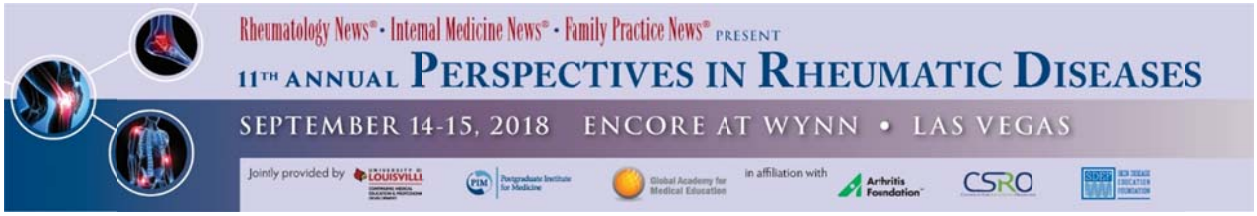

OVERALL 2018 CONFERENCE NEEDS ASSESSMENT

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PROGRAM OVERVIEW

Rheumatology News, Internal Medicine News, and ***Family Practice News*** present the **11th Annual Perspectives in Rheumatic Diseases**, a continuing medical education conference that explores the latest advances in the treatment and management of rheumatic diseases. This activity has been designed to provide a forum for rheumatologists, family practice physicians, internists, nurses, nurse practitioners, pharmacists and physician assistants to receive relevant and timely information regarding the most recent developments in managing patients with rheumatic diseases. By remaining current on the advances in the treatment of rheumatic diseases—particularly the newest evidence regarding the optimum use of the biologic agents—clinicians will be able to provide state-of-the-art therapeutic options to their patients.

A nationally renowned group of faculty leaders will analyze the many areas of research relevant to, and best practices in management of, a wide range of rheumatologic conditions including ankylosing spondylitis, gout, myositis, osteoporosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, and systemic lupus erythematosus. Faculty will also discuss management of comorbidities associated with rheumatic diseases, including gastrointestinal complications and pain. Special focus will be given to the role of biosimilar agents. All sessions offer evidence-based lectures from leading experts while providing an opportunity for participants to engage in interactive case presentations and panel discussions. This conference will help clinicians who manage patients with various rheumatic diseases maintain and improve their clinical diagnostic and therapeutic skills, leading to improved patient care and optimal patient outcomes.

Practice surveys indicate that more than half of patients' rheumatologic conditions receive their care from family physicians, many of whom are not familiar with or comfortable using current medications to treat these diseases and are not aware of the recent innovations in management. In response to this finding, this meeting offers attendees the opportunity to follow their choice of agendas with small group breakouts: one track is designed for the rheumatologist, and one track targeted to the primary care clinician.

Learning Objectives

After completing this live activity, participants should be better able to:

- Identify the potential gastrointestinal complications that commonly emerge in the setting of rheumatologic disease, including those induced by immunological therapies.
- Design effective multidisciplinary strategies for managing gastrointestinal complications in patients with autoimmune disorders.
- Establish treatment plans for gout that achieve targeted levels of serum uric acid.
- Integrate imaging options to aid in the diagnosis of gout.
- Recognize evidence-based recommendations for dosing urate-lowering therapies to optimize efficacy in patients with gout.
- Develop monitoring regimens to measure serum urate levels.
- Identify patients at elevated risk of osteoarthritis so as to initiate preventive interventions.
- Compare and contrast the safety, efficacy, and mechanisms of various agents available for managing pain in the context of autoimmune disorders.
- Demonstrate awareness of current guidelines for management of psoriasis.
- Outline treatment plans for psoriasis that consider the use of new agents, with new mechanisms, and that include strategies for modifying treatment as needed based on results and patient satisfaction.
- Create a treatment plan for psoriatic arthritis that incorporates tools for assessing the impact of psoriatic arthritis and that anticipates the potential need to switch or augment therapy.
- Describe the safety and efficacy of available agents for psoriatic arthritis
- Identify the various cytokine pathways that underlie the process by which rheumatoid arthritis develops and progresses and that serve as potential targets for therapy.
- Discuss current ACR/EULAR guidelines for managing rheumatoid arthritis, including the treat-to-target approach.
- Design effective treatment strategies for managing rheumatoid arthritis
- Describe the ACR/EULAR classifications used in the diagnosis of scleroderma.
- Design effective treatment strategies for the various manifestations of localized and systemic scleroderma.
- Summarize current and emerging research on the mechanisms of the pathology of systemic lupus erythematosus.
- Review data from clinical trials – including failed trials – on candidate therapies that target various pathways involved in systemic lupus erythematosus.
- Outline the current and emerging therapeutic options that target established and newly recognized pathways in the pathogenesis of ankylosing spondylitis.
- Clinically identify vasculitis and its mimics and how to institute appropriate therapy.

EVALUATIONS OF 10TH ANNUAL PERSPECTIVES IN RHEUMATIC DISEASES 2017

1. This activity should improve my: Medical or Practice Knowledge. N=229

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree

56%	35%	6%	0%	1%

2. This activity should improve my: Procedural or Cognitive Skills. N=229

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
45%	31%	18%	4%	<1%

3. This activity should improve my: Practice Behavior. N=XXX

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
44%	33%	17%	<1%	<1%

4. Based on the content of the activity, what will you do differently in the care of your patients and/or regarding your professional responsibilities? N=XXX

Statement	% Responding
Implement a change in my practice/workplace.	19%
Seek additional information on this topic.	29%
Implement a change in my practice/workplace and seek additional information on this topic.	29%
Do nothing differently. Current practice/job responsibilities reflect activity recommendations.	22%
Do nothing differently as the content was not convincing.	0%
Do nothing differently. System barriers prevent me from changing my practice/workplace.	1%

REPRESENTATIVE COMMENTS ON POST-MEETING ACTIONS FROM 2017 CONFERENCE

The following comments were provided in response to the request, "If you anticipate changing one or more aspects of your practice and/or professional responsibilities as a result of your participation in this activity, please describe how you plan to do so."

- Start DMARDS Rx early in treating arthritis.
- Learn more about HLS=B5801 allele in allopurinol toxicity
- I would take the evidence and use evidence-based medicine to implement
- Apply a metric in my record keeping in RA patients
- Conduct regular conferences with colleagues, and discuss similar cases, intervention and management
- Monitor for co-morbidities
- Collaborative care model
- Know the new treatment modalities for various diseases sates and know the MOA to apply to day to day practice. Know side effects associated with meds so that it can be applied to different patient groups with different comorbidities
- Follow new guidelines
- Look into new medications
- Educate my patients more than I already do. Advise them of new treatments available
- I will aggressively treat RA and PsA patients and refer to a rheumatologist if patients don't respond to treatment
- I will inform my patients that the depression and fatigue that they experience is a result of their diseases and that they will likely feel significantly better with appropriate treatment
- More intensive lupus monitoring broader use of non-anti TNFs in psoriasis
- Management of chronic pain using SNRIs
- Provide more education as learned from this conference
- I will look for undiagnosed rheumatic patients in my practice
- Being more aggressive with treatment of PsA
- Treat gout aggressively.
- Address CV risk in patients with arthritis
- Feel more comfortable with less frequently used meds and understand their optional benefits for therapy in certain selceted patients

