practice for all in the team, as well as assisting with academic study and research. We also offer one-to-one or small group training in **literature searching, critical appraisal and medical statistics**. Get in touch: library@uhbristol.nhs.uk

Literature searching: We provide a literature searching service for any library member. For those embarking on their own research it is advisable to book some time with one of the librarians for a one-to-one session where we can guide you through the process of creating a well-focused literature research. Please email requests to library@uhbristol.nhs.uk

Contents

Updates

NICE National Institute for Health and Care Excellence

Prevention and control of healthcare-associated infections

Everything NICE has said on preventing and controlling healthcare-associated infections in an interactive flowchart

NICE Pathway Published March 2012 Last updated October 2017

Cochrane Library

Goldenberg JZ, Yap C, Lytvyn L, Lo CKF, Beardsley J, Mertz D, Johnston BC. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD006095. DOI: 10.1002/14651858.CD006095.pub4.

Jacobson Vann JC, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. Patient reminder and recall interventions to improve immunization rates. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD003941. DOI: 10.1002/14651858.CD003941.pub3.

Norman G, Atkinson RA, Smith TA, Rowlands C, Rithalia AD, Crosbie EJ, Dumville JC. Intracavity lavage and wound irrigation for prevention of surgical site infection. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD012234. DOI: 10.1002/14651858.CD012234.pub2.

UpToDate®

OpenAthens login required. Register here: https://openathens.nice.org.uk/

Treatment of seasonal influenza in adults
Author: Kimon C Zachary, MD
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Jan 05, 2018.

Seasonal influenza in children: Prevention and treatment with antiviral drugs
Author: Flor M Munoz, MD, MSc
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Jan 15, 2018.

Overview of control measures for prevention of surgical site infection in adults
Authors: Deverick J Anderson, MD, MPH; Daniel J Sexton, MD
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Oct 24, 2017.

Antimicrobial prophylaxis for prevention of surgical site infection in adults
Authors: Deverick J Anderson, MD, MPH; Daniel J Sexton, MD
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Nov 28, 2017.

Bronchiolitis in infants and children: Treatment, outcome, and prevention
Authors: Pedro A Piedra, MD; Ann R Stark, MD
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Jan 05, 2018.

Respiratory syncytial virus infection: Prevention
Authors: Frederick E Barr, MD; Barney S Graham, MD, PhD
All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Dec 2017. | **This topic last updated:** Sep 14, 2017.

UpToDate® Anywhere

UpToDate® is now available as a Mobile App, free for all UHBristol staff

Interested in staying up to date?

Sign up at the Library, or email:

library@uhbristol.nhs.uk

University Hospitals Bristol NHS
NHS Foundation Trust

Recent Database Articles

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

- C Difficile
- Bronchiolitis
- RSV
- Surgical Site Infection
- Influenza
- Norovirus

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

C Difficile

1. Updated meta-analysis of controlled observational studies: proton-pump inhibitors and risk of Clostridium difficile infection.

Author(s): Cao, F; Chen, C X; Wang, M; Liao, H R; Wang, M X; Hua, S Z; Huang, B; Xiong, Y; Zhang, J Y; Xu, Y L

Source: The Journal of hospital infection; Jan 2018; vol. 98 (no. 1); p. 4-13

Publication Type(s): Journal Article Review

Abstract: Attention has recently been directed toward a plausible link between Clostridium difficile infection (CDI) and proton-pump inhibitors (PPIs). However, the results of studies on the association between CDI and PPI remain controversial. We searched the literature databases from their inception to December 2016, without restriction of language, including all controlled observational studies examining the association between acid-suppressive therapy and CDI. Pooled analysis of 50 studies showed a significant association between PPI use and risk of developing CDI (odds ratio: 1.26; 95% confidence interval: 1.12-1.39) as compared with non-users. When stratified by study patients, the relative risk of hospital-acquired CDI and community-associated CDI were 1.29 (1.14-1.44) and 1.17 (0.74-1.59). After restricting the studies according to hospital department, the relative risks of hospital-acquired CDI in ICUs and general wards were 1.43 (0.74-2.11) and 1.29 (1.13-1.45). By implementing cumulative meta-analysis, it was clear that earlier trials of CDI conducted in the early 2000s demonstrated a high degree of heterogeneity and a high percentage of negative results. Since 2011, the overall association between PPI use and risk of developing CDI has remained relatively stable within an effect size between OR 1.20 and 1.26. Our findings indicate a significant associated risk of incident CDI among PPI users, especially in general ward patients. The

totality of evidence, when using cumulative meta-analysis, showed that further trials are unlikely to overturn this positive result. Therefore establishing a guideline for the use of PPIs may help in future with the control of CDI.

2. Magnitude and direction of the association between Clostridium difficile infection and proton pump inhibitors in adults and pediatric patients: a systematic review and meta-analysis.

Author(s): Oshima, Tadayuki; Wu, Liping; Li, Min; Fukui, Hirokazu; Watari, Jiro; Miwa, Hiroto

Source: Journal of gastroenterology; Jan 2018; vol. 53 (no. 1); p. 84-94

Publication Type(s): Journal Article

Abstract:BACKGROUNDClostridium difficile infection (CDI) is a cause of increased morbidity and health care costs among hospitalized patients. Proton pump inhibitors (PPIs) are mainly used for the treatment of acid-related upper gastrointestinal diseases. The aim of the study was to assess the risks associated with initial and recurrent CDI in adult and pediatric patients treated with PPIs.METHODSA systematic search was performed using PubMed (Medline), Embase, and Web of Science with the following search terms: ("proton pump inhibitor," "PPI," or "acid suppression") AND ("infection," "diarrhea," "diarrhoea," "colitis," or "disease") AND ("Clostridium difficile"). Meta-analysis was performed using Revman5.3 software. Pooled odds ratios (ORs) presented as standard plots with 95% confidence intervals (CIs) were determined.RESULTSSixty-seven eligible studies were selected. PPI use was significantly associated with risk of CDI (OR 2.34, 95% CI 1.94-2.82; P < 0.00001). Pooled data from twelve studies demonstrated a significant association between PPI use and recurrent CDI (OR 1.73, 95% CI 1.39-2.15; P = 0.02). Subgroup analysis revealed significant associations between PPI use and an increased incidence of CDI among adult (OR 2.30, 95% CI 1.89-2.80; P < 0.00001) and pediatric (OR 3.00, 95% CI 1.44-6.23; P < 0.00001) patients.CONCLUSIONSPPI use was associated with CDI in adult and pediatric patients, and with recurrent CDI. Although many risk factors are associated with the occurrence and recurrence of CDI, consideration should be given to not administering PPIs at any age if they are unnecessary.

3. Extended-pulsed fidaxomicin versus vancomycin for Clostridium difficile infection in patients 60 years and older (EXTEND): a randomised, controlled, open-label, phase 3b/4 trial.

Author(s): Guery, Benoit; Menichetti, Francesco; Anttila, Veli-Jukka; Adomakoh, Nicholas; Aguado, Jose Maria; Bisnauthsing, Karen; Georgopali, Areti; Goldenberg, Simon D; Karas, Andreas; Kazeem, Gbenga; Longshaw, Chris; Palacios-Fabrega, Jose Alejandro; Cornely, Oliver A; Vehreschild, Maria J G T; EXTEND Clinical Study Group

Source: The Lancet. Infectious diseases; Dec 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDClostridium difficile infection causes severe complications and frequently recurs. An extended-pulsed fidaxomicin regimen might facilitate sustained clinical cure by prolonging C difficile suppression and supporting gut microbiota recovery. We aimed to compare clinical outcomes of extended-pulsed fidaxomicin with standard vancomycin.METHODSIn this randomised, controlled, open-label, superiority study, we recruited hospitalised adults aged 60 years and older with confirmed C difficile infection at 86 European hospitals. Patients were randomly assigned (1:1) using an interactive web response system to receive extended-pulsed fidaxomicin (200 mg oral tablets, twice daily on days 1-5, then once daily on alternate days on days 7-25) or vancomycin (125 mg oral capsules, four times daily on days 1-10), stratified by baseline C difficile infection severity, cancer presence, age (≥75 years vs <75 years), and number of previous C difficile infection occurrences. The primary endpoint was sustained clinical cure 30 days after end of treatment (day 55 for extended-pulsed fidaxomicin and day 40 for vancomycin), assessed in all randomised patients

who met the inclusion criteria and received at least one dose of study medication (modified full analysis set). Adverse events were assessed in all patients who received at least one dose of study drug. The study is registered with ClinicalTrials.gov, number NCT02254967.FINDINGSBetween Nov 6, 2014, and May 5, 2016, 364 patients were enrolled and randomly assigned to receive extended-pulsed fidaxomicin or vancomycin. 362 patients received at least one dose of study medication (181 in each group). 124 (70%) of 177 patients in the modified full analysis set receiving extended-pulsed fidaxomicin achieved sustained clinical cure 30 days after end of treatment, compared with 106 (59%) of 179 patients receiving vancomycin (difference 11% [95% CI 1·0-20·7], p=0·030; odds ratio 1·62 [95% CI 1·04-2·54]). Incidence of treatment-emergent adverse events did not differ between extended-pulsed fidaxomicin (121 [67%] of 181) and vancomycin (128 [71%] of 181) treatment arms. One death in the vancomycin arm was considered by the investigator to be related to study drug.INTERPRETATIONExtended-pulsed fidaxomicin was superior to standard-dose vancomycin for sustained cure of C difficile infection, and, to our knowledge, extended-pulsed fidaxomicin recurrence rates in this study are the lowest observed in a randomised clinical trial of antibiotic treatment for C difficile infection.FUNDINGAstellas Pharma, Inc.

4. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children.

Author(s): Goldenberg, Joshua Z; Yap, Christina; Lytvyn, Lyubov; Lo, Calvin Ka-Fung; Beardsley, Jennifer; Mertz, Dominik; Johnston, Bradley C

Source: The Cochrane database of systematic reviews; Dec 2017; vol. 12 ; p. CD006095

Publication Type(s): Journal Article Review

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract:BACKGROUNDAntibiotics can disturb gastrointestinal microbiota which may lead to reduced resistance to pathogens such as Clostridium difficile (C. difficile). Probiotics are live microbial preparations that, when administered in adequate amounts, may confer a health benefit to the host, and are a potential C. difficile prevention strategy. Recent clinical practice guidelines do not recommend probiotic prophylaxis, even though probiotics have the highest quality evidence among cited prophylactic therapies.OBJECTIVESTo assess the efficacy and safety of probiotics for preventing C.difficile-associated diarrhea (CDAD) in adults and children.SEARCH METHODSWe searched PubMed, EMBASE, CENTRAL, and the Cochrane IBD Group Specialized Register from inception to 21 March 2017. Additionally, we conducted an extensive grey literature search.SELECTION CRITERIARandomized controlled (placebo, alternative prophylaxis, or no treatment control) trials investigating probiotics (any strain, any dose) for prevention of CDAD, or C. difficile infection were considered for inclusion.DATA COLLECTION AND ANALYSISTwo authors (independently and in duplicate) extracted data and assessed risk of bias. The primary outcome was the incidence of CDAD. Secondary outcomes included detection of C. difficile infection in stool, adverse events, antibiotic-associated diarrhea (AAD) and length of hospital stay. Dichotomous outcomes (e.g. incidence of CDAD) were pooled using a random-effects model to calculate the risk ratio (RR) and corresponding 95% confidence interval (95% CI). We calculated the number needed to treat for an additional beneficial outcome (NNTB) where appropriate. Continuous outcomes (e.g. length of hospital stay) were pooled using a random-effects model to calculate the mean difference and corresponding 95% CI. Sensitivity analyses were conducted to explore the impact of missing data on efficacy and safety outcomes. For the sensitivity analyses, we assumed that the event rate for those participants in the control group who had missing data was the same as the event rate for those participants in the control group who were successfully followed. For the probiotic group, we calculated effects using the following assumed ratios of event rates in those with missing data in comparison to those successfully followed: 1.5:1, 2:1, 3:1, and 5:1. To explore possible explanations for heterogeneity, a priori subgroup analyses were conducted on probiotic species, dose, adult versus pediatric population, and risk of bias as well as a post hoc subgroup analysis on baseline risk

of CDAD (low 0% to 2%; moderate 3% to 5%; high > 5%). The overall quality of the evidence supporting each outcome was independently assessed using the GRADE criteria.MAIN RESULTSThirty-nine studies (9955 participants) met the eligibility requirements for our review. Overall, 27 studies were rated as either high or unclear risk of bias. A complete case analysis (i.e. participants who completed the study) among trials investigating CDAD (31 trials, 8672 participants) suggests that probiotics reduce the risk of CDAD by 60%. The incidence of CDAD was 1.5% (70/4525) in the probiotic group compared to 4.0% (164/4147) in the placebo or no treatment control group (RR 0.40, 95% CI 0.30 to 0.52; GRADE = moderate). Twenty-two of 31 trials had missing CDAD data ranging from 2% to 45%. Our complete case CDAD results proved robust to sensitivity analyses of plausible and worst-plausible assumptions regarding missing outcome data and results were similar whether considering subgroups of trials in adults versus children, inpatients versus outpatients, different probiotic species, lower versus higher doses of probiotics, or studies at high versus low risk of bias. However, in a post hoc analysis, we did observe a subgroup effect with respect to baseline risk of developing CDAD. Trials with a baseline CDAD risk of 0% to 2% and 3% to 5% did not show any difference in risk but trials enrolling participants with a baseline risk of > 5% for developing CDAD demonstrated a large 70% risk reduction (interaction P value = 0.01). Among studies with a baseline risk > 5%, the incidence of CDAD in the probiotic group was 3.1% (43/1370) compared to 11.6% (126/1084) in the control group (13 trials, 2454 participants; RR 0.30, 95% CI 0.21 to 0.42; GRADE = moderate). With respect to detection of C. difficile in the stool pooled complete case results from 15 trials (1214 participants) did not show a reduction in infection rates. C. difficile infection was 15.5% (98/633) in the probiotics group compared to 17.0% (99/581) in the placebo or no treatment control group (RR 0.86, 95% CI 0.67 to 1.10; GRADE = moderate). Adverse events were assessed in 32 studies (8305 participants) and our pooled complete case analysis indicates probiotics reduce the risk of adverse events by 17% (RR 0.83, 95% CI 0.71 to 0.97; GRADE = very low). In both treatment and control groups the most common adverse events included abdominal cramping, nausea, fever, soft stools, flatulence, and taste disturbance.AUTHORS' CONCLUSIONSBased on this systematic review and meta-analysis of 31 randomized controlled trials including 8672 patients, moderate certainty evidence suggests that probiotics are effective for preventing CDAD (NNTB = 42 patients, 95% CI 32 to 58). Our post hoc subgroup analyses to explore heterogeneity indicated that probiotics are effective among trials with a CDAD baseline risk >5% (NNTB = 12; moderate certainty evidence), but not among trials with a baseline risk ≤5% (low to moderate certainty evidence). Although adverse effects were reported among 32 included trials, there were more adverse events among patients in the control groups. The short-term use of probiotics appears to be safe and effective when used along with antibiotics in patients who are not immunocompromised or severely debilitated. Despite the need for further research, hospitalized patients, particularly those at high risk of CDAD, should be informed of the potential benefits and harms of probiotics.

5. The Impact of Clostridium difficile Infection on Mortality in Patients With Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis.

Author(s): Tariq, Raseen; Law, Cindy C Y; Khanna, Sahil; Murthy, Sanjay; McCurdy, Jeffrey D

Source: Journal of clinical gastroenterology; Dec 2017

Publication Type(s): Journal Article

Abstract:BACKGROUND AND AIMSClostridium difficile infection (CDI) has been associated with an increased mortality risk among patients with inflammatory bowel disease (IBD) in multiple observational studies. We performed a systematic review and meta-analysis to help clearly define the magnitude of risk in IBD patients with and without CDI, and to assess the risk in individual IBD subtypes.METHODSA systematic search of multiple electronic databases was conducted for observational studies reporting the risk of mortality in IBD, stratified by the presence of CDI. Weighted summary estimates were calculated using generalized inverse variance with random-

effects model. Study quality was assessed using the Newcastle-Ottawa scale.RESULTSTen observational studies were identified (8 from North America and 2 from Europe) and included 40,700 IBD patients with CDI and 1,320,764 IBD controls without CDI. Overall, IBD patients with CDI had a higher risk of mortality compared with IBD patients without CDI [odds ratios (OR), 4.39; 95% confidence interval (CI), 3.56-5.42; I=93%]. The results were stable in high-quality studies and in hospitalized patients. When patients were stratified by IBD type, CDI was associated with increased mortality in patients with ulcerative colitis (7 studies) (OR, 4.39; 95% CI, 3.44-5.61; I), but not in patients with Crohn's disease (4 studies) (OR, 2.21; 95% CI, 0.84-5.77; I). Individual studies were limited by an inability to control for IBD disease activity and therapeutic interventions.CONCLUSIONSOn the basis of 10 observational studies with at least moderate quality, CDI seems to increase mortality risk in IBD, particularly in ulcerative colitis. These findings are a cause for concern and suggest that CDI should be managed aggressively in patients with IBD.

6. Microbiological factors affecting Clostridium difficile recurrence.

Author(s): Chilton, C H; Pickering, D S; Freeman, J

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

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDRecurrent Clostridium difficile infection (rCDI) places a huge economic and practical burden on healthcare facilities. Furthermore, rCDI may impact quality of life, leaving patients in a 'rCDI cycle', and dependant on antibiotic therapy.AIMSThis article discusses the importance of microbiological factors in the development of rCDI.SOURCESLiterature was drawn from a search of PubMed from 2000 onwards with the search term "recurrent Clostridium difficile infection"; and further references quoted within these articles.CONTENTMeta-analysis and systematic reviews have shown that CDI and rCDI risk factors are similar. Development of rCDI is attendant upon many factors including immune status/function, comorbidities and concomitant treatments. Studies suggest that poor bacterial diversity is correlated with clinical rCDI. Narrow spectrum gut microflora-sparing antimicrobials (eg surotomycin, cadazolid, ridinilazole) are in development for CDI treatment; while microbiota therapeutics (faecal microbiota transplantation, non-toxigenic C. difficile, stool substitutes) are increasingly being explored. Recurrent CDI can only occur when viable C. difficile spores are present, either within the gut lumen post-infection, or re-acquired from the environment. C. difficile spore germination can be influenced by gut environmental factors resulting from dysbiosis; and spore outgrowth may be affected stage by some antimicrobials, (eg fidaxomicin, ramoplanin, oritavancin).IMPLICATIONSRecurrent CDI is a significant challenge for healthcare professionals, requiring a multi-faceted approach:optimised infection control to minimise re-infection; C. difficile-targeted antibiotics, to minimise dysbiosis; gut microflora restoration to promote colonisation resistance. These elements should be informed by our understanding of the microbiological factors involved: both C. difficile itself and the gut microbiome.

7. Surotomycin versus vancomycin in adults with Clostridium difficile infection: primary clinical outcomes from the second pivotal, randomized, double-blind, Phase 3 trial.

Author(s): Daley, P; Louie, T; Lutz, J E; Khanna, S; Stoutenburgh, U; Jin, M; Adedoyin, A; Chesnel, L; Guris, D; Larson, K B; Murata, Y

Source: The Journal of antimicrobial chemotherapy; Dec 2017; vol. 72 (no. 12); p. 3462-3470

Publication Type(s): Journal Article

Abstract: BackgroundThe available treatment options for Clostridium difficile infection (CDI) are limited by high recurrence rates. Surotomycin was a novel bactericidal cyclic lipopeptide in development to treat CDI that demonstrated non-inferiority to vancomycin in a Phase 2 trial.ObjectivesTo assess surotomycin safety and clinical response (non-inferiority versus vancomycin) at the end of treatment (EOT) of CDI. Additionally, to assess surotomycin response over time and sustained response at 30-40 days post-EOT (superiority versus vancomycin).Patients and methodsPatients with CDI were randomized (1:1) to receive twice-daily oral surotomycin 250 mg alternating with twice-daily placebo or four-times-daily oral vancomycin 125 mg for 10 days in this Phase 3, double-blind, multicentre, international trial. Clinical response over time and sustained clinical response were monitored until the end of the trial, through a follow-up period of 30-40 days. Clinical Trial Registration: NCT01598311.ResultsA total of 285 and 292 patients with confirmed CDI were randomized to receive surotomycin and vancomycin, respectively. Surotomycin-associated clinical response at EOT was non-inferior to vancomycin (surotomycin/vancomycin: 83.4%/82.1%; difference 1.4%, 95% CI - 4.9, 7.6). Following treatment with surotomycin, both clinical response over time (stratified log-rank test, P = 0.277) and sustained clinical response (63.3%/59.0%; difference 4.3%, 95% CI - 3.6, 12.2) did not demonstrate superiority versus vancomycin at end of trial. Both treatments were generally well tolerated.ConclusionsSurotomycin demonstrated non-inferiority to vancomycin for CDI clinical response at EOT. Surotomycin did not demonstrate superiority to vancomycin for clinical response over time or sustained clinical response rate.

