Rheumatology
Current Awareness Newsletter
August 2015
**Outreach**

Your Outreach Librarian can help facilitate evidence-based practise for all Rheumatology staff, as well as assisting with academic study and research. We can help with literature searching, obtaining journal articles and books, and setting up individual current awareness alerts.

**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 1 to 1 session where we can guide you through the process of creating a well-focused literature research and introduce you to the health databases access via NHS Evidence.

**Critical Appraisal Training**

We also offer one-to-one or small group training in literature searching, accessing electronic journals, and critical appraisal/Statistics. These are essential courses that teach how to interpret clinical papers.

For more information, email: katie.barnard@uhbristol.nhs.uk

**Books**

Books can be searched for using SWIMS our online catalogue at [www.swims.nhs.uk](http://www.swims.nhs.uk). Books and journals that are not available on site or electronically may be requested from other locations. Please email requests to: library@uhbristol.nhs.uk
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New NICE Guidance

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Lunchtime Drop-in Sessions

The **Library and Information Service** provides free specialist information skills training for all UHBristol staff and students.

To book a place, email: **library@uhbristol.nhs.uk**

If you’re unable to attend we also provide **one-to-one or small group** sessions. Contact **library@** or **katie.barnard@** to arrange a session.

**Literature Searching**

An in-depth guide on how to search the evidence base, including an introduction to UpToDate and Anatomy.tv.

Useful for anybody who wants to find the best and quickest way to source articles.

**How to understand an article**

How to assess the strengths and weaknesses of published articles.

Examining bias and validity.

**Medical Statistics**

A basic introduction to the key statistics in medical articles.

Giving an overview of statistics that compare risk, test confidence, analyse clinical investigations, and test difference.

**August** (12pm)

- Fri 14th: Literature Searching
- Tues 18th: Understanding articles
- Weds 26th: Statistics

**September** (1pm)

- Thurs 3rd: Literature Searching
- Fri 11th: Understanding articles
- Mon 14th: Statistics
- Tues 22nd: Literature Searching
- Weds 30th: Understanding articles

**October** (12pm)

- Thurs 8th: Statistics
- Fri 16th: Literature Searching
- Mon 19th: Understanding articles
- Tues 27th: Statistics

**November** (1pm)

- Weds 4th: Literature Searching
- Thurs 12th: Understanding articles
- Fri 20th: Statistics
- Mon 23rd: Literature Searching

**December** (12pm)

- Tues 1st: Understanding articles
- Weds 9th: Statistics
- Thurs 17th: Literature Searching
Latest relevant Systematic Reviews from the Cochrane Library

Non-steroidal anti-inflammatory drugs (NSAIDs) for axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis)

Pilates for low back pain

Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease

New activity in Uptodate

www.uptodate.com

You will need your NHS Athens username/password (register through http://openathens.nice.org.uk/)

Monoclonal antibody to reduce tissue amyloid deposits (July 2015)

Tissue deposition of amyloid results in potentially fatal organ dysfunction. Clinical trials are investigating agents designed to remove amyloid from the tissues since current treatment options primarily limit further tissue deposition. In a phase 1, dose-escalation trial, 15 patients with amyloidosis (primary, secondary, or genetic) received an investigational monoclonal antibody directed against serum amyloid P (anti-SAP) [19]. The antibody was well tolerated and the nine patients receiving higher doses had evidence of reduced tissue amyloid. Further studies are needed to confirm the safety and efficacy of this treatment. (See "Overview of amyloidosis", section on 'Treatment' and "Prognosis and treatment of immunoglobulin light chain (AL) amyloidosis and light and heavy chain deposition diseases", section on 'Clinical trials'.)

International consensus on management of IgG4-related disease (July 2015)

The optimal treatment for immunoglobulin G4-related disease (IgG4-RD) has not been established, nor have randomized trials been performed to inform treatment approaches. Nonetheless, broad international consensus has been achieved among experts on several major management strategies [20]. These include the importance of biopsy confirmation of the diagnosis to exclude malignancy and other disorders that may mimic IgG4-RD; the need to treat symptomatic patients, sometimes urgently, as well as some asymptomatic patients; use of glucocorticoids as first-line therapy; use of maintenance therapy in certain patients; and retreatment strategies for patients who relapse after successful remission induction. Consensus was not reached on the use of steroid-sparing immunosuppressive agents from the start of treatment, and largely reflects different practice styles between countries. (See "Overview of IgG4-related disease", section on 'Diagnostic studies' and "Overview of IgG4-related disease", section on 'Treatment principles and observations'.)
Quick Exercise

Sensitivity and Specificity

**Sensitivity:**
If a person has a disease, how often will the test be positive (true positive rate)?

Put another way, if the test is highly sensitive and the test result is negative you can be nearly certain that they don’t have disease.

**Specificity:**
If a person does not have the disease how often will the test be negative (true negative rate)?

In other terms, if the test result for a highly specific test is positive you can be nearly certain that they actually have the disease.

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**Quick Quiz:**

1. **A very sensitive test, when negative, helps you:**
   a: Rule-in disease
   b: Rule-out disease
   c: Confuse medical students
   d: Save money

2. **A test which is highly specific, when positive, helps you:**
   a: Rule-in disease
   b: Rule-out disease
   c: Confuse medical students
   d: Save money

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Title: A randomized controlled trial for improving patient self-assessment of synovitis in rheumatoid arthritis with education by ultrasonography: the RAEBUS Study.

Citation: Rheumatology (Oxford, England), Jul 2015, vol. 54, no. 7, p. 1161-1169 (July 2015)

Author(s): Cheung, Peter P, Lahiri, Manjari, Teng, Gim Gee, Lim, Anita Y N, Lau, Tang Ching, Lateef, Aisha, Mak, Anselm, Gossec, Laure, March, Lyn

Abstract: Patients can potentially monitor disease activity of RA through self-assessed swollen joints (clinical synovitis), but reliability is poor. The objective is to evaluate the use of education by US feedback on the ability of patients to assess for clinical synovitis in RA. We performed a 6 month, single-centre, randomized controlled trial on patients with established RA to study the effect of education on self-assessment of joints that included initial brief patient training on tender (TJC) and swollen (SJC) joint counts followed by US feedback every 3 months vs standard care without education. Patient and physician independently performed 28-joint counts at each visit. Outcome variables included the percentage of patients with good agreement with physician-derived swollen joints [prevalence-adjusted bias-adjusted kappa (PABAK) >0.6] as well as agreement in the SJC (Bland and Altman 95% limits of agreement), feasibility/patient satisfaction survey and disease activity at 6 months. Of the 101 randomized patients, 95 were included (51 in the education arm and 44 in the standard care arm). At 6 months there was a significant difference in the proportion of patients with good agreement with physician-derived swollen joints [prevalence-adjusted bias-adjusted kappa (PABAK) >0.6] in the education arm compared with standard care (98 vs 85%, P = 0.02). Limits of agreement for the SJC difference between physician and patients were reduced only in the education arm. The training method is considered feasible, with 94% of patients reporting it as useful. A trend of higher rates of disease remission (28-joint DAS <2.6) in the education arm vs standard care (47% vs 29%, P = 0.07) was seen. A short course of education with US feedback may be helpful in educating patients to assess for clinical synovitis. Clinical trials.gov, https://clinicaltrials.gov, NCT02351401. © The Author 2014. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

Title: Long-term follow-up of patients who received repeat-dose rituximab as maintenance therapy for ANCA-associated vasculitis.

