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Current Awareness Bulletin – Rheumatology
February and March 2015

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New and updated Cochrane Systematic Reviews

Full-text evidence-based systematic reviews prepared by the Cochrane Collection

Updated Review – February 2015

Mobile bearing vs fixed bearing prostheses for posterior cruciate retaining total knee arthroplasty for postoperative functional status in patients with osteoarthritis and rheumatoid arthritis

New Reviews – January 2015

Chondroitin for osteoarthritis

Rituximab for rheumatoid arthritis

Zonisamide for neuropathic pain in adults

Updated Review – January 2015

Exercise for osteoarthritis of the knee

New from UpToDate

What’s New in Rheumatology?
New additions to UpToDate considered by the editors to be of particular interest.
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1. Advances in the diagnosis of large vessel vasculitis

Citation: Rheumatic Disease Clinics of North America, February 2015, vol./is. 41/1(125-140), 0889-857X;1558-3163 (01 Feb 2015)


Language: English

Abstract: The diagnosis of large-vessel vasculitis has experienced substantial improvement in recent years. While Takayasu arteritis diagnosis relies on imaging, the involvement of epicranial arteries by giant-cell arteritis facilitates histopathological confirmation. When appropriately performed temporal artery biopsy has high sensitivity and specificity. However, an optimal biopsy is not always achievable and, occasionally, the superficial temporal artery may not be involved. Imaging in its various modalities including colour-duplex ultrasonography, computed tomography angiography, magnetic resonance angiography and positron emission tomography, are emerging as important procedures for the diagnosis and assessment of disease extent in large-vessel vasculitis. Recent contributions to the better performance and interpretation of temporal artery biopsies as well as advances in imaging are the focus of the present review.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Rheumatic diseases clinics of North America at No link? Ask Salisbury Healthcare Library - please click here to request article.

2. Arthritogenic alphaviruses: New insights into arthritis and bone pathology

Citation: Trends in Microbiology, January 2015, vol./is. 23/1(35-43), 0966-842X;1878-4380 (01 Jan 2015)

Author(s): Chen W., Foo S.-S., Sims N.A., Herrero L.J., Walsh N.C., Mahalingam S.

Language: English

Abstract: Arthritogenic alphaviral infection begins as a febrile illness and often progresses to joint pain and rheumatic symptoms that are described as polyarthritis. Alphaviral arthritis and classical arthritides share many similar cellular and immune mediators involved in their pathogenesis. Recent in vitro and in vivo evidence suggests that bone loss resulting from increased expression of bone resorption mediators may accompany alphaviral infection. In addition, several longitudinal studies have reported more severe and delayed recovery of alphaviral disease in patients with pre-existing arthritic conditions. This review aims to provide insights into alphavirus-induced bone loss and focuses on aspects of disease exacerbation in patients with underlying arthritis and on possible therapeutic targets.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Trends in microbiology at No link? Ask Salisbury Healthcare Library - please click here to request article.

3. Autoantibodies to the mitochondrial RNA processing (MRP) complex also known as Th/To autoantigen

Citation: Autoimmunity Reviews, March 2015, vol./is. 14/3(254-257), 1568-9972;1873-0183 (01 Mar 2015)

Author(s): Mahler M., Fritzler M.J., Satoh M.

Language: English

Abstract: Antinuclear antibodies (ANA) represent valuable biomarkers in the diagnosis of systemic sclerosis (SSc) being present in the vast majority of the patients. Besides anti-topoisomerase I, anti-centromere and anti-RNA polymerase III antibodies as the main specificities, several other autoantibodies can be present in SSc patients including autoantibodies targeting the PM/Scl complex (also known as the exosome), U3-RNP/fibrillarin and the Th/To autoantigens. Anti-Th/To antibodies are one of the specificities that reportedly show homogenous nucleolar staining in conventional indirect immunofluorescence (IIF) ANA tests. Almost all protein components of the mitochondrial RNA processing (MRP) and the evolutionarily related RNase P complex have been reported to be the target of anti-Th/To antibodies in systemic autoimmune rheumatic disease (SARD) patients. However, Rpp25, Rpp38 and hPop1 have been described as the main autoantigen.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Autoimmunity reviews at No link? Ask Salisbury Healthcare Library - please click here to request article.
4. Autoimmune disease in the epigenetic era: How has epigenetics changed our understanding of disease and how can we expect the field to evolve?

Citation: Expert Review of Clinical Immunology, January 2015, vol./is. 11/1(45-58), 1744-666X;1744-8409 (01 Jan 2014)

Author(s): Jeffries M.A., Sawalha A.H.

Language: English

Abstract: Autoimmune diseases are complex and enigmatic, and have presented particular challenges to researchers seeking to define their etiology and explain progression. Previous studies have implicated epigenetic influences in the development of autoimmunity. Epigenetics describes changes in gene expression related to environmental influences without alterations in the underlying genomic sequence, generally classified into three main groups: cytosine genomic DNA methylation, modification of various sidechain positions of histone proteins and noncoding RNAs feedback. The purpose of this article is to review the most relevant literature describing alterations of epigenetic marks in the development and progression of four common autoimmune diseases: systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis and Sjogren's syndrome. The contribution of DNA methylation, histone modification and noncoding RNA for each of these disorders is discussed, including examples both of candidate gene studies and larger epigenomics surveys, and in various tissue types important for the pathogenesis of each. The future of the field is speculated briefly, as is the possibility of therapeutic interventions targeting the epigenome.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Expert review of clinical immunology at No link? Ask Salisbury Healthcare Library - please click here to request article.

5. Autonomic function and rheumatoid arthritis - A systematic review

Citation: Seminars in Arthritis and Rheumatism, December 2014, vol./is. 44/3(283-304), 0049-0172;1532-866X (01 Dec 2014)


Language: English

Abstract: Objectives: Rheumatoid arthritis (RA) is a chronic inflammatory condition with increased all-cause and cardiovascular mortality. Accumulating evidence indicates that the immune and autonomic nervous systems (ANS) are major contributors to the pathogenesis of cardiovascular disease. We performed the first systematic literature review to determine the prevalence and nature of ANS dysfunction in RA and whether there is a causal relationship between inflammation and ANS function. Methods: Electronic databases (MEDLINE, Central and Cochrane Library) were searched for studies of RA patients where autonomic function was assessed. Results: A total of 40 studies were included. ANS function was assessed by clinical cardiovascular reflex tests (CCTs) (. n = 18), heart rate variability (HRV) (. n = 15), catecholamines (. n = 5), biomarkers of sympathetic activity (. n = 5), sympathetic skin responses (. n = 5), cardiac baroreflex sensitivity (cBRS) (. n = 2) and pupillary light reflexes (. n = 2). A prevalence of ~60% (median, range: 20-86%) of ANS dysfunction (defined by abnormal CCTs) in RA was reported in 9 small studies. Overall, 73% of studies (. n = 27/37) reported at least one of the following abnormalities in ANS function: parasympathetic dysfunction (. n = 20/26, 77%), sympathetic dysfunction (. n = 16/30, 53%) or reduced cBRS (. n = 1/2, 50%). An association between increased inflammation and ANS dysfunction was found (. n = 7/19, 37%), although causal relationships could not be elucidated from the studies available to date. Conclusions: ANS dysfunction is prevalent in ~60% of RA patients. The main pattern of dysfunction is impairment of cardiovascular reflexes and altered HRV, indicative of reduced cardiac parasympathetic (strong evidence) activity and elevated cardiac sympathetic activity (limited evidence). The literature to date is underpowered to determine causal relationships between inflammation and ANS dysfunction in RA.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Seminars in arthritis and rheumatism at No link? Ask Salisbury Healthcare Library - please click here to request article.