BEST PRACTICES AND GOALS: ANKYLOSING SPONDYLITIS

Axial spondyloarthritis (axSpA) refers to a group of chronic inflammatory disease mainly involving the axial skeleton. In many cases, the disease progresses to involve the spine, at which point it is considered to be ankylosing spondylitis (AS). AS causes chronic inflammation of the spine and sacroiliac joints; over time, the fusion of tendons and ligaments around the bones and joints typically lead to swelling and irritation. AS is the most common form of the spondyloarthritides, seen in about 0.1% to 0.5% of the adult population. Although it can occur at any age, AS most often strikes men in their teens and 20s. Other types of these axial spondyloarthitides include peripheral spondyloarthritis, causing pain and swelling typically in the arms and legs; reactive arthritis; psoriatic arthritis; and enteropathic arthritis/spondylitis associated with inflammatory bowel diseases (ulcerative colitis and Crohn's disease)

AS can often be diagnosed early, before radiologic damage is evident. However, because many characteristics of AS mimic the symptoms of a wide range of other diseases, the differential diagnosis can be a clinical challenge. In many cases, patients are seen by several specialists before receiving the correct diagnosis. It is estimated that a correct diagnosis is delayed on average, by 5 years. Consequently, they are often diagnosed late, after permanent damage has occurred.

The treatments approved for use in patients with AS in the United States include NSAIDs and biologic agents, including 5 anti-TNF agents (adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab). However, about 30% to 40% of patients do not respond to anti-TNF drugs, a situation that drives the search for more effective medications. Recently, a number of investigators have turned their attention to the possibility of inducing long-term remission with early intervention, particularly by using an aggressive approach that includes biologic agents.

Much attention has been devoted to the development of biologic agents that target different pathways. The IL-17 pathway has recently been identified as a key factor in the pathogenesis of inflammatory arthritis and thus as a potential promising target for its treatment. There are 6 known members of the IL-17 family (A through F). IL-17A was the first such cytokine identified and is the subject of extensive research. In the context of arthritis, the focus is on the role of IL-17 in bone metabolism. IL-17A has been shown to induce production of bone-destructive cytokines and to increase bone resorption. (This is especially true when IL-17A is combined with TNF and IL-1). Conversely, inhibition of IL-17A produces an anti-inflammatory effect and reduces bone destruction. AS involves development of bony growths within the ligaments of intervetebral joints, known as syndesmophytes. Such ectopic bone growths contribute to spinal stiffness, the classic sign of AS. It seems somewhat counterintuitive, then, to block IL-17A activity, since the cytokine participates in breaking down bone. The resolution of this paradox apparently lies in the fact that mesenchymal cells from vertebral ligaments have a different anatomical origin and respond differently to cytokine activity.

Secukinumab, a first-in-class interleukin-17A (IL-17A) inhibitor, was approved in 2016 and is indicated for both AS and psoriatic arthritis. Secukinumab has demonstrated efficacy in clinical trials: nearly 70% of patients given the drug as first-line therapy for AS achieved ASAS20, and 50% of patients who were intolerant or had an inadequate response to anti-TNF therapy achieved ASAS30 at week 16 compared to

placebo. Data indicate that early treatment with this agent is likely to improve outcomes. In contrast to the situation with anti-TNF agents, the use of secukizumab has not been associated with increased risk for Guillain Barré syndrome, a demyelinating condition that causes severe muscle weakness and paralysis. Use of secukizumab for AS has now been integrated into ASAS/EULAR recommendations; the main treatment target is remission, with low disease activity regarded as a secondary target.

Another IL-17A agent, ixekizumab, is currently approved for plaque psoriasis and is under investigation as a potential drug for treatment of AS. Other agents in clinical trials that target other pathways involved in axial spondyloarthritis (of which AS is a subset) include rituximab (CD20 monoclonal antibody), which has proven efficacy; ustekinumab (antibody to IL-12/23), which has shown probable efficacy in a small study; apremilast, a PDE-4 inhibitor, with equivocal results; and tofacitinib, a JAK3 inhibitor, also with equivocal efficacy.

The optimal treatment of ankylosing spondylitis calls for a combination strategy that involves medications to reduce inflammation or suppress immunity, physical therapy, and exercise. Clinicians need education to keep abreast of the latest findings concerning the pathophysiology of the axial spondyloarthritides and new and emerging treatment choices for improving patient outcomes.

EDUCATION AND PRACTICE GAPS: ANKYLOSING SPONDYLITIS

- Clinicians are challenged to differentiate ankylosing spondylitis from other forms of spondyloarthtitides.
- Because early aggressive treatment appears to improve outcomes, earlier diagnosis of AS is needed.
- Clinicians need a better understanding of how to use novel treatments for patient management.

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BEST PRACTICES AND GOALS: GASTROINTESTINAL ISSUES IN THE RHEUMATIC PATIENT

Virtually any systemic autoimmune disorder can trigger gastrointestinal (GI) symptoms and complications. People with systemic autoimmune disorders experience comorbid symptoms and complications problems at a higher rate than do individuals without these disorders, due largely to the higher levels of inflammation and impaired immunity caused by rheumatic diseases. Further complicating the clinical picture is the fact that medications commonly used to treat these diseases often cause GI adverse effects. Clinicians are challenged to provide effective, comprehensive treatment for their rheumatology patients that addresses the primary disease and resolves symptomatic complaints while minimizing the risk for GI complications.

The risk of developing an upper or lower GI event is up to 70% higher in individuals with rheumatoid arthritis compared to those without RA. Such events are more likely to be serious, potentially requiring hospitalization. Common complications include bleeding, GI perforation, ulcers, esophagitis, diverticulitis, and colitis. Upper GI problems are frequently associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs), while lower GI problems may arise with use of corticosteroids.

The pathophysiological effects of scleroderma affect the GI tract in up to 90% of patients with this disease. The fibrotic effects of scleroderma can appear in various sites within the digestive tract, affecting motility, digestion, absorption, and excretion. Patients may experience severe symptoms including pain, dysphagia, vomiting, diarrhea, constipation, incontinence, and weight loss. The consequences are not trivial; approximately 10% of deaths from scleroderma are attributed to GI complications.

GI manifestations of systemic lupus erythematosus (SLE) are common and can affect any site in the digestive tract. Lupus enteritis is commonly affects the oral cavity, leading to mucosal ulcers (approximately 50% of patients) and decreased salivation. The esophagus and stomach can be affected by ulcers and perforation. Intestinal manifestations can include dysmotility, vasculitis, malabsorption, and ischemic bowel disease. SLE can also cause damage in the liver, gall bladder, bile ducts, and pancreas.

Sjögren syndrome, an autoimmune disease affecting the salivary and lacrimal glands, is characterized by dry mouth and dry eyes. Symptoms include difficulty swallowing, esophageal atrophy and dysmotility, epigastric pain, dyspepsia, and nausea. Other organ systems, including the bowels, liver, and pancreas, may be involved.