Citation: Rheumatology (Oxford, England), Jul 2015, vol. 54, no. 7, p. 1153-1160 (July 2015)


Abstract: ANCA-associated vasculitis (AAV) is characterized by a chronic relapsing course. Rituximab (RTX) is an effective maintenance treatment; however, the long-term outcomes after its discontinuation are unclear. The aim of this study was to explore the long-term outcomes of AAV patients treated with repeat-dose RTX maintenance therapy. AAV patients receiving a RTX treatment protocol consisting of an induction and maintenance phase were included. For initial remission induction, RTX was dosed at 1 g every 2 weeks or 375 mg/m(2) weekly for 4 consecutive weeks and for remission maintenance at 1 g every 6 months for 24 months. At the first RTX administration, ongoing immunosuppressives were withdrawn. Sixty-nine patients were identified, 67 of whom were failing other therapies. Nine relapsed during the RTX treatment protocol consisting of an induction and maintenance phase were included. For initial remission induction, RTX was dosed at 1 g every 2 weeks or 375 mg/m(2) weekly for 4 consecutive weeks and for remission maintenance at 1 g every 6 months for 24 months. At the first RTX administration, ongoing immunosuppressives were withdrawn. Sixty-nine patients were identified, 67 of whom were failing other therapies. Nine relapsed during the RTX treatment protocol; however, all 69 were in remission at the end of the maintenance phase on a median prednisolone dose of 2.5 mg/day and 9% were receiving additional immunosuppression. During subsequent observation, 28 patients relapsed a median of 34.4 months after the last RTX infusion. Risk factors for relapse were PR3-associated disease (P = 0.039), B cell return within 12 months of the last RTX infusion (P = 0.0038) and switch from ANCA negativity to positivity (P = 0.0046). Two patients died and two developed severe hypogammaglobulinaemia. This study supports the efficacy and safety of a fixed-interval RTX maintenance regimen in relapsing/refractory AAV. Relapses after discontinuation of maintenance therapy did occur, but at a lower rate than after a single RTX induction course. PR3-associated disease, the switch from ANCA negative to positive and the return of B cells within 12 months of the last RTX administration were risk factors for further relapse. © The Author 2014.
Title: Occurrence of adverse events in patients with JIA receiving biologic agents: long-term follow-up in a real-life setting.


Author(s): Tarkiainen, Maari, Marrat, Tynjälä, Pirjo, Vähäsalo, Paula, Lahdenne, Pekka

Abstract: The aim of this study was to carry out a safety evaluation of biologic agents in patients with JIA and associated uveitis. In three tertiary centres in Finland, all adverse events (AEs) in 348 consecutive patients were collected. AEs were classified according to the Common Terminology Criteria for AEs. A total of 1516 patient-years (py) were included: 710 on etanercept, 591 on infliximab, 188 on adalimumab, 8 on rituximab, 5 on anakinra, 6 on tocilizumab, 6 on abatacept and 1 on golimumab. The median follow-up of an individual patient was 51 months (range 1-155). The most common of the 2902 AEs (191/100 py) observed were mild infections, infusion or injection site reactions and alanine aminotransferase elevations. At least one AE occurred in 319 (92%) patients and 121 (35%) had at least one serious AE (SAE). The rate of SAEs was 11.4/100 py on etanercept, 11.8 on infliximab, 10.1 on adalimumab, 15.7 on abatacept, 31.2 on tocilizumab and 87.5 on rituximab, higher than with most anti-TNF agents (P = 0.005). No cases of malignant neoplasms or tuberculosis were detected. New-onset uveitis occurred in 9 patients, psoriasis or psoriasiform lesions in 13 and IBD in 6. Mild and moderate AEs in patients with JIA treated with biologics were more frequent than previously reported. SAEs were observed in one-third of the patients, but SAEs seldom led to drug discontinuation. © The Author 2014. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

Title: Spanish Rheumatology Society and Hospital Pharmacy Society Consensus on recommendations for biologics optimization in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis.

Citation: Rheumatology (Oxford, England), Jul 2015, vol. 54, no. 7, p. 1200-1209 (July 2015)

Author(s): González-Álvaro, Isidoro, Martínez-Fernández, Carmen, Dorantes-Calderón, Benito, García-Vicuña, Rosario, Hernández-Cruz, Blanca, Herrero-Ambrosio, Alicia, Ibarra-Barruet, Olatz, Martín-Mola, Emilio, Monte-Boquet, Emilio, Morell-Baladrón, Alberto, Sanmartí, Raimon, Sanz-Sanz, Jesús, de Toro-Santos, Francisco Javier, Vela, Paloma, Román Ivorra, José Andrés, Poveda-Andrés, José Luis, Muñoz-Fernández, Santiago

Abstract: The aim of this study was to establish guidelines for the optimization of biologic therapies for health professionals involved in the management of patients with RA, AS and PsA. Recommendations were established via consensus by a panel of experts in rheumatology and hospital pharmacy, based on analysis of available scientific evidence obtained from four systematic reviews and on the clinical experience of panellists. The Delphi method was used to evaluate these recommendations, both between panellists and among a wider group of rheumatologists. Previous concepts concerning better management of RA, AS and PsA were reviewed and, more specifically, guidelines for the optimization of biologic therapies used to treat these diseases were formulated. Recommendations were made with the aim of establishing a plan for when and how to taper biologic treatment in patients with these diseases. The recommendations established herein aim not only to provide advice on how to improve the risk:benefit ratio and efficiency of such treatments, but also to reduce variability in daily clinical practice in the use of biologic therapies for rheumatic diseases. © The Author 2014. Published by Oxford University Press on behalf of the British Society for Rheumatology.

Title: Drug adherence, response and predictors thereof for tocilizumab in patients with rheumatoid arthritis: results from the Swedish biologics register.


Author(s): Forsblad-d'Elia, Helena, Bengtsson, Karin, Kristensen, Lars Erik, Jacobsson, Lennart T H
Abstract: To evaluate drug adherence, clinical response and predictors thereof for tocilizumab in patients with RA in routine care based on prospectively collected data from the Swedish biologics register. Anti-Rheumatic Therapies in Sweden. RA patients who had started with tocilizumab from September 2008 until March 2012 were included. Cox regression and logistic regression models were used. A total of 530 RA patients were included, of whom 80.6% were female, 64.7% were on concomitant DMARDs, of which 300 were on MTX and 12% were biologic naive. The overall 6 month, 1 and 2 year estimated drug continuations were 79%, 64% and 50%, respectively. In the multivariate analyses, a low initial level of CRP [hazard ratio (HR) 0.76/1s.d. (95% CI 0.63, 0.91)], high HAQ score [HR 1.23/1s.d. (95% CI 1.06, 1.44)] and prior exposure to different biologics [HR 1.43 (95% CI 1.12, 1.83)] were predictors for drug termination, whereas concomitant DMARD therapy was not.

European League Against Rheumatism (EULAR) good, moderate, and no response were achieved by 184 (46.7%), 133 (33.8%) and 77 (19.5%) patients, respectively. Predictors for EULAR good response vs no response (at 2.5-8 months) were low HAQ [odds ratio (OR) 0.56/1s.d. (95% CI 0.40, 0.78)], high 28-joint DAS [OR 2.0/1s.d. (95% CI 1.44, 2.78)] and not being on prednisolone [OR 0.47 (95% CI 0.25, 0.88)] at baseline. In this RA cohort treated with tocilizumab, the estimated 1 year drug continuation was 64% and 80% of the patients achieved an EULAR response. Drug discontinuation was not predicted by no concomitant DMARD, but by low CRP, high HAQ and prior exposure to biologics. © The Author 2014. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved.

Title: Surgical and clinical efficacy of sacroiliac joint fusion: a systematic review of the literature.


Author(s): Zaidi, Hasan A, Montoure, Andrew J, Dickman, Curtis A

Abstract: OBJECT The sacroiliac joint (SIJ) and surgical intervention for treating SIJ pain or dysfunction has been a topic of much debate in recent years. There has been a resurgence in the implication of this joint as the pain generator for many patients experiencing low-back pain, and new surgical methods are gaining popularity within both the orthopedic and neurosurgical fields. There is no universally accepted gold standard for diagnosing or surgically treating SIJ pain. The authors systematically reviewed studies on SIJ fusion in the neurosurgical and orthopedic literature to investigate whether sufficient evidence exists to support its use.

