I34. METABOLIC BONE DISEASES

Juliet Compston

University of Cambridge, Cambridge, United Kingdom

Osteoporosis is characterized by low bone mass and disruption of bone structure, leading to increased risk of fragility fracture. One woman in two and one man in three aged 50 years or older will suffer at least one osteoporotic fracture during their remaining lifetime; these fractures are associated with significant morbidity, increased mortality, and high economic costs. Fracture risk can be assessed using the FRAX algorithm, based on clinical risk factors with or without bone mineral density measurement. Approved treatment options in post-menopausal women include the bisphosphonates (alendronate, risedronate,ibandronate and zoledronate), denosumab, raloxifene, strontium ranelate and parathyroid hormone peptides. Of these, alendronate is the most cost-effective and is generally regarded as the first line option. The optimal duration of therapy has not been established but treatment is usually given for five years in the first instance, followed by reassessment of risk and the need for continued treatment. Alendronate, risedronate, zoledronate and teriparatide are also approved for the management of glucocorticoid-induced osteoporosis. Fracture risk increases rapidly after the onset of oral glucocorticoid therapy and primary prevention with a bone protective agent should be advised in patients at increased risk and should be continued for the duration of glucocorticoid therapy.

Paget’s disease of bone is the second most frequent metabolic bone disease, affecting up to 3% of adults. It is a progressive disorder characterized by focal abnormalities of bone remodeling. Its aetiology has not been fully established, although several genetic mutations have been linked to Paget’s disease including in the sequestrosome-1 and RANK genes. It is often asymptomatic, but may present with pain, deformity and pathological fractures. Neurological complications may occur as a result of spinal canal stenosis or cranial involvement. Plain X-rays are often diagnostic and isotope bone scans show increased uptake in involved areas. Bisphosphonates provide the main treatment option and zoledronate is regarded as the treatment of choice because of its potency and long lasting action.

Osteomalacia is an uncommon condition. Causes include intestinal malabsorption, privational vitamin D deficiency, renal disease and inherited conditions. It presents with bone pain and muscle weakness; pathological fractures may also occur. The most common biochemical abnormality is a raised serum alkaline phosphatase, although reduced serum calcium and phosphate levels may also be seen. Serum 25-hydroxyvitamin D is low in the majority of cases and serum PTH is increased. Pseudofractures or Looser’s zones may be seen on X-ray and histologically the disease is characterized by a mineralization defect. Vitamin D repletion with colecalciferol or active vitamin D metabolites provides effective treatment, although several years of treatment may be required to achieve complete resolution.

Disclosures: J.C., Amgen - Consultation and honoraria, GSK - Consultation fees and research grant, Servier - Honoraria, Nycomed - Research grant, MSD - Consultation fees, Roche - Research Grant, Roche - Research Grant, UCB - Research Grant.

I35. PSORIATIC ARTHRITIS

Oliver Fitzgerald

St Vincent’s University Hospital, Dublin, Ireland

Psoriatic arthritis is a multigenic autoimmune disease which involves synovial tissue, enthesal sites and skin and which may result in significant joint damage. While there are no diagnostic tests for psoriatic arthritis, classification criteria have been agreed and research has identified consistent features which help distinguish the condition from other common rheumatic diseases. Composite disease activity and response measures are being proposed and tested in large-scale RCT datasets. Screening questionnaires have been developed which may assist in identifying patients with musculoskeletal involvement among dermatology clinic patients. Analysis of HLA-B27 and -C regions in psoriatic arthritis compared to psoriasis only demonstrates significant differences such that psoriatic arthritis cannot be viewed simply as a subset of genetically homogeneous psoriasis. Results from a recent genome-wide association study in psoriatic arthritis point to involvement of the IL-17 cytokine pathway. While anti-TNF therapies have been successful in treating many patients, novel therapeutic strategies, perhaps targeting the IL-17 pathway, may well prove effective.

Disclosures: O.F., Pfizer - Research Grant, Consultation Fees, Abbott - Research Grant, Consultation Fees, MSD - Research Grant, Roche - Research Grant, UC B - Research Grant.

I36. ANTIPHOSPHOLIPID SYNDROME

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The antiphospholipid syndrome (APS) is a condition characterized by thrombosis, pregnancy morbidity and strokes in patients whose blood tests persistently positive for antiphospholipid antibodies (aPL). The only evidence-based treatments for patients with APS rely on anticoagulation. Typically, warfarin is used long-term to prevent recurrent thrombosis whereas heparin and aspirin have become the standard management of at-risk pregnancies in APS. As knowledge of the pathogenesis of APS has grown, it has become clear that the pathogenic aPL exert effects on various target cells by acting through cell surface receptors and intracellular signalling pathways. This may enable researchers to develop novel treatments that do not require long-term anticoagulation.

In this lecture, the following topics will be addressed:

1. What should we advise the asymptomatic patient with persistently positive blood tests for aPL?
2. Warfarin for prevention of recurrent thrombosis - is high intensity or low intensity anticoagulation best?
3. Pregnancy:- how does heparin work and can we do better than the current management protocol?
4. What are the prospects for new treatments in APS?

Disclosures: The author has declared no conflicts of interest.

