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SUPPORTING PATIENT CARE AND RESEARCH IN RHEUMATIC DISEASES

CLINICAL RESEARCH ON E6 - Dr Deepak Jadon



Dr Deepak Jadon is a consultant rheumatologist and Director of the Rheumatology Research Unit (RRU) at Addenbrooke's Hospital. He is also a honorary senior lecturer (associate PI) in the Department of Medicine at the University of Cambridge. His major clinical and research interests relate to psoriatic arthritis (PsA), ankylosing spondylitis (AS) and rheumatoid arthritis (RA).

It has been a busy year on the RRU both in terms of new staff and in terms of research activity. There are currently 24 clinical studies active and ten in the pipeline; with a balanced portfolio of academic and non-academic (often clinical trials of new medications) research.

We now have five research nurses (Sisters Yin Peng Fan, Jolanta Mil, Dominique Raut-Roy, Alina Cezar and Deniska Kemeny) and one administrative assistant (Tracey Jarvis). There are five research fellows (senior doctors undertaking a period of research, as described below).

Dr Jobie Evans is about to undertake a 2-year study (**ProSpA-IBD**) investigating how MRI scans of the abdomen in patients with Crohn's disease or ulcerative colitis can be used to screen for patients with spondyloarthritis (inflammation of the spine). He will aim to recruit 300 patients.

Dr Mark Sapsford is a fellow from New Zealand comparing the burden of enthesitis (inflammation where tendons, ligaments and joint capsules insert into bone) as measured by ultrasound versus clinical examination, in patients with PsA. If you are interested in taking part in the **CLUE-PsA** study, he is currently recruiting with a target of 85 patients by December 2018.

Dr Joe Hutton is developing a research study investigating extreme forms of PsA, including PsA-mutilans and enthesitis using imaging (x-rays, MRI, ultrasound) and immunology.

Dr Maeve Fifield is undertaking the **APRIL** trial assessing the safety of abatacept in patients with rheumatoid arthritis (RA) and interstitial lung disease (ILD). The trial is recruiting, with a target of 30 patients over the coming year.

Dr Shahryar Hadavi is the fellow dedicated to the clinical trials on the RRU. In PsA he is recruiting to the: **MONITOR** study which is an inception (from first diagnosis) cohort study of patients with PsA running for 5 years and recruiting 500 patients across Cambridge, Oxford and Bath; **ASSESS** study which is assessing the impact of disease in PsA; and later this year the British Society of Rheumatology **PsA Registry** will open to recruitment and assess the safety of biologic treatments in clinical practice. In RA we are recruiting to the **STRAP** study of precision medicine whereby patients' response to biologic treatment is compared with their joint biopsy; and the **SECARA** study where an 'add-on treatment' is given to RA patients with insufficient response to anti-TNF therapy.

Dr Gavin Clunie (Consultant) is leading on a study assessing MRI features before and after NSAID use in axial spondyloarthritis (**DYNAMISM**). Dr Kenneth Poole (Consultant) is leading two studies relating to osteoporosis and osteogenesis imperfecta (ToPAZ and Asteroid studies).

CARE kindly supported the '**East of England Spondyloarthritis Academy**' in 2017/2018, which through four whole-day educational events aimed to raise awareness, promote a deeper understanding and improve the management of patients with PsA and axial spondyloarthritis in the region. The academy was hosted by myself and Dr Karl Gaffney (consultant rheumatologist in Norwich) and attended by approaching 200 delegates including doctors, clinical and research nurses, pharmacists, physiotherapists, occupational therapists, chiropractors, osteopaths and psychologists. The SpA Academy will be launching in London in January 2019.

CARE hosted the Psoriatic Arthritis Genetics Europe (**PAGE**) annual meeting in October 2017. Attended by twenty professors, consultants and researchers from the UK, Germany, Italy, Sweden, Denmark and Ireland, the meeting at the Varsity Hotel in Cambridge was a great success. A key-note talk was given by Professor Gaston.

If you are interested in taking part in any of the research studies mentioned above, then please do not hesitate to contact the team via CARE. More information will be available on the soon to launch **new CARE website!**

Studies in Autoimmune Connective Tissue Diseases (CTD) – Dr Natasha Jordan



Dr Natasha Jordan is a consultant rheumatologist at Addenbrooke's Hospital. Her major clinical and research interests are the autoimmune connective tissue diseases (CTD) including systemic lupus erythematosus (SLE) and Sjögren's syndrome. Dr Jordan is principal investigator for Addenbrooke's on a number of studies in these areas. She is Deputy Director of the Rheumatology Clinical Research Unit (RCRU) and is the CRN Eastern Specialty Group Lead for Musculoskeletal Disorders.