METHODS A literature search was performed using MEDLINE, Google Scholar, and OvidSP-Wolters Kluwer Health for all articles regarding SIJ fusion published from 2000 to 2014. Original, peer-reviewed, prospective or retrospective scientific papers with at least 2 patients were included in the study. Exclusion criteria included follow-up shorter than 1-year, nonsurgical treatment, inadequate clinical data as determined by 2 independent reviewers, non-English manuscripts, and nonhuman subjects. RESULTS A total of 16 peer-reviewed journal articles met the inclusion criteria: 5 consecutive case series, 8 retrospective studies, and 3 prospective cohort studies. A total of 430 patients were included, of whom 131 underwent open surgery and 299 underwent minimally invasive surgery (MIS) for SIJ fusion. The mean duration of follow-up was 60 months for open surgery and 21 months for MIS. SIJ degeneration/arthrosis was the most common pathology among patients undergoing surgical intervention (present in 257 patients [59.8%]), followed by SIJ dysfunction (79 [18.4%]), postpartum instability (31 [7.2%]), posttraumatic (28 [6.5%]), idiopathic (25 [5.8%]), pathological fractures (6 [1.4%]), and HLA-B27+/rheumatoid arthritis (4 [0.9%]). Radiographically confirmed fusion rates were 20%-90% for open surgery and 13%-100% for MIS. Rates of excellent satisfaction, determined by pain reduction, function, and quality of life, ranged from 18% to 100% with a mean of 54% in open surgical cases. For MIS patients, excellent outcome, judged by patients' stated satisfaction with the surgery, ranged from 56% to 100% (mean 84%). The reoperation rate after open surgery ranged from 0% to 65% (mean 15%). Reoperation rate after MIS ranged from 0% to 17% (mean 6%). Major complication rates ranged from 5% to 20%, with 1 study that addressed safety reporting a 56% adverse event rate. CONCLUSIONS Surgical intervention for SIJ pain is beneficial in a subset of patients. However, with the difficulty in accurate diagnosis and evidence for the efficacy of SIJ fusion itself lacking, serious consideration of the cause of pain and alternative treatments should be given before performing the operation.

Title: Safety of long-term biologic therapy in rheumatologic patients with a previously resolved hepatitis B viral infection.

Citation: Hepatology (Baltimore, Md.), Jul 2015, vol. 62, no. 1, p. 40-46 (July 2015)
**Author(s):** Barone, Michele, Notarnicola, Antonella, Lopalco, Giuseppe, Viggiani, Maria Teresa, Sebastiani, Francesco, Covelli, Michele, Iannone, Florenzo, Avolio, Alfonso W, Di Leo, Alfredo, Cantarini, Luca, Lapadula, Giovanni

**Abstract:** European and Asian studies report conflicting data on the risk of hepatitis B virus (HBV) reactivation in rheumatologic patients with a previously resolved HBV (prHBV) infection undergoing long-term biologic therapies. In this patient category, the safety of different immunosuppressive biologic therapies, including rituximab, was assessed. A total of 1218 Caucasian rheumatologic patients, admitted consecutively as outpatients between 2001 and 2012 and taking biologic therapies, underwent evaluation of anti-HCV and HBV markers as well as liver amino transferases every 3 months. Starting from January 2009, HBV DNA monitoring was performed in patients with a prHBV infection who had started immunosuppressive biologic therapy both before and after 2009. Patients were considered to have elevated amino transferase levels if values were >1× upper normal limit at least once during follow-up. We found 179 patients with a prHBV infection (14 treated with rituximab, 146 with anti-tumor necrosis factor-alpha, and 19 with other biologic therapies) and 959 patients without a prHBV infection or other liver disease (controls). The mean age in the former group was significantly higher than the controls. Patients with a prHBV infection never showed detectable HBV DNA serum levels or antibody to hepatitis B surface antigen/hepatitis B surface antigen seroreversion. However, when the prevalence of elevated amino transferases in patients with prHBV infection was compared to controls, it was significantly higher in the former group only for amino transferase levels >1× upper normal limit but not when amino transferase levels >2× upper normal limit were considered. Among patients with a prHBV infection and rheumatologic indications for long-term biologic therapies, HBV reactivation was not seen; this suggests that universal prophylaxis is not justified and is not cost-effective in this clinical setting. (Hepatology 2015;62:40-46). © 2015 by the American Association for the Study of Liver Diseases.

**Title:** Active-comparator design and new-user design in observational studies.

**Citation:** Nature reviews. Rheumatology, Jul 2015, vol. 11, no. 7, p. 437-441 (July 2015)

**Author(s):** Yoshida, Kazuki, Solomon, Daniel H, Kim, Seoyoung C

**Abstract:** Over the past decade, an increasing number of observational studies have examined the effectiveness or safety of treatments for rheumatoid arthritis. Unlike randomized controlled trials (RCTs), however, observational studies of drug effects have methodological limitations such as confounding by indication. Active-comparator designs and new-user designs can help mitigate such biases in observational studies and improve the validity of their findings by making them more closely approximate RCTs. In an active-comparator study, the drug of interest is compared with another agent commonly used for the same indication, rather than with no treatment (a ‘non-user’ group). This principle helps to ensure that treatment groups have similar treatment indications, attenuating both measured and unmeasured differences in patient characteristics. The new-user study includes a cohort of patients from the time of treatment initiation, enabling assessment of patients’ pretreatment characteristics and capture of all events occurring during follow-up. These two principles should be considered when designing or reviewing observational studies of drug effects.

**Title:** Dose modifications of anti-TNF drugs in rheumatoid arthritis patients under real-world settings: a systematic review.

**Citation:** Rheumatology international, Jul 2015, vol. 35, no. 7, p. 1193-1210 (July 2015)

**Author(s):** Ferriols-Lisart, Rafael, Ferriols-Lisart, Francisco

**Abstract:** Anti-TNF dose modifications in rheumatoid arthritis have implications on healthcare resource utilization. The objective was to systematically review the dose modifications, both escalations and reductions, of currently available anti-TNF drugs (adalimumab, certolizumab, etanercept, golimumab and infliximab) in the real-world setting. We performed a systematic literature search of MEDLINE, ISI Web of Science, EMBASE, Indice Médico Español databases and American College of Rheumatology and European League Against Rheumatism annual congresses databases. PRISMA and MOOSE guidelines were followed. Only observational studies were included. Clinical trials were excluded since they do not reflect routine clinical practice. Dose escalations and reductions of the anti-TNF drug and their magnitude were collected. Thirty-four studies fulfill the inclusion criteria. Etanercept was associated with the lower percentage of patients under dose escalation (4.5
Title: Imaging of systemic vasculitis in childhood.

Citation: Pediatric radiology, Jul 2015, vol. 45, no. 8, p. 1110-1125 (July 2015)

Author(s): Soliman, Magdy, Laxer, Ronald, Manson, David, Yeung, Rae, Doria, Andrea S

Abstract: The term "systemic vasculitis" encompasses a diverse set of diseases linked by the presence of blood-vessel inflammation that are often associated with critical complications. These diseases are uncommon in childhood and are frequently subjected to a delayed diagnosis. Although the diagnosis and treatment may be similar for adult and childhood systemic vasculitides, the prevalence and classification vary according to the age group under investigation. For example, Kawasaki disease affects children while it is rarely encountered in adults. In 2006, the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PReS) proposed a classification system for childhood vasculitis adopting the system devised in the Chapel Hill Consensus Conference in 1993, which categorizes vasculitides according to the predominant size of the involved blood vessels into small, medium and large vessel diseases. Currently, medical imaging has a pivotal role in the diagnosis of vasculitides given recent developments in the imaging of blood vessels. For example, early diagnosis of coronary artery aneurysms, a serious complication of Kawasaki disease, is now possible by magnetic resonance imaging (MRI) of the heart and multidetector computed tomography (MDCT); positron emission tomography/CT (PET/CT) helps to assess active vascular inflammation in Takayasu arteritis. Our review offers a unique approach using the integration of the proposed classification criteria for common systemic childhood vasculitides with their most frequent imaging findings, along with differential diagnoses and an algorithm for diagnosis based on common findings. It should help radiologists and clinicians reach an early diagnosis, therefore facilitating the ultimate goal of proper management of affected children.