8. Enteric microbiome profiles during a randomized Phase 2 clinical trial of surotomycin versus vancomycin for the treatment of Clostridium difficile infection.

Author(s): Cannon, Kristine; Byrne, Brendan; Happe, Jennifer; Wu, Kaiyu; Ward, Linda; Chesnel, Laurent; Louie, Thomas

Source: The Journal of antimicrobial chemotherapy; Dec 2017; vol. 72 (no. 12); p. 3453-3461

Publication Type(s): Journal Article

Abstract: ObjectivesThe effects of surotomycin (CB-183,315, MK-4261), a bactericidal cyclic lipopeptide, and vancomycin, the current standard-of-care for Clostridium difficile infection (CDI), on intestinal pathogens and microbiota were evaluated parallel to a Phase 2 randomized, double-blind clinical trial.MethodsThe single-centre cohort included 26 patients receiving surotomycin [125 or 250 mg twice daily (n = 9 each)] or oral vancomycin [125 mg four times daily (n = 8)] for 10 days. Faecal samples were collected at days 0-42 to quantify both C. difficile by conventional culture and the major components of the microbiome by quantitative PCR.ResultsSurotomycin 250 mg twice daily or vancomycin 125 mg four times daily reduced faecal C. difficile counts from ∼105-107 log10 cfu/g at baseline to ≤ 102 cfu/g by days 4-10 of treatment. Day 10 counts of C. difficile in 3/9 patients receiving surotomycin 125 mg twice daily remained detectable, including one patient who failed to achieve clinical cure. Bacteroidetes and Prevotella mean counts increased 0.7 log10 or remained unchanged with surotomycin 125 and 250 mg twice daily, respectively, whereas vancomycin reduced counts by 2.5-3.2 log10 (P < 0.02). Vancomycin reduced Firmicutes counts by 2.5-2.8 log10; surotomycin moderately suppressed these microbes in a dose-dependent manner.ConclusionsIn this Phase 2 trial substudy, compared with vancomycin 125 mg four times daily, surotomycin 250 mg twice daily is as active in vivo against C. difficile, but was more sparing of microbiota. Surotomycin is no longer in development due to failed Phase 3 efficacy results.

9. Evaluation of the cobas Cdiff Test for Detection of Toxigenic Clostridium difficile in Stool Samples.

Author(s): Peterson, Lance R; Young, Stephen A; Davis, Thomas E; Wang, Zi-Xuam; Duncan, John; Noutsios, Christopher; Liesenfeld, Oliver; Osiecki, John C; Lewinski, Michael A

Source: Journal of clinical microbiology; Dec 2017; vol. 55 (no. 12); p. 3426-3436

Publication Type(s): Journal Article

Abstract: Nucleic acid amplification tests (NAATs) are reliable tools for the detection of toxigenic Clostridium difficile from unformed (liquid or soft) stool samples. The objective of this study was to evaluate performance of the cobas Cdiff test on the cobas 4800 system using prospectively collected stool specimens from patients suspected of having C. difficile infection (CDI). The performance of the cobas Cdiff test was compared to the results of combined direct and broth-enriched toxigenic culture methods in a large, multicenter clinical trial. Additional discrepancy analysis was performed by using the Xpert C. difficile Epi test. Sample storage was evaluated by using contrived and fresh samples before and after storage at -20°C. Testing was performed on samples from 683 subjects (306 males and 377 females); 113 (16.5%) of 683 subjects were positive for toxigenic C. difficile by direct toxigenic culture, and 141 of 682 subjects were positive by using the combined direct and enriched toxigenic culture method (reference method), for a prevalence rate of 20.7%. The sensitivity and specificity of the cobas Cdiff test compared to the combined direct and enriched culture method were 92.9% (131/141; 95% confidence interval [CI], 87.4% to 96.1%) and 98.7% (534/541; 95% CI, 97.4% to 99.4%), respectively. Discrepancy analysis using results for retested samples from a second NAAT (Xpert C. difficile/Epi test; Cepheid, Sunnyvale, CA) found no false-negative and 4 false-positive cobas Cdiff test results. There was no difference in positive and negative results in comparisons of fresh and stored samples. These results support the use of the cobas Cdiff test as a robust aid in the diagnosis of CDI.

10. Metronidazole or Rifaximin for Treatment of Clostridium difficile in Pediatric Patients with Inflammatory Bowel Disease: A Randomized Clinical Trial.

Author(s): Gawronska, Agnieszka; Banasiuk, Marcin; Lachowicz, Dominika; Pituch, Hanna; Albrecht, Piotr; Banaszkiewicz, Aleksandra

Source: Inflammatory bowel diseases; Dec 2017; vol. 23 (no. 12); p. 2209-2214

Publication Type(s): Journal Article

Abstract:BACKGROUNDInterestingly, Clostridium difficile infection (CDI) worsens the course of inflammatory bowel disease (IBD); however, there is a paucity of data regarding the treatment of CDI in this group of patients.METHODSThis was a prospective, single-blind trial. Children with flare of IBD and CDI were randomly assigned to receive metronidazole or rifaximin orally for 14 days. CDI was diagnosed based on a positive well-type enzyme immunoassay (EIA) toxins A/B stool test for C. difficile toxins A and/or B. The cure rate was defined as the percentage of patients with a negative EIA stool test for C. difficile toxins A/B measured 4 weeks after the end of treatment. Recurrence was defined as a repeat CDI within 2 to 8 weeks.RESULTSIn total, we included 31 patients with IBD including 12 patients with Crohn's disease and 19 with ulcerative colitis. Of them, 17 received metronidazole and 14 received rifaximin. There were no statistically significant differences between the 2 study groups including age, type of treatment, and disease activity. There was no statistically significant difference in the cure rate between patients treated with metronidazole and rifaximin (70.6% versus 78.6%, respectively, P = 0.5). We found no difference in recurrence rate between the 2 study treatment types (17% versus 0%, respectively, P = 0.3). We did not find an association between immunosuppressive therapy and CDI cure rate or CDI recurrence rate.CONCLUSIONSMetronidazole and rifaximin were similarly effective treatments for CDI in pediatric patients with IBD.

11. Randomized clinical trial to evaluate the effect of fecal microbiota transplant for initial clostridium difficile infection in intestinal microbiome

Author(s): Camacho-Ortiz A.; Palau-Davila L.; Gutierrez-Delgado E.M.; Garcia-Mazcorro J.F.; Mendoza-Olazaran S.; Maldonado-Garza H.; Garza-Gonzalez E.; Martinez-Melendez A.; Baines S.D.

Source: PLoS ONE; Dec 2017; vol. 12 (no. 12)

Publication Type(s): Article

Available at PLoS ONE - from Public Library of Science (PLoS)

Available at PLoS ONE - from Europe PubMed Central - Open Access

Available at PLoS ONE - from EBSCO (MEDLINE Complete)

Abstract: Objective The aim of this study was to evaluate the impact of fecal donor-unrelated donor mix (FMT-FURM) transplantation as first-line therapy for C. difficile infection (CDI) in intestinal microbiome. Methods We designed an open, two-arm pilot study with oral vancomycin (250mg every 6 h for 10-14 days) or FMT-FURM as treatments for the first CDI episode in hospitalized adult patients in Hospital Universitario "Dr. Jose Eleuterio Gonzalez". Patients were randomized by a closed envelope method in a 1: 1 ratio to either oral vancomycin or FMT-FURM. CDI resolution was considered when there was a reduction on the Bristol scale of at least 2 points, a reduction of at least 50% in the number of bowel movements, absence of fever, and resolution of abdominal pain (at least two criteria). From each patient, a fecal sample was obtained at days 0, 3, and 7 after treatment. Specimens were cultured to isolate C. difficile, and isolates were characterized by PCR. Susceptibility testing of isolates was performed using the agar dilution method. Fecal samples and FMT-FURM were analyzed by 16S rRNA sequencing. Results We included 19 patients; 10 in the vancomycin arm and 9 in the FMT-FURM arm. However, one of the patients in the vancomycin arm and two patients in the FMT-FURM arm were eliminated. Symptoms resolved in 8/9 patients (88.9%) in the vancomycin group, while symptoms resolved in 4/7 patients (57.1%) after the first FMT-FURM dose (P = 0.26) and in 5/7 patients (71.4%) after the second dose (P = 0.55). During the study, no adverse effects attributable to FMT-FURM were observed in patients. Twelve isolates were recovered, most isolates carried tcdB, tcdA, cdtA, and cdtB, with an 18-bp deletion in tcdC. All isolates were resistant to ciprofloxacin and moxifloxacin but susceptible to metronidazole, linezolid, fidaxomicin, and tetracycline. In the FMT-FURM group, the bacterial composition was dominated by Firmicutes, Bacteroidetes, and Proteobacteria at all-time points and the microbiota were remarkably stable over time. The vancomycin group showed a very different pattern of the microbial composition when comparing to the FMT-FURM group over time. Conclusion The results of this preliminary study showed that FMT-FURM for initial CDI is associated with specific bacterial communities that do not resemble the donors' sample. Copyright © 2017 Camacho-Ortiz et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

12. Effect of Oral Capsule- vs Colonoscopy-Delivered Fecal Microbiota Transplantation on Recurrent Clostridium difficile Infection: A Randomized Clinical Trial.

Author(s): Kao, Dina; Roach, Brandi; Silva, Marisela; Beck, Paul; Rioux, Kevin; Kaplan, Gilaad G; Chang, Hsiu-Ju; Coward, Stephanie; Goodman, Karen J; Xu, Huiping; Madsen, Karen; Mason, Andrew; Wong, Gane Ka-Shu; Jovel, Juan; Patterson, Jordan; Louie, Thomas

Source: JAMA; Nov 2017; vol. 318 (no. 20); p. 1985-1993

Publication Type(s): Comparative Study Randomized Controlled Trial Multicenter Study Journal Article Equivalence Trial

Available at JAMA - from EBSCO (MEDLINE Complete)

Abstract: ImportanceFecal microbiota transplantation (FMT) is effective in preventing recurrent Clostridium difficile infection (RCDI). However, it is not known whether clinical efficacy differs by route of delivery.ObjectiveTo determine whether FMT by oral capsule is noninferior to colonoscopy delivery in efficacy.Design, Setting, and ParticipantsNoninferiority, unblinded, randomized trial

conducted in 3 academic centers in Alberta, Canada. A total of 116 adult patients with RCDI were enrolled between October 2014 and September 2016, with follow-up to December 2016. The noninferiority margin was 15%.InterventionsParticipants were randomly assigned to FMT by capsule or by colonoscopy at a 1:1 ratio.Main Outcomes and MeasuresThe primary outcome was the proportion of patients without RCDI 12 weeks after FMT. Secondary outcomes included (1) serious and minor adverse events, (2) changes in quality of life by the 36-Item Short Form Survey on a scale of 0 (worst possible quality of life) to 100 (best quality of life), and (3) patient perception on a scale of 1 (not at all unpleasant) to 10 (extremely unpleasant) and satisfaction on a scale of 1 (best) to 10 (worst).ResultsAmong 116 patients randomized (mean [SD] age, 58 [19] years; 79 women [68%]), 105 (91%) completed the trial, with 57 patients randomized to the capsule group and 59 to the colonoscopy group. In per-protocol analysis, prevention of RCDI after a single treatment was achieved in 96.2% in both the capsule group (51/53) and the colonoscopy group (50/52) (difference, 0%; 1-sided 95% CI, -6.1% to infinity; P < .001), meeting the criterion for noninferiority. One patient in each group died of underlying cardiopulmonary illness unrelated to FMT. Rates of minor adverse events were 5.4% for the capsule group vs 12.5% for the colonoscopy group. There was no significant between-group difference in improvement in quality of life. A significantly greater proportion of participants receiving capsules rated their experience as "not at all unpleasant" (66% vs 44%; difference, 22% [95% CI, 3%-40%]; P = .01).Conclusions and RelevanceAmong adults with RCDI, FMT via oral capsules was not inferior to delivery by colonoscopy for preventing recurrent infection over 12 weeks. Treatment with oral capsules may be an effective approach to treating RCDI.Trial Registrationclinicaltrials.gov Identifier: NCT02254811.

13. Impact of antimicrobial stewardship interventions on Clostridium difficile infection and clinical outcomes: segmented regression analyses.

Author(s): Patton, Andrea; Davey, Peter; Harbarth, Stephan; Nathwani, Dilip; Sneddon, Jacqueline; Marwick, Charis A

Source: The Journal of antimicrobial chemotherapy; Nov 2017

Publication Type(s): Journal Article

Abstract: BackgroundAntimicrobial exposure is associated with increased risk of Clostridium difficile infection (CDI), but the impact of prescribing interventions on CDI and other outcomes is less clear.ObjectivesTo evaluate the effect of an antimicrobial stewardship intervention targeting high-risk antimicrobials (HRA), implemented in October 2008, and to compare the findings with similar studies from a systematic review.MethodsAll patients admitted to Medicine and Surgery in Ninewells Hospital from October 2006 to September 2010 were included. Intervention effects on HRA use (dispensed DDD), CDI cases and mortality rates, per 1000 admissions per month, were analysed separately in Medicine and Surgery using segmented regression of interrupted time series (ITS) data. Data from comparable published studies were reanalysed using the same method.ResultsSix months post-intervention, there were relative reductions in HRA use of 33% (95% CI 11-56) in Medicine and 32% (95% CI 19-46) in Surgery. At 12 months, there was an estimated reduction in CDI of 7.0 cases/1000 admissions [relative change -24% (95% CI - 55 to 6)] in Medicine, but no change in Surgery {estimated 0.1 fewer cases/1000 admissions [-2% (95% CI - 116 to 112)]}. Mortality reduced throughout the study period, unaffected by the intervention. In all six comparable studies, HRA use reduced significantly, but reductions in CDI rates were only statistically significant in two and none measured mortality. Pre-intervention CDI rates and trends influenced the intervention effect.ConclusionsDespite large reductions in HRA prescribing and reductions in CDI, demonstrating real-world impact of stewardship interventions remains challenging.

14. Comparison of the Hospital-Acquired Clostridium difficile Infection Risk of Using Proton Pump Inhibitors versus Histamine-2 Receptor Antagonists for Prophylaxis and Treatment of Stress Ulcers: A Systematic Review and Meta-Analysis.

Author(s): Azab, Mohamed; Doo, Loomee; Doo, Daniel H; Elmofti, Yousif; Ahmed, Muazer; Cadavona, John Jay; Liu, Xibei B; Shafi, Amaan; Joo, Moon Kyung; Yoo, Ji Won

Source: Gut and liver; Nov 2017; vol. 11 (no. 6); p. 781-788

Publication Type(s): Journal Article

Available at Gut and liver - from Europe PubMed Central - Open Access

Abstract: Background/AimsAlthough proton pump inhibitors (PPIs) have been widely used for the prevention and treatment of stress gastric ulcers in hospital settings, there are concerns that PPIs increase the risk of Clostridium difficile infection (CDI). However, little is known about the risk of CDI following PPI and histamine-2 receptor antagonist (H2RA) use. We evaluated the comparative hospital-acquired CDI occurrence risk associated with the concurrent use of PPIs versus H2RAs.MethodsA systematic search of PubMed, MEDLINE/Ovid, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, and Google Scholar through August 19, 2016, identified 12 studies that reported the hospital-acquired CDI occurrence following H2RA and PPI use for the prevention and treatment of stress gastric ulcers. Random-effects pooled odds ratios and 95% confidence intervals were estimated. Heterogeneity was measured using I^2, and a meta-regression analysis was conducted. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was used to assess the overall quality of the evidence.ResultsA total of 74,132 patients from 12 observational studies were analyzed. Compared to H2RAs, PPIs increased the risk of CDI by 38.6% (pooled odds ratio, 1.386; 95% confidence interval, 1.152 to 1.668; p=0.001; I^2=42.81%). Subgroup analyses of the purpose of study medication use, study site, and study design confirmed the consistency of a greater CDI risk with PPIs than with H2RAs. The overall quality of evidence was rated as low.ConclusionsThe use of PPIs for both the prevention and treatment of stress ulcers was associated with a 38.6% increased risk of hospital-acquired CDI occurrence compared to H2RA use.

15. Identifying predictive features of Clostridium difficile infection recurrence before, during, and after primary antibiotic treatment.

Author(s): Pakpour, Sepideh; Bhanvadia, Amit; Zhu, Roger; Amarnani, Abhimanyu; Gibbons, Sean M; Gurry, Thomas; Alm, Eric J; Martello, Laura A

Source: Microbiome; Nov 2017; vol. 5 (no. 1); p. 148

Publication Type(s): Journal Article

Available at Microbiome - from BioMed Central

Available at Microbiome - from Europe PubMed Central - Open Access

Abstract:BACKGROUNDColonization by the pathogen Clostridium difficile often occurs in the background of a disrupted microbial community. Identifying specific organisms conferring resistance to invasion by C. difficile is desirable because diagnostic and therapeutic strategies based on the human microbiota have the potential to provide more precision to the management and treatment of Clostridium difficile infection (CDI) and its recurrence.METHODSWe conducted a longitudinal study of adult patients diagnosed with their first CDI. We investigated the dynamics of the gut microbiota during antibiotic treatment, and we used microbial or demographic features at the time of diagnosis, or after treatment, to predict CDI recurrence. To check the validity of the predictions, a meta-analysis using a previously published dataset was performed.RESULTSWe observed that patients' microbiota "before" antibiotic treatment was predictive of disease relapse, but surprisingly, post-antibiotic microbial community is indistinguishable between patients that recur or not. At the

individual OTU level, we identified Veillonella dispar as a candidate organism for preventing CDI recurrence; however, we did not detect a corresponding signal in the conducted meta-analysis.CONCLUSIONAlthough in our patient population, a candidate organism was identified for negatively predicting CDI recurrence, results suggest the need for larger cohort studies that include patients with diverse demographic characteristics to generalize species that robustly confer colonization resistance against C. difficile and accurately predict disease relapse.

16. A randomized controlled trial of probiotics for Clostridium difficile infection in adults (PICO).

Author(s): Barker, Anna K; Duster, Megan; Valentine, Susan; Hess, Timothy; Archbald-Pannone, Laurie; Guerrant, Richard; Safdar, Nasia

Source: The Journal of antimicrobial chemotherapy; Nov 2017; vol. 72 (no. 11); p. 3177-3180

Publication Type(s): Journal Article

Abstract: BackgroundClostridium difficile is the most common cause of hospital-acquired infections, responsible for >450000 infections annually in the USA. Probiotics provide a promising, well-tolerated adjunct therapy to standard C. difficile infection (CDI) treatment regimens, but there is a paucity of data regarding their effectiveness for the treatment of an initial CDI.ObjectivesWe conducted a pilot randomized controlled trial of 33 participants from February 2013 to February 2015 to determine the feasibility and health outcomes of adjunct probiotic use in patients with an initial mild to moderate CDI.MethodsThe intervention was a 28 day, once-daily course of a four-strain oral probiotic capsule containing Lactobacillus acidophilus NCFM, Lactobacillus paracasei Lpc-37, Bifidobacterium lactis Bi-07 and B. lactis Bl-04. The control placebo was identical in taste and appearance. Registered at clinicaltrials.gov: trial registration number = NCT01680874.ResultsProbiotic adjunct therapy was associated with a significant improvement in diarrhoea outcomes. The primary duration of diarrhoea outcome (0.0 versus 1.0 days; P = 0.039) and two exploratory outcomes, total diarrhoea days (3.5 versus 12.0 days; P = 0.005) and rate of diarrhoea (0.1 versus 0.3 days of diarrhoea/stool diary days submitted; P = 0.009), all decreased in participants with probiotic use compared with placebo. There was no significant difference in the rate of CDI recurrence or functional improvement over time between treatment groups.ConclusionsProbiotics are a promising adjunct therapy for treatment of an initial CDI and should be further explored in a larger randomized controlled trial.

17. Which antibiotics drive gut microbiome compositions towards those typical of individuals with recurrent clostridium difficile infection?: A meta-analysis and template for antibiotic development

Author(s): Hazleton K.; Lozupone C.