Citation: Arthritis Care and Research, February 2015, vol./is. 67/2(169-179), 2151-464X;2151-4658 (01 Feb 2015)


Language: English
Abstract: Objective. Cardiovascular disease (CVD) is a leading cause of mortality in rheumatoid arthritis (RA). This study systematically reviewed and appraised guidelines and quality indicators (QIs) pertaining to CVD risk management in patients with RA. Methods. Four electronic medical databases (Medline, Embase, CINAHL, and Web of Science) and gray literature publications were searched using terms and keywords pertaining to guidelines, QIs, RA, and CVD (RA and general population literature searched). Abstracts were screened for inclusion and rated using the Appraisal of Guidelines for Research and Evaluation II instrument independently by 2 of 3 reviewers. Results. In total, 16,064 abstracts were screened and 808 underwent full-text review. A total of 17 guidelines and 3 QI sets published between 2008 and 2013 were included. A number of consistent themes emerged, including the increased CV risk faced by RA patients and the need to address modifiable risk factors on a regular basis. The role of the multidisciplinary team in risk optimization was also highlighted. Ten guidelines provided recommendations for CVD prevention in patients with RA. Unfortunately, most recommendations lacked the specificity required to determine adherence to the recommendation. Only 4 RA-specific CVD QIs were identified (1 general comorbidity screening, formal CVD risk estimation, exercise, and minimizing steroid use). Conclusion. Regular screening for CVD risk factors is an important part of care in patients with RA. Unfortunately, existing RA-specific CVD QIs do not adequately address risk factor management, and existing guideline recommendations lack specificity for measurement and use in quality improvement initiatives.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Arthritis Care & Research (2151464X) at No link? Ask Salisbury Healthcare Library - please click here to request article.

Citation: Expert Review of Clinical Immunology, January 2015, vol./is. 11/1(109-116), 1744-666X;1744-8409 (01 Jan 2014)
Author(s): Leone A., Sciascia S., Kamal A., Khamashta M.
Language: English
Abstract: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease resulting from the dysregulation of various immunological pathways. There has been major progress in recent years in the understanding of the pathogenesis of SLE, which has led to an emergence of a new class of drugs designed to target specific components of the disease process. Evidence from a number of open-label, uncontrolled studies has supported the use of rituximab (an anti-CD20 monoclonal antibody) in SLE for more than one decade. However, these promising results are in clear contrast with the poor results of the completed Efficacy and Safety of Rituximab in Patients with Severe SLE (EXPLORER) and Efficacy and Safety of Rituximab in Subjects with class III or IV Lupus Nephritis (LUNAR) randomized controlled trials. In contrast to EXPLORER and LUNAR results, controlled trials for belimumab (a fully humanized monoclonal antibody against B lymphocyte stimulator) showed positive results and subsequently, belimumab was the first drug approved for the treatment of SLE patients. This has paved the way for the development of further biological agents, potentially revolutionizing the treatment of SLE. In this study, the potential benefits of novel biological agents are explored, obstacles to the development of a treatment target in SLE are identified, and possible strategies to achieve this goal are discussed.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Expert review of clinical immunology at No link? Ask Salisbury Healthcare Library - please click here to request article.

8. Challenging mimickers of primary systemic vasculitis
Citation: Rheumatic Disease Clinics of North America, February 2015, vol./is. 41/1(141-160), 0889-857X;1558-3163 (01 Feb 2015)
Author(s): Miloslavsky E.M., Stone J.H., Unizony S.H.
Language: English
Abstract: The need to distinguish true primary systemic vasculitis from its multiple potential mimickers is one of the most challenging diagnostic conundrums in clinical medicine. This article reviews 9 challenging vasculitis mimickers: fibromuscular dysplasia, calciphylaxis, segmental arterial mediolysis, antiphospholipid syndrome, hypereosinophilic syndrome, lymphomatoid granulomatosis, malignant atrophic papulosis, livedoid vasculopathy, and immunoglobulin G4-related disease.

Publication type: Journal: Review
9. Clinical effectiveness of glucosamine and chondroitin sulphate in treatment of osteoarthritis

**Citation:** International Journal of Pharmaceutical Sciences and Research, 2015, vol./is. 6/2(S41-545), 2320-5148;0975-8232 (2015)

**Author(s):** Batool F., Sohail M., Ashraf F., Rana B., Mahmood F., Tanveer S.

**Language:** English

**Abstract:** Osteoarthritis is a form of arthritis, and is the most common form of arthritis. Persons suffering from osteoarthritis have symptoms of pain, stiffness, decreased range of motion of affected joints. Although NSAIDS are the most commonly prescribed agents for this disorder but can cause of serious adverse effects. Two compounds Glucosamine and chondroitin which are extracted from animal products have been used in various forms for OA. To assess the clinical effectiveness of glucosamine and chondroitinsulphate in treatment of osteoarthritis symptoms like joint pain, joint space narrowing, reduced walking time, swelling etc. We searched articles separately for glucosamine and chondroitin sulphate using internet. Fifteen articles met the inclusion criteria. Data from articles was extracted using a standardized data extraction tables i.e. table1 and table 2. Glucosamine and Chondroitin sulphate are effective in the treatment of Osteoarthritis because these can reduce pain, prevent further joint space narrowing and solve other related problems of this disease. The two agents can be used in osteoarthritis treatment as their safety is already assured as compared to other symptomatic treatment for OA. But these agents can take more time to treat disease as compared to conventional medicine like NSAIDS.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available ProQuest at International Journal of Pharmaceutical Sciences and Research

10. Cogan and Behcet syndromes

**Citation:** Rheumatic Disease Clinics of North America, February 2015, vol./is. 41/1(75-91), 0889-857X;1558-3163 (01 Feb 2015)

**Author(s):** Singer O.

**Language:** English

**Abstract:** Cogan and Behcet syndromes are considered large vessel vasculitides. Both are rare diseases, with varied clinical manifestations affecting multiple organ systems. Although both have hallmark symptoms (ocular and vestibuloadunditory inflammation in Cogan syndrome and aphthous ulcers in Behcet syndrome), neither has confirmatory diagnostic testing. Delayed diagnosis can result in poor outcomes. In both syndromes, large vessel arterial inflammation may result in severe morbidity and mortality. Treatment strategies in both syndromes vary based on organ system involvement and severity of manifestations. In this article, the epidemiology, proposed pathogenesis, manifestations, and the most current treatment paradigms for these syndromes are reviewed.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available Rheumatic diseases clinics of North America at No link? Ask Salisbury Healthcare Library - please click here to request article.

11. Connective tissue disorders associated with vasculitis and vaso-occlusive disease of the hand

**Citation:** Hand Clinics, February 2015, vol./is. 31/1(63-73), 0749-0712;1558-1969 (01 Feb 2015)

**Author(s):** Michelotti B., Rizzo M., Moran S.L.

**Language:** English

**Abstract:** Hand ischemia caused by vasculitis is a secondary finding in many autoimmune processes. Many of these autoimmune diseases are managed primarily with medications that can prevent the development of occlusive disease, tissue ischemia, and tissue loss. Unfortunately several disease conditions can be recalcitrant to medical management and can result in ischemic changes within the hand, which may require operative intervention. This article briefly reviews the major connective tissue disorders associated with vasculitis and vaso-occlusive disease of the hand, including scleroderma, lupus, and Buerger disease, and their surgical treatment.