Ankylosing spondylitis is associated with inflammatory bowel disease and reactive arthritis. Systemic vasculitis (polyarteritis nodosa) often involves mesenteric ischemia and abdominal pain in up to 70% of patients. GI ulceration, most commonly affecting the jejunum, is found in approximately 6% of patients with polyarteritis nodosa. Inflammatory muscle disorders such as polymyositis and dermatomyositis can manifest along the entire length of the digestive tract, especially the proximal esophagus, contributing to complaints of dysphagia, regurgitation, bloating, and constipation. Up to 60% of patients with Behçet disease have gastrointestinal involvement.

Pain relief is an integral part of most treatment plans for many rheumatic disorders, but drugs used for pain can contribute to GI complications. For example, non-narcotic analgesics pose a risk for liver damage. Narcotic analgesics (opioids) can induce nausea, vomiting, dry mouth, and constipation. NSAIDs can cause stomach upset and ulcers. With short-term use, corticosteroids can cause fluid retention, increased appetite, and weight gain; with long-term use, adverse events may include osteoporosis and hypertension. Disease-modifying antirheumatic drugs (DMARDs) are associated with renal or liver toxicity and gastrointestinal disturbance. Some DMARDs may also interact with other drugs, such as NSAIDs, that are used to treat rheumatologic conditions, further exacerbating their adverse GI effects. Newer biologic agents, including TNF-alpha blockers, are often associated with GI complications, including infections and perforation.

Clinicians should be vigilant concerning the development of gastrointestinal complaints in their patients with rheumatic conditions. Screening tools may be of value. For example, the updated UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract questionnaire (SCTC GIT 2.0) is a validated instrument with subscales for assessing symptoms in 7 domains: reflux, distention and/or bloating, diarrhea, fecal soilage, constipation, emotional well-being and social functioning, and a total gastrointestinal score.[Khanna] The Patient-Reported Outcomes Measurement Information System (PROMIS) has been validated in systemic sclerosis and is being increasingly used in idiopathic gastrointestinal disorders such as IBD and IBS. Clinicians should also interrogate patients about the impact of their symptoms on quality of life and should target those symptoms that are identified as most bothersome. In addition, clinicians should be especially vigilant in identifying patients at risk for malnutrition, which is associated with increased disease severity and poorer prognosis.[Emmanuel] The malnutrition universal screening tool (MUST) can be useful in identified patients at various degrees of risk for malnutrition.[Baron]

In many cases, referral to other specialists may be appropriate. In addition to the rheumatologist in charge of managing the main disease, members of a multidisciplinary team might include gastroenterologists, dietitians, radiologists, nurse practitioners, and physician assistants. Tests for making a differential diagnosis of gastrointestinal complaints include endoscopy, gastric scintigraphy,

hydrogen breath test, radiography, CT, MRI, and so on.[Emmanuel] No therapy is available that can reverse the pathophysiology of systemic involvement of the GI tract. Therapeutic management depends on the specific symptoms present, on the underlying disease, and on the risk for potential drug interactions and adverse effects. In some cases, specific agents might provide targeted symptom relief, such as proton pump inhibitors for GERD or naloxegol for opioid-induced constipation. Results of ongoing clinical trials will clarify whether the use of novel these gut-mucosa-targeted agents such as prokinetic agents (eg, prucalopride) or secretagogues (eg, linaclotide and lubiprostone) offer efficacy for patients with rheumatic diseases.[Emmanuel]

EDUCATION AND PRACTICE GAPS: GASTROINTESTINAL ISSUES IN THE RHEUMATIC PATIENT

- While the focus of managing rheumatologic disorders is on addressing the skeletal, muscular, and dermatologic symptomatology, clinicians need to consider the potential for serious complications that can potentially affect one or more sites along the digestive tract.
- As the therapeutic options for treating rheumatologic diseases continue to expand, clinicians need to increase their awareness of the potential GI adverse effects and drug interactions.
- Clinicians should be prepared to offer their patients treatment for GI symptoms that is compatible with the therapeutic strategy targeting the underlying rheumatologic disease.

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BEST PRACTICES AND GOALS: GOUT

Gout is the most common inflammatory arthritis among adults in Western nations; its prevalence exceeds that of rheumatoid arthritis.[Singh 2016; Doherty 2012] The underlying pathophysiology of gout is well understood: It is a disease of crystal deposition caused by persistent elevation of serum urate (sUA) levels above the saturation point for monosodium urate (MSU) crystal formation.[Doherty 2012] A leading risk factor for development of gout is lifestyle, especially obesity and excessive intake of purines, alcohol, and fructose.[Fay] Use of certain medications (eg, diuretics) can increase risk, as can the presence of comorbid conditions including diabetes, metabolic syndrome, hypertension, cardiovascular disease, and chronic kidney disease.

Up to 40% of patients with hyperuricemia have asymptomatic sUA deposits around joints. The risk for recurrent acute attacks of gout is associated with sUA levels above approximately 6.0 mg/dL; but, according to an MD-IQ quiz, 37% of the respondents did not know the level of sUA that is associated with higher risk for recurrent attacks. Recent evidence indicates that even “normal” levels of sUA may play a role in cardiovascular, renal, skeletal, and metabolic disorders and that levels <6.0 mg/dL should be considered as normal for healthy individuals. According to recent practice data, an estimated 40% to 70% of patients with gout who are receiving the accepted current standard of care are not being successfully treated to low enough target levels of sUA. Clinicians would benefit from education that reviews the target levels of serum uric acid to minimize gout attacks and related consequences.

Diagnosis of gout can be confirmed through visualization of monosodium urate crystals in the synovial fluid through such modalities as conventional radiography, ultrasonography, and MRI. However, aspiration of synovial fluid, although the standard of care, is often deferred because of inaccessibility of small joints, patient assessment during intervals between flares, or clinicians’ unfamiliarity with the technology. Dual energy computed tomography (DECT) is a relatively new imaging modality that provides a noninvasive alternative to synovial fluid aspiration. In addition to providing greater sensitivity for erosion detection compared to conventional radiography, DECT can identify and color-code tophaceous material and provide an overview of the tophus burden of a joint area. Clinicians need education about new and emerging imaging modalities to better diagnose gout.

Gout is a highly treatable disease; in many cases appropriate management can prevent future attacks and can often lead to a cure.[Doherty] Because the disease usually remains unrecognized unless symptoms develop, most patients do not seek treatment until they experience an acute flare. Patients often will present to a primary care provider (PCP) (eg, internist, family doctor, or podiatrist), whose approach is aimed at treating current symptoms using NSAIDs and corticosteroids. Ideally, the importance of lifestyle changes, including diet and alcohol consumption, is included in the overall treatment plan. Often, however, PCPs fail to offer comprehensive treatment that is aimed at long-term management or cure.