Source: Journal of Pediatric Gastroenterology and Nutrition; Nov 2017; vol. 65

Publication Type(s): Conference Abstract

Abstract: The human intestine houses a community of trillions of bacteria and there is mounting evidence that they are vital in maintaining human health. The bacterial community of our intestines are susceptible to killing by antibiotics. The disruption caused by these medications has been associated with an increased susceptibility to Clostridium diffcile associated diarrhea (CDAD). To better defne the changes to the bacterial community that lead to this increased risk of CDAD we conducted a meta-analysis of several published gut microbiome studies of patients with recurrent CDAD. Our analysis shows that the gut microbiome of adults with CDAD very closely resembles that of infants, with high levels of facultative anaerobes including Proteobacteria and relatively low levels of strict anaerobes such as the Bacteroidetes. These fndings suggest that the normal anaerobic environment of the distal intestines is disrupted and allows for C. diffcile to cause disease. Using studies of healthy individuals given antibiotics, we found that treatment with amoxicillin and

clindamycin push the microbiome of the participants towards that seen in recurrent CDAD and infants, and that this effect is stronger than for minocycline. This result is consistent with clinical data showing an increased risk of CDAD with these more disruptive antibiotics. This analysis could provide a metric to assess the CDAD-causing potential of novel antibiotics.

18. Vancomycin followed by fecal microbiota transplantation versus vancomycin for initial clostridium difficile infection: An open-label randomised controlled trial

Author(s): Ng S.C.C.; Wong S.H.; Cheung K.; Ching J.Y.L.; Tang W.; Kyaw M.; Tao Z.; Ho K.T.; Chan F.K.L.; Sung J.J.Y.; Wu J.C.; Lam L.Y.K.; Lui R.N.; Ip M.; Chan P.

Source: United European Gastroenterology Journal; Oct 2017; vol. 5 (no. 5)

Publication Type(s): Conference Abstract

Available at United European Gastroenterology Journal - from Europe PubMed Central - Open Access

Abstract: Introduction: Fecal microbiota transplantation (FMT) is effective for the treatment of recurrent Clostridium difficile infection (CDI) but its role as an initial therapy for patients with CDI has not been studied. Aims & Methods: We assessed the efficacy of FMT in patients with an initial episode of CDI compared with standard vancomycin regimen. In a single center, open-label, randomised study, we assigned 30 patients with an initial episode of CDI to receive either: oral vancomycin (500 mg four times daily) followed by FMT consisting of a single infusion of donor feces through a nasoduodenal tube; or a standard oral vancomycin regimen (500 mg four times daily for 10 days). The primary end point was resolution of diarrhea associated with CDI without relapse within 10 weeks after initiation of therapy. Secondary outcomes included 30-day and 6-month mortality, 30-day colectomy rates, length of hospital stay, adverse effects and alteration of fecal microbiota after FMT using metagenomic sequencing. Results: Baseline characteristics including age, gender and co-morbidities were comparable between the vancomycin and FMT arm. 60% and 47% of subjects in the vancomycin and FMT arm, respectively, had severe CDI. Resolution of C. difficile infection occurred in 10 of 15 patients (66.7%) receiving vancomycin and 11 of 15 patients (73.3%) receiving FMT (p=1.00). Two deaths occurred in the vancomycin group and none in the FMT group within 30 days. Nine (60%) and three deaths (20%) occurred in the vancomycin and FMT arms, respectively, within 6 months. None of the patients had a colectomy. Median length of hospital did not differ between both arms (13 vs 15 days; p=0.95). No serious adverse events attributed to FMT were observed. A restoration of healthy control enriched bacteria in recipients was observed after FMT, with a decrease in abundance of CDI-enriched bacteria. FMT, but not vancomycin treatment, resulted in marked virome alterations. Conclusion: In this pilot randomised controlled trial, FMT was not superior to vancomycin in patients with an initial episode of CDI. 30-day and 6-month mortality was higher in the vancomycin arm. A restoration of healthy control enriched bacteria in recipients was observed after FMT, with a decrease in abundance of CDI-enriched bacteria.

19. A randomised controlled trial of rifaximin to prevent relapse of clostridium difficile associated diarrhoea after resolution with standard therapy

Author(s): Major G.; Spiller R.; Bradshaw L.; Sprange K.; Montgomery A.; Boota N.; Jawhari A.; Diggle M.

Source: United European Gastroenterology Journal; Oct 2017; vol. 5 (no. 5)

Publication Type(s): Conference Abstract

Available at United European Gastroenterology Journal - from Europe PubMed Central - Open Access

Abstract: Introduction: Clostridium difficile associated diarrhoea (CDAD) is a common nosocomial infection. The most commonly prescribed treatments, metronidazole and vancomycine, have a primary cure rat of 90% but 1 in 4 cases suffer a relapse in the following months. A disrupted microbiota is thought to increase the risk of relapse. Rifaximin is a non-absorbable antibiotic that suppresses C.difficile proliferation. In a trial of 68 patients Garey et al. found that a course of rifaximin after standard therapy reduced relapse rate though not significantly1. Aims & Methods: We aimed to further investigate the efficacy of rifaximin to prevent CDAD relapse in a parallel group, randomised, placebo controlled trial in 23 hospitals in England. Population: age>=18 with resolution of CDAD after treatment with metronidazole or vancomycin, defined as cessation of diarrhoea for >=2 days. CDAD diagnosis required evidence of toxin production or pseudomembranes at endoscopy. Exclusion criteria were pregnancy or breast feeding; life expectancy 5 days elapsed since treatment. Randomisation was stratified by hospital using a remote, internet-based system. Participants, clinicians and researchers were blind to allocation. Intervention: Rifaximin 1200 mg daily for two weeks then 600 mg daily for two weeks, in three divided doses. Comparator: identical placebo. Primary Outcome: relapse =3 type 6 or 7 stools per day) for 2 days with evidence of toxin production. Sample size: The planned sample size was 180 to detect a difference in relapse of 20% (30% placebo, 10% rifaximin) with 80% power, allowing for loss to follow-up of 20%. EudraCT 2012-003205-10; www.clinicaltrials.gov NCT01670149; ISRCTN 65163992 Results: Recruitment occurred December 2012-March 2016. Of 2157 patients screened, 151 were eligible, willing and randomised before funding limits were reached (74 placebo, 77 rifaximin). Primary outcome data were available on 130. Mean age was 71.9 (SD 15.3). 36% were in-patients at start of intervention. 13% had a prior recorded episode of CDAD. 26% were using proton pump inhibitors pror to CDAD diagnosis, with a higher rate of use in the rifaximin group (32% vs. 20%). 18/61 (29.5%) on placebo relapsed within 12 weeks compared to 11/69 (15.9%) on rifaximin, a difference between groups of -13.7% (95% CI -28.1% to 0.7%, p=0.06). The risk ratio was 0.54 (95% CI 0.28 to 1.05, p=0.07). During 6-month safety follow up 9 participants died in each group (12%). Adverse event rates were similar between groups. Conclusion: CDAD relapse rate was 13.7% lower than on placebo. The confidence interval means that lack of effect remains possible but the estimated effect size is similar to Garey's trial1 with meta-analysis of the trials showing a statistically significant effect. The effect size is similar to that reported for fidaxomicin at 40 days2, or for bezlotoxumab at 3 months3. Age and mortality rate were higher in our trial which may reflect greater similarity to the population at risk. Comparative trials of the effectiveness and cost effectiveness of alternative treatment strategies should follow.

20. Accuracy of Xpert Clostridium difficile assay for the diagnosis of Clostridium difficile infection: A meta analysis

Author(s): Bai Y.; Jin Y.; Wang Y.; Sun X.; Li J.

Source: PLoS ONE; Oct 2017; vol. 12 (no. 10)

Publication Type(s): Article

PubMedID: 29016644

Abstract: Background: There is an urgent need for rapid and accurate microbiological diagnostic assay for detection of Clostridium difficile infection (CDI). We assessed the diagnostic accuracy of the Xpert Clostridium difficile assay (Xpert CD) for the diagnosis of CDI. Methods: We searched PubMed, EMBASE, and Cochrane Library databases to identify studies according to predetermined criteria. STATA 13.0 software was used to analyze the tests for sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and area under the summary receiver operating

characteristic curves (AUC). QUA-DAS-2 was used to assess the quality of included studies with RevMan 5.2. Heterogeneity in accuracy measures was tested with Spearman correlation coefficient and Chi-square. Results: A total of 22 studies were included in the meta-analysis. The pooled sensitivity (95% confidence intervals [CI]) was 0.97 (0.95-0.99) and specificity was 0.95 (0.94-0.96). The AUC was 0.99 (0.97-0.99). Significant heterogeneity was observed when we pooled most of the accuracy measures of selected studies. Conclusions: The Xpert CD assay is a useful diagnostic tool with high sensitivity and specificity in diagnosing toxigenic CDI, and this method has excellent usability due to its rapidity and simplicity.

21. Proton pump inhibitors therapy and risk of Clostridium difficile infection: Systematic review and meta-analysis.

Author(s): Trifan, Anca; Stanciu, Carol; Girleanu, Irina; Stoica, Oana Cristina; Singeap, Ana Maria; Maxim, Roxana; Chiriac, Stefan Andrei; Ciobica, Alin; Boiculese, Lucian

Source: World journal of gastroenterology; Sep 2017; vol. 23 (no. 35); p. 6500-6515

Publication Type(s): Journal Article

Available at World journal of gastroenterology - from Europe PubMed Central - Open Access

Abstract:AIMTo perform a systematic review and meta-analysis on proton pump inhibitors (PPIs) therapy and the risk of Clostridium difficile infection (CDI). METHODS We conducted a systematic search of MEDLINE/PubMed and seven other databases through January 1990 to March 2017 for published studies that evaluated the association between PPIs and CDI. Adult case-control and cohort studies providing information on the association between PPI therapy and the development of CDI were included. Pooled odds ratios (ORs) estimates with 95% confidence intervals (CIs) were calculated using the random effect. Heterogeneity was assessed by I2 test and Cochran's Q statistic. Potential publication bias was evaluated via funnel plot, and quality of studies by the Newcastle-Otawa Quality Assessment Scale (NOS).RESULTSFifty-six studies (40 case-control and 16 cohort) involving 356683 patients met the inclusion criteria and were analyzed. Both the overall pooled estimates and subgroup analyses showed increased risk for CDI despite substantial statistical heterogeneity among studies. Meta-analysis of all studies combined showed a significant association between PPI users and the risk of CDI (pooled OR = 1.99, CI: 1.73-2.30, P < 0.001) as compared with non-users. The association remained significant in subgroup analyses: by design-case-control (OR = 2.00, CI: 1.68-2.38, P < 0.0001), and cohort (OR = 1.98, CI: 1.51-2.59, P < 0.0001); adjusted (OR = 1.95, CI: 1.67-2.27, P < 0.0001) and unadjusted (OR = 2.02, CI: 1.41-2.91, P < 0.0001); unicenter (OR = 2.18, CI: 1.72-2.75, P < 0.0001) and multicenter (OR = 1.82, CI: 1.51-2.19, P < 0.0001); age ≥ 65 years (OR = 1.93, CI: 1.40-2.68, P < 0.0001) and < 65 years (OR = 2.06, CI: 1.11-3.81, P < 0.01). No significant differences were found in subgroup analyses (test for heterogeneity): P = 0.93 for case-control vs cohort, P = 0.85 for adjusted vs unadjusted, P = 0.24 for unicenter vs multicenter, P = 0.86 for age ≥ 65 years and < 65 years. There was significant heterogeneity across studies (I2 = 85.4%, P < 0.001) as well as evidence of publication bias (funnel plot asymmetry test, P = 0.002).CONCLUSIONThis meta-analysis provides further evidence that PPI use is associated with an increased risk for development of CDI. Further high-quality, prospective studies are needed to assess whether this association is causal.

Database: Medline

Bronchiolitis

1. Nitric oxide inhalations in bronchiolitis: A pilot, randomized, double-blinded, controlled trial.

Author(s): Tal, Asher; Greenberg, David; Av-Gay, Yossef; Golan-Tripto, Inbal; Feinstein, Yael; Ben-Shimol, Shalom; Dagan, Ron; Goldbart, Aviv D

Source: Pediatric pulmonology; Jan 2018; vol. 53 (no. 1); p. 95-102

Publication Type(s): Journal Article

Abstract:AIMThe aims of this pilot study were to determine safety, tolerability (primary outcome) and efficacy (secondary outcome) of high-dose inhaled nitric oxide for the treatment of infants with moderately severe bronchiolitis.METHODSThis was a pilot, double-blinded, randomized controlled study (phase IIa). Intermittent inhalations of nitric oxide 160 ppm for 30 min or oxygen/air (control) were given 5 times/day to hospitalized infants (2-11 months) with acute bronchiolitis. Oxygen saturation, methemoglobin, and nitric dioxide (NO_2) levels and vital signs were monitored.RESULTSForty-three infants were enrolled. Baseline characteristics were comparable in both study groups. Mean clinical score, comprised of four components: respiratory rate, use of accessory muscles, wheezes and crackles, and % room-air oxygen saturation, was 7.86 (±1.1) and 8.09 (±1.2) in the NO and control groups, respectively, consistent with moderate severity. The overall frequency of adverse events was similar between the groups. Repeated nitric oxide inhalations did not result in increased inhaled NO_2 levels or cumulative effect on methemoglobin levels. Secondary outcomes of efficacy were measured by length of hospitalization (LOS) in hours: LOS did not differ between groups. However, in a post-hoc analysis of a subgroup of infants hospitalized for >24 h (n = 24), the median LOS was shorter in the nitric oxide (41.9 h) than in the control group (62.5 h) (P = 0.014).CONCLUSIONOur study was unable to detect a difference in side effects using intermittent high-dose nitric-oxide inhalation or supportive treatment alone, in infants with moderate bronchiolitis. Preliminary efficacy outcomes are encouraging.

2. Reducing unnecessary chest X-rays, antibiotics and bronchodilators through implementation of the NICE bronchiolitis guideline.

Author(s): Breakell, Richard; Thorndyke, Benjamin; Clennett, Julie; Harkensee, Christian

Source: European Journal of Pediatrics; Jan 2018; vol. 177 (no. 1); p. 47-51

Publication Type(s): Academic Journal

Abstract: Chest X-rays (CXR), antibiotics and inhaled/nebulized therapy are overused in bronchiolitis, despite evidence-based guidelines suggesting supportive management only. This study investigates the effect of the implementation of the NICE bronchiolitis guideline in a secondary paediatric unit in England. We present a quality improvement project with a completed audit cycle (winter 2014-2015 and 2015-2016) pre- and post-implementation of the NICE bronchiolitis guideline. The educational intervention included sessions for raising awareness of appropriate and inappropriate management of bronchiolitis for both clinicians and nursing staff. As a result, the number of chest radiographs reduced fivefold (from 20 to 4% of patients, absolute reduction 16%), antibiotics reduced more than threefold (from 22 to 6% of patients, absolute reduction 16%) and inhaled/nebulised treatment up to twofold (from 30 to 16%, absolute reduction 14%). Overall NICE guideline compliance rose from 28 to 63%.Conclusion: Implementation of the NICE bronchiolitis guideline supported by a simple educational intervention can effectively reduce the number of inappropriate chest radiographs and antibiotic prescribing in bronchiolitis, and enhance compliance with the NICE guideline. What is Known: • Bronchiolitis management in paediatric units in the UK is variable, with poor evidence for existing guidance. Best available evidence was compiled into the NICE guideline, aiming to standardize care. • Some evidence exists for the effectiveness of quality improvement approaches to

improve the management of bronchiolitis. What is New: • NICE guidance can be effectively applied to a department using simple educational tools. • Effective NICE implementation reduces the rates of unnecessary chest radiograph and antibiotic administration for patients admitted with bronchiolitis in District General Hospitals.

3. Respiratory Syncytial Virus Genotypes, Host Immune Profiles and Disease Severity in Young Children Hospitalized with Bronchiolitis.

Author(s): Rodriguez-Fernandez, Rosa; Tapia, Lorena I.; Chin-Fen Yang; Torres, Juan Pablo; Chavez-Bueno, Susana; Garcia, Carla; Jaramillo, Lisa M.; Moore-Clingenpee, Melissa; Jafri, Hasan S.; Peeples, Mark E.; Piedra, Pedro A.; Ramilo, Octavio; Mejias, Asuncion

Source: Journal of Infectious Diseases; Jan 2018; vol. 217 (no. 1); p. 24-34

Publication Type(s): Academic Journal

Abstract: Background: Data on how RSV genotypes influence disease severity and host immune responses is limited. We characterized the genetic variability of RSV during five seasons, and evaluated the role of RSV subtypes, genotypes and viral loads on disease severity and host transcriptional profiles.Methods: Prospective, observational study including a convenience sample of healthy infants hospitalized with RSV bronchiolitis. Nasopharyngeal samples for viral load quantitation, typing and genotyping, and blood samples for transcriptome analyses were obtained within 24h of hospitalization. Multivariate models were constructed to identify virologic and clinical variables predictive of clinical outcomes.Results: From 3/2004 to 4/2011, we enrolled 253 infants (57% males; median age 2.1 [1.1-4.0] moths). RSV-A infections predominated over RSV-B (69% vs. 31%; p<0.001) and showed greater genotype variability. RSV A/GA2, A/GA5 and RSV B/BA were the most common genotypes identified. Compared to GA2 or BA, infants with GA5 infections had higher viral loads (p<0.01). Adjusted for other covariates, GA5 infections were also associated with longer hospital stay, and with less activation of interferon and increased overexpression of neutrophil genes.Conclusions: RSV-A infections were more frequent than RSV B, and displayed greater variability. GA5 infections were associated with enhanced disease severity and distinct host immune responses.

4. Viral bronchiolitis in young infants: new perspectives for management and treatment.

Author(s): Caballero, Mauricio T; Polack, Fernando P; Stein, Renato T

Source: Jornal de pediatria; 2017; vol. 93

Publication Date: 2017

Publication Type(s): Journal Article Review

PubMedID: 28859915

Available at Jornal de pediatria - from EBSCO (MEDLINE Complete)

Abstract:OBJECTIVEThe aim of this review was to address advances in management and treatment of acute viral bronchiolitis in infants.SOURCESA systematic review search was made including all articles published in English between 2010 and 2017, and available in the electronic databases PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) and specialized register of the Acute Respiratory Infections Group (Cochrane review group). The following MESH terms in English were included, using different Boolean operators for the search strategy: "bronchiolitis, viral," "diagnosis," "epidemiology," "etiology," "therapy," "virology," "prevention and control," "respiratory syncytial virus, human." Additional filters were used.SUMMARY OF FINDINGSFew effective interventions are recommended for the management of RSV bronchiolitis in young infants. The main goal is to ensure an adequate oxygen supplementation and fluid balance whenever deemed

necessary. Hypertonic saline nebulization is helpful only for hospitalized infants. Numerous antiviral drugs and specific vaccines for RSV are under evaluation and foretell advances in disease management in the near future.CONCLUSIONA number of promising new technologies are advancing in the field. Until new interventions became feasible, early detection and modification of preventable risk factors is essential to improve outcomes.

5. Hypertonic saline inhalations in bronchiolitis-A cumulative meta-analysis.

Author(s): Heikkilä, Paula; Renko, Marjo; Korppi, Matti

Source: Pediatric pulmonology; Dec 2017

Publication Type(s): Journal Article Review

Abstract: We undertook a cumulative meta-analysis for the efficacy of hypertonic saline (HS) compared to normal saline (NS) inhalations or no inhalations as controls in bronchiolitis. We performed literature searches from PubMed, Scopus, and by hand search until 20 June 2017. We accepted published randomized controlled trials of HS inhalations in children with bronchiolitis aged <24 months. We evaluated the differences between treatment group with HS and control group without HS inhalations for the length-of-stay in hospital (LOS) by cumulative mean difference (MD) and in hospitalization rate by cumulative risk ratio (RR). We identified 18 studies including 2102 children treated in hospital, and the cumulative MD in LOS was -0.471 days (95% confidence interval [CI] -0.765 to -0.177, Higgins heterogeneity test [I2] 72.9%). The cumulative MD reduced in more recently published papers. In studies with the upper age limit of 12 months, the cumulative MD was -0.408 days (95%CI -0.733 to -0.083) without any important heterogeneity (I2 = 0%). If only studies with a very low risk of bias were included, the cumulative MD was 0.034 (95%CI -0.361 to 0.293) without any important heterogeneity (I2 = 0%). We identified eight studies including 1834 children in the outpatient setting, and the cumulative risk ratio for hospitalization was 0.771 (95%CI 0.619-0.959, I2 55.8%). In conclusion, HS inhalations offered only limited clinical benefits, though the differences between HS and control groups were statistically significant. The heterogeneity between the studies was substantial. Further studies are warranted with consistent definitions of bronchiolitis and comparable research frames.