Title: Yoga in Sedentary Adults with Arthritis: Effects of a Randomized Controlled Pragmatic Trial.

Citation: Journal of Rheumatology, 01 July 2015, vol./is. 42/7(1194-1202), 0315162X

Author(s): Moonaz, Steffany Haaz, Bingham 3rd, Clifton O, Wissow, Lawrence, Bartlett, Susan J

Abstract: OBJECTIVE: To evaluate the effect of Integral-based hatha yoga in sedentary people with arthritis.

METHODS: There were 75 sedentary adults aged 18+ years with rheumatoid arthritis (RA) or knee osteoarthritis randomly assigned to 8 weeks of yoga (two 60-min classes and 1 home practice/wk) or waitlist. Poses were modified for individual needs. The primary endpoint was physical health [Medical Outcomes Study Short Form-36 (SF-36) physical component summary (PCS)] adjusted for baseline; exploratory adjusted outcomes included fitness, mood, stress, self-efficacy, SF-36 health-related quality of life (HRQOL), and RA disease activity. In everyone completing yoga, we explored longer-term effects at 9 months. RESULTS: Participants were mostly female (96%), white (55%), and college-educated (51%), with a mean (SD) age of 52 years (12 yrs). Average disease duration was 9 years and 49% had RA. At 8 weeks, yoga was associated with significantly higher PCS (6.5, 95% CI 2.0-10.7), walking capacity (125 m, 95% CI 15-235), positive affect (5.2, 95% CI 1.4-8.9), and lower Center for Epidemiologic Studies Depression Scale (-3.0, 95% CI -4.8 - -1.3). Significant improvements (p < 0.05) were evident in SF-36 role physical, pain, general health, vitality, and mental health scales. Balance, grip strength, and flexibility were similar between groups. Twenty-two out of 28 in the waitlist group completed yoga. Among all yoga participants, significant (p < 0.05) improvements were observed in mean PCS, flexibility, 6-min walk, and all psychological and most HRQOL domains at 8 weeks with most still evident 9 months later. Of 7 adverse events, none were associated with yoga. CONCLUSION: Preliminary evidence suggests yoga may help sedentary individuals with arthritis safely increase physical activity, and improve physical and psychological health and HRQOL. Clinical Trials NCT00349869.
Title: Outcome After Operative Fusion of the Tarsal Joints: A Systematic Review.

Citation: Journal of Foot & Ankle Surgery, 01 July 2015, vol./is. 54/4(636-645), 10672516

Author(s): Stegeman, Mark, Louwerens, Jan Willem Karel, van der Woude, Jan Ton, Jacobs, Wilhelms Cornelis Hermina, van Ginneken, Berbke To Josephine

Abstract: Arthrodesis of 1 or more joints of the hindfoot is performed to treat severe functional impairment due to pain, deformity, and/or instability. Evaluation of the results of hindfoot arthrodesis from the published data has been difficult owing to the great variety of pathologic entities and surgical techniques reported in the studies. A comprehensive search for relevant reports, reference lists, and citation tracking of the included studies was conducted using the PubMed®, Embase®, and CINAHL® databases. The studies had to have been prospective, included patients with hindfoot problems, evaluated arthrodesis of 1 or more tarsal joints, and had at least 1 of the following primary clinical outcome parameters: pain, function, or complications. Two of us independently selected the relevant studies using predefined criteria and graded the quality of evidence using a 0 to 9 star scale according to the Newcastle-Ottawa Scale. A total of 16 prospective case series were included; 5 studies scored 6 stars, 8 scored 5 stars, 2 scored 4 stars, and 1 scored 3 stars. A best evidence synthesis was performed, and improvement in function and pain was found for 3 combinations: talonavicular arthrodesis for rheumatoid arthritis, triple arthrodesis for rheumatoid arthritis, and subtalar arthrodesis for post-traumatic arthritis showed good results for pain and function, the last especially when performed arthroscopically. The best evidence syntheses revealed good results for pain and function for these disease-operative technique combinations.

Title: Juvenile spondyloarthritis.

Citation: Current Opinion in Rheumatology, 01 July 2015, vol./is. 27/4(364-372), 10408711

Author(s): Gmuca, Sabrina, Weiss, Pamela F

Abstract: PURPOSE OF REVIEW: This article provides a comprehensive update of the pathogenesis, diagnostic imaging, treatments, and disease activity measurements of juvenile spondyloarthritis (JSpA).

RECENT FINDINGS: Genetic and microbiome studies have provided new information regarding possible pathogenesis of JSpA. Recent work suggests that children with JSpA have decreased thresholds for pain in comparison to healthy children. In addition, pain on physical examination and abnormalities on ultrasound of the enthesis are not well correlated. Treatment guidelines for juvenile arthritis, including JSpA, were published by the American College of Rheumatology and are based on active joint count and presence of sacroiliitis. Recent studies have established the efficacy of tumor necrosis factor inhibitors in the symptomatic treatment of axial disease, although their efficacy for halting progression of structural damage is less clear. Newly developed disease activity measures for JSpA include the Juvenile Arthritis Disease Activity Score and the JSpA disease activity index. In comparison to other categories of juvenile arthritis, children with JSpA are less likely to attain and sustain inactive disease. SUMMARY: Further microbiome and genetic research may help elucidate JSpA pathogenesis. More randomized therapeutic trials are needed and the advent of new composite disease activity measurement tools will hopefully allow the design of these greatly needed trials.

Title: Systematic review and meta-analysis of effects of foot orthoses on pain and disability in rheumatoid arthritis patients.

Citation: Disability & Rehabilitation, 01 July 2015, vol./is. 37/14(1209-1213), 09638288

Author(s): Conceição, Cristiano Sena da, Gomes Neto, Mansueto, Mendes, Selena M. D., S, Kátia Nunes, Baptista, Abrahão Fontes

Abstract: Purpose: This meta-analysis examined the effects of foot orthoses (FO) on pain and disability in rheumatoid arthritis (RA) patients. Methods: MEDLINE, Cochrane Controlled Trials Register, EMBASE, SPORT Scielo, and CINAHL were searched through July 2014 for randomized controlled trials (RCTs) examining the effects of orthoses on pain and disability in RA patients. Two reviewers selected studies
independently. Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated, and heterogeneity was assessed using the I(2) test. Results: Three studies, involving 110 patients who received FO and 108 control patients, met the study criteria. Relative to controls, FO had a positive impact on pain (WMD 0.40; 95% CI 0.04-0.57). Between group differences in disability were not statistically significant. Conclusions: FO may improve pain in RA patients, but their impact on disability remains undetermined. Additional large RCTs are needed to investigate the effects of these devices in RA patients.

Title: Individual variations in treatment decisions by Swedish rheumatologists regarding biological drugs for rheumatoid arthritis.