Part of the confusion among clinicians on how best to treat gout arises from the fact that different specialty societies – including the American College of Physicians (ACP), The American College of Rheumatology (ACR), and the European League Against Rheumatism (EULAR) – have produced guidelines that offer conflicting recommendations.[Qaseem; Khanna + Fitzgerald 2012; Khanna + Khanna 2012; Kiltz] Of these, the EULAR guidelines recommend a treat-to-target approach. In addition, it is necessary to treat gout not as an episodic attack but rather as a chronic disease. Clinicians need education about the similarities and differences between the various guidelines, as well as the need to develop long-term strategies that both address acute flares and prevent future ones**.**

Despite the availability of various medications and recommendations for treating gout, management of the disease remains poor. At least 3 population-based studies (in the United States, United Kingdom, and Taiwan) have reported that gout is significantly undertreated. In a 2016 survey among primary care physicians and rheumatologists, 89% of respondents agreed that achieving serum uric acid levels <6 mg/dL – the goal established by ACR – is imperative, yet only 51% reported that their patients achieve this goal. Nearly 9 out of 10 clinicians said they wished there were additional treatment options available. New agents or combinations have been introduced, including febuxostat, pegloticase, lesinurad, a combination of lesinurad and allopurinol, and canakimumab. Other agents are under investigation. Unfortunately, many clinicians fail to prescribe gout medications at guideline-recommended effective doses, and they are hesitant to titrate the dosage to achieve optimal results. Clinicians would benefit from education that reviews the efficacy and safety of each of the available and emerging agents, including appropriate dosages.

The Task Force Panel of the ACR tasked with developing the gout guidelines recommend regular monitoring of serum urate every 2 to 5 weeks during titration of urate-lowering therapy, and continuing measurements every 6 months once target levels have been achieved.[Khanna + Fitzgerald] In addition to providing a gauge of treatment efficacy, regular sUA assessment also helps monitor (and promote) adherence to therapy. Finally, several comorbidities are commonly associated with gout.[Vaccher] Clinicians should be aware of the risk for potential adverse events and other complications arising from the presence of comorbidities in a patient who is being treated for gout. Clinicians would also benefit from education that provides clear guidance about the appropriate use of available medications, that addresses myths and misconceptions about the disease, and that presents evidence-based strategies for nonpharmacologic and supportive care for patients with gout.

EDUCATION AND PRACTICE GAPS: GOUT

- Clinicians need education on the various imaging options to aid in the diagnosis of gout.
- Clinicians must measure serum urate levels and should know the target levels of sUA to control hyperuricemia.
- Clinicians need to develop comprehensive treatment plans that address gout as a curable chronic disease requiring the appropriate first-line treatment as well as ongoing monitoring and management.
- Clinicians need to prescribe sufficient doses of urate-lowering therapies to be optimally effective.

- ❖ Clinicians need to develop treatment plans using monotherapy or appropriate sequential combinations of agents to achieve target low serum urate levels.
- ❖ Clinicians should facilitate treatment adherence through a treat-to-target approach.
- ❖ Clinicians should minimize risk of progression of hyperuricemia to chronic kidney disease and potential cardiovascular mortality.

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BEST PRACTICES AND GOALS: PAIN MANAGEMENT IN RHEUMATIC DISEASES

According to the American College of Rheumatology Pain Management Task Force, pain plays a central role in the clinical spectrum of rheumatic disorders and is the most common complaint of patients presenting to a rheumatologist. Non-severe acute pain represents one of the most frequent complaints of patients presenting to primary care physicians (PCPs), accounting for nearly 50% of all patient visits.[McCarberg 2011] Despite the ubiquity of pain as a symptom, few clinicians have adequate experience with nonopioid pharmacologic and nonpharmacologic modalities of pain management. Instead, they may concentrate on reducing inflammation and modifying the disease. Importantly, in the absence of timely pain assessment and treatment, central nociceptive pathways may undergo potentially irreversible changes that sensitize the system to subsequent inputs and exaggerate pain responses over the long term. About 15% to 30% of patients with autoimmune or rheumatic disorders have a centralized pain state. However, clinicians may not be aware that opioid medications – besides posing a significant risk for addiction and dependence – often are ineffective in central pain states.

The goals of treatment for pain associated with rheumatic conditions are to improve function and reduce global complaints. Effective pain management usually involves combination strategies using pharmacologic analgesics and anti-inflammatories as well as nonpharmacologic interventions such as cognitive-behavioral therapy, exercise, hydrotherapy, massage, mindfulness-based stress reduction (MBSR), and other palliative measures.[Anheyer 2017; Maserejian 2014] This multidisciplinary approach has proved to be highly effective. Effective treatment stratification requires a full assessment of pain

mechanisms by clinical history and examination, as well as objective assessment of synovitis and joint damage. Treatments vary from person to person, and treatment choices may change as the underlying disease progresses. Even though two patients receive the same diagnosis, they may be given different treatments based on the severity and types of problems each one experiences. However, despite current recommendations, fewer than 1 in 3 PCPs would provide advice on exercise, and newer physicians are more likely to provide guidance on lifestyle changes than those in practice for longer durations.[Maserejian 2014]Clinicians must better inform their patients about the key role they play in managing their own pain therapy, for example by reminding them of the importance of adhering to their therapeutic regimens and by tracking and communicating their progress.

Several categories of drugs are available to treat pain resulting from rheumatic diseases. A number of pharmacologic agents have been studied for central pain; the strongest evidence exists for dual reuptake inhibitors (including tricyclic compounds and highly selective reuptake inhibitors of serotonin or norepinephrine or both; SSRI, SNRI) and the anticonvulsants gabapentin and pregabalin. Other data recommend against the use of gabapentinoids for chronic back pain.[Shanthanna 2017] Modest evidence exists for tramadol, older less-selective serotonin reuptake inhibitors, gamma-hydroxybutyrate, and low-dose naltrexone. Three medications, duloxetine, pregabalin, and milnacipran, have received FDA approval for fibromyalgia. However, a recent retrospective analysis found that treatment of fibromyalgia pain is suboptimal. Numerous agents are currently under investigation. PCPs are particularly challenged to identify patients with legitimate medical needs for pain management from those without need who are seeking drugs.[McCarberg 2011] Clinicians would benefit from education that reviews the available (and emerging) pharmacologic interventions for pain management, including how to determine appropriate candidates for each option.

EDUCATION AND PRACTICE GAPS: PAIN MANAGEMENT IN RHEUMATIC DISEASES

- Clinicians need to consistently and adequately assess, monitor, and treat pain in their patients with rheumatologic diseases to improve efficacy and improve quality of life.
- Many clinicians may lack adequate experience with the full spectrum of pharmacologic modalities of pain management.
- As new agents are currently being investigated for pain management, clinicians need to remain current on these developments in order to provide their patients with the best care possible.

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BEST PRACTICES AND GOALS: PSORIASIS

Psoriasis is an inflammatory chronic, immune-mediated systemic disease affecting 3.2% of the adult US population (approximately 8 million people). Characterized by pruritic inflammatory plaques with a chronic remitting and relapsing disease course, psoriasis is associated with significant comorbidities including obesity, metabolic syndrome, cardiovascular disease, psoriatic arthritis, autoimmune disease, psychiatric illness, liver disease, malignancy, chronic obstructive pulmonary disease, sleep apnea, and alcohol abuse, resulting in a markedly decreased quality of life.[Oliveira Mde 2015; Kim 2010] Psoriatic arthritis develops in 10% to 30% of these patients approximately 10 years after the onset of skin disease.[Mease 2014; Young 2017]

Clinicians may lack a thorough understanding of psoriasis beyond its dermatologic manifestations. For example, in a recent survey, 75% of dermatologists and rheumatologists acknowledged that psoriatic arthritis may be underdiagnosed because of a failure to connect skin and joint symptoms. Fewer than half of primary care physicians reported screening psoriasis patients for cardiovascular risk factors, as recommended by National Psoriasis Foundation guidelines.[Parsi]. Thus, accurate diagnosis and effective management of psoriasis and its comorbidities requires a deeper understanding of its pathophysiology.