**Publication type:** Journal: Review

**Source:** EMBASE
12. Current and emerging treatment options for ANCA-associated vasculitis: Potential role of belimumab and other BAFF/APRIL targeting agents

Citation: Drug Design, Development and Therapy, January 2015, vol./is. 9/(333-347), 1177-8881; 1177-8881 (07 Jan 2015)

Author(s): Lenert A., Lenert P.

Language: English

Abstract: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) comprises several clinical entities with diverse clinical presentations, outcomes, and nonuniforming pathogenesis. AAV has a clear potential for relapses, and shows unpredictable response to treatment. Cyclophosphamide-based therapies have remained the hallmark of induction therapy protocols for more than four decades. Recently, B-cell depleting therapy with the anti-CD20 antibody rituximab has proved beneficial in AAV, leading to Food and Drug Administration approval of rituximab in combination with corticosteroids for the treatment of AAV in adults. Rituximab for ANCA-associated vasculitis and other clinical trials provided clear evidence that rituximab was not inferior to cyclophosphamide for remission induction, and rituximab appeared even more beneficial in patients with relapsing disease. This raised hopes that other B-cell targeted therapies directed either against CD19, CD20, CD22, or B-cell survival factors, B-cell activating factor of the tumor necrosis factor family (BAFF) and a proliferation-inducing ligand could also be beneficial for the management of AAV. BAFF neutralization with the fully humanized monoclonal antibody belimumab has already shown success in human systemic lupus erythematosus and, along with another anti-BAFF reagent blisibimod, is currently undergoing Phase II and III clinical trials in AAV. Local production of BAFF in granulomatous lesions and elevated levels of serum BAFF in AAV provide a rationale for BAFF-targeted therapies not only in AAV but also in other forms of vasculitis such as Behcet’s disease, large-vessel vasculitis, or cryoglobulinemic vasculitis secondary to chronic hepatitis C infection. BAFF-targeted therapies have a very solid safety profile, and may have an additional benefit of preferentially targeting newly arising autoreactive B cells over non-self-reactive B cells.

Publication type: Journal: Review

Source: EMBASE

Full text: Available National Library of Medicine at Drug Design, Development and Therapy

13. Current and future trends in biomarker discovery and development of companion diagnostics for arthritis

Citation: Expert Review of Molecular Diagnostics, February 2015, vol./is. 15/2(219-234), 1473-7159; 1744-8352 (01 Feb 2015)


Language: English

Abstract: Musculoskeletal diseases such as rheumatoid arthritis are complex multifactorial disorders that are chronic in nature and debilitating for patients. A number of drug families are available to clinicians to manage these disorders but few tests exist to target these to the most responsive patients. As a consequence, drug failure and switching to drugs with alternate modes of action is common. In parallel, a limited number of laboratory tests are available which measure biological indicators or ‘biomarkers’ of disease activity, autoimmune status, or joint damage. There is a growing awareness that assimilating the fields of drug selection and diagnostic tests into 'companion diagnostics' could greatly advance disease management and improve outcomes for patients. This review aims to highlight: the current applications of biomarkers in rheumatology with particular focus on companion diagnostics; developments in the fields of proteomics, genomics, microbiomics, imaging and bioinformatics and how integration of these technologies into clinical practice could support therapeutic decisions.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Expert review of molecular diagnostics at No link? Ask Salisbury Healthcare Library - please click here to request article.

14. Current serological possibilities for the diagnosis of arthritis with special focus on proteins and proteoglycans from the extracellular matrix

Citation: Expert Review of Molecular Diagnostics, January 2015, vol./is. 15/1(77-95), 1473-7159; 1744-8352 (01 Jan 2015)
Abstract: This review discusses our current understanding of how the expression and turnover of components of the cartilage extracellular matrix (ECM) have been investigated, both as molecular markers of arthritis and as indicators of disease progression. The cartilage ECM proteome is well studied; it contains proteoglycans (aggrecan, perlecan and inter-alpha-trypsin inhibitor), collagens and glycoproteins (cartilage oligomeric matrix protein, fibronectin and lubricin) that provide the structural and functional changes in arthritis. However, the changes that occur in the carbohydrate structures, including glycosaminoglycans, with disease are less well studied. Investigations of the cartilage ECM proteome have revealed many potential biomarkers of arthritis. However, a clinical diagnostic or multiplex assay is yet to be realized due to issues with specificity to the pathology of arthritis. The future search for clinical biomarkers of arthritis is likely to involve both protein and carbohydrate markers of the ECM through the application of glycoproteomics.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Expert review of molecular diagnostics at No link? Ask Salisbury Healthcare Library - please click here to request article.

15. Cytokine-modulating strategies and newer cytokine targets for arthritis therapy

Citation: International Journal of Molecular Sciences, December 2015, vol./is. 16(1)/1(887-906), 1661-6596;1422-0067 (31 Dec 2015)

Author(s): Venkatesha S.H., Dudics S., Acharya B., Moudgil K.D.

Abstract: Cytokines are the key mediators of inflammation in the course of autoimmune arthritis and other immune-mediated diseases. Uncontrolled production of the pro-inflammatory cytokines such as interferon- (IFN-), tumor necrosis factor alpha (TNFalpha), interleukin-6 (IL-6), and IL-17 can promote autoimmune pathology, whereas anti-inflammatory cytokines including IL-4, IL-10, and IL-27 can help control inflammation and tissue damage. The pro-inflammatory cytokines are the prime targets of the strategies to control rheumatoid arthritis (RA). For example, the neutralization of TNFalpha, either by engineered anti-cytokine antibodies or by soluble cytokine receptors as decoys, has proven successful in the treatment of RA. The activity of pro-inflammatory cytokines can also be downregulated either by using specific siRNA to inhibit the expression of a particular cytokine or by using small molecule inhibitors of cytokine signaling. Furthermore, the use of anti-inflammatory cytokines or cytokine antagonists delivered via gene therapy has proven to be an effective approach to regulate autoimmunity. Unexpectedly, under certain conditions, TNFalpha, IFN-, and few other cytokines can display anti-inflammatory activities. Increasing awareness of this phenomenon might help develop appropriate regimens to harness or avoid this effect. Furthermore, the relatively newer cytokines such as IL-32, IL-34 and IL-35 are being investigated for their potential role in the pathogenesis and treatment of arthritis.

Publication type: Journal: Review

Source: EMBASE

Full text: Available International Journal of Molecular Sciences at International Journal of Molecular Sciences

16. Efficacy of patient-initiated follow-up clinics in secondary care: A systematic review

Citation: Internal Medicine Journal, December 2014, vol./is. 44/12(1156-1160), 1444-0903;1445-5994 (01 Dec 2014)

Author(s): Taneja A., Su'a B., Hill A.G.