6. A Randomized Controlled Trial of a Single Dose Furosemide to Improve Respiratory Distress in Moderate to Severe Bronchiolitis.

Author(s): Williamson, Kristy; Bredin, Gabriel; Avarello, Jahn; Gangadharan, Sandeep

Source: The Journal of emergency medicine; Nov 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDBronchiolitis is one of the most common disorders of the lower respiratory tract in infants. While historically diuretics have been used in severe bronchiolitis, no studies have looked directly at their early use in children in the emergency department.OBJECTIVEThe primary objective of this study was to determine whether a single early dose of a diuretic in infants with moderate to severe bronchiolitis would improve respiratory distress. Secondary objectives examined whether it reduced the use of noninvasive ventilation and hospital length of stay.METHODSPatients diagnosed with clinical bronchiolitis were enrolled at a tertiary care, academic children's hospital over a 3-year period. This was a double-blind, randomized controlled trial in which subjects were randomly assigned to either furosemide or placebo. Respiratory rate and oxygen saturation at the time of medication delivery and at 2 and 4 h post-intervention were recorded, as well as other data. Exact logistic regression was used to examine associations.RESULTSThere were 46 subjects enrolled and randomized. There was no difference in respiratory rates, measured as a decrease of ≥ 25%, at both 2 and 4 h after intervention between furosemide and placebo groups (odds ratios 1.13 and

1.13, respectively). There was also no difference in oxygen saturation, intensive care unit admission rate, or hospital length of stay between groups.CONCLUSIONSWhile theoretically a single dose of a diuretic to reduce lung fluid would improve respiratory distress in children with bronchiolitis, our randomized controlled medication trial showed no difference in outcomes. ClinicalTrials.gov ID: NCT02469597.

RSV

1. Determining the outcomes of interventions to prevent respiratory syncytial virus disease in children: What to measure?

Author(s): Karron R.A.; Zar H.J.

Source: The Lancet Respiratory Medicine; 2017

Publication Type(s): Article In Press

Abstract: Respiratory syncytial virus (RSV) is the most common cause of viral acute lower respiratory tract illness (LRTI) in young children, and a major cause of hospital admissions and health-care utilisation globally. Substantial efforts have been made to develop RSV vaccines and vaccine-like monoclonal antibodies to prevent acute RSV LRTI. Prevention of acute disease could improve long-term lung health, with potential effects on wheezing, asthma, and chronic lung disease. This Personal View describes assessments that should be initiated during clinical trials and continued after licensure to fully evaluate the effect of RSV preventive interventions. These assessments include recording the incidence of RSV-specific LRTI and all-cause LRTI through two RSV seasons, and assessment of the prevalence and severity of recurrent wheezing or asthma in children aged up to 6 years. Standardised assessments in diverse settings are needed to fully determine the effect of interventions for the prevention of RSV disease.

2. Palivizumab in the prevention of severe respiratory syncytial virus infection in children with congenital heart disease; a novel cost-utility modeling study reflecting evidence-based clinical pathways in Spain.

Author(s): Schmidt, Ralph; Majer, Istvan; García Román, Natalia; Rivas Basterra, Alejandra; Grubb, ElizaBeth; Medrano López, Constancio

Source: Health economics review; Dec 2017; vol. 7 (no. 1); p. 47

Publication Type(s): Journal Article

Available at Health economics review - from Europe PubMed Central - Open Access

Abstract:BACKGROUNDRespiratory syncytial virus (RSV) infection remains one of the major reasons of re-hospitalization among children with congenital heart disease (CHD). This study estimated the cost-effectiveness of palivizumab prophylaxis versus placebo, in Spain, from the societal perspective, using a novel cost-effectiveness model reflecting evidence-based clinical pathways.METHODSA decision-analytic model, combining a decision tree structure in the first year and a Markov structure in later years, was constructed to evaluate the benefits and costs associated with palivizumab versus no prophylaxis among children with CHD. In the first year of the model, children were at risk of mild (i.e. medically attended, MA-RSV) and severe (hospitalized, RSV-H) RSV infection. The impact of delayed corrective CHD surgery due to RSV infection and the consequence of performed surgery despite severe infection were considered. In later years, patients were at risk of developing asthma and allergic sensitization as sequelae of RSV infection. Input data for the model were derived from the pivotal clinical trial and systematic literature reviews. Indirect costs included parental absence

from work and nosocomial infections. In agreement with Spanish guidelines, costs and effects were discounted at 3%.RESULTSOver a lifetime horizon, palivizumab prophylaxis yielded 0.11 and 0.07 additional quality-adjusted life years (QALYs) and life years (LYs), respectively, at additional costs of € 1,693, resulting in an ICER of € 15,748 per QALY gained and € 24,936 per LY gained. Probabilistic sensitivity analyses demonstrated that the probability of palivizumab prophylaxis being cost-effective at a € 30,000 per QALY threshold was 92.7%. The ICER remained below this threshold for most extreme scenario analyses.CONCLUSIONSThe model demonstrated that palivizumab prophylaxis results in more QALYs than no prophylaxis in children with CHD. Palivizumab prophylaxis was shown to be a cost-effective health care intervention according to the commonly accepted standards of cost-effectiveness in Spain (ICER below the threshold of € 30,000 per QALY).

3. An Adjuvanted, Postfusion F Protein-Based Vaccine Did Not Prevent Respiratory Syncytial Virus Illness in Older Adults.

Author(s): Falloon, Judith; Yu, Jing; Esser, Mark T; Villafana, Tonya; Yu, Li; Dubovsky, Filip; Takas, Therese; Levin, Myron J; Falsey, Ann R

Source: The Journal of infectious diseases; Dec 2017; vol. 216 (no. 11); p. 1362-1370

Publication Type(s): Randomized Controlled Trial Clinical Trial, Phase Ii Journal Article

Abstract: BackgroundRespiratory syncytial virus (RSV) is an important cause of illness in older adults. This study assessed efficacy of a vaccine for prevention of RSV-associated acute respiratory illness (ARI), defined by specified symptoms with virologic confirmation.MethodsThis phase 2b study evaluated RSV postfusion F protein (120 µg) with glucopyranosyl lipid adjuvant (5 µg) in 2% stable emulsion. Subjects aged ≥60 years were randomly assigned at a ratio of 1:1 to receive vaccine or placebo (all received inactivated influenza vaccine). Ill subjects recorded symptoms and provided blood and nasal swab samples.ResultsIn the per-protocol population (n = 1894), the incidence of RSV-associated ARI occurring ≥14 days after dosing was 1.7% and 1.6% in the vaccine and placebo groups, respectively, for a vaccine efficacy (VE) of -7.1% (90% confidence interval [CI], -106.9%-44.3%). Efficacy was not observed in secondary analyses that included seroresponse to nonvaccine RSV antigens (VE, 8.9%; 90% CI, -28.5%-35.4%) or symptoms combined with seroresponse (VE, 10.0%; 90% CI, -45.4%-44.4%). On day 29, 92.9% of vaccinees had an anti-F immunoglobulin G antibody seroresponse. Overall, 48.5% and 30.9% of RSV vaccine recipients reported local and systemic solicited symptoms, respectively.ConclusionThe RSV vaccine was immunogenic but did not protect older adults from RSV illness.Clinical Trials RegistrationNCT02508194.

4. Chronologic Age at Hospitalization for Respiratory Syncytial Virus Among Preterm and Term Infants in the United States.

Author(s): Parikh, Rohan C; McLaurin, Kimmie K; Margulis, Andrea V; Mauskopf, Josephine; Ambrose, Christopher S; Pavilack, Melissa; Candrilli, Sean D

Source: Infectious diseases and therapy; Dec 2017; vol. 6 (no. 4); p. 477-486

Publication Type(s): Journal Article

Available at Infectious diseases and therapy - from Europe PubMed Central - Open Access

Available at Infectious diseases and therapy - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:INTRODUCTIONRespiratory syncytial virus (RSV) is the leading cause of hospitalization among infants in the United States, and the risk for RSV hospitalizations is greater for infants born preterm. Recent studies in preterm and term infants have shown that RSV hospitalization rates vary considerably depending on infant chronologic age. This study sought to aggregate the data available

from published literature and from nationally representative databases of US infant hospitalizations to generate a composite description of the effect of young chronologic age on RSV hospitalizations among US preterm and term infants by individual month of age.METHODSData describing the relative incidence of RSV hospitalizations by individual month of chronologic age during the first year of life were obtained from recently published studies, the 2006-2011 National Inpatient Sample databases, and the 2006 and 2009 Kids Inpatient Databases.RESULTSAll data sources showed that ≥20% of infant RSV hospitalizations occurred in the second month of life and >50% and >75% of RSV hospitalizations were observed during the first 3 and 6 months of life, respectively. These findings were consistent for both preterm and term infants.CONCLUSIONData from multiple sources demonstrate that the greatest risk of RSV hospitalization occurs during the first 6 months of life among US preterm and term infants. Strategies to prevent infant RSV hospitalizations should be targeted to infants during the first months of life.FUNDINGAstraZeneca.

5. Respiratory syncytial virus seasonality and its implications on prevention strategies.

Author(s): Janet, Sophie; Broad, Jonathan; Snape, Matthew D

Source: Human vaccines & immunotherapeutics; Dec 2017 ; p. 1-11

Publication Type(s): Journal Article

Abstract: With maternal and infant vaccines against respiratory syncytial virus (RSV) in development, it is timely to consider how the deployment of these vaccines might vary according to local RSV disease seasonality. In temperate regions RSV infection is predictably limited to a period of 3 to 5 months, while in tropical regions disease seasonality is often both more variable and more prolonged. Accordingly, in tropical regions a year-round immunisation schedule for both maternal and infant immunisation might be appropriate. In contrast, in temperate regions the benefit of year-round maternal immunisation would be heavily dependent on the duration of protection this provided, potentially necessitating a strategy directed at children due to be born in the months immediately prior to the RSV season. This review will consider the impact of seasonality on maternal and infant immunisation strategies against RSV, and the potential of an alternative approach of passive immunisation for all infants immediately prior to the RSV season.

6. RI-002, an intravenous immunoglobulin containing high titer neutralizing antibody to RSV and other respiratory viruses for use in primary immunodeficiency disease and other immune compromised populations

Author(s): Wasserman R.L.; Greener B.N.; Mond J.

Source: Expert Review of Clinical Immunology; Dec 2017; vol. 13 (no. 12); p. 1107-1119

Publication Type(s): Article

Abstract: Introduction: Novel immune globulin (IG) products (RI-002, RI-001) have been designed to provide protection against respiratory syncytial virus (RSV) mediated respiratory illness while at the same time meeting the manufacturing requirements established by FDA for antibody supplementation in immunocompromised subjects. Areas covered: This review covers the manufacture and development of both RI-001 and RI-002, including the selection of plasma donors for IG preparation with high-titers of anti-RSV antibody, in vitro, and preclinical data in the cotton rat model S. hispidus, and clinical trials including Phase II and compassionate use studies of RI-001 and a multi-center, pivotal Phase III study of RI-002 in PIDD patients. Expert commentary: The data demonstrate that RI-002 is efficacious in the prevention and treatment of RSV in preclinical normal and immune suppressed animal models and is safe and efficacious in the treatment of patients with various forms of primary immunodeficiency disease (PIDD). This product offers potential advantages over other available IG's for prophylaxis in immunocompromised patients requiring polyclonal

immunoglobulin supplementation because of its unique antibody composition. In addition to its enhanced neutralizing anti-RSV activity and its polyclonal IG composition, there is preclinical data to support the use of RI-002 for humoral protection against other respiratory pathogens.

7. A human challenge model for respiratory syncytial virus kinetics, the pharmacological effect of a novel fusion inhibitor, and the modelling of symptoms scores.

Author(s): Korell, Julia; Green, Bruce; DeVincenzo, John; Huntjens, Dymphy

Source: European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences; Nov 2017; vol. 109

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) causes acute lower respiratory tract infections, and is a major cause of hospital admissions and death in young children. Limited treatments currently exist that can prevent or minimise exacerbation of the disease. The aims of this work were: 1) to develop a population pharmacodynamic model to describe RSV kinetics (RSVK) in nasal lavage, 2) evaluate the impact of an investigational fusion inhibitor, JNJ-53718678, on RSVK, and 3) determine the relationship between RSVK and symptoms scores. The best model to fit the RSVK data was a target-cell limited viral kinetics model previously developed for influenza A infections (Baccam et al., 2006), which included a series of compartments for infected, non-producing and infected, and producing cell populations. The model was adapted to account for longer incubation times seen in RSV, by including 4 additional transit compartments, with the virus elimination rate constant and initial number of target cells fixed to literature values to ensure model parameter identifiability. Between-subject variability was included on the infection rate constant and virus production rate constant. The effect of JNJ-53718678 on RSVK was best described by a non-dose dependent transformation of the infectious virions into a non-infectious state, with a proportional odds model successfully describing symptoms scores, using individual model predicted viral loads as predictor.

8. Prospective and Retrospective Evaluation of the Performance of the FDA-Approved Cepheid Xpert Flu/RSV XC Assay.

Author(s): Arbefeville, Sophie; Thonen-Kerr, Elizabeth; Ferrieri, Patricia

Source: Laboratory medicine; Nov 2017; vol. 48 (no. 4); p. e53

Publication Type(s): Journal Article

Abstract: Rapid and accurate detection of respiratory viruses is important in patient care and in guiding therapy and infection prevention policy. Rapid viral antigen assays are simple to perform and provide results within 15 to 30 minutes but are limited by their modest-to-moderate sensitivity. Molecular assays are more sensitive and specific but require more technical time and expertise and are more expensive. We verified the performance of the Xpert Flu/RSV XC assay prospectively, using patient respiratory samples from the 2014-2015 respiratory season, and, retrospectively, with frozen patient samples from the previous respiratory season. A total of 60 specimens were assayed on the Xpert Flu/RSV XC assay and by the GenMark Diagnostics eSensor Respiratory Viral Panel. The sensitivity of the Xpert Flu/RSV XC for Flu A was 100% (23/23), for Flu B, 80% (8/10), and for respiratory syncytial virus (RSV), 94.1% (16/17), compared to the reference assay (GenMark). The specificity was 100%. Eight specimens were positive for viruses other than Flu A/B or RSV, and this did not interfere with detection of targets in the Xpert assay. We demonstrated that the performance of the Xpert Flu/RSV XC was comparable to the more comprehensive molecular respiratory assay.

9. Respiratory Syncytial Virus (RSV): Targeting the G Protein Provides a New Approach for an Old Problem.

Author(s): Tripp, Ralph A; Power, Ultan F; Openshaw, Peter J M; Kauvar, Lawrence M

Source: Journal of virology; Nov 2017

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection (LRTI) annually affecting >2 million children in the US 65 years old), RSV results in ∼175,000 hospitalizations annually in the US with worldwide incidence ∼34 million. There is no approved RSV vaccine and treatments are limited. Recently, a Phase 3 trial in the elderly using a recombinant RSV F protein vaccine failed to meet its efficacy objectives, namely prevention of moderate-to-severe RSV-associated LRTI and reduced incidence of acute respiratory disease. Moreover, a recent Phase 3 trial evaluating suptavumab (REGN2222), an antibody to RSV F protein, did not meet its primary endpoint of preventing medically attended RSV infections in pre-term infants. Despite these setbacks, numerous efforts targeting the RSV F protein with vaccines, antibodies, and small molecules continue based on the commercial success of a monoclonal antibody (mAb) against the RSV F protein (palivizumab). As the understanding of RSV biology has improved, the other major coat protein, the RSV G protein, has re-emerged as an alternative target reflecting progress in understanding its roles in infecting bronchial epithelial cells and in altering the host immune response. In mouse models, a high-affinity, strain-independent human mAb to the RSV G protein has shown potent direct antiviral activity combined with the alleviation of virus-induced immune system effects that contribute to disease pathology. This mAb, being prepared for clinical trials, provides a qualitatively new approach to managing RSV for populations not eligible for prophylaxis with palivizumab.

10. Prolonged viral replication and longitudinal viral dynamic differences among respiratory syncytial virus infected infants.

Author(s): Brint, Monica E; Hughes, Joshua M; Shah, Aditya; Miller, Chelsea R; Harrison, Lisa G; Meals, Elizabeth A; Blanch, Jacqueline; Thompson, Charlotte R; Cormier, Stephania A; DeVincenzo, John P

Source: Pediatric research; Nov 2017; vol. 82 (no. 5); p. 872-880

Publication Type(s): Journal Article

Abstract: BackgroundLongitudinal respiratory syncytial virus (RSV) dynamics have not been well studied despite the existence of factors favoring prolonged RSV replication including high mutation rates allowing rapid evolution and potential escape from immune control. We therefore measured viral load in previously RSV-naive infants over prolonged time spans.MethodsDuring 2014-2015, quantitative nasal aspirates were collected from 51 RSV-PCR+ infants. Multiple parallel assessments of viral loads were quantified at each collected time point using a well-validated real-time quantitative reverse transcriptase polymerase chain reaction assay. After observing viral load rebound phenomenon in some infants, the viral dynamics of 27 infants with sufficient longitudinal viral load data points were analyzed using the pre-defined criteria for viral rebound. Additional analyses were performed comparing age with viral rebound, viral clearance rates, and viral load area-under-the-curve (AUCVL).ResultsThe 51 infants (303 nasal aspirate samples; mean of 5.9 per patient) exhibited slower than expected viral clearance. Lower age trended toward slower viral clearance and greater AUCVL. Six infants had detectable viral loads ≥1 month after symptom onset. Ten of twenty-seven evaluable subjects exhibited viral rebound and this rebound was age-dependent (P=0.0259). All but one rebounder were <70 days old.ConclusionInfants struggle to control primary RSV infections allowing prolonged viral replication and previously undescribed viral rebound; likely representing viral mutational immune escape.

11. Recombinant baculovirus-based vaccine expressing M2 protein induces protective CD8+ T-cell immunity against respiratory syncytial virus infection.

Author(s): Lee, Jeong-Yoon; Chang, Jun

Source: Journal of microbiology (Seoul, Korea); Nov 2017; vol. 55 (no. 11); p. 900-908

Publication Type(s): Journal Article

Abstract: Respiratory syncytial virus (RSV) is an important cause of acute lower respiratory tract disease in infants, young children, immunocompromised individuals, and the elderly. However, despite ongoing efforts to develop an RSV vaccine, there is still no authorized RSV vaccine for humans. Baculovirus has attracted attention as a vaccine vector because of its ability to induce a high level of humoral and cellular immunity, low cytotoxicity against various antigens, and biological safety for humans. In this study, we constructed a recombinant baculovirus- based vaccine expressing the M2 protein of RSV under the control of cytomegalovirus promoter (Bac_RSVM2) to induce CD8+ T-cell responses which play an important role in viral clearance, and investigated its protective efficacy against RSV infection. Immunization with Bac_RSVM2 via intranasal or intramuscular route effectively elicited the specific CD8+ T-cell responses. Most notably, immunization with Bac_RSVM2 vaccine almost completely protected mice from RSV challenge without vaccine-enhanced immunopathology. In conclusion, these results suggest that Bac_RSVM2 vaccine employing the baculovirus delivery platform has promising potential to be developed as a safe and novel RSV vaccine that provides protection against RSV infection.

12. Respiratory Syncytial Virus Infection Control Challenges with a Novel Polymerase Chain Reaction Assay in a Tertiary Medical Center.

Author(s): Sendi, Parham; Egli, Adrian; Dangel, Marc; Frei, Reno; Tschudin-Sutter, Sarah; Widmer, Andreas F

Source: Infection control and hospital epidemiology; Nov 2017; vol. 38 (no. 11); p. 1291-1297

Publication Type(s): Journal Article

Abstract:OBJECTIVES To evaluate host characteristics, mode of infection acquisition, and infection control procedures in patients with a positive respiratory syncytial virus (RSV) test result after the introduction of the GenXpert Influenza/RSV polymerase chain reaction (PCR) assay. DESIGN Retrospective cohort study. PATIENTS Adults with a positive PCR test result for RSV who were hospitalized in a tertiary academic medical center between January 2015 and December 2016 were included in this study. Our infection control policy applies contact isolation precautions only for immunocompromised patients. METHODS Patients were identified through 2 databases, 1 consisting of patients isolated because of RSV infection and 1 with automatically collected laboratory results. Baseline and clinical characteristics were collected through a retrospective medical chart review. The rate of and clinical factors associated with healthcare-associated RSV infections were evaluated. RESULTS In total, 108 episodes in 106 patients hospitalized with a positive Xpert RSV test result were recorded during the study period. Among them, 11 episodes were healthcare-associated infections (HAIs) and 97 were community-acquired infections (CAIs). The mean length of hospital stay (LOS, 40.2 vs 11.2 days), the mean number of room switches (3.5 vs 1.7) and ward switches (1.5 vs 0.4), and the mean numbers of contact patients (9.9 vs 3.8) were significantly longer and higher in the HAI group than in the CAI group (P<.0001). Surveillance of microbiology records and clinical data did not reveal evidence for a cluster or an epidemic during the 2-year observation period. CONCLUSIONS The introduction of a rapid molecular diagnostic test systematically applied to patients with influenza-like illness may challenge current infection control policies. In our study, patients with HAIs

had a prolonged hospital stay and a high number of contact patients, and they switched rooms and wards frequently.