In a recent survey of dermatologists, 92% acknowledged that the disease burden of psoriasis is frequently underestimated and that the condition is undertreated.[van de Kerkhof 2015] Among patients with psoriasis, 24% to 35% of those with moderate psoriasis, and 9% to 30% with severe psoriasis, were untreated.[Armstrong, 2017] In a 2016 survey, only 1 in 3 patients were satisfied with their treatment plan, and more than 80% reported emotional impact resulting, in part, from lack of knowledge about what to expect.[Gould 2016] Barriers to guideline adherence frequently cited by

clinicians include lack of knowledge and fear of side effects, suggesting the need for further educational strategies.[van de Kerkhof 2015]

Clinicians also need expanded knowledge and improved clinical confidence in assessing disease severity, treatment results, and quality of life.[Gottlieb 2016] Clinicians should discuss treatment goals with patients, stressing that control of the disease is the primary aim and that remission may be achievable with appropriate use of therapies in appropriately chosen patients. Treatment goals for psoriasis include rapidly controlling the disease process; achieving and maintaining remission; minimizing adverse events; and enhancing quality of life. For mild-to-moderate disease, topical therapies may suffice. Severe psoriasis (affecting >5% to 10% of body surface area) requires phototherapy or systemic therapies such as retinoids, methotrexate, cyclosporine, apremilast, or biologic immune modifying agents.[Young 2017] Keeping the regimen simple and acceptable to the patient can maximize adherence.

The National Psoriasis Foundation (NPF) suggests that clinicians need to understand and use defined treatment targets, citing clinical assessment tools including changes in BSA (Body Surface Area), Psoriasis Area and Severity Index (PASI), Physician Global Assessment (PGA), and Dermatology Life Quality Index (DLQI).[Armstrong 2017] The treat-to-target strategy allows patients and their health care providers to take better control of psoriatic disease by setting specific targets and goals for improved health outcomes.[NPF Treat to Target, 2017] However, many clinicians have not adopted treat-to-target strategies for their patients and thus are not evaluating progress and adjusting treatments as recommended.[Duffy 2016]

The advent of biologic agents has allowed treatment goals for psoriasis to be more aggressive and has made remission a potential and realistic goal.[Feldman 2017] Biologic immune-modifying agents act through targeted inhibition of specific cytokines associated with inflammatory immune responses and skin lesions.[Leonardi 2015, Young 2017] Several biologic agents have already been approved for the treatment of psoriasis, including a biosimilar, and others are currently under investigation.

However, despite the availability of guidelines and effective treatments, a substantial number of patients with moderate-to-severe psoriasis are not receiving appropriate, aggressive management.[Eissing 2016] Barriers to providing optimal care include lack of knowledge (regarding the guidelines and treatments) and poor understanding and appreciation of psoriasis comorbidities.[Eissing 2016] Clinicians need education on these topics so they can to optimally manage their patients with psoriasis. Primary care clinicians would also benefit from guidance regarding when to refer patients with psoriasis to specialists.[Gottlieb 2016]

EDUCATION AND PRACTICE GAPS: PSORIASIS

- Clinicians need to understand the pathophysiology of psoriasis and the associated comorbidities of the disease in order to optimize treatment selection.
- Clinicians require substantive knowledge and improved clinical confidence in assessing disease severity, treatment results, and impact on a patient's quality of life
- Many clinicians fail to apply updated treat-to-target guidelines for diagnosis, treatment, and assessment of progress in patients with psoriasis.
- Despite available systemic therapies, a significant proportion of patients with psoriasis are not receiving guideline-concordant care.

- ❖ Because psoriasis is a chronic condition and most patients with psoriasis are dissatisfied with their treatment, clinicians must be prepared to make ongoing modifications in patient treatment.
- ❖ Clinicians must keep pace with treatment advances to incorporate such therapies into clinical practice as prudently as possible to improve outcomes in patients with psoriasis.

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BEST PRACTICES AND GOALS: PSORIATIC ARTHRITIS

The scientific understanding of psoriatic arthritis (PsA) – its natural history, pathogenesis, treatment, and clinical sequelae – continues to advance. This growing body of knowledge mandates that clinicians who care for patients with PsA must keep abreast of results of clinical trials exploring new therapeutic options.

PsA is a clinically diverse inflammatory arthritis that can affect peripheral joints and the axial skeleton. Up to 40% of patients with psoriasis also develop PsA, and many suffer from pain, physical limitations, and disability. If untreated, PsA can cause irreversible damage.[Mease 2014] Duration of disease does not correlate with how rapidly joint destruction may progress; some patients demonstrate progressive disease within the first year after diagnosis. Unless PsA is treated effectively, patients may experience persistent inflammation, progressive and debilitating joint destruction, and increased mortality.[Gottlieb 2016] Furthermore, many patients with PsA have serious comorbidities, primarily cardiovascular disease and inflammation-related insulin resistance leading to diabetes, but also including autoimmune ophthalmic disease, inflammatory bowel disease, and osteoporosis.[Coates 2014]

Clinicians must be prepared to address the identification, assessment, and treatment of PsA; the similarities and differences in the treatment of cutaneous and musculoskeletal manifestations of the disease; and comorbidities and quality-of-life issues. However, persistent gaps in clinicians' awareness of appropriate treatment options means there are unmet needs in the management of PsA. According to the Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP), a population-based survey that included 1005 patients, 101 dermatologists, and 100 rheumatologists, more than one third of dermatologists reported that their greatest challenging in managing PsA patients was in differentiating between PsA and other arthritic diseases.[van der Kerkhof, MAPP]

There also is a gap between patients' and clinicians' perceptions of PsA. In the MAPP survey, nearly half of patients with a diagnosis of psoriasis reported pain in more than 4 joints, while dermatologists reported that only about 19% of their psoriasis patients complained of joint pain. About 87% of dermatologists and 85% of rheumatologists acknowledged that PsA is likely underdiagnosed because

clinicians may not assess joint pain effectively (or at all) in patients with skin symptoms. Only about 7% of dermatologists thought they would need to refer to or involve other specialists in the care of their PsA patients, while 1 in 4 rheumatologists said that delayed referral by dermatologists of patients with PsA is one of their greatest challenges. [MAPP]

Different sets of PsA treatment recommendations have been developed. The European League Against Rheumatism (EULAR) published an algorithm that guides the clinician through serial treatment steps and choice of medications based on the severity of clinical domains involved (ie, arthritis, enthesitis, and spondylitis) and on the patient's response to therapy.[Gossec, EULAR 2016] The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) developed its recommendations based on evidence derived from a literature review of treatment of the various clinical domains, including skin.[GRAPPA] The American Academy of Dermatology (AAD) guidelines recommend that clinicians first ascertain whether a patient with psoriasis also has PsA; patients who have PsA should receive systemic medications that treat both psoriasis and PsA.[Gottlieb 2008] Clinicians need to become familiar with these guidelines and with strategies for optimally applying them in their clinical practice.