Abstract: Patient-initiated follow up (PIFU) is an initiative that allows patients to initiate hospital follow-up appointments on an 'as required' basis compared with the traditional 'physician-initiated' model. The main principle is to reduce inappropriate regular follow-up appointments. In this systematic review, we attempt to address its efficacy for outpatient secondary level care. Using Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines, an electronic literature search was performed independently by two authors using pre-defined search terms across EMBASE, Ovid MedLine, PubMed, PSYCINFO and the Cochrane Library databases. Articles were included if they specifically evaluated any aspect of PIFU. Studies evaluating non-outpatient-based, primary level-based and nurse-led clinic appointments were excluded. A total of 747 articles was reviewed, and six were finally included for the systematic review. Three studies analysed efficacy of PIFU with regards to rheumatological disease and found that there was no deleterious clinical effect and a trend towards increased satisfaction and quality of life including lower
costs in the PIFU group. Two studies looked at PIFU and inflammatory bowel disease and identified some clinical benefit and lower costs and equivalent satisfaction and QoL with the PIFU group. A further study looked at PIFU in stage 1 breast cancer and did not find any significant differences in outcomes. There is evidence to suggest that PIFU systems result in fewer overall outpatient appointments in secondary care led services while maintaining equivalent if not better patient satisfaction, quality of life and clinical outcomes across a range of chronic conditions.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Internal medicine journal at No link? Ask Salisbury Healthcare Library - please click here to request article.

17. Febuxostat for the treatment of gout  
**Citation:** Expert Opinion on Pharmacotherapy, February 2015, vol./is. 16/3(395-398), 1465-6566;1744-7666 (01 Feb 2015)  
**Author(s):** Bridgeman M.B., Chavez B.  
**Language:** English  
**Abstract:** Introduction: Gout is a rheumatologic condition associated with elevated serum uric acid levels and deposition of monosodium urate crystals in joints and soft tissues. The xanthine oxidase inhibitor, allopurinol, has historically been the principle agent utilized for reducing elevated uric acid levels and treating underlying cause of gout symptoms; the availability of febuxostat, a newer non-purine selective xanthine oxidase inhibitor, represents an alternative therapy for those patients with contraindications or intolerance to allopurinol. Areas covered: This article reviews the published literature on the pharmacologic characteristics and clinical safety and efficacy data on the use of febuxostat in the treatment of gout. A literature search of MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations Databases (1996-November 2014) was conducted utilizing the key words 'febuxostat', 'allopurinol', and 'gout'. All published articles regarding febuxostat were evaluated. References of selected articles, data from poster presentations, and abstract publications were additionally reviewed. Expert opinion: Febuxostat has shown benefit with respect to symptomatic relief and uric acid level reduction. The safety profile of this agent makes it an ideal alternative in those patients with contraindications to or who are intolerant of allopurinol.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Expert opinion on pharmacotherapy at No link? Ask Salisbury Healthcare Library - please click here to request article.

18. Giant Cell Arteritis and Polymyalgia Rheumatica: an Update  
**Citation:** Current Rheumatology Reports, 2015, vol./is. 17/2, 1523-3774;1534-6307 (2015)  
**Author(s):** Gonzalez-Gay M.A., Pina T.  
**Language:** English  
**Abstract:** Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two closely related diseases in people aged 50 years and older, which are more frequently observed in Western countries. Despite being common entities, concern still exists about the epidemiology, pathogenesis, and diagnosis of both entities. New imaging techniques, such as 18 fluorodeoxyglucose-positron emission tomography, have proved to be useful in detecting large-vessel involvement in GCA. Corticosteroids are the cornerstone of the therapy in GCA and PMR. Relapses are frequent in these conditions. Unlike methotrexate and tumor necrosis factor-alpha antagonists, anti-interleukin-6 receptor therapy appears to be useful in patients with GCA and PMR who are refractory to corticosteroids. This review summarizes recent studies on GCA and PMR.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Current rheumatology reports at No link? Ask Salisbury Healthcare Library - please click here to request article.

19. Interferon regulatory factors: Critical mediators of human lupus  
**Citation:** Translational Research, February 2015, vol./is. 165/2(283-295), 1931-5244;1878-1810 (01 Feb 2015)  
**Author(s):** Jensen M.A., Niewold T.B.  
**Language:** English  
**Abstract:** The pathogenesis of systemic lupus erythematosus (SLE) is multifactorial, and the interferon regulatory factors (IRFs) play an important role. Autoantibodies formed in SLE target nuclear antigens, and immune complexes
formed by these antibodies contain nucleic acid. These immune complexes can activate antiviral pattern recognition receptors (PRRs), resulting in the downstream activation of IRFs, which can induce type I interferon (IFN-I) and other inflammatory mediators. Genetic variations in IRFs have been associated with susceptibility to SLE, and current evidence supports the idea that these polymorphisms are gain of function in humans. Recent studies suggest that these genetic variations contribute to the break in humoral tolerance that allows for nucleic acid binding autoantibodies, and that the same polymorphisms also augment IFN-I production in the presence of these autoantibody immune complexes, forming a feed-forward loop. In this review, we will outline major features of the PRR/IRF systems and describe the role of the IRFs in human SLE pathogenesis.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Translational research : the journal of laboratory and clinical medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

20. Inflammatory eye reactions with bisphosphonates and other osteoporosis medications: what are the risks?

Citation: Therapeutic Advances in Musculoskeletal Disease, February 2015, vol./is. 7/1(11-16), 1759-720X;1759-7218 (05 Feb 2015)
Author(s): Clark E.M., Durup D.
Language: English
Abstract: Inflammatory eye reactions (IERs) are rare but have been associated with medications to treat osteoporosis. The aim of this review is to summarize the current literature on the association between IERs and specific medications to treat osteoporosis (bisphosphonates, selective estrogen receptor modulators, strontium, denosumab and teriparatide). We cover the known epidemiology, potential pathogenic mechanisms and a resume of unanswered questions. Briefly, this review highlights that none of the existing randomized clinical trials were powered to identify these rare adverse events, and the majority of the information available is from spontaneous case reports and case series reporting associations between bisphosphonates and IERs. No case reports describe IERs after other anti-osteoporosis medications. Importantly, some case reports describe recurrence of the IER after affected patients were rechallenged with the same or another bisphosphonate, and that no reported cases resolved without discontinuation of the bisphosphonate. However, three large population-based cohort studies have shown conflicting results between osteoporosis treatments and IERs, but overall these studies suggest that IERs may actually be part of underlying inflammatory disease processes that also cause osteoporosis, rather than due to the medications used to treat osteoporosis themselves. There are no clear pathogenic mechanisms for how bisphosphonates could potentially cause IERs. However, the drug is secreted into the tears by the lacrimal gland and could cause irritation to the mucous membranes with subsequent release of inflammatory mediators, similar to the systemic response typically seen after infusion of bisphosphonates. However, in summary it is still not known whether there is a true causal association between bisphosphonates or other anti-osteoporosis medications and IERs, or whether it is confounding by indication and is actually due to underlying inflammatory diseases that cause both osteoporosis and IERs.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Therapeutic Advances in Musculoskeletal Disease at No link? Ask Salisbury Healthcare Library - please click here to request article.