13. Virus-like particle vaccine primes immune responses preventing inactivated-virus vaccine-enhanced disease against respiratory syncytial virus

Author(s): Hwang H.S.; Lee Y.-T.; Kim K.-H.; Ko E.-J.; Lee Y.; Kwon Y.-M.; Kang S.-M.

Source: Virology; Nov 2017; vol. 511 ; p. 142-151

Publication Type(s): Article

Abstract: Formalin inactivated respiratory syncytial virus (FI-RSV) vaccination caused vaccine-enhanced respiratory disease (ERD) upon exposure to RSV in children. Virus-like particles presenting RSV F fusion protein (F VLP) are known to increase T helper type-1 (Th1) immune responses and avoid ERD in animal models. We hypothesized that F VLP would prime immune responses preventing ERD upon subsequent exposure to ERD-prone FI-RSV. Here, we demonstrated that heterologous F VLP priming and FI-RSV boosting of mice prevented FI-RSV vaccine-enhanced lung inflammation and eosinophilia upon RSV challenge. F VLP priming redirected pulmonary T cells toward effector CD8 T cells producing Th1 cytokines and significantly suppressed pulmonary Th2 cytokines. This study suggests that RSV F VLP priming would modulate and shift immune responses to subsequent exposure to ERD-prone FI-RSV vaccine and RSV infection, suppressing Th2 immune-mediated pulmonary histopathology and eosinophilia.

14. Cost-effectiveness of rule-based immunoprophylaxis against respiratory syncytial virus infections in preterm infants

Author(s): Blanken M.O.; Nibbelke E.E.; Sanders E.A.M.; Bont L.; Frederix G.W.; Koffijberg H.; Rovers M.M.

Source: European Journal of Pediatrics; Nov 2017 ; p. 1-12

Publication Type(s): Article In Press

Abstract: The objective of the paper is to assess the cost-effectiveness of targeted respiratory syncytial virus (RSV) prophylaxis based on a validated prediction rule with 1-year time horizon in moderately preterm infants compared to no prophylaxis. Data on health care consumption were derived from a randomised clinical trial on wheeze reduction following RSV prophylaxis and a large birth cohort study on risk prediction of RSV hospitalisation. We calculated the incremental cost-effectiveness ratio (ICER) of targeted RSV prophylaxis vs. no prophylaxis per quality-adjusted life year (QALYs) using a societal perspective, including medical and parental costs and effects. Costs and health outcomes were modelled in a decision tree analysis with sensitivity analyses. Targeted RSV prophylaxis in infants with a first-year RSV hospitalisation risk of > 10% resulted in a QALY gain of 0.02 (0.931 vs. 0.929) per patient against additional cost of 472 compared to no prophylaxis (ICER 214,748/QALY). The ICER falls below a threshold of 80,000 per QALY when RSV prophylaxis cost would be lowered from 928 (baseline) to 406 per unit. At a unit cost of 97, RSV prophylaxis would be cost saving. Conclusions: Targeted RSV prophylaxis is not cost-effective in reducing RSV burden of disease in moderately preterm infants, but it can become cost-effective if lower priced biosimilar palivizumab or a vaccine would be available. Copyright © 2017 The Author(s)

15. Clinical Potential of Prefusion RSV F-specific Antibodies.

Author(s): Rossey, Iebe; McLellan, Jason S; Saelens, Xavier; Schepens, Bert

Source: Trends in microbiology; Oct 2017

Publication Type(s): Journal Article Review

Abstract: Human respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections in the very young. The RSV fusion protein (F) is essential for virus entry because it mediates viral and host membrane fusion. During this fusion process F is converted from a metastable prefusion conformation into an energetically favored postfusion state. Antibodies that target F can prevent viral entry and reduce disease caused by RSV. During recent years, many prefusion F-specific antibodies have been described. These antibodies typically have stronger RSV-neutralizing activity compared to those that also bind F in the postfusion conformation. Here, we describe how F-specific antibodies protect against RSV and why specifically targeting prefusion F could have great clinical potential.

16. Cost-utility analysis of Palivizumab for Respiratory Syncytial Virus infection prophylaxis in preterm infants: update based on the clinical evidence in Spain.

Author(s): Sanchez-Luna, M; Burgos-Pol, R; Oyagüez, I; Figueras-Aloy, J; Sánchez-Solís, M; Martinón-Torres, F; Carbonell-Estrany, X

Source: BMC infectious diseases; Oct 2017; vol. 17 (no. 1); p. 687

Publication Type(s): Journal Article

Available at BMC infectious diseases - from BioMed Central

Available at BMC infectious diseases - from Europe PubMed Central - Open Access

Available at BMC infectious diseases - from EBSCO (MEDLINE Complete)

Abstract:BACKGROUNDThis study aimed at estimating the efficiency of palivizumab in the prevention of Respiratory Syncytial Virus (RSV) infection and its sequelae in preterm infants (32day 1-35day 0weeks of gestational age -wGA-) in Spain.METHODSA decision-tree model was developed to compare health benefits (Quality Adjusted Life Years-QALYs) and costs of palivizumab versus a non-prophylaxis strategy over 6 years. A hypothetical cohort of 1,000 preterm infants, 32day 1-35day 0 wGA (4.356 kg average weight) at the beginning of the prophylaxis (15 mg/kg of palivizumab; 3.88 average number of injections per RSV season) was analysed. The model considered the most recent evidence from Spanish observational and epidemiological studies on RSV infection: the FLIP II study provided hospital admission and Intensive Care Unit (ICU) admission rates; in-hospital mortality rate was drawn from an epidemiological study from 2004 to 2012; recurrent wheezing rates associated to RSV infection from SPRING study were adjusted by the evidence on the palivizumab effect from clinical trials. Quality of life baseline value, number of hospitalized infants and the presence of recurrent wheezing over time were granted to estimate QALYs. National Health Service and societal perspective (included also recurrent wheezing indirect cost) were analysed. Total costs (€, 2016) included pharmaceutical and administration costs, hospitalization costs and recurrent wheezing management annual costs. A discount rate of 3.0% was applied annually for both costs and health outcomes.RESULTSOver 6 years, the base case analysis showed that palivizumab was associated to an increase of 0.0731 QALYs compared to non-prophylaxis. Total costs were estimated in €2,110.71 (palivizumab) and €671.68 (non-prophylaxis) from the National Health System (NHS) perspective, resulting in an incremental cost utility ratio (ICUR) of €19,697.69/QALYs gained (prophylaxis vs non-prophylaxis). Results derived from the risk-factors population subgroups analysed were in line with the total population results. From the societal perspective, the incremental cost associated to palivizumab decreased to an €1,253.14 (ICUR = €17,153.16€/QALYs gained for palivizumab vs non-prophylaxis). One-way and probabilistic sensitivity analyses confirmed the robustness of the model.CONCLUSIONSThe prophylaxis with palivizumab is efficient for preventing from RSV infections in preterm infants 32day 1-35day 0 wGA in Spain.

17. Deep sequencing of RSV from an adult challenge study and from naturally infected infants reveals heterogeneous diversification dynamics.

Author(s): Lau, Jessica W; Kim, Young-In; Murphy, Ryan; Newman, Ruchi; Yang, Xiao; Zody, Michael; DeVincenzo, John; Grad, Yonatan H

Source: Virology; Oct 2017; vol. 510 ; p. 289-296

Publication Type(s): Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Journal Article

Abstract: As RNA virus mutation occurs during replication within host cells, we hypothesized that viral evolution during acute infections in healthy hosts reflects host immune pressure. We therefore investigated the within-host diversification of human respiratory syncytial virus (RSV), a highly prevalent cause of acute respiratory infections. We evaluated healthy adults experimentally infected with an identical inoculum and infants hospitalized with naturally acquired infections. In aggregate, viral diversification in adults peaked at day 3, with overrepresentation of diversity in the matrix protein 2 (M2) and non-structural protein 2 (NS2) genes. In one subject, delayed viral clearance was accompanied by a late peak of diversity at day 10 in known and predicted B and T cell epitopes. In contrast, infant infections showed much less viral diversity. Our findings suggest multiple overlapping mechanisms for early control of acute viral infections, which may differ between age groups and host immune responses.

Surgical Site Infection

1. Methodology and Background for the World Health Organization Global Guidelines on the Prevention of Surgical Site Infection

Author(s): Sway A.; Solomkin J.S.; Pittet D.; Kilpatrick C.

Source: Surgical Infections; Jan 2018; vol. 19 (no. 1); p. 33-39

Publication Type(s): Article

Abstract: Surgical site infections remain an important topic of concern for surgeons in all specialties and are currently the focus of global health agencies for prevention. Because patients have numerous co-morbidities that increase the risks of surgical site infections, and because of the emergence of more resistant pathogens, it is necessary to revise and update guidelines to assist surgeons in the prevention of these infections. This article will summarize the most recent WHO Global Guidelines for the prevention of Surgical Site Infection that will have applicability for surgeons in all countries.

2. Does surgical site infection after Caesarean section in Polish hospitals reflect high-quality patient care or poor postdischarge surveillance? Results from a 3-year multicenter study.

Author(s): Różańska, Anna; Jarynowski, Andrzej; Kopeć-Godlewska, Katarzyna; Wójkowska-Mach, Jadwiga; Misiewska-Kaczur, Agnieszka; Lech, Marzena; Rozwadowska, Małgorzata; Karwacka, Marlena; Liberda, Joanna; Domańska, Joanna; Polish Society of Hospital Infections Team

Source: American journal of infection control; Jan 2018; vol. 46 (no. 1); p. 20-25

Publication Type(s): Journal Article

Abstract:BACKGROUNDCaesarean sections (CSs) are associated with a high infection risk. Surgical site infection (SSI) incidence is among the markers of effectiveness of infection prevention efforts. The aim of this study was to analyze risk factors for SSI, incidence, and microbiology in patients who

underwent CS.METHODSThe study was conducted during 2013-2015 using active infection surveillance in 5 Polish hospitals according to the European Centre for Disease Prevention and Control surveillance network known as HAI-Net. For each procedure, the following data were registered: age, American Society of Anesthesiologists score, procedure time, elective or emergency procedure, use of perioperative antibiotic prophylaxis, microbiology, the treatment used, and other information.RESULTSSSI incidence was 0.5% and significant differences were noted among hospitals (between 0.1% and 1.8%), for different American Society of Anesthesiologists scales (between 0.2% and 4.8%) and different values of standardized SSI risk index (between 0.0% and 0.8%). In 3.1% of procedures, with no antibiotic prophylaxis, SSI risk was significantly higher. Deep infections dominated: 61.5% with superficial infections in only approximately 30% of cases and 2.6% of infections were detected postdischarge without readmissions.CONCLUSIONSResults showed high incidence of SSI in Poland without perioperative antibiotic prophylaxis, and secondly, ineffective surveillance according to CS status, considering outpatient obstetric care. Without postdischarge surveillance, it is not possible to recognize the epidemiologic situation, and further, to set priorities and needs when it comes to infection prophylaxis, especially because such low incidence may indicate no need for improvement in infection control.

3. Caesarean Delivery Surgical Site Infection: What are Expected Rates and Potentially Modifiable Risk Factors?

Author(s): Haidar, Ziad A; Nasab, Susan Hosseini; Moussa, Hind N; Sibai, Baha M; Blackwell, Sean C

Source: Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC; Dec 2017

Publication Type(s): Journal Article

Abstract:OBJECTIVEThis study sought to determine baseline Caesarean delivery (CD) surgical site infection (SSI) rates in various patient subgroups and to identify potentially modifiable and non-modifiable risk factors for SSI.METHODSThis is a secondary analysis of a multicentre CD registry. Women who underwent CD were divided into SSI versus no SSI. SSI was defined as an infection that occurred in the part of the body where the surgery took place, within 30 days of surgery. Clinical characteristics and potential risk factors were compared between groups.RESULTSOf 57 182 women, 3696 (6.5%) had SSI. SSI rates were higher in primary versus repeat CD (9.7% vs. 4.2%; P <0.001), and in CD after labour vs. no labour (9.5% vs. 3.8%; P <0.001). After adjustment for confounding factors, low transverse CD (adjusted OR [aOR] 0.7 [0.6-0.9]), CD performed between 7 pm and 7 am (aOR 0.9 [0.83-0.98]), primary CD (aOR 0.5 [0.5-0.6]), and intrapartum antibiotics (aOR 0.3 [0.1-0.4]) were associated with a decreased in the rate of SSI. Black race (aOR 1.9 [1.7-2.1]), tobacco use (aOR 1.4 [1.2-1.6]), increasing American Society of Anesthesiologists category (aOR 1.3 [1.1-1.6]), vertical skin incision (aOR 1.2 [1.1-1.3], emergency CD (aOR 1.3 [1.1-1.5]), and postpartum transfusion (aOR 2.7 [2.1-3.6]) were associated with an increase in the rate of SSI.CONCLUSIONThis study estimates the CD SSI rates in different subgroups and serves as a baseline for future trials designed to develop preventive guidelines and protocols.

4. Risk of Surgical Site Infection in Elective Hip and Knee Replacements After Confirmed Eradication of MRSA in Chronic Carriers.

Author(s): Tandon, Tarang; Tadros, Baha J; Akehurst, Harold; Avasthi, Adhish; Hill, Richard; Rao, Madhu

Source: The Journal of arthroplasty; Dec 2017; vol. 32 (no. 12); p. 3711-3717

Publication Type(s): Journal Article

Abstract:BACKGROUNDMethicillin-resistant Staphylococcus aureus (MRSA) is globally endemic and is a leading cause of surgical site infection (SSI). The purpose of this study was to evaluate the incidence of SSI in MRSA carriers undergoing elective hip or knee arthroplasty, who had confirmed eradication and to compare it with incidence of SSI in non-MRSA carriers.METHODSThis is a retrospective analysis of 6613 patients who underwent elective total hip arthroplasty (THA; n = 3347) and total knee arthroplasty (TKA; n = 3266) at our institution. A cohort of patients who were preoperatively colonized with MRSA was identified. We compared the infection rates with non-MRSA carriers.RESULTSWe had a colonization rate of 1.3% (83 patients). A total of 79 patients had confirmed eradication of carrier status before surgical intervention. Of these, 38 were THAs and 41 were TKAs. Five of 79 patients (6.32%; 95% confidence interval [CI]: 2.35%-14.79%) had "deep SSI" within 1 year of surgery. There were 2 MRSA infections in THAs (relative risk 4.46; 95% CI: 1.12-17.82). There were 2 MRSA and 1 methicillin-sensitive Staphylococcus aureus infections in TKAs (relative risk 5.61; 95% CI: 1.81-17.38). A significant statistical difference in infection rates from MRSA negative control group was noted, which had a deep sepsis rate of 1.17% in THAs and 1.3% in TKAs over the same period.CONCLUSIONIn spite of a selective treatment program for carriers and confirmed eradication, there is still a significantly increased risk of SSI in MRSA-colonized patients undergoing hip or knee arthroplasties.

5. Waterless Hand Rub Versus Traditional Hand Scrub Methods for Preventing the Surgical Site Infection in Orthopedic Surgery

Author(s): Iwakiri K.; Kobayashi A.; Seki M.; Ando Y.; Tsujio T.; Hoshino M.; Nakamura H.

Source: Spine; Nov 2017; vol. 42 (no. 22); p. 1675-1679

Publication Type(s): Article

Abstract: Study Design. A retrospective cohort study with prospectively collected data. Objective. The aim of this study was to compare SSI incidences, the cost of hand hygiene agents, and hand hygiene time between the traditional hand scrub and the waterless hand rub protocols before orthopedic surgery. Summary of Background Data. Surgical site infections (SSI) prolong hospitalization and are a leading nosocomial cause of morbidity and a source of excess cost. Recently, a waterless hand rub protocol comprising alcohol based chlorhexidine gluconate for use before surgery was developed, but no studies have yet examined its utility in orthopedic surgery. Methods. Fourteen hundred consecutive patients who underwent orthopedic surgery (spine, joint replacement, hand, and trauma surgeries) in our hospital since April 1, 2012 were included. A total of 712 cases underwent following traditional hand scrub between April 1, 2012 and April 30, 2013 and 688 cases underwent following waterless hand rub between June 1, 2013 and April 30, 2014. We compared SSI incidences within all and each subcategory between two hand hygiene protocols. All patients were screened for SSI within 1 year after surgery. We compared the cost of hand hygiene agents and hand hygiene time between two groups. Results. The SSI incidences were 1.3% (9 of 712) following the traditional protocol (2 deep and 7 superficial infections) and 1.1% (8 of 688) following the waterless protocol (all superficial infections). There were no significant differences between the two groups. The costs of liquids used for one hand hygiene were about $2 for traditional hand scrub and less than $1 for waterless hand rub. The mean hand hygiene time was 264 seconds with the traditional protocol and 160 seconds with the waterless protocol. Conclusion. Waterless hand rub with an alcohol based chlorhexidine gluconate solution can be a safe, quick, and cost-effective alternative to traditional hand scrub.

6. Performance of statistical process control methods for regional surgical site infection surveillance: a 10-year multicentre pilot study.

Author(s): Baker, Arthur W; Haridy, Salah; Salem, Joseph; Ilieş, Iulian; Ergai, Awatef O; Samareh, Aven; Andrianas, Nicholas; Benneyan, James C; Sexton, Daniel J; Anderson, Deverick J

Source: BMJ quality & safety; Nov 2017

Publication Type(s): Journal Article

Available at BMJ quality & safety - from BMJ Journals

Available at BMJ quality & safety - from BMJ Journals - NHS

Abstract:BACKGROUNDTraditional strategies for surveillance of surgical site infections (SSI) have multiple limitations, including delayed and incomplete outbreak detection. Statistical process control (SPC) methods address these deficiencies by combining longitudinal analysis with graphical presentation of data.METHODSWe performed a pilot study within a large network of community hospitals to evaluate performance of SPC methods for detecting SSI outbreaks. We applied conventional Shewhart and exponentially weighted moving average (EWMA) SPC charts to 10 previously investigated SSI outbreaks that occurred from 2003 to 2013. We compared the results of SPC surveillance to the results of traditional SSI surveillance methods. Then, we analysed the performance of modified SPC charts constructed with different outbreak detection rules, EWMA smoothing factors and baseline SSI rate calculations.RESULTSConventional Shewhart and EWMA SPC charts both detected 8 of the 10 SSI outbreaks analysed, in each case prior to the date of traditional detection. Among detected outbreaks, conventional Shewhart chart detection occurred a median of 12 months prior to outbreak onset and 22 months prior to traditional detection. Conventional EWMA chart detection occurred a median of 7 months prior to outbreak onset and 14 months prior to traditional detection. Modified Shewhart and EWMA charts additionally detected several outbreaks earlier than conventional SPC charts. Shewhart and SPC charts had low false-positive rates when used to analyse separate control hospital SSI data.CONCLUSIONSOur findings illustrate the potential usefulness and feasibility of real-time SPC surveillance of SSI to rapidly identify outbreaks and improve patient safety. Further study is needed to optimise SPC chart selection and calculation, statistical outbreak detection rules and the process for reacting to signals of potential outbreaks.

7. Perioperative, local and systemic warming in surgical site infection: a systematic review and meta-analysis.

Author(s): Ousey, K; Edward, K-L; Lui, S; Stephenson, J; Walker, K; Duff, J; Leaper, D

Source: Journal of wound care; Nov 2017; vol. 26 (no. 11); p. 614-624

Publication Type(s): Journal Article

Abstract:OBJECTIVESurgical site infection (SSI) is a common cause of postoperative morbidity. Perioperative hypothermia may contribute to surgical complications including increased risk of SSI. In this systematic review and meta-analysis, the effectiveness of active and passive perioperative warming interventions to prevent SSI was compared with standard (non-warming) care.METHODOvid MEDLINE; Ovid EMBASE; EBSCO CINAHL Plus; The Cochrane Wounds Specialised Register, and The Cochrane Central Register of Controlled Trials were searched, with no restrictions on language, publication date or study setting for randomised controlled trials (RCTs) and cluster RCTs. Adult patients undergoing elective or emergency surgery under general anaesthesia, receiving any active or passive warming intervention perioperatively were included. Selection, risk of bias assessment and data extraction were performed by two review authors, independently. Outcomes studied were SSI (primary outcome), inpatient mortality, hospital length of stay and pain (secondary outcomes).RESULTSWe identified four studies, including 769 patients. The risk ratio (RR) for SSI in warming groups was 0.36 [95% confidence interval (CI): 0.23, 0.56; p<0. 001]. Length of hospitalisation was 1.13 days less in warming groups [95% CI: -3.07, 5.33; p=0.600]. The RR for mortality in the warming groups was 0.77 [95% CI: 0.17, 3.43; p=0.730]. A meta-analysis for pain outcome could not be conducted.CONCLUSIONThis review provides evidence in favour of active warming to prevent SSI, but insufficient evidence of active warming to reduce length of hospital stay and mortality. Benefits of passive warming remain unclear and warrant further research.