Citation: Scandinavian journal of rheumatology, Jul 2015, vol. 44, no. 4, p. 265-270 (July 2015)

Author(s): Kalkan, A, Hallert, E, Carlsson, P, Roback, K, Sjöwall, C

Abstract: In Sweden, reports indicate surprisingly large regional variation in prescription of biological drugs despite a growing number of clinical studies describing their beneficial effects and guidelines by professional organizations and agencies. Our objectives were to ascertain whether there is also variation between individual rheumatologists in prescribing biologics to patients with rheumatoid arthritis (RA) and to evaluate reasons for treatment choices. Ten hypothetical patient cases were constructed and presented to 26 rheumatologists in five regions in Sweden. The cases were based on actual cases and were thoroughly elaborated by a senior rheumatologist and pre-tested in a pilot study. The respondents were asked whether they would treat the patients with a biological agent (Yes/No) and to explain their decisions. The response rate was 26/105 (25%). Treatment choices varied considerably between the rheumatologists, some prescribing biologics to 9/10 patients and others to 2/10. In five of the 10 hypothetical cases, approximately half of the respondents would prescribe biologics. No regions with particularly high or low prescription were identified. Both the decisions to prescribe biologics and also not to prescribe biologics were mainly motivated by medical reasons. Some rheumatologists also referred to lifestyle-related factors or the social function of the patient. The choice of initiation of biologics varied substantially among rheumatologists presented with hypothetical patient cases, and there were also disparities between rheumatologists practicing at the same clinic. Treatment choices were motivated primarily by medical reasons. This situation raises concerns about a lack of consensus in RA treatment strategies.

Title: Young people's decisions about biologic therapies: who influences them and how?


Author(s): Hart, Ruth I, Foster, Helen E, McDonagh, Janet E, Thompson, Ben, Kay, Lesley, Myers, Andrea, Rapley, Tim

Abstract: Young people with inflammatory arthritis can have severe disease warranting biologic therapy. They face complex treatment decisions, with profound consequences. This study aimed to explore the influence of individuals outside the care team (trusted others) on the treatment decisions made by young people, in particular their decisions about biologic therapies. Young people (16-25 years of age) with inflammatory arthritis and experience of treatment decision making were recruited from three NHS Hospital Trusts. Twenty-five were interviewed, plus 11 trusted others identified by young people as being involved in their decision making, as well as 6 health professionals. The data were analysed using coding, memoing and mapping techniques and the findings were tested through a series of focus groups. Young people initially emphasized their decisional autonomy, typically describing people other than health professionals as limited in influence. However, discussions revealed the involvement-in deliberation and enactment-of a range of other people. This cast of trusted others was small and largely consistent; mothers played a particularly prominent role, providing cognitive, practical and emotional support. Members of the wider cast of trusted others were involved in more limited but still significant ways. Young people claim autonomy but other people enable this. The network of relationships in which they are embedded is distinctive and evolving. Mothers play a supporting role well into early adulthood; in contrast, partners are involved in far more limited ways. As such, the applicability of adult models of decision making is unclear. This must be taken into account if the support provided by professionals is to be optimally tailored to young people's needs. © The Author 2015. Published by Oxford University Press on behalf of the British Society for Rheumatology.

Title: Efficacy and safety of biological agents in adult-onset Still's disease.
Citation: Scandinavian journal of rheumatology, Jul 2015, vol. 44, no. 4, p. 309-314 (July 2015)

Author(s): Cavalli, G, Franchini, S, Aiello, P, Guglielmi, B, Berti, A, Campochiaro, C, Sabbadini, M G, Baldissera, E, Dagna, L

Abstract: To describe the efficacy and safety of different biological agents in a large cohort of 20 patients with adult-onset Still's disease (AOSD). We retrospectively evaluated 20 patients with severe or refractory AOSD treated with at least one biological agent (anakinra, etanercept, tocilizumab, and adalimumab), followed up for at least 12 months at our Institution. We collected and analysed data on the disease course, treatment outcome, and adverse effects, and compared our data with other published series. The median duration of follow-up was 5 years. In 12 patients a single biological drug induced a clinical response. In eight patients the biological agent that was first administered proved ineffective, and a switch to a different biologic was necessary. In three patients a third biologic was necessary to achieve disease control. The biologics eventually determined a clinical response in all patients. Patients with systemic disease showed better responses than patients with chronic arthicular disease (p < 0.05). Biological agents allowed either the withdrawal or the tapering of corticosteroid therapy (p < 0.0001) and of disease-modifying anti-rheumatic agents (DMARDs; p < 0.05). Three patients experienced herpes zoster reactivation. This is the longest follow-up of a cohort of AOSD patients treated with biological agents. Our data show that biologics are safe and generally effective in the long-term management of AOSD, particularly in cases with systemic disease, and suggest that a clinical response can be obtained in almost all AOSD patients, although a switch to drugs with a different mechanism of action may be necessary.

Title: Brief Report: Childhood-Onset Systemic Necrotizing Vasculitides: Long-Term Data From the French Vasculitis Study Group Registry.


Author(s): Iudici, Michele, Puéchal, Xavier, Pagnoux, Christian, Quartier, Pierre, Agard, Christian, Aouba, Achille, Büchler, Matthias, Cevallos, Ramiro, Cohen, Pascal, de Moreuil, Claire, Guilpain, Philippe, Le Quellec, Alain, Roblot, Pascal, Serratrice, Jacques, Bachmeyer, Claude, Daugas, Éric, Terrier, Benjamin, Mouthon, Luc, Guillevin, Loïc, French Vasculitis Study Group

Abstract: To describe the initial features and long-term outcomes of childhood-onset small vessel and medium vessel systemic necrotizing vasculitides (SNVs), including antineutrophil cytoplasmic antibody-associated vasculitides (AAVs) and polyarteritis nodosa (PAN). Data on patients with childhood-onset SNV registered in the French Vasculitis Study Group database were reviewed for demographic characteristics, clinical, laboratory, and histologic features, and outcomes. Disease activity was assessed with the Birmingham Vasculitis Activity Score and the Paediatric Vasculitis Activity Score, and damage was scored using the Vasculitis Damage Index. Relapse and survival rates and causes of death were analyzed. Fifty-six patients (35 with AAV and 21 with PAN) (median age at database enrollment 14 years [range 2-17]) were included in the study. The median duration of followup was 96 months (range 1-336); two-thirds of the patients were followed up beyond 18 years of age. Six patients (11%) died, mostly of SNV-related causes. Relapse rates ranged from 33% for microscopic polyangitis to 50% for eosinophilic granulomatosis with polyangitis (Churg-Strauss) and 83% for granulomatosis with polyangiitis (Wegener's), with similar rates among AAV and PAN patients (76% and 75%, respectively); neither overall survival nor relapse-free survival differed significantly between the 2 disease groups. Rates of relapse increased after 18 years of age, both among patients with AAV and among patients with PAN. At the last followup evaluation, AAV patients had more major flares and more severe accrued damage compared with PAN patients. Despite similar relapse rates, patients with childhood-onset AAVs experienced more major flares with more cumulative damage than those with pediatric PAN. Treatments aimed at reducing the rates of mortality and relapse in this patient group need to be developed and assessed. © 2015, American College of Rheumatology.

Title: Neutrophil-Related Gene Expression and Low-Density Granulocytes Associated With Disease Activity and Response to Treatment in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis.