21. Interferon regulatory factors: Critical mediators of human lupus

Citation: Translational Research, February 2015, vol./is. 165/2(283-295), 1931-5244;1878-1810 (01 Feb 2015)
Author(s): Jensen M.A., Niewold T.B.
Language: English
Abstract: The pathogenesis of systemic lupus erythematosus (SLE) is multifactorial, and the interferon regulatory factors (IRFs) play an important role. Autoantibodies formed in SLE target nuclear antigens, and immune complexes formed by these antibodies contain nucleic acid. These immune complexes can activate antiviral pattern recognition receptors (PRRs), resulting in the downstream activation of IRFs, which can induce type I interferon (IFN-I) and other inflammatory mediators. Genetic variations in IRFs have been associated with susceptibility to SLE, and current evidence supports the idea that these polymorphisms are gain of function in humans. Recent studies suggest that these genetic variations contribute to the break in humoral tolerance that allows for nucleic acid binding autoantibodies, and that the same polymorphisms also augment IFN-I production in the presence of these autoantibody immune complexes, forming a feed-forward loop. In this review, we will outline major features of the PRR/IRF systems and
describe the role of the IRFs in human SLE pathogenesis.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Translational research : the journal of laboratory and clinical medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

22. **Kawasaki disease**  
**Citation:** Rheumatic Disease Clinics of North America, February 2015, vol./is. 41/1(63-73), 0889-857X;1558-3163 (01 Feb 2015)  
**Author(s):** Sundel R.P.  
**Language:** English  
**Abstract:** Kawasaki disease (KD) is the archetypal pediatric vasculitis, exemplifying the unique aspects and challenges of vascular inflammation in children. The condition is almost unheard of in adults, is closely associated with infections, and is self-limited, with fever resolving after an average of 12 days even without treatment. Yet KD is also a potentially fatal disease and the most common cause of acquired heart disease in the developed world. Unraveling of the developmental, immunologic, and genetic secrets of Kawasaki disease promises to improve our understanding of vasculitis in particular, and perhaps also to provide a window on the fundamental mysteries of inflammatory diseases in general.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Rheumatic diseases clinics of North America at No link? Ask Salisbury Healthcare Library - please click here to request article.

23. **Management of Osteoarthritis with Avocado/Soybean Unsaponifiables**  
**Citation:** Cartilage, January 2015, vol./is. 6/1(30-44), 1947-6035;1947-6043 (19 Jan 2015)  
**Author(s):** Christiansen B.A., Bhatti S., Goudarzi R., Emami S.  
**Language:** English  
**Abstract:** Osteoarthritis (OA) is a painful and life-altering disease that severely limits the daily activities of millions of Americans, and it is one of the most common causes of disability in the world. With obesity on the rise and the world’s population living longer, the prevalence of OA is expected to increase dramatically in the coming decades, generating burdensome socioeconomic costs. This review summarizes current pharmaceutical, nonpharmaceutical, and prospective new treatments for OA, with primary focus on the dietary supplement avocado/soybean unsaponifiables (ASU). ASU modulates OA pathogenesis by inhibiting a number of molecules and pathways implicated in OA. Anticatabolic properties prevent cartilage degradation by inhibiting the release and activity of matrix metalloproteinases and increasing tissue inhibitors of these catabolic enzymes. ASU also inhibits fibrinolysis by stimulating the expression of plasminogen activator inhibitor. Anabolic properties promote cartilage repair by stimulating collagen and aggrecan synthesis via inhibition of inflammatory cytokines such as interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor, ERK, and prostaglandin E2. Chondroprotective effects are mediated by correcting growth factor abnormalities, increasing TGF-beta, and decreasing vascular endothelial growth factor (VEGF) in synovial fluid. ASU also inhibits cholesterol absorption and endogenous cholesterol biosynthesis, which mediate reactive oxygen species pathology in chondrocytes. At the clinical level, ASU reduces pain and stiffness while improving joint function, resulting in decreased dependence on analgesics.

**Publication type:** Journal: Review  
**Source:** EMBASE

24. **Metabolic triggered inflammation in osteoarthritis**  
**Citation:** Osteoarthritis and Cartilage, January 2015, vol./is. 23/1(22-30), 1063-4584;1522-9653 (01 Jan 2015)  
**Author(s):** Wang X., Hunter D., Xu J., Ding C.  
**Language:** English  
**Abstract:** Osteoarthritis (OA) is a common chronic joint disorder with a multifactorial etiology including genetic and environmental factors. Metabolic triggered inflammation, induced by nutrient overload and metabolic surplus, consists of components such as obesity, pro-inflammatory cytokines and adipokines, abnormal metabolites, acute phase proteins, vitamin D deficiency, and deregulated microRNAs that may play a role in OA pathophysiology. Obesity-related metabolic factors, especially adipokines, contribute to OA development by inducing pro-inflammatory cytokines and degradative enzymes, leading to cartilage matrix impairment and subchondral bone remodeling. Ectopic metabolite
deposition and low-grade systemic inflammation can contribute to a toxic internal environment that exacerbates OA. Complement components highly expressed in osteoarthritic joints have also been proposed as causative factors. Vitamin D deficiency has been associated with obesity and is implicated to be associated with cartilage loss in OA. Metabolic microRNAs may explain the inflammatory link between obesity and OA. Therapies targeting metabolic-triggered inflammation and its components are anticipated to have potential for the treatment of OA.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society at No link? Ask Salisbury Healthcare Library - please click here to request article](http://Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society at No link? Ask Salisbury Healthcare Library - please click here to request article).

### 25. Patient-level analysis of five international cohorts further confirms the efficacy of aspirin for the primary prevention of thrombosis in patients with antiphospholipid antibodies

**Citation:** Autoimmunity Reviews, March 2015, vol./is. 14/3(192-200), 1568-9972;1873-0183 (01 Mar 2015)  
**Language:** English  
**Abstract:** We performed an individual patient meta-analysis to determine whether aspirin has a significant protective effect on the risk of first thrombosis among patients with antiphospholipid antibodies (aPL). Five international cohort studies with available individual patient-level data, reporting on primary prophylaxis with continuous treatment with low-dose aspirin in patients with aPL were included. The main outcome was the occurrence of a first thrombotic event in patients with aPL treated with low-dose aspirin compared to those not treated with low-dose aspirin. Pooled Hazard Ratios (HRs) and 95%CI were calculated using frailty models. We pooled data from 497 subjects and 79 first thrombotic events (3469 patient-years of follow-up). After adjustment on cardiovascular risk factors, aPL profiles, and treatment with hydroxychloroquine, the HR for the risk of a first thrombosis of any type in aPL carriers treated with low-dose aspirin versus those not treated with aspirin was 0.43 (95%CI 0.25-0.75). Subgroup analysis showed a protective effect of aspirin against arterial (HR: 0.43 [95%CI: 0.20-0.93]) but not venous (HR: 0.49 [95%CI: 0.22-1.11]) thrombosis. Subgroup analysis according to underlying disease revealed a protective effect of aspirin against arterial thrombosis for systemic lupus erythematosus (SLE) (HR: 0.43 [95%CI: 0.20-0.94]) and asymptomatic aPL carriers (HR: 0.43 [95%CI 0.20-0.93]). We found no independent protective effect of hydroxychloroquine. This individual patient data meta-analysis shows that the risk of first thrombotic event as well of first arterial thrombotic event is significantly decreased among SLE patients and asymptomatic aPL individuals treated by low-dose aspirin.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Autoimmunity reviews](http://Autoimmunity reviews) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 26. Prolactin: A versatile regulator of inflammation and autoimmune pathology