MIMICKERS OF MYOSITIS AND TREATMENT UPDATE: ROOM FOR IMPROVEMENT AND LESSONS FROM NEUROLOGY

I37. ADULT ONSET METABOLIC/MITOCHONDRIAL MYOPATHIES AND DYSTROPHIES: HOW THESE CASES CAN BE MISSED

Mark Roberts

Consultant Neurologist, Salford Royal NHS Foundation Trust, Salford, United Kingdom

Problem: The acquired inflammatory myopathies and genetic neuromuscular disorders (NMD) such as muscular dystrophy, metabolic and mitochondrial disorders have overlapping clinical (myalgia, weakness, fatigue), and laboratory features (elevated muscle enzyme levels, myopathic change on electromyography, and even inflammatory changes on muscle biopsy). The potential for diagnostic confusion is thus great and results in unnecessary immunosuppression, a lack of genetic counselling and in the future may deny patients gene therapy and other potential treatments.

Solution: Recognition of genetic myopathies requires a working knowledge of subtypes. A clinically focussed approach is outlined: The role of history in diagnosis cannot be over emphasized addressing early development, questions on sporting ability, pigmenturia, cramps, stiffness, and contractures. Of note many genetic NMD present late...
e.g. myofibrillar myopathies. A family history enquiry is often useful though potential confounders such as the frequent new mutations, co-sanginity, variable penetrance and anticipation cause confusion. A system that addresses known and unexpected associations, for e.g. deafness, diabetes is common in mitochondrial disorders. Examination document signs suggestive of a genetic disorder (lumbar lordosis, scoliosis, scapular winging, ptosis) and its associations, cardio-respiratory involvement is common. Elevated and fluctuating (metabolic) CK and neurophylography (myatonic discharges, chronic myopathic change, electrical silence in riling muscle disease, associated neuropathy) are useful in selected patients. Recognition of clinical phenotypes may permit non-invasive gene e.g. Fascioscapular Humeral Muscular dystrophy and other tests e.g. dried blood spot enzymology in Pompe disease. Muscle biopsy is often still required, and must be interpreted in the clinical context, within a multi-disciplinary setting. Muscle MRI scanning is increasingly used to guide biopsy and may suggest a diagnostic pattern.

Discussion: Close cooperation between physicians including rheumatologist, neurologist, metabolic, muscle pathologist, radiologist) will reduce the diagnostic odyssey for patients. Clinical algorithms, data mining techniques and emergent technologies such as Gene chip may further speed diagnosis.

Disclosures: The author has declared no conflicts of interest.

I38. INCLUSION BODY MYOSITIS AND MISDIAGNOSIS OF POLYMYOSITIS

Speaker not confirmed.

I39. TREATMENT UPDATE AND BEST PRACTICE IN INFLAMMATORY MYOPATHY

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The inflammatory myopathies are a heterogeneous group of diseases including dermatomyositis, polymyositis, and inclusion body myositis. Few clinical trials have been conducted in myositis, making it difficult to provide clear recommendations on the treatment of these rare disorders. Although glucocorticoids have not been tested in randomized controlled trials, the general consensus confirms their first-line use. However, additional immunosuppression is often necessary due to unwanted glucocorticoid side effects or an inadequate response to steroids alone. Intravenous immunoglobulin is a reasonable short-term treatment with proven benefit in a controlled trial, but its long-term effectiveness remains unknown. The evidence for other immunosuppressive therapies has been derived mainly from case reports and open studies. These agents include methotrexate and/or azathioprine, as well as cyclosporine or tacrolimus. The latter agents are often used for antitnsynthase antibody-positive patients and the devastating complication of interstitial lung disease. Myophenolate mofetil has been used in adult and pediatric myositis, particularly DM including refractory rash. Newer therapies (e.g. rituximab) are encouraging, and results from the largest randomized controlled trial studying this agent will be discussed. Other data on biologic agents including the use of anti-TNF agents will also be discussed as smaller studies targeting TNF-alpha antibodies have been published. The balance of evidence suggests that immunosuppressive drugs are effective in dermatomyositis and polymyositis, although randomized controlled trials are lacking.

Disclosures: The author has declared no conflicts of interest.

I40. SHOULD WE STOP REGULAR PRESCRIBING OF CALCIUM/VITAMIN D SUPPLEMENTATION BECAUSE OF THE RISK OF ADVERSE CARDIOVASCULAR OUTCOMES?

Bo Abrahamsen,\(^1\)\(^2\)
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Fractional absorption of calcium in man declines with age, is strongly dependent on vitamin D sufficiency and is reduced by systemic glucocorticoids. Combined supplementation with calcium and vitamin D (CaD) in the elderly modestly decreases the risk of fractures at key osteoporotic sites. Further, most but not all studies of osteoporosis medications have addressed a scenario where the active drug was given together with calcium and vitamin D. This has seemed a logical assumption that the net flux of calcium to the skeleton is positive during antiresorptive or anabolic treatment, where it is negative in untreated individuals.

Initial concerns that CaD supplementation could lead to adverse cardiovascular outcomes were based on observations of accelerated vascular calcification in patients with renal failure, especially in the presence of a raised calcium x phosphate product. In accordance with this, vitamin D and analogues have the capacity to enhance vascular calcification in vitro and in animal models.

It is much less clear, however, if CaD supplementation is associated with cardiovascular harm in patients with normal or moderately reduced renal function.

Regrettably, the majority of RCTs with CaD supplements were not set up to address cardiovascular endpoints and outcomes were in some cases self-reported or based on death certificates. Meta-analyses have suggested an excess risk of myocardial infarction with calcium supplements given with or without vitamin D. The risk appeared to be confined - in the case of calcium supplements - to persons with above average baseline intake of calcium (800 mg or over). For CaD, the strongest cardiovascular outcome information comes from the WHI study, but an excess risk could only be inferred by first excluding subjects who also used own supplements, a process that meant that balanced randomization may no longer be present. Moreover, in this analysis there was a significant survival advantage when CaD was added to personal supplements.