For patients with localized mild PsA that affects only 1 or 2 joints, the recommended treatment is NSAIDs with or without intra-articular injections of corticosteroids.[Gossec/Smolen CER2015] Patients whose PsA involves 3 or more joints are at greater risk for joint erosion and functional disability. Experts advise that patients who do not respond adequately to treatment with NSAIDs may need treatment with disease-modifying antirheumatic drugs (DMARDs) such as methotrexate; immunosuppressant medications such as azathioprine, cyclosporine, or leflunomide; or biologic agents to control signs and symptoms. Many of the same medications that are effective in psoriasis are also beneficial in PsA. Anti-tumor necrosis factor (anti-TNF) agents such as certolizumab pegol have emerged as a pivotal treatment for many patients More education is needed about the role of anti-TNF therapy in the management of PsA.

The armamentarium for PsA is rapidly expanding, with additional agents constantly being approved and investigated.[Hilton 2016; Leonardi 2017] As is true of treatment for psoriasis, challenges to the optimal use of therapies for PsA include cost, lack of long-term safety, and lack of efficacy. PsA is undertreated; half of the patients with PsA who participated in the MAPP survey reported they received no treatment or that they were prescribed topical medications only. Among PsA patients, 40% reported being dissatisfied with the long-term safety of conventional oral therapy and 25% reported dissatisfaction with biologic therapy. More than 4 out of 10 PsA patients said that their primary goals of therapy were not met with their current treatment. Tellingly, 88% of patients and 98% of clinicians felt there was a strong or moderate need for better therapy. Nearly half of dermatologists and nearly one third of rheumatologists reported that patients leave their practice because of frustration or dissatisfaction with current therapies.

Finally, there are no treatment algorithms or typical patient profiles to help guide clinicians when switching patients between biologic DMARDs, and only limited data are to be found in the clinical literature.[Merola 2017] Clinicians typically consider disease characteristics, comorbidities,

cardiometabolic risk factors, treatment history, and patient preference when selecting or switching between agents. While the literature suggests that switching between TNF inhibitors may be effective for many patients, switching biologic DMARDs with different mechanisms of action may afford superior outcomes. Clinicians need guidance in selecting initial therapy and in switching therapies when indicated.

EDUCATION AND PRACTICE GAPS: PSORIATIC ARTHRITIS

- Clinicians often fail to assess joint symptoms in patients with psoriasis, causing psoriatic arthritis to remain undiagnosed in up to one third of patients.
- Clinicians need to be aware of the signs and symptoms of psoriatic arthritis and to better assess their patients with psoriasis so that treatment may begin promptly to prevent structural joint damage.
- Clinicians need to stay current on the growing armamentarium of agents for the treatment of PsA to provide optimal care to patients.
- Clinicians must make ongoing modifications to treatment strategies to maximize outcomes and to increase patient satisfaction.

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BEST PRACTICES AND GOALS: RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a complex disease with multiple mechanisms that result in a spectrum of articular and systemic manifestations and associated comorbidities. Treatment of RA is similarly complex, requiring appropriate assessment and evaluation to identify which therapies offer the greatest benefit for individual patients.

The most recent diagnostic criteria are the 2010 RA classification criteria from the ACR/EULAR collaborative initiative, which continue to be extensively validated and well-integrated into clinical practice.[Aletaha 2010; Radner 2014] ACR/EULAR treatment guidelines were most recently updated in 2015, and thus do not include all of the most current available treatment options.[Singh 2015] These guidelines focus on pharmacologic treatment decisions and emphasize the importance of facilitating discussion about individualized decision-making between patients and their clinicians.[Singh] Rheumatologists and primary care providers (PCPs) would benefit from education that keeps them abreast of the latest specialty consensus statements so as to be better prepared to manage patients with RA.

The advent of DMARDs represented a significant advance in the management of RA. However, the probability of achieving American College of Rheumatology criteria (ACR50) with methotrexate alone is about 40%.[Hazlewood] Since research unveiled the role of the proinflammatory cytokine tumor necrosis factor alpha (TNFa) in the pathophysiology of RA, anti-TNFa drugs have become a mainstay of RA treatment. However, up to two-thirds of RA patients have no or only partial response to anti-TNF therapy.[Calabrese; Hetland; Kim; Tanaka]. An even greater percentage lose response over time or experience significant adverse events following treatment with a TNF inhibitor.[Rubbert-Roth] Lack of response means that many patients will need to be switched to another therapy or to treatment with a combination of two or more agents, which increases the risk for adverse events.[Pavelka]

Greater understanding of the underlying pathophysiologic mechanisms of rheumatoid arthritis has led to the development and introduction of new therapies with unique mechanisms of action, including tofacitinib, the first Janus kinase (JAK) inhibitor for use in RA, and tocilizumab, the first biologic DMARD (bDMARD) monoclonal antibody (mAb) targeting the IL-6 receptor. Other newer agents include abatacept (now available in 3 modes of delivery), anakinra, golilumab, infliximab, rituximab, and sarilumab; numerous agents are also under investigation. Canakinumab, which demonstrates anti–IL-1 beta activity, is approved for systemic juvenile idiopathic arthritis.

The goals of RA therapy include achieving remission or low disease activity using a treat-to-target approach.[Smolen] Although biomarkers have not yet been identified that would help determine which patients are likely to respond to a specific therapy, some progress has been made toward the development of a personalized approach to treatment. However, there is still controversy regarding the

most appropriate treatment strategy for patients who fail on a specific biologic agents.[Mehta 2017] Clinicians need education to keep abreast of the current scientific rationale for use of combination therapy, dose escalation, or switching between or among classes of DMARDs and biologic agents.

A particular challenge in the management of patients with RA is the high rate of comorbidities associated with the disease. Among the more common comorbid conditions are diabetes and insulin resistance,[Nicolau 2017] lung disease,[Bluett 2017; Hyldgaard 2017] cardiovascular comorbidities, including numerous components of metabolic syndrome,[Gualtierotti 2017; Müller 2017] and possibly gallstones in women.[Garcia-Gomez 2017] Historically gout was not considered to be a usual comorbidity of RA, but a large population database study in Israel reported a significant proportion of gout in patients with RA versus controls.[Merdler-Rabinowicz 2017] Of concern is an increased risk of several malignancies, including non-Hodgkin lymphoma. In addition to the association between RA and these conditions, biologic agents used in the management for RA can increase susceptibility to infection, tuberculosis, and malignancies. Clinicians must be aware of the elevated risk of comorbid conditions and should continually monitor patients for these diseases throughout the course of treatments.

Recent research has identified an elevated risk of inflammatory and/or rheumatoid arthritis in patients with cancer who are receiving the new immune checkpoint inhibitor drugs (including nivolumab and ipilumumab), which are now the most widely used precision immunotherapy treatments for cancer. Cappelli and colleagues identified 13 patients receiving this treatment who developed rheumatologic complications, including 9 who developed inflammatory arthritis.[Cappelli 2017] They noted that inflammatory arthritis is underappreciated and may have clinically severe consequences. As many as 10% to 15% of patients being treated with immune checkpoint inhibitor drugs may have IA.[Cappelli 2017] Rheumatologists must therefore be aware of all treatments their patients are receiving, and should directly inquire about symptoms of IA in patients undergoing immune checkpoint inhibitor therapy.