**Citation:** Autoimmunity Reviews, March 2015, vol./is. 14/3(223-230), 1568-9972;1873-0183 (01 Mar 2015)  
**Author(s):** Costanza M., Binart N., Steinman L., Pedotti R.  
**Language:** English  
**Abstract:** Prolactin (PRL) has long been proposed as an immune-stimulating and detrimental factor in autoimmune disorders. However, recent findings have challenged this common view, showing that PRL does not play a crucial role in the development of experimental autoimmune encephalomyelitis, animal model for multiple sclerosis (MS), and even protects against adjuvant-induced model of rheumatoid arthritis (RA). In this review we provide a critical overview of data supporting a role for PRL in the regulation of immune responses. In addition, we focus on studies exploring the involvement of PRL in autoimmune diseases, such as systemic lupus erythematosus, MS and RA, in light of the recently-outlined regenerative properties of this hormone.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Autoimmunity reviews](http://Autoimmunity reviews) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 27. Pulmonary Hypertension in Antiphospholipid Syndrome

**Citation:** Current Rheumatology Reports, 2015, vol./is. 17/1, 1523-3774;1534-6307 (2015)  
**Author(s):** Zuily S., Wahl D.
Abstract: Pulmonary hypertension (PH) is a rare but life-threatening condition in antiphospholipid syndrome (APS) patients with or without systemic lupus erythematosus (SLE). The definition of PH is based on hemodynamic parameters estimated by transthoracic echocardiography (TTE) and confirmed by right heart catheterization (RHC). New evidence suggests that antiphospholipid antibodies (aPL) in SLE patients increase the risk of PH; however, studies yield conflicting results. Hypotheses regarding the impact of aPL on PH include large vessel and microvascular thrombosis, and endothelial remodeling. Natural history of PH is progressive worsening mainly due to recurrent pulmonary embolism. The management in APS patients includes anticoagulation; patients undergoing pulmonary endarterectomy need to be closely monitored because of an increased risk of thrombotic complications.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Current rheumatology reports at No link? Ask Salisbury Healthcare Library - please click here to request article.

28. Review of Giant cell arteritis
Citation: Saudi Journal of Ophthalmology, January 2015, vol./is. 29/1(48-52), 1319-4534 (01 Jan 2015)
Author(s): Chacko J.G., Chacko J.A., Salter M.W.
Language: English
Abstract: Giant-cell arteritis (GCA) is a systemic autoimmune disease affecting primarily the elderly. Giant cell arteritis can cause sudden and potentially bilateral sequential vision loss in the elderly. Therefore, it is considered a medical emergency in ophthalmology and a significant cause of morbidity in an increasingly aging population. Ophthalmologists need to be able to recognize the classic symptoms and signs of this disease, and then be able to work-up and treat these patients in an efficient manner. An in-depth review of GCA from the literature as well as personal clinical experience follows.

Publication type: Journal: Review
Source: EMBASE

39. Rituximab and its therapeutic potential in catastrophic antiphospholipid syndrome
Citation: Therapeutic Advances in Musculoskeletal Disease, February 2015, vol./is. 7/1(26-30), 1759-720X;1759-7218 (05 Feb 2015)
Author(s): Rodriguez-Pinto I., Cervera R., Espinosa G.
Language: English
Abstract: The catastrophic antiphospholipid syndrome (CAPS) is characterized by thrombosis in more than three organs or systems developing over a short period of time. Despite conventional treatment with a combination of anticoagulation plus corticosteroids plus plasma exchange, and/or intravenous immunoglobulin, mortality remains high and some patients suffer from recurrent CAPS episodes. In selected patients, new therapies such as rituximab may be a treatment option. In this review, the rationale for using rituximab in CAPS is discussed.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Therapeutic Advances in Musculoskeletal Disease at No link? Ask Salisbury Healthcare Library - please click here to request article.

30. Safety of off-label biologicals in systemic lupus erythematosus
Citation: Expert Opinion on Drug Safety, February 2015, vol./is. 14/2(243-251), 1474-0338;1744-764X (01 Feb 2015)
Author(s): Aringer M., Smolen J.S.
Language: English
Abstract: Introduction: The approval of belimumab and other advances in the field have narrowed the window for off-label use of biologicals in systemic lupus erythematosus (SLE). For consideration in severe and refractory disease, safety will play a major role. Areas covered: We reviewed the literature on safety aspects of off-label biological use in SLE. Significant evidence is available for rituximab, whereas data on the off-label SLE therapy with other biologicals are much more limited. Published trials and open-label experience in SLE allow for some conclusions on abatacept, and on approaches targeting TNF, IL-1 and IL-6 receptors. Expert opinion: Anti-TNF antibodies apparently are the only ones inducing SLE-specific autoantibodies, but even these were not associated with flares. Risks for severe infections
certainly remain a major serious concern, particularly in combinations with glucocorticoids and/or immunosuppressants. These findings reiterate that experience with both the disease and the drugs will be essential for keeping patients safe. The available data suggest a manageable adverse event profile for rituximab and do not prove unacceptable risks for other biologicals. Reports frequently only include very few patients, with the inherent danger of bias due to lacking reports on failed treatment attempts.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Expert opinion on drug safety](#) at No link? Ask Salisbury Healthcare Library - please click here to request article.

31. Safety of supervised exercise therapy in patients with intermittent claudication  
**Citation:** Journal of Vascular Surgery, February 2015, vol./is. 61/2(512-518), 0741-5214;1097-6809 (01 Feb 2015)  
**Author(s):** Gommans L.N.M., Fokkenrood H.J.P., Van Dalen H.C.W., Scheltinga M.R.M., Teijink J.A.W., Peters R.J.G.  
**Language:** English  
**Abstract:** Background Supervised exercise therapy (SET) is recommended as the primary treatment for patients with intermittent claudication (IC). However, there is concern regarding the safety of performing SET because IC patients are at risk for untoward cardiovascular events. The Dutch physical therapy guideline advocates cardiac exercise testing before SET, if indicated. Perceived uncertainties concerning safety may contribute to the underuse of SET in daily practice. The objective of this review was to analyze the safety of supervised exercise training in patients with IC. Methods Two authors independently studied clinical trials investigating SET. Data were obtained from MEDLINE, EMBASE, and The Cochrane Central Register of Controlled Trials. Complication rates were calculated and expressed as number of events per number of patient-hours. The usefulness of cardiac screening before SET was evaluated in a subanalysis. Results Our search strategy revealed 2703 abstracts. We selected 121 articles, of which 74 met the inclusion criteria. Studies represent 82,725 hours of training in 2876 IC patients. Eight adverse events were reported, six of cardiac and two of noncardiac origin, resulting in an all-cause complication rate of one event per 10,340 patient-hours. Conclusions SET can safely be prescribed in patients with IC because an exceedingly low all-cause complication rate was found. Routine cardiac screening before commencing SET is not required. Our results may diminish perceived uncertainties regarding safety and will possibly increase the use of SET in daily practice.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter](#) at No link? Ask Salisbury Healthcare Library - please click here to request article.

32. Scoliosis and the Impact in Neuromuscular Disease  
**Citation:** Paediatric Respiratory Reviews, January 2015, vol./is. 16/1(35-42), 1526-0542;1526-0550 (01 Jan 2015)  
**Author(s):** Mayer O.H.  
**Language:** English  
**Abstract:** Scoliosis can alter respiratory mechanics by changing the orientation of the muscles and joints of the respiratory system and in severe forms can put a patient at risk of severe respiratory morbidity or respiratory failure. However, perhaps the most important factor in determining the pulmonary morbidity in scoliosis is the balance between the "load" or altered respiratory mechanics and the "pump" or the respiratory muscle strength. Therefore, scoliosis in patients with neuromuscular disease will both lead to increased "load" and a weakened "pump", an exceptionally unfortunate combination. While progressive neuromuscular disease by its nature does not respond favorably to attempts to improve respiratory muscle strength, the natural approach of early proactive management of the "load" and in the case of scoliosis a variety of different strategies have been tried with variable short term and long term results. Figuring this out requires both an understanding of the underlying pathophysiology of a particular neuromuscular condition and the available options for and timing of surgical intervention.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Paediatric respiratory reviews](#) at No link? Ask Salisbury Healthcare Library - please click here to request article.