In the absence of better primary study data, it is very difficult to conclude whether calcium/vitamin D supplements are associated with cardiovascular harm or not in subjects with normal or moderately reduced kidney function. However, until this issue has been clarified, clinicians should probably replace the simpler one-size-fits-all policy for CaD supplementation in rheumatology and osteoporosis with an individualized approach where the dietary intake of calcium is taken into account.

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I41. BISPHOSPHONATES: WHAT CAN WE DO TO MAXIMIZE ADHERENCE?

Rob Home
The School of Pharmacy, University of London, London, United Kingdom

The WHO has estimated that approximately a half of medicines prescribed for long-term conditions are not taken as advised and bisphosphonates are no exception. Despite the high health and financial costs of nonadherence for individuals and society, effective interventions remain elusive. Systematic reviews of such interventions to improve adherence have only limited effects. This talk will examine the reasons for this and what we might do to improve the situation. Summarising research across long-term conditions it will dispel common myths about the reasons for nonadherence and present a Perceptions and Practicalities Approach (PAPA) for developing more effective patient-centred interventions to support optimal adherence. The PAPA is based on the principle that nonadherence is best understood as a variable behavior with intentional and unintentional causes: Most of us are nonadherent some of the time. Unintentional nonadherence is linked to limitations in capacity or resources that reduce the ability to adhere to the treatment as intended. Intentional nonadherence is the product of a decision informed by beliefs, emotions and preferences. Research across long-term conditions, including studies of bisphosphonates for osteoporosis, shows that nonadherence is often related to patients' beliefs about medicines. How patients judge their personal need for the treatment (necessity beliefs) relative to their concerns about potential adverse effects, is particularly salient. These evaluations are informed by beliefs about the illness and by social representations of pharmaceuticals (which are often viewed with suspicion). Patients beliefs about their illness and treatment often differ from the medical view, and from the patient’s perspective, can make nonadherence seem like a common sense solution to a scenario where they do not perceive a strong personal need for treatment (e.g. there are fewer symptoms, perceived benefits) and may have concerns about the potential adverse effects of the medication now and in the future. The problem is compounded by the fact that patients are often reluctant to express doubts and concerns or to report non-adherence because they fear being dispelled by the clinician as a doubt in them. The result is that
nonadherence is often a hidden problem. These insights can be used to develop more effective approaches to supporting adherence. The first step is to facilitate an honest and open discussion about adherence by taking a ‘no-blame’ approach that recognizes that some degree of nonadherence may be the norm rather than the exception. Adherence support should be tailored to the needs of the individual. This can be achieved by eliciting and addressing the perceptual barriers (e.g. beliefs, preferences and emotions) affecting motivation to start and continue taking medication as well as the practical barriers (e.g. capacity and resources) influencing ability to adhere to the treatment. Adherence support should begin with the prescribing consultant but should not be limited to this. Innovative intervention need to look beyond the clinic and support both clinicians and patients to get the best from medicines and prescribing-related consultations.

Disclosures: The author has declared no conflicts of interest.

I42. CAUSES OF HIGH BONE MASS AND THE CLINICAL RELEVANCE
Celia Gregson1,2
1Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom; 2Older Person’s Unit, Royal United Hospital Bath, Bath, United Kingdom

In clinical practice high BMD values are not uncommonly identified on routine DXA scanning. High BMD most frequently reflects artefactual changes, but may reveal localized bone pathology or a more generalized skeletal disorder. A number of rare sclerosing bone dysplasias and osteopetroses with characteristic clinical features, such as cranial nerve compression, have been identified. However, more recently, we have found that generalized High Bone Mass (HBM) may reflect a mild skeletal dysplasia characterized by several clinical features including a broad frame, mandible enlargement, extra bone laid down at the site of tendon or ligament insertions, dental abnormalities, larger shoe size and interestingly reduced reported buoyancy. Furthermore, HBM has an associated metabolic phenotype, connecting fat and bone metabolism. Rare genetic skeletal disorders are currently a key focus of therapeutic research, as improved understanding has already identified genes regulating key metabolic pathways, translating into innovative osteoporosis treatments. For example from our knowledge of pycnodysostosis cathepsin K inhibitors have been developed as have anti-SOST antibodies from our insights into sclerosostosis and Van Buchem’s disease. However, currently most HBM is unexplained and therefore it is hoped will offer similar therapeutic potential.

In this presentation I will classify the potential causes of high BMD DXA values, providing a structure to guide clinical investigation. I will include disorders of enhanced bone formation leading to increased bone mass, for example those caused by mutations affecting LRPS and SOST, which up regulate wnt signalling; pertinent to understanding future anabolic therapies. I will then describe the epidemiology of raised BMD values including unexplained HBM within the UK, continuing on to the detail of the clinical features.

Disclosures: The author has declared no conflicts of interest.

ESSENTIALS IN RHEUMATOLOGY: SYMPTOM DIAGNOSIS AND MANAGEMENT

I43. PRIMARY CARE LED RHEUMATOLOGY SERVICES
Jill Firth1
1Pennine Musculoskeletal Partnership, Oldham, United Kingdom

Over the past decade there has been considerable debate around whether the shift from secondary to primary care based service provision will compromise the quality of care for rheumatology patients. NHS Oldham commission primary care based services to provide outpatient and day care in rheumatology, orthopaedics and chronic pain. This presentation will outline the model of care offered to patients with inflammatory arthritis by the multidisciplinary team, to explore the patient and clinician experience of working in primary care.

Disclosures: The author has declared no conflicts of interest.