Current studies running at the RCRU under Dr Jordan's supervision include the **BEAT Lupus Trial**. BEAT Lupus is a multicentre, UK phase II, randomised, double blind, placebo controlled trial investigating the safety and efficacy of belimumab after B-cell depletion therapy in patients with active SLE resistant to conventional therapy. We have successfully recruited our target of 3 patients for this study. A further clinical trial in SLE will be opening at our site later this year.

Dr Jordan and her research team are also recruiting patients for the **GCA Consortium**, a study led by Professor Ann Morgan, University of Leeds. This study aims to establish a database which will permit clinical characterisation of giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) patients with a view to developing a better understanding of these diseases. The research team will also carry out genetic studies on this patient cohort, investigating the contribution of relevant genes to the susceptibility to GCA/PMR and the risk of complications and response to therapy.

We are also taking part in the **United Kingdom primary Sjögren's syndrome registry (UKPSSR)**. This study is being led by Professor Wan Fai Ng, Newcastle University. The aim of the UKPSSR is to establish a cohort of well-characterised primary Sjögren's syndrome (pSS) patients and matched healthy controls, together with samples of DNA, RNA, serum and immune cells from these subjects in order to facilitate clinical trials, genetic and epidemiological studies in this disease area.

Dr Jordan and her team have recently opened two studies in idiopathic inflammatory myopathy (IIM). Both studies are led by Dr Hector Chinoy, University of Manchester. The studies are **MYOPROSP**; a prospective cohort study with the aim of identifying the best approach to the diagnosis and treatment of patients with myositis. We have also opened recruitment to **UKMYONET**. The aim of UKMYONET is to better understand the cause of myositis by collecting clinical information and performing genetic and antibody studies on patients' blood samples.

The team are also actively recruiting to the **British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA)**. The BSRBR-RA aims to monitor the long-term effects of biologic/biosimilar therapies in patients with rheumatoid arthritis treated during routine clinical practice

PAIN RESEARCH - Dr Nicholas Shenker



Pain Research in the rheumatology department continues to be broad and collaborative. Patients with CRPS have had access to the **LIPS** study which disappointedly did not demonstrate any significant benefit to having low dose Intravenous Immunoglobulin and the results were published this year in the *Annals of Internal Medicine*. The understanding of why some people do develop this challenging condition with which to live has been increased by two recent studies that we have participated. The first published in the *Journal of Pain* showed some of the brain changes captured by high density EEG and these intriguingly map onto the area of the brain that helps to process body scheme. Further work is needed but this might be an important marker by which we can diagnose and monitor patients with this condition and this work is being taken further by Maria Neidernhuber supervised by Dr Nick Shenker and Dr Tristan Beckinschtein in the Cognitive Brain Unit. Maria's work will look in more detail at these preliminary tasks in patients with both CRPS and chronic pain conditions and any patients who would be interested in taking part can make contact in the usual way.

The second and perhaps even more exciting study builds on the great strength of Cambridge's Geneticists. Using the **CRPS-UK Registry** set up by Dr Nick Shenker and colleagues across the UK, exome sequencing technology has explored the full genome of patients with CRPS and several interesting findings have been discovered. These will be taken on by Dr Mike Nahorski in the University. This may instruct fundamental understanding on why some patients may develop this condition and why others do not. Furthermore, why do some patients with the condition get better and others do not may be explained by some of these findings. More work will need to be done.

Finally, let us not forget patients who suffer with rheumatoid arthritis and chronic pain and fatigue. In collaboration with Dr Mike Lee in the Academic Division of Anaesthetics, brain scans are being performed to try and understand why some patients feel fatigued with rheumatoid arthritis and others do not. Blood tests are taken to assess for the small proteins (cytokines) that can cause inflammation and this will be factored into any analysis. If you would be interested in taking part in any of these research studies, then please do not hesitate to contact us via CARE.

Current Trials in Connective Tissue Disease - Dr Frances Hall



Lymphocyte Expression Profiling and Phenotyping in Patients with Primary Sjogren's Syndrome

Primary Sjögren's Syndrome (PSS) is an autoimmune disease which attacks secretory glands such as those which produce saliva and tears; some patients develop systemic manifestations and secondary malignancy. Preliminary studies have confirmed known and uncovered novel T-cell abnormalities in PSS. The response of T-cell abnormalities in PSS to biological therapy remains unknown, as does the ability of such responses to predict clinical efficacy. This project is studying circulating and gland-infiltrating T-cells of PSS patients with systemic manifestations enrolled in TRACTISS, an ARUK-funded randomised trial of Rituximab. Blood CD4+ and CD8+ T cells purified before and after treatment will be tested to determine the genes they express and markers on their surface. The same things can sometimes be examined in the cells of the affected glands – there are minor salivary glands in lips which can be biopsied without too much discomfort. Rituximab depletes B cells which make the autoantibodies seen in PSS, but they also interact with T cells, so it is necessary to examine the effect of treatment on these. Given the efficacy of Rituximab in other autoimmune diseases, the studies will have relevance beyond PSS.