8. The Effect of Participating in a Surgical Site Infection (SSI) Surveillance Network on the Time Trend of SSI Rates: A Systematic Review.

Author(s): Abbas, Mohamed; Tartari, Ermira; Allegranzi, Benedetta; Pittet, Didier; Harbarth, Stephan

Source: Infection control and hospital epidemiology; Nov 2017; vol. 38 (no. 11); p. 1364-1366

Publication Type(s): Journal Article

PubMedID: 28836491

Abstract: This systematic literature review reveals that participating in a surgical site infection (SSI) surveillance network is associated with short-term reductions in SSI rates: relative risk [RR] for year 2, 0.80 (95% confidence interval [CI], 0.79-0.82); year 3 RR, 0.92 (95% CI, 0.90-0.94); year 4 RR, 0.98 (95% CI, 0.96-1.00). Infect Control Hosp Epidemiol 2017;38:1364-1366.

9. Prevention of Surgical Site Infection: Analysis and Narrative Review of Clinical Practice Guidelines.

Author(s): Gómez-Romero, Francisco Javier; Fernández-Prada, Maria; Navarro-Gracia, Juan Francisco

Source: Cirugia espanola; Nov 2017; vol. 95 (no. 9); p. 490-502

Publication Type(s): Journal Article

Abstract: Surgical site infection is one of the most prevalent healthcare-associated infections and presents a considerable morbidity. The aim of this comprehensive narrative review is to describe the evidence and grade of recommendation of the preventive measures developed in the three phases of the surgical process (preoperative, perioperative and postoperative phases), as well as coincidences and divergences between selected Clinical Practice Guidelines (CPG). Four preventive measures were recommended with similar high grade evidence in all CPG: Hair removal, antibiotic prophylaxis, surgical site preparation and normothermia. However, critical points, new preventive measures and bundle implementations by surgical process are under discussion. These results represent a significant progress toward improving programs to prevent surgical site infection and they should be taken into account for improved future interventions in this area.

10. Multi-institution analysis of infection control practices identifies the subset that impact surgical site infection: A texas alliance for surgical quality collaborative project

Author(s): Davis C.H.; Kao L.S.; Aloia T.A.

Source: Journal of the American College of Surgeons; Oct 2017; vol. 225 (no. 4)

Publication Type(s): Conference Abstract

Abstract:INTRODUCTION: A large number of infection control practices (ICP), including operating room attire policies, have been recommended with the intent of lowering wound infections (SSI). However, few have proven benefit and many are costly, timeconsuming, and detrimental to provider morale. The goal of this multi-institution study was to determine which ICPs are associated with lower postoperative SSI rates. METHODS: Twenty American College of Surgeons-NSQIP Texas Alliance for Surgical Quality (TASQ) hospitals completed this QIAB-approved study. Surgeon champions at each hospital ranked current adherence to 38 separate ICPs in 6 categories (Attire/ Preop/Intraop/ABX/Postop/Reporting) on 4-point scales for general surgery/anesthesia providers and cases. These data were compared to the risk-adjusted general surgery SSI odds ratios contained in July 2016 American College of Surgeons-NSQIP hospital- level reports. Compliance rates were compared between the 7 highest (median odds ratio [OR]:0.64 [0.56-0.70]) and 7 lowest (median

OR:1.16 [0.94-1.65]) performers using ANOVA tests. RESULTS: Nearly all hospitals reported maximal adherence to hair removal with clippers (SCIP Inf-6) and to best-practice prophylactic antibiotic metrics (SCIP Inf-1-4). There was consistent reporting of surgeons wearing scrubs outside of the operating room. Variable adherence was identified across many ICPs and more frequent compliance with 8 ICPs correlated with lower SSI odds ratios. Operating room attire ICPs, including coverage of non-scrubbed provider head/arm hair, did not correlate with SSI rates. CONCLUSIONS: This analysis suggests that the subset of ICPs that focus on perioperative patient skin/wound hygiene and transparent display of SSI data, not operating room attire issues, correlates with SSI performance. Focusing on changing practice to implement these evidence- based ICPs may improve SSI rates at lower-performing hospitals.

11. An infection prevention bundle to reduce the risk of surgical site infection at caesarean section: Recommendations from a systematic review

Author(s): Martin E.; Halton K.; Graves N.; Beckmann M.; Merollini K.

Source: Australian and New Zealand Journal of Obstetrics and Gynaecology; Oct 2017; vol. 57 ; p. 7

Publication Type(s): Conference Abstract

Abstract: Introduction: The large number of caesarean section review studies on individual surgical site infection risk-reducing strategies are difficult for clinical end-users to decipher. A transparent and structured review of systematic reviews, meta-analyses and other types of reviews has value in informing clinicians of best practice by cutting through the volume of evidence. The objective of this study was to identify a suite of peri-operative strategies and surgical techniques that reduce surgical site infection risk following caesarean section based on the latest published evidence. Methods: Electronic databases were searched to systematically review literature reviews, systematic reviews and meta-analyses published from 2006 to 2016. Reviews, systematic reviews and meta-analyses in which competing peri-operative strategies and surgical techniques relevant for caesarean section were identified, were included in the systematic review. Clinical effectiveness data was extracted. Quality, including bias within individual studies was examined using the AMSTAR tool. Recommendations for surgical site infection risk reducing strategies were developed using the GRADE approach. Results: Of 466 records retrieved, 44 studies were selected for inclusion in the systematic review. Recommended strategies for preventing surgical site infection following caesarean section were: administer pre-incision antibiotic prophylaxis, vaginal preparation and spontaneous placenta removal. Discussion: We recommend clinicians implement pre-incision antibiotic prophylaxis, vaginal preparation and spontaneous placenta removal as an infection prevention bundle for caesarean section. The infection prevention bundle can be implemented with small additional cost through integration into existing surgical processes. Time and costs will be saved through fewer readmissions for surgical site infection.

12. Intracavity lavage and wound irrigation for prevention of surgical site infection

Author(s): Norman G.; Atkinson R.A.; Dumville J.C.; Smith T.A.; Rowlands C.; Rithalia A.D.; Crosbie E.J.

Source: Cochrane Database of Systematic Reviews; Oct 2017; vol. 2017 (no. 10)

Publication Type(s): Review

Available at Cochrane Database of Systematic Reviews - from Cochrane Collaboration (Wiley)

Abstract: Background: Surgical site infections (SSIs) are wound infections that occur after an operative procedure. A preventable complication, they are costly and associated with poorer patient outcomes, increased mortality, morbidity and reoperation rates. Surgical wound irrigation is an

intraoperative technique, which may reduce the rate of SSIs through removal of dead or damaged tissue, metabolic waste, and wound exudate. Irrigation can be undertaken prior to wound closure or postoperatively. Intracavity lavage is a similar technique used in operations that expose a bodily cavity; such as procedures on the abdominal cavity and during joint replacement surgery. Objectives: To assess the effects of wound irrigation and intracavity lavage on the prevention of surgical site infection (SSI). Search methods: In February 2017 we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid Embase and EBSCO CINAHL Plus. We also searched three clinical trials registries and references of included studies and relevant systematic reviews. There were no restrictions on language, date of publication or study setting. Selection criteria: We included all randomised controlled trials (RCTs) of participants undergoing surgical procedures in which the use of a particular type of intraoperative washout (irrigation or lavage) was the only systematic difference between groups, and in which wounds underwent primary closure. The primary outcomes were SSI and wound dehiscence. Secondary outcomes were mortality, use of systemic antibiotics, antibiotic resistance, adverse events, re-intervention, length of hospital stay, and readmissions. Data collection and analysis: Two review authors independently assessed studies for inclusion at each stage. Two review authors also undertook data extraction, assessment of risk of bias and GRADE assessment. We calculated risk ratios or differences in means with 95% confidence intervals where possible. Main results: We included 59 RCTs with 14,738 participants. Studies assessed comparisons between irrigation and no irrigation, between antibacterial and non-antibacterial irrigation, between different antibiotics, different antiseptics or different non-antibacterial agents, or between different methods of irrigation delivery. No studies compared antiseptic with antibiotic irrigation. Surgical site infection Irrigation compared with no irrigation (20 studies; 7192 participants): there is no clear difference in risk of SSI between irrigation and no irrigation (RR 0.87, 95% CI 0.68 to 1.11; I2 = 28%; 14 studies, 6106 participants). This would represent an absolute difference of 13 fewer SSIs per 1000 people treated with irrigation compared with no irrigation; the 95% CI spanned from 31 fewer to 10 more SSIs. This was low-certainty evidence downgraded for risk of bias and imprecision. Antibacterial irrigation compared with non-antibacterial irrigation (36 studies, 6163 participants): there may be a lower incidence of SSI in participants treated with antibacterial irrigation compared with non-antibacterial irrigation (RR 0.57, 95% CI 0.44 to 0.75; I2 = 53%; 30 studies, 5141 participants). This would represent an absolute difference of 60 fewer SSIs per 1000 people treated with antibacterial irrigation than with non-antibacterial (95% CI 35 fewer to 78 fewer). This was low-certainty evidence downgraded for risk of bias and suspected publication bias. Comparison of irrigation of two agents of the same class (10 studies; 2118 participants): there may be a higher incidence of SSI in participants treated with povidone iodine compared with superoxidised water (Dermacyn) (RR 2.80, 95% CI 1.05 to 7.47; low-certainty evidence from one study, 190 participants). This would represent an absolute difference of 95 more SSIs per 1000 people treated with povidone iodine than with superoxidised water (95% CI 3 more to 341 more). All other comparisons found low- or very low-certainty evidence of no clear difference between groups. Comparison of two irrigation techniques: two studies compared standard (non-pulsed) methods with pulsatile methods. There may, on average, be fewer SSIs in participants treated with pulsatile methods compared with standard methods (RR 0.34, 95% CI 0.19 to 0.62; I2 = 0%; two studies, 484 participants). This would represent an absolute difference of 109 fewer SSIs occurring per 1000 with pulsatile irrigation compared with standard (95% CI 62 fewer to 134 fewer). This was low-certainty evidence downgraded twice for risks of bias across multiple domains. Wound dehiscence Few studies reported wound dehiscence. No comparison had evidence for a difference between intervention groups. This included comparisons between irrigation and no irrigation (one study, low-certainty evidence); antibacterial and non-antibacterial irrigation (three studies, very low-certainty evidence) and pulsatile and standard irrigation (one study, low-certainty evidence). Secondary outcomes Few studies reported outcomes such as use of systemic antibiotics and antibiotic resistance and they were poorly and incompletely reported. There was limited reporting of mortality; this may have been partially due to

failure to specify zero events in participants at low risk of death. Adverse event reporting was variable and often limited to individual event types. The evidence for the impact of interventions on length of hospital stay was low or moderate certainty; where differences were seen they were too small to be clinically important. Authors' conclusions: The evidence base for intracavity lavage and wound irrigation is generally of low certainty. Therefore where we identified a possible difference in the incidence of SSI (in comparisons of antibacterial and non-antibacterial interventions, and pulsatile versus standard methods) these should be considered in the context of uncertainty, particularly given the possibility of publication bias for the comparison of antibacterial and non-antibacterial interventions. Clinicians should also consider whether the evidence is relevant to the surgical populations under consideration, the varying reporting of other prophylactic antibiotics, and concerns about antibiotic resistance. We did not identify any trials that compared an antibiotic with an antiseptic. This gap in the direct evidence base may merit further investigation, potentially using network meta-analysis; to inform the direction of new primary research. Any new trial should be adequately powered to detect a difference in SSIs in eligible participants, should use robust research methodology to reduce the risks of bias and internationally recognised criteria for diagnosis of SSI, and should have adequate duration and follow-up.

13. Timing of antibiotic prophylaxis in cesarean section: retrospective, difference-in-differences estimation of the effect on surgical-site-infection.

Author(s): Ben Shoham, Assaf; Bar-Meir, Maskit; Ioscovich, Alexander; Samueloff, Arnon; Wiener-Well, Yonit

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Oct 2017 ; p. 1-5

Publication Type(s): Journal Article

Abstract:BACKGROUNDCesarean section (CS) is one of the most common surgical procedures performed worldwide. Surgical-site-infection (SSI) occurs in approximately 5-10% of CS. The benefit of prophylactic antibiotics for prevention of SSI has been demonstrated in the literature. The optimal timing of antibiotic prophylaxis (prior to surgical incision versus after cord clamping) was investigated in recent studies. In January 2014, the Israeli Ministry of Health introduced a national quality measure which monitors the administration of prophylactic antibiotics in CS. The custom clinical practice in our medical center was to administer prophylactic antibiotics immediately after cord clamping. Upon introduction of the national quality measurement program, the practice was changed to administration of antibiotics prior to surgical incision. Our objective was to examine the effect of timing of prophylactic antibiotics administration on the incidence of SSI following CS, in a single medical center that performs a large volume of deliveries, with a low rate of CS.MATERIAL AND METHODSTaking advantage of a discrete change in clinical practice, we used retrospective data and applied difference-in-differences design to estimate the effect of the timing of prophylactic antibiotics administration on SSI rates. The analysis included all CSs performed during 2012-2015 and all hysterectomies conducted during the study period.RESULTSThe coverage rates of prophylactic antibiotics in CS before and after the policy change were 99.10% and 99.03%, respectively. The rates of SSI following CS, before and after the policy change, were 2.63% (n = 2499) and 2.32% (n = 3840), respectively. The rates of SSI following hysterectomy, before and after the policy, change were 6.82% (n = 396) and 7.09% (n = 437), respectively. Difference-in-differences (DID) estimates of the effect of policy change on the incidence of SSI in linear and logistic regression models were not significant (B = -0.6%, p = .64; odds ratio = 0.84, p = .58, respectively).CONCLUSIONSWe found no effect of the timing of prophylactic antibiotic administration (prior to surgical incision versus after cord clamping) on SSI rates following CS.

14. Temporal trends and epidemiology of Staphylococcus aureus surgical site infection in the Swiss surveillance network: a cohort study.

Author(s): Abbas, M; Aghayev, E; Troillet, N; Eisenring, M-C; Kuster, S P; Widmer, A F; Harbarth, S; SwissNoso

Source: The Journal of hospital infection; Oct 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDStaphylococcus aureus is the leading pathogen in surgical site infections (SSI).AIMTo explore trends and risk factors associated with S. aureus SSI.METHODSRisk factors for monomicrobial S. aureus SSI were identified from the Swiss multi-centre SSI surveillance system using multi-variate logistic regression. Both in-hospital and postdischarge SSI were identified using standardized definitions.FINDINGSOver a six-year period, data were collected on 229,765 surgical patients, of whom 499 (0.22%) developed monomicrobial S. aureus SSI; 459 (92.0%) and 40 (8.0%) were due to meticillin-susceptible S. aureus (MSSA) and meticillin-resistant S. aureus (MRSA), respectively. There was a significant decrease in the rate of MSSA SSI (P = 0.007), but not in the rate of MRSA SSI (P = 0.70). Independent protective factors for S. aureus SSI were older age [≥75 years vs <50 years: odds ratio (OR) 0.60, 95% confidence interval (CI) 0.44-0.83], laparoscopy/minimally invasive surgery (OR 0.68, 95% CI 0.50-0.92), non-clean surgery [OR 0.78 (per increase in wound contamination class), 95% CI 0.64-0.94] and correct timing of pre-operative antibiotic prophylaxis (OR 0.80, 95% CI 0.65-0.98). Independent risk factors were male sex (OR 1.38, 95% CI 1.14-1.66), higher American Society of Anesthesiologists' score (per one-point increment: OR 1.30, 95% CI 1.13-1.51), re-operation for non-infectious reasons (OR 4.59, 95% CI 3.59-5.87) and procedure type: cardiac surgery, laminectomy, and hip or knee arthroplasty had two-to nine-fold increased odds of S. aureus SSI compared with other procedures.CONCLUSIONSSSI due to S. aureus are decreasing and becoming rare events in Switzerland. High-risk procedures that may benefit from specific preventive measures were identified. Unfortunately, many of the independent risk factors are not easily modifiable.

15. Structure, Process, and Outcome Quality of Surgical Site Infection Surveillance in Switzerland.

Author(s): Kuster, Stefan P; Eisenring, Marie-Christine; Sax, Hugo; Troillet, Nicolas; Swissnoso

Source: Infection control and hospital epidemiology; Oct 2017; vol. 38 (no. 10); p. 1172-1181

Publication Type(s): Journal Article

Abstract:OBJECTIVE To assess the structure and quality of surveillance activities and to validate outcome detection in the Swiss national surgical site infection (SSI) surveillance program. DESIGN Countrywide survey of SSI surveillance quality. SETTING 147 hospitals or hospital units with surgical activities in Switzerland. METHODS Site visits were conducted with on-site structured interviews and review of a random sample of 15 patient records per hospital: 10 from the entire data set and 5 from a subset of patients with originally reported infection. Process and structure were rated in 9 domains with a weighted overall validation score, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated for the identification of SSI. RESULTS Of 50 possible points, the median validation score was 35.5 (range, 16.25-48.5). Public hospitals (P<.001), hospitals in the Italian-speaking region of Switzerland (P=.021), and hospitals with longer participation in the surveillance (P=.018) had higher scores than others. Domains that contributed most to lower scores were quality of chart review and quality of data extraction. Of 49 infections, 15 (30.6%) had been overlooked in a random sample of 1,110 patient records, accounting for a sensitivity of 69.4% (95% confidence interval [CI], 54.6%-81.7%), a specificity of 99.9% (95% CI, 99.5%-100%), a positive predictive value of 97.1% (95% CI, 85.1%-99.9%), and a negative predictive value of 98.6% (95% CI, 97.7%-99.2%). CONCLUSIONS Irrespective of a well-defined surveillance

methodology, there is a wide variation of SSI surveillance quality. The quality of chart review and the accuracy of data collection are the main areas for improvement.

Influenza

1. From Original Antigenic Sin to the Universal Influenza Virus Vaccine.

Author(s): Henry, Carole; Palm, Anna-Karin E; Krammer, Florian; Wilson, Patrick C

Source: Trends in immunology; Jan 2018; vol. 39 (no. 1); p. 70-79

Publication Type(s): Journal Article Review

Available at Trends in immunology - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract: Antibody responses are essential for protection against influenza virus infection. Humans are exposed to a multitude of influenza viruses throughout their lifetime and it is clear that immune history influences the magnitude and quality of the antibody response. The 'original antigenic sin' concept refers to the impact of the first influenza virus variant encounter on lifelong immunity. Although this model has been challenged since its discovery, past exposure, and likely one's first exposure, clearly affects the epitopes targeted in subsequent responses. Understanding how previous exposure to influenza virus shapes antibody responses to vaccination and infection is critical, especially with the prospect of future pandemics and for the effective development of a universal influenza vaccine.

2. The evolution of seasonal influenza viruses.

Author(s): Petrova, Velislava N; Russell, Colin A

Source: Nature reviews. Microbiology; Jan 2018; vol. 16 (no. 1); p. 47-60

Publication Type(s): Journal Article Review

Abstract: Despite decades of surveillance and pharmaceutical and non-pharmaceutical interventions, seasonal influenza viruses continue to cause epidemics around the world each year. The key process underlying these recurrent epidemics is the evolution of the viruses to escape the immunity that is induced by prior infection or vaccination. Although we are beginning to understand the processes that underlie the evolutionary dynamics of seasonal influenza viruses, the timing and nature of emergence of new virus strains remain mostly unpredictable. In this Review, we discuss recent advances in understanding the molecular determinants of influenza virus immune escape, sources of evolutionary selection pressure, population dynamics of influenza viruses and prospects for better influenza virus control.

3. Live attenuated influenza vaccine (LAIV): recent effectiveness results from the USA and implications for LAIV programmes elsewhere.