I44. MUSCULOSKELETAL INTERFACE CLINICS: HOW PHYSIOTHERAPY HAS CONTRIBUTED TO THIS MODEL OF CARE
Kay Stevenson1
1University Hospital of North Staffordshire, Stoke on Trent, United Kingdom

This presentation will focus on how physiotherapy has contributed to the development, implementation and delivery of a successful Musculoskeletal Interface Service. This model of care has allowed a broad range of healthcare practitioners to be involved in developing rapid access and management of patients with non surgical musculoskeletal disease.

Rheumatology, General Practice and Physiotherapy professionals have worked together to provide expert clinical skills, clinical leadership, appropriate education and a strong research focus within this model of care. The presentation will highlight examples of each of these aspects and how strong clinical leadership from a Physiotherapy Consultant has worked with Rheumatology to ensure success.

Disclosures: The author has declared no conflicts of interest.

I45. BUSINESS PLANNING FOR A PATIENT CENTRED RHEUMATOLOGY SERVICE
Ann Todd1
1Pennine Musculoskeletal Partnership, Oldham, United Kingdom

A finance role in the NHS is always challenging and can be consumed by balanced budgets and performance targets. It is too easy to lose sight of the primary reason we are all here - the Patient! Working in a clinically led service with a responsive and flexible board of directors demonstrates how with careful business planning, a service can be truly patient focussed.

Disclosures: The author has declared no conflicts of interest.

I46. OCULAR MANIFESTATIONS OF RHEUMATOLOGICAL DISORDERS
Carlos Pavesio1
1Moorfields Eye Hospital, London, United Kingdom

Rheumatological disorders can affect the eye in many different ways and the ocular involvement may actually be the first manifestation of the systemic disease. The problems vary in severity and may involve the surface of the eye, the intraocular compartment and also the orbital tissues. Abnormalities of the tear film are quite common, but mostly not severe, while scleritis and keratitis can be quite painful and potentially visually threatening. Intraocular inflammation, uveitis, may be acute or chronic in nature and many times quite difficult to control, requiring aggressive local and systemic therapy. Retinal vascular disease can also occur, leading in many cases to severe visual loss. Orbital inflammation can produce a wide range of signs and may, for this reason, be missed, which can result in disease progression and visual loss. Another aspect to be considered is related to potential ocular effects of drugs used to treat rheumatological disorders, which can produce toxic effects on the retina and also induce inflammation.

Disclosures: The author has declared no conflicts of interest.

I47. IS THERE INFECTION? ARTHRITIS, BONES AND PROSTHETICS
Tony Berendt1
1Consultant Physician, Nuffield Orthopaedic Centre, Oxford, United Kingdom

Abstract not provided
I48. IMPROVING PATIENT MANAGEMENT: WHAT DO PATIENTS WANT?
Gordon Duff1
1Academic Unit of Rheumatology, University of Sheffield, Sheffield, United Kingdom

Abstract not provided

RHEUMATOLOGICAL CHALLENGES IN PRIMARY CARE

I49. WHAT MUSCULOSKELETONAL PROBLEMS DOES THE AVERAGE GP SEE?
Mark Pocheret1
1Arthritis Research UK Primary Care Centre, Keele University, Keele, United Kingdom

In the UK about 60 million people a year consult their GP and about 13 million of them will consult with a musculoskeletal condition - a lot of problems to see! For the average GP (one with a list size of 1700 patients) this equates to seeing 350 patients a year with musculoskeletal problems, and undertaking 750 musculoskeletal consultations. Data on who these people are and what musculoskeletal problems they have will be presented to provide the context for this session on rheumatological challenges in primary care.

Disclosures: The author has declared no conflicts of interest.

I50. HOW TO BETTER DIAGNOSE EARLY INFLAMMATORY ARTHRITIS IN PRIMARY CARE
Karim Raza1,2
1MRC Centre for Immune Regulation, University of Birmingham, Birmingham, United Kingdom; 2Department of Rheumatology, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom

A new onset of inflammatory arthritis is a common occurrence. In many patients the condition is of short duration, resolving spontaneously. A key clinical challenge is to be able to distinguish such patients from those whose disease will persist in the long term, and in particular from those who will develop rheumatoid arthritis (RA). A number of strategies have been developed to predict disease persistence, and specifically the development of RA, in patients with early arthritis and these will be reviewed with a focus on their strengths and weaknesses. Novel approaches to the early identification of inflammatory arthritis and the prediction of outcome, including the use of imaging, will be reviewed. Finally, important aims for future research in this area will be identified and discussed.

Disclosures: K.R., Pfizer - Consultancy fees, research grant, UCB - Consultancy fees, research grant.

I51. POLYMYALGIA RHEUMATICA: MORE THAN JUST SHOULDER PAIN
Christian Mallen1
1Keele University; Arthritis Research UK Primary Care Centre, Keele, United Kingdom

Polymyalgia rheumatica is a common rheumatological disorder characterized by bilateral shoulder and hip pain, morning stiffness and raised inflammatory markers. The annual incidence is 8.4 per 10,000 person-years, it is more frequently diagnosed in women and is associated with giant cell arteritis. Most patients in the UK are exclusively managed in a primary care setting with the ‘average’ general practice having around 20 patients consulting with this condition per year.

This presentation will consider topical issues associated with the diagnosis and management of polymyalgia rheumatica in a primary care setting, emphasizing that this common but often disabling condition is more than just shoulder pain.

Polymyalgia rheumatica is subject to wide variation in clinical practice due to the uncertainty surrounding diagnosis and the lack of an evidence base to support management strategy. This presentation will provide an evidence based approach to diagnosis and management of this condition that is applicable to a primary care setting. Recent research findings around the current state of polymyalgia rheumatica management in primary care will be presented and the importance of identifying and managing the potential side effects of corticosteroids will be discussed.