33. Sjogren Syndrome-associated lymphomas: An update on pathogenesis and management  
**Citation:** British Journal of Haematology, February 2015, vol./is. 168/3(317-327), 0007-1048;1365-2141 (01 Feb 2015)
the complexity and involvement in osteoarthritis. We illustrate that a comprehensive and multisystem approach is necessary to understand recent progress in the field, including data from novel ‘omics’ technologies and from a number of preclinical and clinical stages of the disease, surgical interventions are often necessary to partially restore joint function. Although the focus of osteoarthritis research has been originally on the articular cartilage, novel findings are now pointing to osteoarthritis as a disease of the whole joint, in which failure of different joint components can occur. In this Review, we summarize the role of different cell types in the pathogenesis of osteoarthritis. We emphasize the importance of the immune system in the development of the disease and to better guide the development of novel therapeutic strategies.


citation: DMM Disease Models and Mechanisms, January 2015, vol./is. 8/1(17-30), 1754-8403;1754-8411 (01 Jan 2015)
author(s): Thysen S., Luyten F.P., Lories R.J.U.
language: English
abstract: Osteoarthritis is a chronic degenerative disorder of the joint and represents one of the most common diseases worldwide. Its prevalence and severity are increasing owing to aging of the population, but treatment options remain largely limited to painkillers and anti-inflammatory drugs, which only provide symptomatic relief. In the late stages of the disease, surgical interventions are often necessary to partially restore joint function. Although the focus of osteoarthritis research has been originally on the articular cartilage, novel findings are now pointing to osteoarthritis as a disease of the whole joint, in which failure of different joint components can occur. In this Review, we summarize recent progress in the field, including data from novel ‘omics’ technologies and from a number of preclinical and clinical trials. We describe different in vitro and in vivo systems that can be used to study molecules, pathways and cells that are involved in osteoarthritis. We illustrate that a comprehensive and multisystem approach is necessary to understand the complexity and heterogeneity of the disease and to better guide the development of novel therapeutic strategies.
for osteoarthritis.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Highwire Press](https://disease-models-and-mechanisms.onhighwire.com) at [Disease Models and Mechanisms](http://disease-models-and-mechanisms.onhighwire.com)

### 36. The association between vibration and vascular injury in rheumatic diseases: A review of the literature

**Citation:** Autoimmunity, February 2015, vol./is. 48/1(61-68), 0891-6934;1607-842X (01 Feb 2015)


**Language:** English

**Abstract:** Vascular manifestations can be seen early in the pathogenesis of inflammatory rheumatic diseases. Animal experiments, laboratory and clinical findings indicated that acute or long-term vibration exposure can induce vascular abnormalities. Recent years, in addition to Raynaud's phenomenon (RP), vibration as a risk factor for other rheumatic diseases has also received corresponding considered. This review is concentrated upon the role of vibration in the disease of systemic sclerosis (SSc). In this review, we are going to discuss the main mechanisms which are thought to be important in pathophysiology of vascular injury under the three broad headings of "vascular", "neural" and "intravascular". Aspects on the vibration and vascular inflammation are briefly discussed. And the epidemiological studies related to vibration studies in SSc and other rheumatic diseases are taken into account.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Autoimmunity](http://www.sagepub.com/journals) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 37. The Challenge of Bleeding in Antiphospholipid Antibody-Positive Patients

**Citation:** Current Rheumatol Reports, 2015, vol./is. 17/2, 1523-3774;1534-6307 (2015)

**Author(s):** Pazzola G., Zuily S., Erkan D.

**Language:** English

**Abstract:** Antiphospholipid antibody-positive patients can develop bleeding due to capillaritis, microthrombosis, antiprothrombin antibodies, thrombocytopenia, and/or excessive antithrombotic therapy. Clinical characteristics of patients, e.g., renal impairment, elderly, or concomitant medications, are closely related to the risk of bleeding. The management of bleeding in antiphospholipid antibody (aPL)-positive patients is challenging due to the baseline increased risk of thrombosis. If anticoagulation is stopped, it should be restarted as soon as possible once the acute bleeding is controlled; the continuation of anticoagulation despite active bleeding may be required in selected cases. High-dose corticosteroid is the mainstay treatment for diffuse alveolar hemorrhage, lupus anticoagulant-hypoprothrombinemia syndrome, and severe thrombocytopenia; immunosuppressive drugs are also required to improve the long-term outcomes. Hydrocortisone is critical in adrenal hemorrhage patients due to concomitant adrenal insufficiency; despite bleeding, anticoagulation should be maintained as much as possible. Plasma exchange should be considered in catastrophic antiphospholipid syndrome patients with concurrent bleeding. This article will review the causes of bleeding in aPL-positive patients as well as the management strategies.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Current rheumatology reports](http://www.sagepub.com/journals) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 38. The efficacy of calcineurin inhibitors for the treatment of interstitial lung disease associated with polymyositis/dermatomyositis

**Citation:** Lupus, January 2015, vol./is. 24/1(3-9), 0961-2033;1477-0962 (16 Jan 2015)

**Author(s):** Kurita T., Yasuda S., Amengual O., Atsumi T.

**Language:** English

**Abstract:** Interstitial lung disease (ILD) in patients with polymyositis (PM) and dermatomyositis (DM) is often resistant to treatment and life threatening, being recognized as one of the severest complication in these autoimmune disorders. Patients with clinically amyopathic dermatomyositis (CADM) or those with anti-CADM140/MDA5 antibody are especially prone to develop rapidly progressive interstitial pneumonia. We retrospectively analyzed 46 patients with PM/DM admitted to our hospital and identified DM, rapidly progressive disease, honeycomb lung, CADM and extensive ILD as risk factors for recurrence or death. In the presence of two or more risk factors, the sensitivity and specificity for the prediction of death or relapse were 81.3% and 76.7%, respectively. Calcineurin inhibitors have been widely used as induction and maintenance therapy for PM/DM-associated ILD. Recently we reported the benefit of
tacrolimus on the disease-free survival and event-free survival of the patients with PM/DM-associated ILD. Among those patients treated with tacrolimus, poor prognostic factors for death, recurrence or severe adverse event were identified as acute progression of the disease, honeycomb lung, forced vital capacity (FVC) less than 80% and having DM. The potential effectiveness of an intensive therapy protocol with triple therapy that comprises high-dose corticosteroids, calcineurin inhibitors and cyclophosphamide has been reported.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Lupus* at [Lupus](#).

**39. The risk of ischemic stroke in major rheumatic disorders**

**Citation:** *Journal of Neuroimmunology*, December 2014, vol./is. 277/1-2(1-5), 0165-5728;1872-8421 (15 Dec 2014)  
**Author(s):** Behrouz R.  
**Language:** English  
**Abstract:** Rheumatic disorders (RD) are a range of conditions associated with inflammation of joints and connective tissue. They can manifest beyond the musculoskeletal system. Recent focus has been placed on the association of ischemic stroke with these conditions. Traditional vascular risk factors seem to be more prevalent in patients with certain types of RD than in the general population, but these factors do not fully explain the enhanced vascular risk in this population. Four major RD will be discussed in terms of their relationship with ischemic stroke: rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, and psoriatic arthritis.  