EDUCATION AND PRACTICE GAPS: RHEUMATOID ARTHRITIS

- Clinicians lack awareness of the latest understanding of the pathophysiology of rheumatoid arthritis (RA), including the role of interleukin-6 and its receptors (IL-6/IL-6R).
- Because response to treatment of RA is often inadequate or fades with time, even with the use of appropriately selected drugs, clinicians should be prepared to monitor patient response and switch or augment therapy as needed, to reach treatment targets.
- Clinicians may be uninformed about the rapidly evolving guidelines for managing patients with RA. Clinicians may lack guidance in designing appropriate treatment strategies that align individual patient needs with various therapeutic options for RA.

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BEST PRACTICES AND GOALS: SCLERODERMA

Scleroderma refers to a heterogeneous group of chronic autoimmune rheumatic disorders characterized by hardening of the skin.[Brady 2016; Fett 2013] It affects an estimated 300,000 Americans, and about one-third of them have the systemic form. There are 2 major classifications – localized scleroderma (LoS), which is generally benign and is limited to the skin and/or underlying tissues; and systemic sclerosis (SSc), which manifests with cutaneous sclerosis and visceral involvement.[Careta 2015] Each major classification is further subdivided into its own subclassifications: LoS into plaque morphea, generalized morphea, bullous morphea, linear scleroderma, and deep morphea; and SSc into limited cutaneous SSc, diffuse cutaneous SSc, and SSc sine scleroderma.[Fett 2013; Careta 2015] However, it can be challenging to distinguish between the different types of morphea.[Beilsa Marsol 2013] ACR/EULAR guidelines for classification of SSc, published in 2013, were designed for use as entrance criteria into SSc clinical trials; these classifications are not diagnostic, and may overlook early patients.[Vanden Hoogen 2013] They incorporate important elements not previously included: proximal scleroderma, sclerodactyly, digital pit, pulmonary fibrosis, Raynaud phenomenon, and Sc-specific autoantibodies.[Johnson 2015]

The symptoms of scleroderma vary greatly, often depending on the parts of the body affected and the extent to which they are affected. Consequently, scleroderma can range from very mild severity to a life-threatening disorder. Generally, localized scleroderma affects children and SSc is more common in adults. While morphea (LoS) is associated with substantial morbidity but does not affect mortality, SSc has the highest disease-specific mortality of all autoimmune rheumatologic diseases.[Fett 2013] The etiology and pathogenesis of this disease remain unclear.

Diagnosis is based on the individual's symptomatic manifestations; blood work, specialized imaging (Doppler, laser Doppler) and other tests may be necessary depending upon the organs affected.[Zulian 2013] Because many symptoms of scleroderma are similar to those of autoimmune diseases, diagnosis can be difficult, leading to misdiagnoses or missed diagnoses.[Brady 2016] It is important for clinicians to

be educated on the most recent recommendations for diagnostic assessment in order to be able to provide an early diagnosis and promptly initiate treatment.

Currently there is no cure for scleroderma. Treatment is based on symptomatic manifestations, although some patients benefit from treatments that decrease the activity of the immune system, such as methotrexate.[Zulian 2013] SSc that involves the lung, kidney, and heart is frequently treated with corticosteroids and immunosuppressives; in contrast, there are limited options to manage the cutaneous manifestations.[Kuhn 2016] A survey of pediatric rheumatologists and dermatologists who manage children and young adults with juvenile localized scleroderma (JLS) in the UK found substantial variation in their respective use of monitoring tools and treatment approaches.[Hawley 2014] Hematopoietic stem cell transplantation (HSCT) has been shown to prevent disease progression in some SSc patients but is associated with a high incidence of treatment-related mortality.[Farge 2017] The European Society for Blood and Marrow Transplantation (EBMT) recently published guidelines to evaluate SSc patients undergoing HSCT; careful patient selection is needed to minimize mortality.[Farge 2017; Sullivan 2018] Lack of universal guidelines and identification of appropriate candidates can interfere with diagnosis, monitoring, and selection of treatment strategies, leading to suboptimal outcomes.

EDUCATION AND PRACTICE GAPS: SCLERODERMA

- Clinicians lack awareness of how to utilize the ACR/EULAR classifications in the diagnosis of scleroderma.
- Physicians would benefit from education regarding available treatments for the various manifestations of localized and systemic scleroderma.

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BEST PRACTICES AND GOALS: SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is an autoimmune disease with a polymorphic presentation. The various forms of this inflammatory connective tissue disorder – systemic, discoid (cutaneous), drug-induced, and neonatal – can follow an unpredictable pattern of flares and remission. About half of SLE cases progress to involve the kidneys (lupus nephritis). The Lupus Foundation of America estimates that 1.5 million Americans, and at least 5 million people worldwide, have some form of chronic SLE. More than 16,000 new cases of lupus are reported annually in the US.

The complex immunopathology of SLE, the variability in its clinical expression and severity, and the unpredictable response to treatment poses significant challenges to rheumatologists, PCPs, and other clinicians responsible for managing the disease.

Education is needed to help clinicians keep current on research into the pathophysiology of the disease; its potential therapeutic targets; safety and efficacy findings from the latest clinical trials; and strategies for choosing appropriate therapy. The ultimate goal is to develop a personalized approach to diagnosing and managing SLE, one that identifies the specific biomarkers and disease mechanisms active within a given individual and that supports therapeutic choices to offer the best hope for treating SLE.

The Systemic Lupus International Collaborating Clinics (SLICC) group developed a set of diagnosis criteria that include 17 variables derived by expert consensus and statistical analysis using real-life patient scenarios. SLICC criteria require that at least 4 criteria need to be met – including at least 1 clinical criterion and 1 immunologic criterion – to establish a classification of SLE.[Petri 2012] The SLICC criteria demonstrate greater sensitivity (97% vs 83%, $P<0.0001$) but less specificity (84% vs 96%, $P<0.0001$) than the current ACR criteria. The SLICC criteria are considered to be more clinically relevant and will probably identify more patients with clinically defined SLE than would the current ACR criteria. Similarly, validated diagnostic recommendations and disease-specific indices for lupus nephritis in children with SLE have been developed and are evolving into consensus treatment practices.[Wenderfer 2016] Most recently, the British Society for Rheumatology published guidelines on non-renal manifestations of SLE. Unlike prior guidelines, the British Society's version uses clinical descriptions for disease activity severity and offers treatment approaches for each disease activity category.[Gordon 2018a; Gordon 2018b] PCPs are often the initial physicians to evaluate patients with possible SLE; as such, they need to be familiar with the many manifestations of SLE to facilitate early diagnosis.[Pramanik 2014] PCPs also need

familiarity with warning signs that warrant referral to a rheumatologist.[Lam 2016] Clinicians would benefit from education on these new guidelines, including means for integrating them into clinical practice.