Disclosures: The author has declared no conflicts of interest.

I52. SEEING THE WOOD FOR THE TREES: DIAGNOSING INFLAMMATORY BACK PAIN IN PRIMARY CARE
Ingemar Peterson1
1Departments of Orthopedics and Rheumatology, Musculoskeletal Research Center, Lund, Sweden

Back pain remains to be a major health problem and there is still much to learn about the mechanisms behind. Although for many patients with back pain the problems are quickly resolved, some patients experience long term problems causing harm both for the patients, their families, the health care system and the society.

A minor part of back pain is related to inflammatory processes as a part of inflammatory back pain/spondylarthrits with or without peripheral joint involvement.

Recent European studies suggest the overall prevalence/consultation rates of Spondyloarthritides (SpA) to be approximately 0.5% including Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), SpA connected to Inflammatory Bowel Disease and Undifferentiated SpAs. Some patients, mainly males, show the first symptoms of SpA already between the age of 20 and 30 resulting in a life long suffering. Other patients present their symptoms in the middle ages with an equal sex distribution. Thus, different age and sex patterns seem to characterize the different SpA-forms.

Recent development in the diagnostic criteria (ASAS criteria for axial and peripheral SpA respectively) can be used in both Primary Health Care (PHC) and within specialized rheumatological care to easier identify those patients.

The recent development of modern pharmacological treatment of the more severe cases with SpAs with biological drugs as well as modern tailored rehabilitation and sell care for patients with SpAs makes it even more important to early identify and diagnose those patients.

Thus, strategies to detect patients with possible inflammatory back pain in PHC will be described and practical experiences shared. Further, the different branches of the SpA tree will be described in diagnostic and prognostic terms.

Disclosures: I.P., Pfizer - Consultation fees. Research grant, Abbott - Consultation fees. Research grant. The author has declared no conflicts of interest.

HOW TO GET YOUR ABSTRACT PUBLISHED

I53. HOW TO GET YOUR ABSTRACT PUBLISHED
Tricia Cornall1, Sarah Ryan2 and Diane Finney3
1Poole Hospital NHS Foundation Trust, Poole, United Kingdom; 2Rheumatology, Haywood Hospital, Stoke on Trent, United Kingdom; 3Rheumatology, Sussex Community Trust, Brighton, United Kingdom

This session will consist of both presentation and workshop format. The presentations will highlight what the reviewers are looking for in a quality abstract submission including structure, grammar, content, tables, findings and conclusion. The workshops will consist of critically analysing several abstracts with feedback and discussion in a friendly non threatening environment.

Disclosures: The author has declared no conflicts of interest.
ESSENTIALS IN RHEUMATOLOGY: KEEPING UP TO DATE, CLINICAL DECISION MAKING: WHAT IS THE EVIDENCE?

I54. ANKYLOSING SPONDYLITIS
Roger Sturrock1
1Centre for Rheumatic Diseases, Glasgow Royal Infirmary, Glasgow, United Kingdom

Abstract not provided

I55. VASCULITIS
David Jayne1
1Medicine, Addenbrookes Hospital, Cambridge, United Kingdom

A revision to the nomenclature of vasculitis was made in 2011 by the Chapel Hill Consensus Committee and results from the first genome wide association study in ANCA vasculitis have shed new light on how these syndromes may be classified. Delayed diagnosis remains a major factor in driving poor outcomes of death and end stage renal disease, while emerging cohort data is defining the malignancy and cardiovascular risks associated with current therapies. The major unmet needs are less toxic and faster acting remission induction regimens and better relapse prevention strategies. Ongoing poor quality of life is not well understood and harder to address. Conventional induction regimens using lower dose cyclophosphamide (short courses or intravenous administration), or using alternative immunosuppressives (methotrexate or mycophenolate mofetil) have been validated but are associated with higher relapse rates. Relapse prevention studies have demonstrated equivalence of azathioprine and methotrexate but inferiority of mycophenolate mofetil. Uncertainty exists as to optimal steroid dosing and duration and while evidence exists for a role of plasma exchange in severe presentations, meta-analysis has not confirmed sustained benefit. Rituximab has been shown to be equivalent to cyclophosphamide for remission induction in ANCA vasculitis but little evidence exists in other vasculitides. Cohort studies have explored the role of rituximab in refractory disease and in remission maintenance. Patient monitoring in order to minimize treatment related toxicity and optimize disease control is central to good long term outcomes and ANCA plays a role in estimating relapse risk in an individual case.

Disclosures: D.J., Roche - Research grant.

CURRENT THINKING ON CONSERVATIVE MANAGEMENT OF BACK PAIN

I56. CAN WE CHOOSE THE BEST TREATMENT FOR BACK PAIN PATIENTS?
Jonathan Hill1
1Rheumatology, Keele University, Keele, United Kingdom

The clinical problem: Primary care clinicians such as GPs and physiotherapists are unclear about which patients with common low back pain to select for the provision of extra health resources beyond standard care involving analgesics, advice and education. Although clinical trials have reported the benefits of a wide range of treatments such as exercise, manual therapy and cognitive behavioural approaches compared with standard care, there is a lack of evidence about which patients are likely to benefit from these interventions. This reduces the efficiency of primary care management as it leads to inconsistent and sometimes inappropriate referral decision-making. The results of this trial specifically sought to address this gap in the existing evidence to better inform commissioners and service providers about how back pain can be better managed in the early stages using a risk stratification approach to help GPs and physiotherapists.