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Journal of neuroimmunology* at No link? Ask Salisbury Healthcare Library - please click here to request article.

**40. The role of microRNAs in cellular senescence and age-related conditions of cartilage and bone: A review**

**Citation:** *Acta Orthopaedica*, 2015, vol./is. 86/1(92-99), 1745-3674;1745-3682 (2015)  
**Author(s):** Weilner S., Grillari-Voglauer R., Redl H., Grillari J., Nau T.  
**Language:** English  
**Abstract:** Background and purpose - We reviewed the current state of research on microRNAs in age-related diseases in cartilage and bone. Methods - PubMed searches were conducted using separate terms to retrieve articles on (1) the role of microRNAs on aging and tissue degeneration, (2) specific microRNAs that influence cellular and organism senescence, (3) microRNAs in age-related musculoskeletal conditions, and (4) the diagnostic and therapeutic potential of microRNAs in age-related musculoskeletal conditions. Results - An increasing number of studies have identified microRNAs associated with cellular aging and tissue degeneration. Specifically in regard to frailty, microRNAs have been found to influence the onset and course of age-related musculoskeletal conditions such as osteoporosis, osteoarthritis, and posttraumatic arthritis. Both intracellular and extracellular microRNAs may be suitable to function as diagnostic biomarkers. Interpretation - The research data currently available suggest that microRNAs play an important role in orchestrating age-related processes and conditions of the musculoskeletal system. Further research may help to improve our understanding of the complexity of these processes at the cellular and extracellular level. The option to develop microRNA biomarkers and novel therapeutic agents for the degenerating diseases of bone and cartilage appears to be promising.  

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Acta orthopaedica* at No link? Ask Salisbury Healthcare Library - please click here to request article.

**41. Thoracic Manifestations of Connective Tissue Diseases**

**Citation:** *Current Problems in Diagnostic Radiology*, January 2015, vol./is. 44/1(47-59), 0363-0188;1535-6302 (01 Jan 2015)  
**Author(s):** Ruano C.A., Lucas R.N., Leal C.I., Lourenco J., Pinheiro S., Fernandes O., Figueiredo L.  
**Language:** English  
**Abstract:** Connective tissue diseases (CTDs) comprise several immunologic systemic disorders, each of which associated with a particular set of clinical manifestations and autoimmune profile. CTDs may cause numerous thoracic abnormalities, which vary in frequency and pattern according to the underlying disorder. The CTDs that most commonly involve the respiratory system are progressive systemic sclerosis, systemic lupus erythematosus,
rheumatoid arthritis, Sjogren syndrome, polymyositis, dermatomyositis, and mixed connective tissue disease. Pulmonary abnormalities in this group of patients may result from CTD-related lung disease or treatment complications, namely drug toxicity and opportunistic infections. The most important thoracic manifestations of CTDs are interstitial lung disease and pulmonary arterial hypertension, with nonspecific interstitial pneumonia being the most common pattern of interstitial lung disease. High-resolution computed tomography is a valuable tool in the initial evaluation and follow-up of patients with CTDs. As such, general knowledge of the most common high-resolution computed tomographic features of CTD-related lung disease allows the radiologist to contribute to better patient management.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Current problems in diagnostic radiology](http://www.ncbi.nlm.nih.gov/pubmed) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 42. Undifferentiated Connective Tissue Disease at risk for systemic sclerosis (SSc) (so far referred to as very early/early SSc or pre-SSc)

**Citation:** Autoimmunity Reviews, March 2015, vol./is. 14/3(210-213), 1568-9972;1873-0183 (01 Mar 2015)  
**Author(s):** Valentini G.  
**Language:** English  
**Abstract:** In the last few years, a number of studies have been published on a condition characterized by Raynaud's phenomenon (RP) associated with systemic sclerosis (SSc) marker autoantibodies and/or scleroderma-type capillaroscopic abnormalities and referred to as very early/early SSc. The present review is devoted to analyze pathophysiologic, clinical, and evolutive aspects of the condition that would induce to label it as Undifferentiated Connective Tissue Disease at risk for SSc and to split it into 3 subsets (i.e. RP associated to marker autoantibodies and scleroderma-type capillaroscopic abnormalities; RP associated to marker autoantibodies in the absence of scleroderma-type capillaroscopic abnormalities; and RP associated to scleroderma-type capillaroscopic abnormalities without any detectable marker autoantibody), which have been shown to carry different degrees of risk, but not the certainty, to develop overt SSc over time. This nosographic approach is instrumental to plan future studies devoted to investigate validated biomarkers heralding the development of major vascular disease manifestations as well as skin and/or organ fibrosis in patients at risk.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Autoimmunity reviews](http://www.ncbi.nlm.nih.gov/pubmed) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 43. Update on the diagnosis and management of Behcet's disease

**Citation:** Open Access Rheumatology: Research and Reviews, December 2015, vol./is. 7/(1-8), 1179-156X (30 Dec 2014)  
**Author(s):** Rokutanda R., Kishimoto M., Okada M.  
**Language:** English  
**Abstract:** Behcet's disease is a multi-organ disorder that is more common in countries around the Silk Road, and manifests as mucosal ulcers and skin lesions, and with ocular involvement. As a systemic disease, it can also involve gastrointestinal organs and the central nervous or cardiovascular systems. Although the etiology of Behcet's disease is not clearly identified, the pathogenesis of the disease is most commonly hypothesized as a profound inflammatory response triggered by an infectious agent in a genetically susceptible host. As there are no single specific manifestations or specific diagnostic tests, various diagnostic criteria have been proposed around the world, and, among them, the International Study Group criteria have been most commonly used. As the clinical expression of Behcet's disease is heterogeneous, the treatment should be individualized based on involved organs, severity of the disease, and patient's background. The choice of therapeutic agents is limited by lack of clinical trials and is based largely on case reports, case series, and several open-label clinical trials. Corticosteroids, colchicine, and traditional immunosuppressive agents, including azathioprine and cyclosporine, have been used for the treatment of Behcet's disease. Recently, tumor necrosis factor (TNF) inhibitors have become available for several rheumatic diseases, and considerable published data suggest that TNF inhibitors represent an important therapeutic advance for patients with severe and resistant disease, as well as for those with contraindications or intolerance to these treatments.

**Publication type:** Journal: Review  
**Source:** EMBASE
44. Vasculitis in antiphospholipid syndrome

Citation: Rheumatic Disease Clinics of North America, February 2015, vol./is. 41/1(109-123), 0889-857X;1558-3163 (01 Feb 2015)

Author(s): Lally L., Sammaritano L.R.

Language: English

Abstract: The major manifestations of antiphospholipid syndrome (APS) are caused by thrombosis within the venous or arterial vasculature, whereas the vascular lesions in systemic vasculitis result from an inflammatory infiltrate in the vessel wall. There is an association between vascular thrombosis and inflammation, however, as vasculitis can occur in APS and thromboembolic complications are seen in systemic vasculitis. Although differentiating between vasculitis and antiphospholipid-associated thrombosis can be difficult, it may be crucial to do so given the different therapeutic implications for immunosuppression or anticoagulation. This article explores the relationship between thrombosis and inflammation as it relates to APS and systemic vasculitis.

Publication type: Journal: Review

Source: EMBASE

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British Society for Rheumatology

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