Citation: Arthritis & rheumatology (Hoboken, N.J.), Jul 2015, vol. 67, no. 7, p. 1922-1932 (July 2015)
Abstract: To discover biomarkers involved in the pathophysiology of antineutrophil cytoplasmic antibody-associated vasculitis (AAV) and to determine whether low-density granulocytes (LDGs) contribute to gene expression signatures in AAV. The source of clinical data and linked biologic specimens was a randomized controlled treatment trial in AAV. RNA sequencing of whole blood from patients with AAV was performed during active disease at the baseline visit and during remission 6 months later. Gene expression was compared between patients who met versus those who did not meet the primary trial outcome of clinical remission at 6 months (responders versus nonresponders). Measurement of neutrophil-related gene expression was confirmed in peripheral blood mononuclear cells (PBMCs) to validate the findings in whole blood. A negative-selection strategy isolated LDGs from PBMC fractions. Differential expression between responders (n = 77) and nonresponders (n = 35) was detected in 2,346 transcripts at the baseline visit (P < 0.05). Unsupervised hierarchical clustering demonstrated a cluster of granulocyte-related genes, including myeloperoxidase (MPO) and proteinase 3 (PR3). A granulocyte multigene composite score was significantly higher in nonresponders than in responders (P < 0.01) and during active disease than during remission (P < 0.01). This signature strongly overlapped an LDG signature identified previously in lupus (false discovery rate by gene set enrichment analysis <0.01). Transcription of PR3 measured in PBMCs was associated with active disease and treatment response (P < 0.01). LDGs isolated from patients with AAV spontaneously formed neutrophil extracellular traps containing PR3 and MPO. In AAV, increased expression of a granulocyte gene signature is associated with disease activity and decreased response to treatment. The source of this signature is likely LDGs, a potentially pathogenic cell type in AAV. © 2015, American College of Rheumatology.

Source: Medline

Title: Policy-Into-Practice for Rheumatoid Arthritis: Randomized Controlled Trial and Cohort Study of E-Learning Targeting Improved Physiotherapy Management.

Citation: Arthritis care & research, Jul 2015, vol. 67, no. 7, p. 913-922 (July 2015)

Author(s): Fary, Robyn E, Slater, Helen, Chua, Jason, Ranelli, Sonia, Chan, Madelynn, Briggs, Andrew M

Abstract: To examine the effectiveness of a physiotherapy-specific, web-based e-learning platform, “RAP-el,” in best-practice management of rheumatoid arthritis (RA) using a single-blind, randomized controlled trial (RCT) and prospective cohort study. Australian-registered physiotherapists were electronically randomized into intervention and control groups. The intervention group accessed RAP-el over 4 weeks. Change in self-reported confidence in knowledge and skills was compared between groups at the end of the RCT using linear regression conditioned for baseline scores by a blinded assessor, using intent-to-treat analysis. Secondary outcomes included physiotherapists’ satisfaction with RA management and responses to RA-relevant clinical statements and practice-relevant vignettes. Retention was evaluated in a cohort study 8 weeks after the RCT. Eighty physiotherapists were randomized into the intervention and 79 into the control groups. Fifty-six and 48, respectively, provided baseline data. Significant between-group differences were observed for change in confidence in knowledge (mean difference 8.51; 95% confidence interval [95% CI] 6.29, 10.73; effect size 1.62) and skills (mean difference 7.26; 95% CI 5.1, 9.4; effect size 1.54), with the intervention group performing better. Satisfaction in ability to manage RA, 4 of the 6 clinical statements, and responses to vignettes demonstrated significant improvement in the intervention group. Although 8-week scores showed declines in most outcomes, their clinical significance remains uncertain. RAP-el can improve self-reported confidence, likely practice behaviors and satisfaction in physiotherapists’ ability to manage people with RA, and improve their clinical knowledge in several areas of best-practice RA management in the short term. © 2015, American College of Rheumatology.

Title: Comprehensive Appraisal of Magnetic Resonance Imaging Findings in Sustained Rheumatoid Arthritis Remission: A Substudy.

Citation: Arthritis care & research, Jul 2015, vol. 67, no. 7, p. 929-939 (July 2015)
Author(s): Ranganath, Veena K, Motamedi, Kambiz, Haavardsholm, Espen A, Maranian, Paul, Elashoff, David, McQueen, Fiona, Duffy, Erin L, Bathon, Joan M, Curtis, Jeffrey R, Chen, Weiling, Moreland, Larry, Louie, James, Amjadi, Sogol, O'Dell, James, Cofield, Stacey S, St Clair, E William, Bridges, S Louis, Paulus, Harold E

Abstract: To evaluate the effect of sustained American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Boolean remission on residual joint inflammation assessed by magnetic resonance imaging (MRI) and to secondarily evaluate other clinical definitions of remission, within an early seropositive rheumatoid arthritis (RA) cohort. A subcohort of 118 RA patients was enrolled from patients who completed the 2-year, double-blind randomized Treatment of Early Aggressive Rheumatoid Arthritis (TEAR) trial. Patients received a single contrast-enhanced 1.5T MRI of their most involved wrist. Two readers scored MRIs for synovitis, osteitis, tenosynovitis, and erosions. Clinical assessments were performed every 3 months during the trial and at time of MRI. The subcohort was 92% seropositive with mean age 51 years, duration 4.1 months, and Disease Activity Score in 28 joints using the erythrocyte sedimentation rate 5.8 at TEAR entry. Total MRI inflammatory scores (tenosynovitis + synovitis + osteitis) were lower among patients in clinical remission. Lower MRI scores were correlated with longer duration of Clinical Disease Activity Index (CDAI) remission (p = 0.22, P = 0.03). At the time of MRI, 89 patients had no wrist pain/tenderness/swelling; however, all 118 patients had MRI evidence of residual joint inflammation after 2 years. No statistically significant differences in damage or MRI inflammatory scores were observed across treatment groups. This is the first detailed appraisal describing the relationship between clinical remission cut points and MRI inflammatory scores within an RA randomized controlled trial. The most stringent remission criteria (2011 ACR/EULAR and CDAI) best differentiate the total MRI inflammatory scores. These results document that 2 years of triple therapy or tumor necrosis factor plus methotrexate treatment in early RA does not eliminate MRI evidence of joint inflammation. © 2015, American College of Rheumatology.

Title: Synthesis and biological evaluation of spirocyclic antagonists of CCR2 (chemokine CC receptor subtype 2).

Citation: Bioorganic & medicinal chemistry, Jul 2015, vol. 23, no. 14, p. 4034-4049 (July 15, 2015)
**Author(s):** Strunz, Ann Kathrin, Zweemer, Annelien J M, Weiss, Christina, Schepmann, Dirk, Junker, Anna, Heitman, Laura H, Koch, Michael, Wünsch, Bernhard

**Abstract:** Activation of chemokine CC receptors subtype 2 (CCR2) plays an important role in chronic inflammatory processes such as atherosclerosis, multiple sclerosis and rheumatoid arthritis. A diverse set of spirocyclic butanamides 4 (N-benzyl-4-(3,4-dihydrospiro[2]benzopyran-1,4'-piperidin]-1'-yl)butanamides) was prepared by different combination of spirocyclic piperidines 8 (3,4-dihydrospiro[2]benzopyran-1,4'-piperidines)) and γ-halobutanamides 11. A key step in the synthesis of spirocyclic piperidines 8 was an Oxa-Pictet-Spengler reaction of β-phenylethanols 5 with piperidone acetal 6. The substituted γ-hydroxybutanamides 11c-e were prepared by hydroxyethylation of methyl acetates 13 with ethylene sulfate giving the γ-lactones 14c and 14e. Aminolysis of the γ-lactones 14c and 14e with benzylamines provided the γ-hydroxybutanamides 15c-e, which were converted into the bromides 11c-e by an Appel reaction using polymer-bound PPh3. In radioligand binding assays the spirocyclic butanamides 4 did not displace the iodinated radioligand (125)I-CCL2 from the human CCR2. However, in the Ca(2+)-flux assay using human CCR2 strong antagonistic activity of butanamides 4 was detected. Analysis of the IC50-values led to clear relationships between the structure and the inhibition of the Ca(2+)-flux. 4g (4-(3,4-dihydrospiro[2]benzopyran-1,4'-piperidin]-1'-yl)-N-[3,5-bis(trifluoromethylbenzyl)]-2-(4-fluorophenyl)butanamide) and 4o (N-[3,5-bis(trifluoromethyl)benzyl]-2-cyclopropyl-4-(3,4-dihydrospiro[2]benzopyran-1,4'-piperidin]-1'-yl)butanamide) represent the most potent CCR2 antagonists with IC50-values of 89 and 17nM, respectively. Micromolar activities were found in the β-arrestin recruitment assay with murine CCR2, but the structure-activity-relationships detected in the Ca(2+)-flux assay were confirmed. Copyright © 2015 Elsevier Ltd. All rights reserved.