Methods – to test risk stratification: A novel approach, gaining interest in other medical specialties, but not previously tested in the management of back pain, is risk stratification, with care provision structured according to an individual’s estimated risk of poor prognosis (persistent disability because of back pain). With research funding of academic staff from the NIHR and Arthritis Research UK, we developed a new stratified model of primary care management of back pain, consisting of two complementary components. First, a previously validated, simple-to-use prognostic screening method (the Keele STarT Back Screening tool), to allocate patients into one of three risk-defined groups—low, medium, and high risk groups; second, three separate care pathways, were designed with clinical experts, to match treatments to these risk groups. We then conducted a large randomized controlled trial funded by Arthritis Research UK - the STarT Back Trial - to test our main hypothesis that a stratified approach to primary care management for low back pain results in clinical and economic benefits compared with current best practice. With 1,675 patients recruited (85% patients aged 18 and over who consulted their GP with non-specific low back pain were recruited to the trial from 10 general practices within the North Staffordshire area of the UK ahead of target. They were randomized to receive either targeted treatment (the STarT Back risk stratification approach), or current best physiotherapy care.

Results – a potential solution: The results (Hill et al, 2011 The Lancet) suggest that, when compared to best current care, the STarT Back risk stratification approach improved disability, pain and distress, and, importantly, helped patients take less time off work and improved their treatment satisfaction rates. The reasons for this were in part due to the new approach affecting the pattern of referral to physiotherapy in a way that was more appropriate to individual patient needs, with low risk patients receiving a single session of advice to help them self manage, and medium and high risk patients receiving more intensive treatment. Crucially, those patients at highest risk of their back pain becoming long-term benefited from a more intensive approach to address their specific worries. The economic analysis also demonstrated that a risk stratification approach was cheaper than current best practice.

Implications for clinical practice: The results of this study have previously been presented at the BSR. This talk will therefore primarily be focussed at the widespread implementation of risk stratification across numerous UK NHS Trusts (n = 20) and the lessons being learnt. GPs are being encouraged to use the Keele STarT Back Screening Tool to assist their early referral decision-making and physiotherapy services to organize themselves to differentiate their treatment provision according to a patients risk status. This is leading to a considerable re-configuration of services to ensure that low risk patients are not being over treated, and high risk patients are better identified and their individual risk factors addressed in the early stages to prevent long term disabling problems. An independent external audit was recently conducted of the first 8 NHS Trusts who had embedded the approach within their back pain pathways, by a team of clinicians in Scotland, to survey the experiences of early adopter Centres, which revealed strong supportive for the ongoing use of the risk stratification tool (see www.keele.ac.uk/stb). This is largely because clinical services are finding that substantial efficiency gains can be made by preventing over treatment among low risk patients, and better identifying those at high risk of persistent disabling problems who benefit from early referral to additional services such as physiotherapy. Risk stratification may not help in choosing the best specific treatment for back pain patients. However, it does appear to have an important role in helping to shape the configuration of services in primary care. This talk will, therefore, focus on sharing the lessons being learnt from early adopter Centres, to ensure that across the UK we achieve the best services possible for sufferers of common low back pain.

Disclosures: The author has declared no conflicts of interest.

I57. LOW BACK PAIN IN PRIMARY CARE
Duncan Critchley1
1School of Medicine, King’s College London, London, United Kingdom

The ideas and language of health economics will be introduced. An example cost-utility analysis will be presented. How knowledge of health economics can inform service planning and clinical decision-making in back pain will be discussed.

Disclosures: The author has declared no conflicts of interest.

I58. CURRENT THINKING ON CONSERVATIVE MANAGEMENT OF BACK PAIN
Martin Underwood1
1University of Warwick, Coventry, United Kingdom

NICE guidance on the management of non-specific low back pain was published in 2009. Since then several important studies have been published widening the treatment options available to patients with low back pain. For example, both a cognitive behavioural approach and
yoga have been shown to be both effective and cost effective treatments. Now that there are a range of treatment options for low back pain, each with a small to moderate potential benefit, the challenge is around deciding which patients will get the greatest benefit from each of these treatment options. In addition to reviewing the major nes trials published since the NCIE guidance was published I will discuss approaches to targeting treatment options at different individuals and how these might reduce the community burden of back pain.

Disclosures: The author has declared no conflicts of interest.

I59. THE DIRECT AND INDIRECT IMPACT OF HEALTH BELIEFS IN LOW BACK PAIN ON OUTCOMES
Tamar Pincus1
Royal Holloway University of London, Egham, United Kingdom

Research has established that patients’ beliefs about their pain, their own resources, and their treatment are associated with long-term outcomes. More recently, the beliefs of clinicians have been investigated, in reference to clinical decision making and professional behaviours. This research will be described, and the implications for patients, clinicians and policy makers will be evaluated.

Disclosures: The author has declared no conflicts of interest.

I60. MECHANICAL EFFECTIVENESS OF ORTHOSES IN FOOT OSTEOARTHRITIS
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New radiographic research suggests foot osteoarthritis maybe more common than previously suspected. Historically large population studies have suggested osteoarthritis in the foot was most common at the first metatarsal phalangeal joint, using standard anterior-posterior clinical radiographs. The publication of a newly developed radiographic foot atlas and the results from an elderly cohort suggests an alternative distribution pattern of foot osteoarthritis. Osteoarthritis was more common at the tarsal joints (60%) and strongly associated with foot pain when compared to the first metatarsal phalangeal joint. Assessment of foot biomechanics in people with foot osteoarthritis suggests altered patterns of foot movement and foot pressures can occur during walking and climbing stairs. This research suggests there maybe a role for mechanical intervention in the treatment of foot osteoarthritis. Wearing foot orthoses for first metatarsal phalangeal joint and tarsal osteoarthritis can improve foot pain and adverse biomechanics. As part of an Arthritis Research UK studentship from 2008 to 2011, we undertook a study of mechanical mid foot pain in which we identified that some of the cohort had MRI features of osteoarthritis in the tarsal joints. As part of this study we explored the relationship between foot biomechanics and pain. This work highlighted the poor recognition and understanding of foot osteoarthritis and the potential role of mechanical interventions to modify foot pain and mechanics.