Research into the immunopathology of SLE is expanding at rapid pace. These emerging findings, as they become validated, have enormous potential for improving the ability of clinicians to recognize patients at risk for SLE, for recognizing SLE earlier in the disease process, and for identifying potential therapeutic targets. For example, researchers are investigating possible biomarkers and genetic markers that may enable better understanding of the underlying pathophysiology of SLE, while identifying potential targets for emerging therapies.[Wang; Motawi; Navarro Quiroz; Lee; Sá; Kröger; Patra; Hu; Rai; Mahieu] Clinicians would benefit from education that summarizes the most relevant current research findings on the mechanisms of SLE pathology and that provides expert perspectives on the clinical utility of emerging data.

The most recently approved drug for treatment of SLE in the United States is belimumab, a fully human IgG1-lambda recombinant monoclonal antibody directed against B-lymphocyte stimulator that was approved in 2011. Before that, the only approved agents were aspirin (1948) and hydroxychloroquine and corticosteroids (1955). Not all patients respond to belimumab treatment. Given that SLE is a highly heterogeneous disease with variable response to treatment, clinicians may be challenged to find optimal treatment for patients on an individualized basis. In order to optimize ongoing treatment, PCPs and rheumatologists need to work together and communicate to best coordinate care.[Lam 2016]

Recent clinical trials have produced mixed results. Many once-promising drug candidates have proved disappointing, and the search for optimal therapy is ongoing and is exploring a number of pathways.[Merrill; Rovin; Mota; Haarhaus; Mysler; Isenberg 2016; Isenberg 2015; Clause; Scheinberg; Zimmer; Kalunian] Clinicians need to keep abreast of the latest developments in this fast-moving field.

Recent advances in the understanding of SLE disease mechanisms have raised interest in the role the interferon pathway plays in the pathogenesis of SLE. [Kalunian; Merrill; Khamashta; Furie] Clinicians would benefit from education that helps provide context for the flood of data – positive and negative – emerging from clinical trials and that helps them incorporate newly available drugs into treatment plans for appropriately selected patients.

EDUCATION AND PRACTICE GAPS: SYSTEMIC LUPUS ERYTHEMATOSUS

- Clinicians may overlook or mistake the heterogeneous signs and symptoms of systemic lupus erythematosus (SLE) and thus may miss making the diagnosis.
- Clinicians may not be using current findings on the underlying pathophysiological mechanisms of SLE and its various biomarkers to design treatment strategies.
- Clinicians who are unable to keep abreast of results of clinical trials of targeted therapies for SLE may not be providing optimal treatment for their patients.

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BEST PRACTICES AND GOALS: VASCULITIS

Vasculitis, a condition that involves inflammation of the blood vessels, including veins, arteries, and capillaries, is a rare and heterogeneous disease with signs and symptoms that vary widely in type and severity. The condition, however, can be life-threatening as inflamed blood vessels can become weak and stretched, causing aneurysm, or conversely, can narrow and constrict to the point of completely occluding blood flow. This disorder can also damage a wide variety of organ systems, including the skin, joints, lungs, kidneys, gastrointestinal tract, eyes, sinuses, nose, ears, and central nervous system. Vasculitides can affect people of all ages, genders, and ethnicities. There are more than 15 vasculitides affecting the small, medium and large vessels. Although the various forms of vasculitides share many of the same symptoms and treatment courses, each is different; therefore, more research is needed to learn more about the various types of vasculitis and their causes, treatments and remission patterns.

The pathophysiology of vasculitis is not completely understood but is known to be either primary or secondary. Primary vasculitides result from an inflammatory response that targets the vessel walls and has no known cause. Secondary vasculitides may be triggered by a viral infection, a drug, or a toxin or may occur as part of another inflammatory disorder or cancer. In some cases, secondary vasculitis is caused by an autoimmune reaction that produces anti-neutrophil cytoplasm antibodies (ANCA). ANCA-associated vasculitis results in rare autoimmune vasculitides that can damage the small blood vessels of the kidneys, lungs, and eyes. Better biomarkers are needed for guiding management of patients with vasculitis. Large cohorts and technological advances had led to an increase in preclinical studies of potential biomarkers. The most interesting markers described recently include a gene expression signature in CD8+ T cells that predicts tendency to relapse or remain relapse-free in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, and a pair of urinary proteins that are elevated in Kawasaki disease but no other febrile illnesses. According to investigators, a crucial need exists to identify the pathogenic pathways in developing therapeutic modalities. Clinicians need to identify the triggers that initiate the inflammatory response and recognize that the signature of chronic inflammation may not reflect the initial trigger response

Vasculitis is usually classified by the size and type of type of vessels affected, but there is considerable overlap in symptoms among the disorders. Because in many cases the pathogenetic causes cannot be pinpointed, precise and early classification of this family of related disorders is incomplete with many types being known only as “unclassified.” Some patients manifest a persistent vasculitis limited to the skin known as cutaneous vasculitis. Cutaneous vasculitis can be acute, subacute or chronic, but all cases are characterized by a rash that usually presents on the limbs, particularly the lower legs. Some cases of vasculitis are chronic with no period of remission. Long-term treatment with medications often can control the signs and symptoms of chronic vasculitis.

Because of its wide variety of possible presentations, diagnosing vasculitis can be a clinical challenge, especially since classification and diagnostic criteria are still evolving. Diagnosis currently involves clinical evaluation, ANCA testing, angiography, and biopsy.

Treatment is largely designed to reduce inflammation in affected blood vessels, typically by slowing or halting the inflammatory cascade. Common prescription agents used to treat vasculitis include corticosteroids, nonsteroidal anti-inflammatory drugs, immunosuppressants, and cytotoxic therapies. Treatment typically is most successful if the disease is diagnosed early before organ damage occurs. Clinical trials have yielded a wealth of data about less toxic alternatives to standard therapy, including new agents and methods of delivery. All aim to reduce long-term exposure to cyclophosphamide and glucocorticoids and so maintain safety while effectively preventing relapse. Individualized evaluation of risk and treatment selection will help maximize effectiveness and minimize toxicity.

Granulomatosis with polyangiitis (GPA) is a common form of small-vessel vasculitis, remarkable for its tendency toward multisystem manifestations. Standard induction treatment calls for the use of low-dose daily cyclophosphamide (CYC) and glucocorticoids. Treatment goals for newly diagnosed patients include increased survival, induction of remission, reduction of relapse frequency, and minimization of treatment toxicity. Induction and maintenance treatments with CYC, lucocorticoids, and other immunosuppressive therapies improve the disease course, but relapse- and treatment-related toxicity and infections demand consistent, patient-specific monitoring.

EDUCATIONAL AND PRACTICE GAPS: VASCULITIS

- With symptoms that vary widely, clinicians must be familiar with characteristic disease manifestations and the potential disease manifestations of the individual vasculitides.
- Because treatment is more effective when vasculitis is diagnosed and treated early, clinicians need to be aware of possible presentations since classification and diagnostic criteria are still evolving.
- Despite the success of treatments that increase the survival rates of GPA patients, clinicians need to be aware of increased risk of treatment-related toxicity in patients who are inadequately monitored.

References: Vasculitis

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