Author(s): Pebody, Richard; McMenamin, Jim; Nohynek, Hanna

Source: Archives of disease in childhood; Jan 2018; vol. 103 (no. 1); p. 101-105

Publication Type(s): Journal Article Review

Available at Archives of disease in childhood - from BMJ Journals - NHS

Available at Archives of disease in childhood - from BMJ Journals

Available at Archives of disease in childhood - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract: The USA has a long-standing paediatric influenza vaccination programme, including use of live attenuated influenza vaccine (LAIV). Following US evidence of apparent lack of vaccine effectiveness (VE) of LAIV in 2015/2016, particularly against A(H1N1)pdm09, the USA suspended the use of LAIV in the 2016/2017 season. The UK introduced LAIV for children in 2013/2014 and Finland in 2015/2016. Both countries have since been closely monitoring programme performance. In 2015/2016, the UK and Finland, unlike the USA, found evidence of significant VE of LAIV against laboratory-confirmed influenza. Several studies, however, reported relatively lower VE of LAIV against A(H1N1)pdm09 infection compared with inactivated influenza vaccine, although not for A(H3N2) or B. The reasons for these apparent differences remain under investigation. Both the UK and Finland continue to recommend the use of LAIV in children for the 2017/2018 season and are intensifying further monitoring of their childhood programmes against a range of end-points.

4. Randomized Comparison of Immunogenicity and Safety of Quadrivalent Recombinant Versus Inactivated Influenza Vaccine in Healthy Adults 18-49 Years of Age.

Author(s): Dunkle, Lisa M; Izikson, Ruvim; Patriarca, Peter A; Goldenthal, Karen L; Muse, Derek; Cox, Manon M J

Source: The Journal of infectious diseases; Dec 2017; vol. 216 (no. 10); p. 1219-1226

Publication Type(s): Randomized Controlled Trial Multicenter Study Journal Article Clinical Trial, Phase Iii

Abstract: BackgroundSeasonal influenza vaccines are transitioning to quadrivalent formulations including the hemagglutinins of influenza A subtypes H1N1 and H3N2 and B lineages Yamagata and Victoria.MethodsA new quadrivalent recombinant influenza vaccine (RIV4) was compared directly with a standard-dose, egg-grown, quadrivalent-inactivated influenza vaccine (IIV4) for immunogenicity and safety in adults 18-49 years of age. The coprimary endpoints for noninferiority were hemagglutination inhibition seroconversion rates and postvaccination geometric mean titer ratios for each antigen using US regulatory criteria. Reactogenicity solicited for 7 days, other safety events collected for 28 days, and serious or medically attended adverse events collected for 6 months after vaccination comprised the safety evaluation.ResultsThe immunogenicity of RIV4 was comparable to that of IIV4; the coprimary noninferiority criteria were met for 3 antigens, and the antibody responses to the fourth antigen, influenza B/Brisbane/60/2008, were low in each group, making comparisons uninterpretable. Systemic and injection site reactions were mild, transient, and similar in each group, whereas none of the spontaneously reported adverse events, serious or nonserious, were considered related to study vaccine.ConclusionsThis first head-to-head comparison of recombinant versus inactivated quadrivalent influenza vaccines in 18-49 year old adults showed comparable immunogenicity, safety, and tolerability for both vaccines.

5. Oseltamivir, amantadine, and ribavirin combination antiviral therapy versus oseltamivir monotherapy for the treatment of influenza: a multicentre, double-blind, randomised phase 2 trial.

Author(s): Beigel, John H; Bao, Yajing; Beeler, Joy; Manosuthi, Weerawat; Slandzicki, Alex; Dar, Sadia M; Panuto, John; Beasley, Richard L; Perez-Patrigeon, Santiago; Suwanpimolkul, Gompol; Losso, Marcelo H; McClure, Natalie; Bozzolo, Dawn R; Myers, Christopher; Holley, H Preston; Hoopes, Justin; Lane, H Clifford; Hughes, Michael D; Davey, Richard T; IRC003 Study Team

Source: The Lancet. Infectious diseases; Dec 2017; vol. 17 (no. 12); p. 1255-1265

Publication Type(s): Randomized Controlled Trial Clinical Trial, Phase Ii Multicenter Study Journal Article

Abstract:BACKGROUNDInfluenza continues to have a substantial socioeconomic and health impact despite a long established vaccination programme and approved antivirals. Preclinical data suggest that combining antivirals might be more effective than administering oseltamivir alone in the treatment of influenza.METHODSWe did a randomised, double-blind, multicentre phase 2 trial of a combination of oseltamivir, amantadine, and ribavirin versus oseltamivir monotherapy with matching placebo for the treatment of influenza in 50 sites, consisting of academic medical centre clinics, emergency rooms, and private physician offices in the USA, Thailand, Mexico, Argentina, and Australia. Participants who were aged at least 18 years with influenza and were at increased risk of complications were randomly assigned (1:1) by an online computer-generated randomisation system to receive either oseltamivir (75 mg), amantadine (100 mg), and ribavirin (600 mg) combination therapy or oseltamivir monotherapy twice daily for 5 days, given orally, and participants were followed up for 28 days. Blinded treatment kits were used to achieve masking of patients and staff. The primary endpoint was the percentage of participants with virus detectable by PCR in nasopharyngeal swab at day 3, and was assessed in participants who were randomised, had influenza infection confirmed by the central laboratory on a baseline nasopharyngeal sample, and had received at least one dose of study drug. Safety assessment was done in all patients in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, number NCT01227967.FINDINGSBetween March 1, 2011, and April 29, 2016, 633 participants were randomly assigned to receive combination antiviral therapy (n=316) or monotherapy (n=317). Seven participants were excluded from analysis: three were not properly randomised, three withdrew from the study, and one was lost to follow-up. The primary analysis included 394 participants, excluding 47 in the pilot phase, 172 without confirmed influenza, and 13 without an endpoint sample. 80 (40·0%) of 200 participants in the combination group had detectable virus at day 3 compared with 97 (50·0%) of 194 (mean difference 10·0, 95% CI 0·2-19·8, p=0·046) in the monotherapy group. The most common adverse events were gastrointestinal-related disorders, primarily nausea (65 [12%] of 556 reported adverse events in the combination group vs 63 [11%] of 585 reported adverse events in the monotherapy group), diarrhoea (56 [10%] of 556 vs 64 [11%] of 585), and vomiting (39 [7%] of 556 vs 23 [4%] of 585). There was no benefit in multiple clinical secondary endpoints, such as median duration of symptoms (4·5 days in the combination group vs 4·0 days in the monotherapy group; p=0·21). One death occurred in the study in an elderly participant in the monotherapy group who died of cardiovascular failure 13 days after randomisation, judged by the site investigator as not related to study intervention.INTERPRETATIONAlthough combination treatment showed a significant decrease in viral shedding at day 3 relative to monotherapy, this difference was not associated with improved clinical benefit. More work is needed to understand why there was no clinical benefit when a difference in virological outcome was identified.FUNDINGNational Institute of Allergy and Infectious Diseases, National Institutes of Health, USA.

6. Influenza in Older Adults.

Author(s): Talbot, H Keipp

Source: Infectious disease clinics of North America; Dec 2017; vol. 31 (no. 4); p. 757-766

Publication Type(s): Journal Article Review

Abstract: Annually, influenza viruses cause significant disease in older adults, varying with the virulence of the circulating strain, prior exposure to circulating strain, and influenza vaccine effectiveness. Older adults often present atypically (eg, without fever) and with complications of influenza infection such as chronic obstructive pulmonary disease and congestive heart failure exacerbations. Prevention methods include antiviral medications and vaccines. Current influenza

vaccines have moderate effectiveness for the prevention of hospitalization, but newer more immunogenic vaccines designed for adults 65 years of age and older have been licensed.

7. Universal influenza virus vaccines: what can we learn from the human immune response following exposure to H7 subtype viruses?

Author(s): Stadlbauer, Daniel; Nachbagauer, Raffael; Meade, Philip; Krammer, Florian

Source: Frontiers of medicine; Dec 2017; vol. 11 (no. 4); p. 471-479

Publication Type(s): Journal Article Review

Abstract: Several universal influenza virus vaccine candidates based on eliciting antibodies against the hemagglutinin stalk domain are in development. Typically, these vaccines induce responses that target group 1 or group 2 hemagglutinins with little to no cross-group reactivity and protection. Similarly, the majority of human anti-stalk monoclonal antibodies that have been isolated are directed against group 1 or group 2 hemagglutinins with very few that bind to hemagglutinins of both groups. Here we review what is known about the human humoral immune response to vaccination and infection with H7 subtype influenza viruses on a polyclonal and monoclonal level. It seems that unlike vaccination with H5 hemagglutinin, which induces antibody responses mostly restricted to the group 1 stalk domain, H7 exposure induces both group 2 and cross-group antibody responses. A better understanding of this phenomenon and the underlying mechanisms might help to develop future universal influenza virus vaccine candidates.

8. A systematic review and meta-analysis of fetal outcomes following the administration of influenza A/H1N1 vaccination during pregnancy.

Author(s): Zhang, Chuan; Wang, Xiaodong; Liu, Dan; Zhang, Lingli; Sun, Xin

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Nov 2017

Publication Type(s): Journal Article Review

Abstract:BACKGROUNDPregnant women were identified as a population of priority for vaccination during the H1N1 influenza pandemic outbreak in 2009.OBJECTIVESTo assess adverse fetal outcomes following the administration of H1N1 pandemic vaccination during pregnancy.SEARCH STRATEGYPubMed, Embase, and Cochrane Library were searched up to January 2017.SELECTION CRITERIACohort studies investigating fetal outcomes after H1N1 influenza vaccination during pregnancy were eligible. The language was limited to English.DATA COLLECTION AND ANALYSISPairs of reviewers independently screened studies for eligibility, assessed the risk of bias, and extracted data from the included studies.MAIN RESULTSA total of 19 cohort studies were eligible. The use of vaccines during any period of pregnancy was associated with lower risk of stillbirth (adjusted hazard ratio 0.80, 95% confidence interval 0.69-0.92). No significant differences were found between the vaccinated versus unvaccinated groups in terms of the risks of spontaneous abortion, premature birth, and small for gestational age.CONCLUSIONSThe administration of H1N1 vaccines during pregnancy might reduce the risk of stillbirth, a complication associated with H1N1 infection. The quality of evidence was, however, not adequate to reach a definitive conclusion.

9. Population Diversity and Collective Interactions during Influenza Virus Infection.

Author(s): Brooke, Christopher B

Source: Journal of virology; Nov 2017; vol. 91 (no. 22)

Publication Type(s): Journal Article Review

Abstract: Influenza A virus (IAV) continues to pose an enormous and unpredictable global public health threat, largely due to the continual evolution of escape from preexisting immunity and the potential for zoonotic emergence. Understanding how the unique genetic makeup and structure of IAV populations influences their transmission and evolution is essential for developing more-effective vaccines, therapeutics, and surveillance capabilities. Owing to their mutation-prone replicase and unique genome organization, IAV populations exhibit enormous amounts of diversity both in terms of sequence and functional gene content. Here, I review what is currently known about the genetic and genomic diversity present within IAV populations and how this diversity may shape the replicative and evolutionary dynamics of these viruses.

10. Perspectives from the Society for Pediatric Research: Decreased Effectiveness of the Live Attenuated Influenza Vaccine.

Author(s): Gill, Michelle A; Schlaudecker, Elizabeth P

Source: Pediatric research; Nov 2017

Publication Type(s): Journal Article Review

Abstract: The intranasal live attenuated influenza vaccine (LAIV), FluMist, has been widely appreciated by pediatricians, parents, and children alike for its ease of administration. However, concerns regarding lack of effectiveness in recent influenza seasons led to the CDC Advisory Committee on Immunization Practices (ACIP) recommendation to administer inactivated influenza vaccines (IIVs), and not LAIV, during the 2016-17 and 2017-18 seasons. Given that data from previous years demonstrated equivalent and even improved efficacy of LAIV compared with IIV, these recent data were surprising, raising many questions about the potential mechanisms underlying this change. This review seeks to summarize the history of LAIV studies and ACIP recommendations with a focus on the recent decrease in vaccine effectiveness (VE) and discordant results among studies performed in different countries. Decreased VE for A/H1N1pdm09 viruses represents the most consistent finding across studies, as VE has been low every season these viruses predominated since 2010-11. Potential explanations underlying diminished effectiveness include the hypothesis that prior vaccination, reduced thermostability of A/H1N1pdm09, addition of a fourth virus, or reduced replication fitness of A/H1N1pdm09 strains may have contributed to this phenomenon. Ongoing studies and potential alterations to LAIV formulations provide hope for a return of effective LAIV in future influenza seasons.Pediatric Research advance online publication, 8 November 2017; doi:10.1038/pr.2017.239.

11. Influenza burden, prevention and treatment in asthma - a scoping review by the EAACI Influenza in Asthma Task Force.

Author(s): Schwarze, Jürgen; Openshaw, Peter; Jha, Akhilesh; Del Giacco, Stefano R; Firinu, Davide; Tsilochristou, Olympia; Roberts, Graham; Selby, Anna; Akdis, Cezmi; Agache, Ioana; Custovic, Adnan; Heffler, Enrico; Pinna, Georgia; Khaitov, Musa; Nikonova, Alexandra; Papadopoulos, Nikolaos; Akhlaq, Ather; Nurmatov, Ulugbek; Renz, Harald; Sheikh, Aziz; Skevaki, Chrysanthi

Source: Allergy; Nov 2017

Publication Type(s): Journal Article Review

Abstract: To address uncertainties in the prevention and management of influenza in people with asthma, we performed a scoping review of the published literature on influenza burden; current vaccine recommendations; vaccination coverage; immunogenicity, efficacy, effectiveness and safety of influenza vaccines; and the benefits of antiviral drugs in people with asthma. We found significant variation in the reported rates of influenza detection in individuals with acute asthma exacerbations making it unclear to what degree influenza causes exacerbations of underlying asthma. The

strongest evidence of an association was seen in studies of children. Countries in the European Union currently recommend influenza vaccination of adults with asthma; however, coverage varied between regions. Coverage was lower among children with asthma. Limited data suggest that good seroprotection and seroconversion can be achieved in both children and adults with asthma and that vaccination confers a degree of protection against influenza illness and asthma related morbidity to children with asthma. There were insufficient data to determine efficacy in adults. Overall, influenza vaccines appeared to be safe for people with asthma. We identify knowledge gaps and make recommendations on future research needs in relation to influenza in patients with asthma.

12. Safety and effectiveness assessment of 2011-2012 seasonal influenza vaccine produced in China: a randomized trial.

Author(s): Jing-Xia, Gao; Yu-Liang, Zhao; Jin-Feng, Liu; Shu-Zhen, Liu; Guo-Yang, Liao; Qi, Li

Source: Postgraduate medicine; Nov 2017; vol. 129 (no. 8); p. 907-914

Publication Type(s): Randomized Controlled Trial Journal Article

Abstract:OBJECTIVEThis study evaluated the effectiveness and safety of the egg-based, trivalent, inactivated split influenza vaccine produced by the Institute of Medical Biology, Chinese Academy of Medical Sciences, Peking Union Medical College, China.METHODSFrom March 2012 through May 2012, we enrolled a total of 1390 healthy volunteers between the ages of 3 and 80 years in a randomized clinical trial at the Hebei Disease Control Center Vaccine Clinical Evaluation Center. For all subjects, body part adverse reactions and whole-body adverse reactions were observed 30 min, 6 h, and 1-7 days' post-inoculation. If no severe adverse effects were observed 7 days' post-vaccination, the local and systemic reactions of preliminary test participants were recorded until day 28. There was no placebo group in this study. Blood samples were taken for serological testing before vaccination and 28 days' post-vaccination.RESULTSTwenty-eight days after vaccination, the seroconversion rates of experimental and control groups were H1N1 75.3% and 75.7%, H3N2 75.8% and 71.8%, B 70.7% vs. 69.4%, (P > 0.05). The antibody Geometric Mean Titer（GMT）of experimental and control groups were H1N1 (179.7, 182.4), H3N2 (584.0, 445.7), B (201.4,191.6). The protection rate of experimental and control groups was not statistically significant (H1N1: 86% vs. 87%, H3N2: 99% vs. 98%, B: 98% vs. 98%). Also, 95% confidence intervals of the protection rate difference between the experimental and the control group were H1N1: -0.1% (-4.1,3.8) %, H3N2: 0.3% (-1.0,1.7) % and B: 0.2% (-1.5,1.9) %; confidence intervals exceeded the limit of -5%. The rates of adverse reactions between experimental and control groups were 6.3% and 7.7% in local response reactions, and 19.5% and 18.0% in systemic reactions. Three hundred and twenty-seven adverse events (AEs) in 1200 (27.76%) subjects were reported within 28 d after vaccination. No serious adverse events occurred during the study.CONCLUSIONSThe experimental vaccine three-antibody protection rate was non-inferior to the control vaccine. Our results demonstrated that the experimental vaccine achieved the primary immunogenic end point of the intended clinical protocol, as well as a secondary immunogenic end-point, with an acceptable level of safety. IRB approval for this study was issued under #2012Y0005 and registered as Clinical Trial No. NCT01551810.

13. Individual versus superensemble forecasts of seasonal influenza outbreaks in the United States.

Author(s): Yamana, Teresa K; Kandula, Sasikiran; Shaman, Jeffrey

Source: PLoS computational biology; Nov 2017; vol. 13 (no. 11); p. e1005801

Publication Type(s): Comparative Study Journal Article

Available at PLoS computational biology - from Public Library of Science (PLoS)

Available at PLoS computational biology - from Europe PubMed Central - Open Access

Available at PLoS computational biology - from EBSCO (MEDLINE Complete)

Abstract: Recent research has produced a number of methods for forecasting seasonal influenza outbreaks. However, differences among the predicted outcomes of competing forecast methods can limit their use in decision-making. Here, we present a method for reconciling these differences using Bayesian model averaging. We generated retrospective forecasts of peak timing, peak incidence, and total incidence for seasonal influenza outbreaks in 48 states and 95 cities using 21 distinct forecast methods, and combined these individual forecasts to create weighted-average superensemble forecasts. We compared the relative performance of these individual and superensemble forecast methods by geographic location, timing of forecast, and influenza season. We find that, overall, the superensemble forecasts are more accurate than any individual forecast method and less prone to producing a poor forecast. Furthermore, we find that these advantages increase when the superensemble weights are stratified according to the characteristics of the forecast or geographic location. These findings indicate that different competing influenza prediction systems can be combined into a single more accurate forecast product for operational delivery in real time.

14. Intravenous Zanamivir in Hospitalized Patients With Influenza.

Author(s): Bradley, John S; Blumer, Jeffrey L; Romero, José R; Michaels, Marian G; Munoz, Flor M; Kimberlin, David W; Pahud, Barbara; DeBiasi, Roberta L; Yamamoto, Go; Roberts, Grace; Hossain, Mohammad; Shortino, Denise; Yates, Phillip J; Adams, Bryan; Peppercorn, Amanda

Source: Pediatrics; Nov 2017; vol. 140 (no. 5)

Publication Type(s): Clinical Trial, Phase Ii Multicenter Study Journal Article

Available at Pediatrics - from American Academy of Pediatrics (AAP)

Abstract:BACKGROUNDChildren with severe influenza infection may require parenteral therapy if oral or inhaled therapies are ineffective or cannot be administered. Results from a study investigating intravenous (IV) zanamivir for the treatment of hospitalized infants and children with influenza are presented.METHODSThis phase II, open-label, multicenter, single-arm study assessed the safety of investigational IV zanamivir in hospitalized children with influenza. Safety outcomes included treatment-emergent adverse events (TEAEs), clinical laboratory measurements, and vital signs. Clinical outcomes, pharmacokinetics, and virologic efficacy data were collected as key secondary outcomes.RESULTSIn total, 71 children received treatment with investigational IV zanamivir (exposure comparable to 600 mg twice daily in adults). TEAEs and serious TEAEs (STEAEs) were reported in 51 (72%) and 15 (21%) patients, respectively. The mortality rate was 7%, and median durations of hospital and ICU stays were 6 and 7.5 days, respectively. No STEAEs or deaths were considered related to IV zanamivir treatment, and no patterns of TEAEs, laboratory abnormalities, or vital signs were observed. The mean zanamivir exposures from 34 patients with normal renal function who received 12 mg/kg, 14 mg/kg, or 600 mg of IV zanamivir ranged from 64.5 to 110 hour·μg/mL. The median change from baseline in the viral load was -1.81 log10 copies per mL after 2 days of treatment.CONCLUSIONSThe safety profile of IV zanamivir was favorable, with no drug-related STEAEs reported. The majority of children experienced virologic response and clinical improvement during the treatment course. Systemic zanamivir exposures in children were consistent with adults.