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I61. VARYING EFFECTIVENESS OF MECHANICAL INTERVENTIONS IN KNEE OA
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Knee osteoarthritis is the most common form of osteoarthritis and both prevention opportunities and treatment are unfortunately limited. It has been shown that roughly 25% of the UK population aged 55 and over suffers from knee pain on most days. New approaches to treatment are desperately needed for osteoarthritis that will alleviate the suffering that many patients experience and that might delay the need for a knee replacement. Devices such as shoe inserts, footwear and knee braces are available and help to reduce the dynamic biomechanical loads present in the medial tibiofemoral compartment. However, there is varying biomechanical response with these devices and this talk will introduce these, and aim to identify strategies and classifications, to improve the effectiveness of conservative treatments in individuals with osteoarthritis of the knee joint.

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I62. TISSUE STRUCTURE MODIFICATION IN LATE STAGE OSTEOARTHRITIS IS FEASIBLE
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Modification of joint tissue damage is challenging in late stage osteoarthritis (OA). Few options are available for treating end-stage knee OA other than joint replacement. However, animal studies have demonstrated that the synovial joint has intrinsic repair capacities provided the proper biomechanical conditions are provided. Temporary joint distraction, providing absence of mechanical stresses on the cartilage, maintaining intra-articular fluid pressure oscillations for nutrition of chondrocytes, and inducing significant peri-articular bone turnover changing the subchondral biomechanics and providing a source for growth factors to facilitate cartilage repair, might provide such a condition. Distraction in case of severe ankle OA proved clinically to be beneficial for prolonged periods of time. Moreover, tissue structure modification was observed in cartilage and bone.

An exploratory trial was performed to examine whether joint distraction can effectively modify joint tissue damage in end stage disease and has the potential to delay prosthesis surgery.

Twenty patients (60 yrs) with end-stage fibo-femoral OA were treated surgically using joint distraction. Distraction (~5mm) was applied for two months using an external fixation frame. Tissue structure modification between baseline and one and two years follow up were evaluated by non-weight bearing MRI (3D cartilage morphometry), weight bearing radiography (joint space width; JSW), and by biochemical markers (collagen type II). All structural changes were assessed blinded. Clinical improvement was evaluated by WOMAC and VAS-pain score.

MRI revealed a significant increase in cartilage thickness (2.4, 3.0, and 2.8 mm at baseline, 1, and 2 yrs follow-up, resp.) and a decrease of denuded bone areas (22%, 5%, and 8%). Radiography demonstrated a significant increase in mean and min JSW (2.7, 3.6, and 3.3 mm and 1.0, 1.9, and 1.7 mm). Biomarker levels showed an increased collagen type II synthesis from 6 months on (+18% and +25%) and a decrease in breakdown (~17%, and ~36%), and an increase in the ratio synthesis over breakdown (~115% and +43%). Starting directly after distraction the total WOMAC index increased from 45 via 77 to 78 points, and VAS pain decreased from 73, via 31 to 28 mm. All changes from baseline were stat. sig. difference between 1 and 2 yrs follow-up was observed, although a tendency towards a decline of the effects was seen.

Pin tract infections, treated successfully with local and oral antibiotics, and discomfort during distraction where clear adverse events.

Joint distraction can induce tissue structure modification in end-stage knee OA accompanied by significant clinical benefit, within one year sustaining for at least an additional year. No current treatment is able to induce such changes. Larger, longer, and randomized studies on joint distraction are warranted and have been initiated.

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I63. THE ROLE OF STRONTIUM IN TREATING OSTEOARTHRITIS
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Abstract not provided.

JUVENILE-ONSET SLE AND CHILDHOOD SCLERODERMA: NEW INSIGHTS INTO PATHOLOGY, TREATMENT AND OUTCOMES

I64. WHAT IS THE NATURAL HISTORY OF SCLERODERMA WITH ITS ONSET IN CHILDHOOD?
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Scleroderma is a very rare disorder in childhood with a UK incidence of 3.4 per million children for localized scleroderma and 0.2 per million
for systemic sclerosis. In this BPSU study 89% of patients were said by their physicians to have improved in the first 12 months of follow-up, with the majority being on treatment. Outcome measures for scleroderma in childhood are currently being developed to assist the comparison of cases. The disease rarity means that there are no reported large cohort studies of the natural history of the various types of disorders linked under the scleroderma heading.

However, valuable publications exist from the PRINTO collaborative group in childhood SLE cases seen over a long period spanning different approaches to care and treatment. However, the fact that 750 cases of localized scleroderma have been studied showing that 22.4% have extracutaneous manifestations immediately confirms that outlook of localized cases will be affected by the cosmetic, local growth and functional effects of the localized lesions as well as associated autoimmune features having their own long-term sequelae. The PRINTO study of 137 patients with systemic sclerosis with at least a five year followup reported a 4 year survival rate of 95% and with 90% of patients leading a fully active life.