**Title:** Discovery of Benzylidene Derivatives as Potent Syk Inhibitors: Synthesis, SAR Analysis, and Biological Evaluation.

**Citation:** Archiv der Pharmazie, Jul 2015, vol. 348, no. 7, p. 463-474 (July 2015)

**Author(s):** Zhang, Lingling, Liu, Wei, Mao, Fei, Zhu, Jin, Dong, Guoqiang, Jiang, Hualiang, Sheng, Chunquan, Miao, Liyan, Huang, Lixin, Li, Jian

**Abstract:** Four scaffolds of varied benzylidene derivatives were synthesized and evaluated as Syk inhibitors for the treatment of rheumatoid arthritis (RA). Among these 31 compounds, 3-benzylidene pyrrolidine-2,5-dione derivatives (including 12k) universally showed good Syk inhibitory activities in the low micromolar to submicromolar range. In the cellular profiling, compound 12k, the most efficient compound, showed excellent antiproliferative activity against fibroblast-like synoviocytes (FLS)-RA, and demonstrated potencies for suppression of IL-6 and MMP-3 secretion almost equal to R406 (positive control). The oral efficacy of 12k in the murine collagen-induced arthritis model was significant, despite being weaker than R406. Taken together, all preliminary pharmacological results supported 12k as a potential small-molecule inhibitor targeting Syk for the treatment of RA. © 2015 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

**Title:** Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis.

**Citation:** Lancet (London, England), Jul 2015, vol. 386, no. 9990, p. 258-265 (July 18, 2015)

**Author(s):** Singh, Jasvinder A, Cameron, Chris, Noorbaloochi, Shahrazad, Cullis, Tyler, Tucker, Matthew, Christensen, Robin, Ghogomu, Elizabeth Tanjong, Coyle, Doug, Clifford, Tammy, Tugwell, Peter, Wells, George A

**Abstract:** Serious infections are a major concern for patients considering treatments for rheumatoid arthritis. Evidence is inconsistent as to whether biological drugs are associated with an increased risk of serious infection compared with traditional disease-modifying antirheumatic drugs (DMARDs). We did a systematic review and meta-analysis of serious infections in patients treated with biological drugs compared with those treated with traditional DMARDs. We did a systematic literature search with Medline, Embase, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from their inception to Feb 11, 2014. Search terms included “biologics”, “rheumatoid arthritis” and their synonyms. Trials were eligible for inclusion if they included any of the approved biological drugs and reported serious infections. We assessed the risk of bias with the Cochrane Risk of Bias Tool. We did a Bayesian network meta-analysis of published trials using a binomial likelihood
model to assess the risk of serious infections in patients with rheumatoid arthritis who were treated with biological drugs, compared with those treated with traditional DMARDs. The odds ratio (OR) of serious infection was the primary measure of treatment effect and calculated 95% credible intervals using Markov Chain Monte Carlo methods. The systematic review identified 106 trials that reported serious infections and included patients with rheumatoid arthritis who received biological drugs. Compared with traditional DMARDs, standard-dose biological drugs (OR 1.31, 95% credible interval [CrI] 1.09-1.58) and high-dose biological drugs (1.90, 1.50-2.39) were associated with an increased risk of serious infections, although low-dose biological drugs (0.93, 0.65-1.33) were not. The risk was lower in patients who were methotrexate naive compared with traditional DMARD-experienced or anti-tumour necrosis factor biological drug-experienced patients. The absolute increase in the number of serious infections per 1000 patients treated each year ranged from six for standard-dose biological drugs to 55 for combination biological therapy, compared with traditional DMARDs. Standard-dose and high-dose biological drugs (with or without traditional DMARDs) are associated with an increase in serious infections in rheumatoid arthritis compared with traditional DMARDs, although low-dose biological drugs are not. Clinicians should discuss the balance between benefit and harm with the individual patient before starting biological treatment for rheumatoid arthritis. Rheumatology Division at the University of Alabama at Birmingham. Copyright © 2015 Elsevier Ltd. All rights reserved.

Source: Medline

Title: 14-3-3 in Thoracic Aortic Aneurysms: Identification of a Novel Autoantigen in Large Vessel Vasculitis.

Citation: Arthritis & rheumatology (Hoboken, N.J.), Jul 2015, vol. 67, no. 7, p. 1913-1921 (July 2015)


Abstract: Large vessel vasculitides (LVV) are a group of autoimmune diseases characterized by injury to and anatomic modifications of large vessels, including the aorta and its branch vessels. Disease etiology is unknown. This study was undertaken to identify antigen targets within affected vessel walls in aortic root, ascending aorta, and aortic arch surgical specimens from patients with LVV, including giant cell arteritis, Takayasu arteritis, and isolated focal aortitis. Thoracic aortic aneurysm specimens and autologous blood were acquired from consenting patients who underwent aorta reconstruction procedures. Aorta proteins were extracted from both patients with LVV and age-, race-, and sex-matched disease controls with noninflammatory aneurysms. A total of 108 serum samples from patients with LVV, matched controls, and controls with antinuclear antibodies, different forms of vasculitis, or sepsis were tested. Evaluation of 108 serum samples and 22 aortic tissue specimens showed that 78% of patients with LVV produced antibodies to 14-3-3 proteins in the aortic wall (93.7% specificity), whereas controls were less likely to do so (6.7% produced antibodies). LVV patient sera contained autoantibody sufficient to immunoprecipitate 14-3-3 protein(s) from aortic lysates. Three of 7 isoforms of 14-3-3 were found to be up-regulated in aorta specimens from patients with LVV, and 2 isoforms (ε and ζ) were found to be antigenic in LVV. This is the first study to use sterile, snap-frozen thoracic aorta biopsy specimens to identify autoantigens in LVV. Our findings indicate that 78% of patients with LVV have antibody reactivity to 14-3-3 protein(s). The precise role of these antibodies and 14-3-3 proteins in LVV pathogenesis deserves further study. © 2015, American College of Rheumatology.

Title: Rheumatoid arthritis: biological drugs and risk of infection.


Author(s): Dixon, William G

Title: Safety of biologic therapies for the treatment of juvenile idiopathic arthritis.

Citation: Expert opinion on drug safety, Jul 2015, vol. 14, no. 7, p. 1111-1126 (July 2015)

Author(s): Horneff, Gerd
Abstract: The introduction of biological therapies opened a new era of treatment of juvenile idiopathic arthritis. After 15 years of experience with the first biologics for treatment of pediatric rheumatic disease, long-term safety effects are of great interest. This review summarizes published knowledge about safety aspects from clinical trials as well as from biologic registries in juvenile idiopathic arthritis patients. Beside infusion and injection reactions, the occurrence and aggravation of infections, the occurrence of a second autoimmune diseases, including uveitis, psoriasis, chronic inflammatory bowel disease, multiple sclerosis, diabetes mellitus, as well as cytopenias and the development of malignancies are major concerns regarding treatment with biologics. The safety profiles of approved biologics, the TNF-α inhibitors etanercept and adalimumab, and the IL-6-inhibitor tocilizumab are highly acceptable. This conclusion is not easily expandable to the IL-1 inhibitor canakinumab as well as the T-cell-activation-inhibitor abatacept due to lack of experience; however, both have showed an excellent safety profile so far. An increase in knowledge about risk profiles in national and international collaborations, with national as well as international registries, is necessary.