15. Effect of Probiotics and Prebiotics on Immune Response to Influenza Vaccination in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.

Author(s): Lei, Wei-Te; Shih, Pei-Ching; Liu, Shu-Jung; Lin, Chien-Yu; Yeh, Tzu-Lin

Source: Nutrients; Oct 2017; vol. 9 (no. 11)

Publication Type(s): Journal Article Review

Available at Nutrients - from Europe PubMed Central - Open Access

Abstract: We conducted a meta-analysis to evaluate the effects of probiotics and prebiotics on the immune response to influenza vaccination in adults. We conducted a literature search of Pubmed, Embase, the Cochrane Library, the Cumulative Index to Nursing and Allied Health (CINAHL), Airiti Library, and PerioPath Index to Taiwan Periodical Literature in Taiwan. Databases were searched from inception to July 2017. We used the Cochrane Review risk of bias assessment tool to assess randomized controlled trial (RCT) quality. A total of 20 RCTs comprising 1979 adults were included in our systematic review. Nine RCTs including 623 participants had sufficient data to be pooled in a meta-analysis. Participants who took probiotics or prebiotics showed significant improvements in the H1N1 strain seroprotection rate (with an odds ratio (OR) of 1.83 and a 95% confidence interval (CI) of 1.19-2.82, $p = 0.006$, $I^2 = 0\%$), the H3N2 strain seroprotection rate (OR = 2.85, 95% CI = 1.59-5.10, $p < 0.001$, $I^2 = 0\%$), and the B strain seroconversion rate (OR = 2.11, 95% CI = 1.38-3.21, $p < 0.001$, $I^2 = 0\%$). This meta-analysis suggested that probiotics and prebiotics are effective in elevating immunogenicity by influencing seroconversion and seroprotection rates in adults inoculated with influenza vaccines.

16. Recommendations for Prevention and Control of Influenza in Children, 2017 - 2018.

Author(s): COMMITTEE ON INFECTIOUS DISEASES

Source: Pediatrics; Oct 2017; vol. 140 (no. 4)

Publication Type(s): Practice Guideline Journal Article

Available at Pediatrics - from American Academy of Pediatrics (AAP)

Abstract: This statement updates the recommendations for routine use of the seasonal influenza vaccine and antiviral medications for the prevention and treatment of influenza in children. The American Academy of Pediatrics recommends annual seasonal influenza immunization for everyone 6 months and older, including children and adolescents. Highlights for the upcoming 2017-2018 season include the following:1. Annual universal influenza immunization is indicated with either a trivalent or quadrivalent (no preference) inactivated vaccine;2. The 2017-2018 influenza A (H1N1) vaccine strain differs from that contained in the 2016-2017 seasonal vaccines. The 2017-2018 influenza A (H3N2) vaccine strain and influenza B vaccine strains included in the trivalent and quadrivalent vaccines are the same as those contained in the 2016-2017 seasonal vaccines: a. trivalent vaccine contains an A/Michigan/45/2015 (H1N1)pdm09-like virus, an A/Hong Kong/4801/2014 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus (B/Victoria lineage); and b. quadrivalent vaccine contains an additional B virus (B/Phuket/3073/2013-like virus [B/Yamagata lineage]);3. Quadrivalent live attenuated influenza vaccine (LAIV4) is not recommended for use in any setting in the United States during the 2017-2018 influenza season. This interim recommendation, originally made in 2016, followed observational data from the US Influenza Vaccine Effectiveness Network revealing that LAIV4 performed poorly against influenza A (H1N1)pdm09 viruses in recent influenza seasons;4. All children with an egg allergy of any severity can receive an influenza vaccine without any additional precautions beyond those recommended for any vaccine;5. All health care personnel should receive an annual seasonal influenza vaccine, a crucial step in preventing influenza and reducing health care-associated influenza infections, because health care personnel often care for individuals at high risk for influenza-related complications; and6. Pediatricians should attempt to promptly identify children suspected of having influenza infection for timely initiation of antiviral treatment, when indicated, to reduce morbidity and mortality. Best results are seen when treated within 48 hours of symptom onset.

Norovirus

1. Norovirus Infection in Older Adults: Epidemiology, Risk Factors, and Opportunities for Prevention and Control.

Author(s): Cardemil, Cristina V; Parashar, Umesh D; Hall, Aron J

Source: Infectious disease clinics of North America; Dec 2017; vol. 31 (no. 4); p. 839-870

Publication Type(s): Journal Article Review

Abstract: Norovirus is the leading cause of acute gastroenteritis. In older adults, it is responsible for an estimated 3.7 million illnesses; 320,000 outpatient visits; 69,000 emergency department visits; 39,000 hospitalizations; and 960 deaths annually in the United States. Older adults are particularly at risk for severe outcomes, including prolonged symptoms and death. Long-term care facilities and hospitals are the most common settings for norovirus outbreaks in developed countries. Diagnostic platforms are expanding. Several norovirus vaccines in clinical trials have the potential to reap benefits. This review summarizes current knowledge on norovirus infection in older adults.

2. Infectious Gastroenteritis and the Need for Strict Contact Precaution Procedures in Adults Presenting in the Emergency Department - a Danish Register-based Study.

Author(s): Skyum, Florence; Andersen, Vibeke; Chen, Ming; Pedersen, Court; Mogensen, Christian Backer

Source: The Journal of hospital infection; Nov 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDAcute infectious gastroenteritis requires contact precautions to prevent spreading. On acute admission the cause of diarrhoea is unknown, so the decision of whom to isolate has to be made on clinical information with a risk of inexpedient use of contact precautions.AIMThe aims of the study were to investigate how often gastroenteritis occurs, and thus the isolation indication has to be assessed, in Danish emergency departments, and how often patients have to remain on contact precaution according to the results of the faecal samples.METHODSThis Danish register based retrospective cohort study on adults in Danish emergency departments linked three data sources: discharge diagnoses from the Danish National Patient Register; microbiologically results from faecal samples delivered in the emergency department; and the causes of hospital admission based on the chief complaint.FINDINGSAmong 66,885 acute admissions 4.3% patients had at least one feature of gastroenteritis: admission with a chief complaint of diarrhoea (1.6%); faecal sample microbiology examination (2.8%); discharged with a gastroenteritis diagnosis (1.7%). 19% of those who had a faecal sample tested were norovirus or Clostridium difficile cases, who should remain on strict contact precautions.CONCLUSIONThe initiation of contact precaution has to be assessed for 4.3% of all emergency department patients; 19% of the patients who had a sample tested had highly contagious gastroenteritis and required strict contact precautions. Further studies for developing tools to determine whom to isolate are needed.

3. Super-infections and relapses occur in chronic norovirus infections

Author(s): Brown J.R.; Breuer J.; Roy S.; Tutill H.; Williams R.

Source: Journal of Clinical Virology; Nov 2017; vol. 96 ; p. 44-48

Publication Type(s): Article

Abstract: Background Norovirus causes chronic infections in immunocompromised patients with considerable associated morbidity. It is not known whether chronic infections involve super- or re-infections or relapses. Objectives To retrospectively investigate whether longitudinal sampling in chronically infected patients demonstrates persistent infection with the same virus, or super- or re-infection. Study design Norovirus full genomes were generated from 86 longitudinal samples from 25 paediatric patients. Consensus sequences were used for phylogenetic analysis and genotyping. Results Super-infections occurred in 17% of chronically infected patients who were continuously PCR positive; including two with mixed norovirus infections. The median duration of infection was 107 days longer in those with super-infections; however this was not statistically significant. A third of patients with interrupted norovirus shedding continued to be infected with the same virus despite up to 2 months of PCR negative stools, classified as a relapse. The majority (67%) of patients with interrupted shedding were re-infected with a different genotype. Conclusions Chronically infected patients who are continuously PCR positive are most likely to remain infected with the same virus; however super-infections do occur leading to mixed infection. Patients with interrupted shedding are likely to represent re-infection with a different genotype, however relapsing infections also occur. Our findings have implications for infection control as immunosuppressed patients remain susceptible to new norovirus infections despite current or recent infection and may continue to be infectious after norovirus is undetectable in stool. The relevance to children without co-morbidities remains to be determined.

4. Norovirus and Rotavirus disease severity in children: Systematic Review and Meta-Analysis.

Author(s): Riera-Montes, Margarita; O'Ryan, Miguel; Verstraeten, Thomas

Source: The Pediatric infectious disease journal; Nov 2017

Publication Type(s): Journal Article

Abstract:BACKGROUNDRotaviruses (RV) and Noroviruses (NoV) are the most common causes of severe acute gastroenteritis (AGE) in children. It is generally accepted that RV causes severe AGE in a higher proportion of cases compared with NoV. To our knowledge, there are no systematic reviews and meta-analyses comparing the severity of NoV and RV disease.METHODSWe searched MEDLINE for studies reporting data for NoV and RV medically-attended disease severity in children. We included studies where all children had been tested for both NoV (RT-PCR) and RV (ELISA or RT-PCR) and that reported disease severity using the Vesikari or modified Vesikari score, or provided clinical information on severity. We generated pooled estimates of the mean with 95% confidence intervals using random effects meta-analysis.RESULTSWe identified 266 publications, of which 31 were retained for qualitative analysis and 26 for quantitative analysis. Fourteen studies provided data on severity score for the meta-analysis. The pooled mean severity scores (95% CI) among outpatients were 10 (8-12) and 11 (8-14) for NoV and RV, respectively. Among inpatients, they were 11 (9-13) for NoV and 12 (10-14) for RV. The difference was statistically significant among inpatients, but relatively small (1 point in a 20-point scale). About 20% more children with RV required rehydration when compared with children with NoV.CONCLUSIONSNoV causes moderate to severe disease similar to RV in young children. This information should be useful for future evaluations of an eventual introduction of NoV vaccines in national immunization programs.

5. Methods for ascertaining norovirus disease burdens.

Author(s): Allen, David J; Harris, John P

Source: Human vaccines & immunotherapeutics; Nov 2017; vol. 13 (no. 11); p. 2630-2636

Publication Type(s): Journal Article

Abstract: Norovirus is the commonest cause of gastrointestinal disease worldwide in. Infections with norovirus occur in all age groups, however, the highest incidence is in children aged less than five years. Surveillance of norovirus is complicated because most people do not contact medical services when they are ill. Nevertheless, Public health laboratory surveillance worldwide has demonstrated the dominance of GII.4 viruses in the population. Better epidemiological surveillance and outbreak investigations, coupled with wider implementation of molecular-based laboratory diagnostics are leading to better estimates of the burden of norovirus infections as well as improved outbreak control. Recent advances in cell culture systems for norovirus and current research investigating the distribution of norovirus-associated disease in the population, for whom the disease burden is greatest, understanding host susceptibility factors, and methodologies for ascertaining cases, are important in increasing our understanding of norovirus. The key to surveillance of norovirus is allying the epidemiology with surveillance of virology. With recent advances in laboratory culture systems for norovirus, next generation sequencing technologies, improved diagnostics and measuring phenotypic characteristics of noroviruses, there are new opportunities to advance understanding of this common and important human pathogen that will help design strategies for vaccine and antiviral development, and how these might be best deployed to control norovirus infection.

6. High genetic variability of norovirus leads to diagnostic test challenges.

Author(s): Zhuo, Ran; Cho, Joanne; Qiu, YuanYuan; Parsons, Brendon D; Lee, Bonita E; Chui, Linda; Freedman, Stephen B; Pang, Xiaoli; Alberta Provincial Pediatric EnTeric Infection TEam (APPETITE)

Source: Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology; Nov 2017; vol. 96 ; p. 94-98

Publication Type(s): Journal Article

Abstract:BACKGROUNDIt is important to understand the diagnostic accuracy of multiplex panels such as the Luminex xTAG® Gastrointestinal Pathogen Panel (GPP) as they are increasingly employed for routine diagnostics worldwide. Recent evaluations in our laboratory identified lower detection rates of norovirus genogroup II (NoV GII) using GPP compared to our laboratory-developed RT-qPCR, Gastroenteritis Virus Panel (GVP).OBJECTIVESTo characterize the cases of discordant NoV GII results between GPP and GVP and determine the sensitivity of the two assays for specific NoV GII genotypes.STUDY DESIGNWe genotyped discordant NoV GII strains identified in stool samples or rectal swabs collected prospectively from a cohort of children with acute gastroenteritis between December 2014 and July 2016. The sensitivities of GVP and GPP for NoV GII were compared by analyses of GVP threshold cycle (Ct) and ten-fold serial dilutions of positive samples of various NoV GII genotypes.RESULTSAll discordant samples (63/607) were NoV GII positive by GVP but negative by GPP. Twenty-two were successfully genotyped, fourteen of which were NoV GII genotype 2 (GII.2). The median Ct value of concordant positives was lower than that of discordant results (19.8 vs. 33.7; P<0.0001). GVP was 10 and at least 10,000-fold more sensitive than GPP in detecting NoV GII.3 and GII.2, respectively, but has similar sensitivity for NoV GII.4. Discordant GII.2 variant differed genetically from concordant GII.2 variants.CONCLUSIONSGPP has lower sensitivity to detect NoV GII.2 than GVP and its use may lead to undetected cases clinically, and an underestimation of NoV disease burden at the population level.

7. Rapid diagnosis of acute norovirus-associated gastroenteritis: evaluation of the Xpert Norovirus assay and its implementation as a 24/7 service in three hospitals in Jonkoping County, Sweden

Author(s): Henningsson A.J.; Nilsson Bowers A.; Quttineh M.; Matussek A.; Haglund S.; Nordgren J.

Source: European Journal of Clinical Microbiology and Infectious Diseases; Oct 2017; vol. 36 (no. 10); p. 1867-1871

Publication Type(s): Article

Available at European Journal of Clinical Microbiology and Infectious Diseases - from doi.org

Abstract: Noroviruses are a leading cause of epidemic and sporadic cases of acute gastroenteritis worldwide. The rapid diagnosis of norovirus infection is important for prompt infection control measures and may reduce the need for additional diagnostic testing. Here we evaluated the performance of the rapid Xpert Norovirus assay, and assessed the turn-around time (TAT) before and after the implementation of the analysis as a 24/7 service at all the three hospitals in Jonkoping County, Sweden. We describe the implementation process which was performed in two steps during 2014. A total number of 276 clinical samples (stool and vomitus) from patients with symptoms of acute gastroenteritis were included in 2014-2015. The samples were analysed with the Xpert Norovirus assay and the already existing routine method: an in-house reverse transcription real-time PCR. Samples showing discrepant results with the two assays were further analysed by a third PCR method. The Xpert Norovirus assay performed well with a sensitivity of 100% and a specificity of 93% compared to the gold standard (defined as the result obtained by at least two of the three PCR methods). The median TAT decreased from 22 hours in 2013 to 2.4 hours in 2015 ($p<0.001$). We conclude that the performance of the Xpert Norovirus assay was excellent, and that the implementation of the analysis as a 24/7 service at all three hospitals in the county has greatly reduced the time to diagnosis which is beneficial for both patients and healthcare providers.

8. Hospital-acquired rotavirus and norovirus acute gastroenteritis in a pediatric unit, in 2014-2015.

Author(s): Valentini, Diletta; Ianiro, Giovanni; Di Bartolo, Ilaria; Di Camillo, Chiara; Boccuzzi, Elena; Vittucci, Anna C; Ruggeri, Franco M; Monini, Marina

Source: Journal of medical virology; Oct 2017; vol. 89 (no. 10); p. 1768-1774

Publication Type(s): Journal Article

Abstract: The occurrence of hospital-acquired acute gastroenteritis (AGE) is a major concern for public health. RotavirusA (RVA) and norovirus (NoV) are common causes of viral AGE in the pediatric population, and their role in nosocomial infections has been proven, remaining poorly investigated. To investigate RVA and NoV in hospital-acquired AGE, 55 stool samples from children with nosocomial AGE were collected between May 2014 and May 2015. To evaluate virus spreading routes, 51 environmental swabs were collected from staff and patients' rooms. Stools were tested for both RVA and NoV RNA by reverse-transcription-PCR. Nucleotide sequencing and phylogenetic analysis were performed to characterize the viruses. Forty-seven of 55 cases analyzed resulted positive for RVA. The predominant genotype was G4P[8] (18/55) followed by G1P[8] (14/55). Mixed RVA infections were also detected (7/55). Twenty-two samples were positive for NoV, and GII.4 was revealed to be the predominant genotype. Seventeen samples were positive for both RVA and NoV. This study aimed to evaluate the burden of norovirus and rotavirus nosocomial AGE, contributing to identify the environment source of infections and to activate effective strategies for intervention. The reduction in nosocomial AGE cases is an important aspect, considered the worsened disease course in transplant, cancer, and intensive care unit inpatients.

9. Community-based surveillance of norovirus disease: a systematic review.

Author(s): Inns, Thomas; Harris, John; Vivancos, Roberto; Iturriza-Gomara, Miren; O'Brien, Sarah

Source: BMC infectious diseases; Sep 2017; vol. 17 (no. 1); p. 657

Publication Type(s): Journal Article

Abstract:BACKGROUNDNorovirus is a common cause of infectious gastrointestinal disease. Despite the increased ability to detect norovirus in affected people, the number of reported cases and outbreaks in the community is still substantially underestimated. We undertook a systematic review to determine the nature, scope and scale of community-based surveillance systems which capture information on norovirus disease.METHODSWe searched MEDLINE, EMBASE and Scopus for studies published between 01 January 1995 and 31 December 2015, using terms relating to norovirus and surveillance. Publications were screened independently by two reviewers using exclusion criteria. Data extraction from included papers was performed using a standardized data extraction form. Outcomes were descriptions of the methods reported in included papers, and any estimates of incidence rate of norovirus disease in each community, stratified by age.RESULTSAfter exclusions, we reviewed 45 papers of which 23 described surveillance studies and 19 included estimates of incidence. The estimates of incidence varied by outcome measure, type of laboratory test and study population. There were two estimates of norovirus hospitalisation; 0.72 and 1.04 per 1000 person-years. Estimates of norovirus disease ranged between 0.024 cases per 1000 person-years and 60 cases per 1000 person-years and estimates of all gastroenteritis varied between 49 and 1100 cases per 1000 person-years.CONCLUSIONSOur systematic review found few papers describing community-based surveillance for norovirus disease. Standardised age-specific estimates of norovirus incidence would be valuable for calculating the true global burden of norovirus disease; robust community surveillance systems would be able to produce this information.TRIAL REGISTRATIONPROSPERO 2016: CRD42016048659 .

Journal Tables of Contents

Click on the hyperlinked journal title (+ Ctrl) for the most recent tables of contents. If you would like any of the papers in full text then please get in touch: Library@uhbristol.nhs.uk

Journal of Infection Prevention

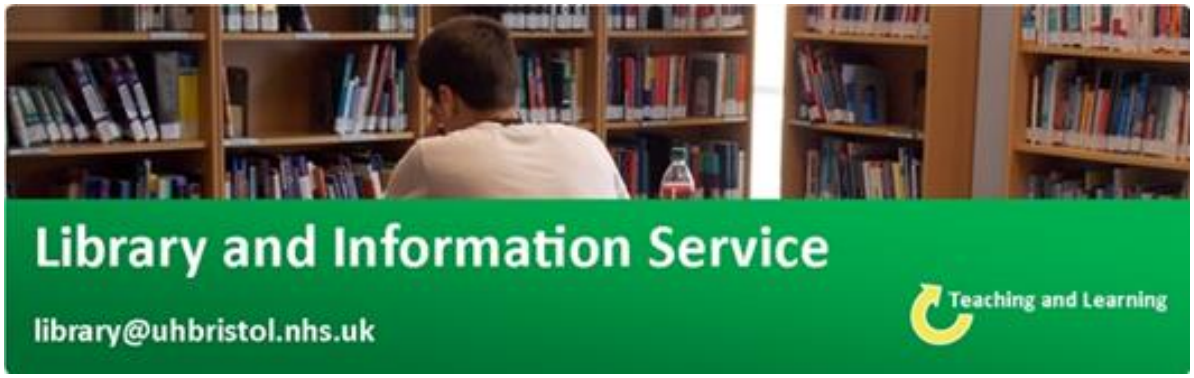
January 2018, Volume 19, Issue 1

Public Health England (Portal)

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

Departmental News

News, Research, Conferences, Training etc
Please contact us with any departmental news you wish to share with your colleagues in your Evidence Update bulletin. **library@uhbristol.nhs.uk**



Library Opening Times

Level Five, Education and Research Centre
University Hospitals Bristol

Staffed hours: 8am-5pm, Monday to Friday
Swipe-card access: 7am-11pm, seven days a week

Contact your Outreach Librarian:

Sarah Barrett

library@uhbristol.nhs.uk

Ext. 20105