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I65. WHY IS IT IMPORTANT TO KNOW ABOUT LUPUS IN CHILDREN?
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SLE is a complex illness at any age. Diagnosis can be particularly challenging during childhood and adolescence. There is a marked difference in the pattern and severity of organ involvement in juvenile-onset SLE (JSLE) compared to adult-onset SLE (aSLE). Significantly more major organ disease occurs in childhood compared to adult-onset disease. As many as 80% of JSLE patients have renal involvement, 90% haematological, and 25% neurological involvement reported within 5 years post-diagnosis.

Greater use of corticosteroids and disease-modifying immunosuppressants characterize JSLE compared to aSLE, and damage accumulates quicker with up to 25% of children accruing damage with less than 5 years disease duration.

The severe phenotype of JSLE offers a unique opportunity for studying the immunopathogenesis of this archetypal systemic autoimmune disease. Increased and dysregulated apoptosis occurs in JSLE. Autoantigens typical of lupus cluster in surface blebs of apoptotic cells, increasing their immune-exposure. Increased toll like receptors capable of recognizing these autoantigens are activated by apoptotic neutrophils leading to downstream activation of the immune pathway.

To date, no single drug has ever been licensed for use in JSLE. Hence, off-label use of all JSLE therapies is routine in clinical practice. With the advent of biologics, and more specific methods of modulating components of this developmental pathway, such as IL17 or the IL23 pathway inflammatory effectors, and more specific methods of modulating the complex autoantibody dysregulation that occurs in JSLE, the need for developing internationally acceptable and robust criteria for appropriate effects of routine clinical practice and future clinical trials has become urgent.

The burden disease of JSLE is considerable. The management of JSLE requires special consideration towards both the significant long-term consequences of the disease, and its onset during a crucial time in growth and development.

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I66. IMPROVING AND OPTIMIZING LONG TERM OUTCOMES OF PATIENTS WITH JUVENILE-ONSET SLE
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Mortality in adult patients with SLE has improved, but adult SLE patients are known to have a higher risk of cardiovascular disease at a younger age than healthy women. Evidence is emerging on the deleterious effect of long-term steroid use in adult patients, suggesting that more aggressive use of DMARDs may be beneficial.

Mortality for patients with juvenile-onset SLE (JSLE) has also improved considerably over the last two decades, but the long-term outlook for morbidity and mortality is not well documented for this group. New cohort studies, designed to allow transfer of data into adulthood, will produce this data in the future.

One such study is the UK JSLE Cohort study, started in 2009, using standardized forms to collect the ACR criteria at diagnosis, BIJAG assessments at each clinic visit, and annual assessments including the SLICC damage assessment. This allows the accrual of damage to be studied, including underlying risk factors. Patients are known to benefit from enrollment in research studies, and inclusion in this cohort study is likely to improve the baseline care and the expertise of the care. The increased use of aggressive DMARDs and the regular documentation of risk factors should lead to an accurate skeletal morbidity and mortality for this group of patients. Long-term follow-up into adult life will be needed to determine this.

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HEBERDEN ORATION
I67. GENETICS AND RHEUMATOLOGY: LESSONS FROM EXTREME PHENOTYPES AND SUBTLE GENOTypes
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The past 30 years have seen unparalleled advances in human genetics. Polymerase chain reaction-based DNA technology has revolutionized the investigation of human disease and experiments that would have taken the life-time of a project grant can now be completed in days. Consequently, not only have the mutations underlying the majority of monogenic skeletal disorders been identified but attention has turned increasingly towards the investigation of complex multifactorial disorders. Better understanding of some of the rather more esoteric monogenic diseases (eg, familial expansile osteolysis and sclerosteosis) has proved highly instructive for insights into normal bone biology. In some cases this has even laid the foundations for new treatments of common conditions, such as Paget’s disease and osteoporosis. Accurate definition of the genetic causes of the skeletal dysplasias and other heritable connective tissue disorders now allows a more logical and accurate classification and diagnosis of many of these disorders. The underlying mutations are often in structural genes, encoding components of the mesenchymal matrix, but there have been important surprises. For example, Marfan syndrome does not simply reflect structural failure of the elastic tissues due to deficiency of the fibrillin microfibrils; there are also important secondary effects on TGFβ signalling that account for many of its clinical features. Crucially these can be effectively antagonized in animal models, thereby holding out the very real prospect of preventive treatments for the disease in man. The use of genome-wide association studies (GWAS) of polygenic disorders was pioneered in type 1 diabetes but rapidly found success in the rheumatic diseases. Nowadays this is more apparent than in the dissection of the polygenic component of rheumatoid arthritis and ankylosing spondylitis (AS). To achieve this numerous large pan-global consortia have been established and more than 30 genes have been identified in each of these disorders. At least some of these will undoubtedly give useful clues towards potential new drug targets. For example, in AS the associations with IL23R, IL12B, STAT3 and PTGER5 all highlight the likely pathogenic involvement of Th17 lymphocytes. Targeting components of this developmental pathway, such as IL17 or the IL23 receptor are already showing exciting therapeutic potential. The exceptionally strong association with ERAP1 in the first GWAS in AS was unexpected but has been widely replicated. It is particularly exciting because it shows clear evidence of a synergistic effect with HLA-B27, the oldest and strongest genetic association with AS. ERAP1 encodes an endoplasmic reticulum-associated aminopeptidase involved in trimming peptide antigens to optimal length for binding to HLA molecules. Structural and functional studies demonstrate that variants of ERAP1 protecting against AS have reduced peptidase activity, suggesting that specific peptidase inhibitors could have important therapeutic applications in AS.