Title: Juvenile spondyloarthritis.

Citation: Current opinion in rheumatology, Jul 2015, vol. 27, no. 4, p. 364-372 (July 2015)

Author(s): Gmuca, Sabrina, Weiss, Pamela F

Abstract: This article provides a comprehensive update of the pathogenesis, diagnostic imaging, treatments, and disease activity measurements of juvenile spondyloarthritis (JSpA). Genetic and microbiome studies have provided new information regarding possible pathogenesis of JSpA. Recent work suggests that children with JSpA have decreased thresholds for pain in comparison to healthy children. In addition, pain on physical examination and abnormalities on ultrasound of the entheses are not well correlated. Treatment guidelines for juvenile arthritis, including JSpA, were published by the American College of Rheumatology and are based on active joint count and presence of sacroiliitis. Recent studies have established the efficacy of tumor necrosis factor inhibitors in the symptomatic treatment of axial disease, although their efficacy for halting progression of structural damage is less clear. Newly developed disease activity measures for JSpA include the Juvenile Arthritis Disease Activity Score and the JSpA disease activity index. In comparison to other categories of juvenile arthritis, children with JSpA are less likely to attain and sustain inactive disease. Further microbiome and genetic research may help elucidate JSpA pathogenesis. More randomized therapeutic trials are needed and the advent of new composite disease activity measurement tools will hopefully allow the design of these greatly needed trials.

Title: Psychological correlates of fatigue in rheumatoid arthritis: A systematic review.

Citation: Clinical Psychology Review, Jul 2015, vol. 39, p. 16-29, 0272-7358 (Jul 2015)

Author(s): Matcham, F., Ali, S., Hotopf, M., Chalder, T.

Abstract: Fatigue is common and debilitating in Rheumatoid Arthritis (RA). A focus on the psychological variables associated with fatigue may help to identify targets for intervention which could enhance the treatment of fatigue in RA. The purpose of this review was to systematically identify psychological variables related to fatigue in RA, with the overall aim of suggesting evidence-based targets for fatigue intervention in RA. Twenty-nine studies met inclusion criteria and were included in the narrative synthesis. A wide range of psychological variables were addressed, spanning 6 categories: affect and common mental disorders; RA-related cognitions; non-RA-related cognitions; personality traits; stress and coping; and social support/interpersonal relationships. The most consistent relationship was found between mood and fatigue, with low mood frequently associated with increased fatigue. Some evidence also highlighted the relationship between RA-related cognitions (such as RA self-efficacy) and fatigue, and non-RA-cognitions (such as goal ownership) and fatigue. Limited evidence was found to support the relationship between stress and coping or personality traits and fatigue, although mixed evidence was found for the relationship between social support and fatigue. The results of this review suggest the interventions for fatigue in RA may benefit from a focus on mental health, and disease-related cognitions.

Source: PsycInfo
Efficacy and safety of a biosimilar rituximab in biologic naïve patients with active rheumatoid arthritis.

Citation: Clinical rheumatology, Jul 2015, vol. 34, no. 7, p. 1289-1292 (July 2015)

Author(s): Roshique, Kuttipurath Kandi, Ravindran, Vinod

Abstract: Biosimilar usage in rheumatology is set to increase over the next few years. This study reports the efficacy and toxicity of a rituximab biosimilar in biologic naïve patients with active rheumatoid arthritis who had inadequately responded to methotrexate. In 21 patients, over a follow-up period of 36 months, it demonstrated prolonged benefit in a majority (10 in remission with disease activity score 28 (DAS28) erythrocyte sedimentation rate (ESR) <2.6 and 9 in low disease activity state with DAS28 ESR between 3.2 and 2.6) and was well tolerated.

Source: Medline

Chikungunya infection in the general population and in patients with rheumatoid arthritis on biological therapy.

Citation: Clinical rheumatology, Jul 2015, vol. 34, no. 7, p. 1285-1287 (July 2015)


Abstract: Chikungunya infection is a febrile illness, which currently is afflicting the Caribbean islands including the Dominican Republic. We would like to report our experience with Chikungunya-related musculoskeletal manifestations in our arthritis clinics in the Dominican Republic. A total of 514 patients presented for the first time to our arthritis clinic exhibiting musculoskeletal manifestations, 473/514 (92 %) exhibiting symmetric polyarthralgias, 344/514 (67 %) arthritis, and 385 (75 %) skin rash. The great majority 457.46 (89 %) exhibited very good clinical response to nonsteroidal anti-inflammatory drugs (NSAIDs), 370 (72 %) require low-dose steroids, and only 5 patients (0.97 %) required methotrexate therapy. In addition, of a total of 328 patients with rheumatoid arthritis on biological treatment, 53 exhibited Chikungunya-related musculoskeletal manifestations; 51/53 (96.2 %) exhibited symmetric polyarthralgias, 25/53 (47.1 %) arthritis, and 13/53 (24.5 %) tendinopathy. Of most patients, 51/53 responded to NSAIDs, of which, 23 patients only responded partially, and in total 25 (47.1 %) required low-dose steroids. Disease-modifying antirheumatic drug (DMARD) therapy remained unchanged in this population.


Citation: Autoimmunity reviews, Jul 2015, vol. 14, no. 7, p. 601-608 (July 2015)

Author(s): Ceccarelli, Fulvia, Perricone, Carlo, Massaro, Laura, Cipriano, Enrica, Alessandri, Cristiano, Spinelli, Francesca Romana, Valesini, Guido, Conti, Fabrizio

Abstract: The assessment of disease activity in patients affected by Systemic Lupus Erythematosus (SLE) represents an important issue, as recommended by the European League Against Rheumatism (EULAR). Two main types of disease activity measure have been proposed: the global score systems, providing an overall measure of activity, and the individual organ/system assessment scales, assessing disease activity in different organs. All the activity indices included both clinical and laboratory items, related to the disease manifestations. However, there is no gold standard to measure disease activity in patients affected by SLE. In this review, we will analyze the lights and shadows of the disease activity indices, by means of a critical approach. In particular, we will focus on SLE Disease Activity Index (SLEDAI) and British Isles Lupus Assessment Group (BILAG), the most frequently used in randomized controlled trials and observational studies. The evaluation of data from the literature underlined some limitations of these indices, making their application in clinical practice difficult and suggesting the possible use of specific tools in the different subset of SLE patients, in order to capture all the disease features. Copyright © 2015 Elsevier B.V. All rights reserved.

Title: Differential risk of herpes zoster infection with biologic agent use in rheumatoid arthritis: comment on the article by Yun et al.
Abstract: It is unclear whether an intensive program of weight loss combined with exercise prevents the onset of knee pain among those at high risk. We examined whether an intensive lifestyle intervention (ILI) prevents incident knee pain compared with a diabetes mellitus support and education (DSE) comparison group among overweight adults with diabetes mellitus. We conducted a secondary analysis of the Action for Health in Diabetes (Look AHEAD) study, which is a randomized intervention trial of adults who were obese and had type 2 diabetes mellitus starting in 2001. We studied a subcohort of 2,889 subjects who reported no knee pain at baseline but were at high risk due to obesity. Risk ratios (RRs) were calculated to examine the association of ILI versus DSE with incident knee pain at year 1 and year 4. All analyses were adjusted for potential confounders. Age, sex, and body mass index were similar among ILI and DSE participants with no knee pain at baseline. At year 1, ILI participants were 15% less likely to develop knee pain compared with DSE participants (RR 0.85, 95% confidence interval 0.74-0.98). At year 4, this difference decreased to 5% and was no longer statistically significant. An ILI of diet and exercise may prevent the development of knee pain among those at high risk in the short term. Health care providers may consider recommending diet and exercise as a means to prevent the development of knee pain among those at high risk. © 2015, American College of Rheumatology.
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