This project involves collaboration with Dr Paul Lyons (Cambridge), who analyses gene expression and Dr Michele Bombardieri (QMUL) who studies lymphocyte in the minor salivary gland biopsies. Initial analyses have focused on the CD8 T cell samples collected at baseline, and suggest that their gene expression might be able to predict the severity of clinical symptoms over the succeeding months and thus prediction of disease prognosis in Primary Sjogrens Syndrome.

A randomized, double blind controlled trial comparing Rituximab against intravenous Cyclophosphamide in Connective Tissue Disease (CTD) associated Interstitial Lung Disease (ILD) (RECITAL)

Cambridge is participating in this multicentre trial, run from the Royal Brompton & Harefield Trust. It aims to demonstrate that intravenous Rituximab is more effective than the current best treatment (intravenous Cyclophosphamide) for interstitial lung disease in CTD. It will also compare the safety profile of Rituximab to intravenous Cyclophosphamide, and assess the health economic benefits of Rituximab compared to current standard of care for CTD-ILD. It will also look for markers (e.g. blood tests) of disease severity, prognosis and treatment response.

The trial, and the associated exploratory laboratory work, underpins the MD project of research fellow Dr Maeve Fifield (Co-supervised by Dr Hall

A Phase II Randomised Controlled Study of Oral Prednisolone in Early Diffuse Cutaneous Systemic Sclerosis (PredSS)

Cambridge has joined this multicentre study, which is run from Manchester. It will determine if moderate dose Prednisolone (steroid) is effective in reducing pain and disability and improving skin score in patients with early diffuse cutaneous systemic sclerosis.

Addenbrooke's recognised as LUPUS UK Centre of Excellence



Chris Maker (CEO, LUPUS UK), Yvonne Norton (Trustee, LUPUS UK), Professor Graham Hughes, Dr Natasha Jordan, Davina Frost (Chairperson, Cambridgeshire LUPUS UK), Dr Frances Hall, Sr Stella Burns, Professor David Jayne, Hugo Tordesillas (Lupus specialist nurse)

ORTHOPAEDIC RESEARCH – Professor Andrew McCaskie



The University Division of Trauma and Orthopaedic Surgery seeks to deliver excellence in research, clinical care, teaching and training as it relates to the surgery of bones, joints and other structures relevant to movement. We adopt a translational approach to seek advances in fundamental musculoskeletal sciences that apply to patient care in the operating theatre and clinic. The Division is led by Professor McCaskie who is also the Head of the University Department of Surgery. He is supported a number of clinical academics including Stephen McDonnell and Wasim Khan, basic scientists

including Mike Birch and Roger Brookes and veterinary scientists including Fran Henson. There are a number of post-doctoral and doctoral students in the group. Jenny O'Calaghan has joined the research group in the last year to provide clinical research support.

The theme of Movement was showcased in the Division's participation in the Cambridge Science Festival this year. There was a Lecture by Professor McCaskie, and a hands on workshop where the public got to know more about the musculoskeletal tissue that keep us moving, and how treatments help repair, replace and reconstruct these tissue.

There are a number of studies in clinical trials undertaken within the department. These have been split into trauma, elective and cell therapies. The trauma lead is Peter Hull who has recently completed the **KFORT** trial comparing fixation and replacement of the knee joint in trauma. We were also a site for the **HEALTH** study comparing hemiarthroplasty and total hip replacement in patients with intracapsular neck of femur fractures. Ongoing trials include the **AceFIT** trial investigating fracture fixation and hip replacements in acetabular fractures, the **WhiST** study looking at wound healing in surgical trauma, and the **FORTIFY** trial evaluating a bone graft for open tibial fractures. The elective surgery study lead is Vikas Khanduja. For elective surgery we have completed a study looking at patient specific instrumentation in total knee replacement and the **FAIT** trial looking at femoral acetabular impingement. We are the only UK Centre in the **ADIPOA 2** trial. This is a study using adipose/ fat derived stem cells cultured to treat early knee osteoarthritis.

The **Arthritis Research UK tuition centre** is led by the University of Cambridge and has a unique collaboration of scientists and clinicians at the University of Aberdeen, Keele University, Newcastle University, the Robert Jones and Agnes Hunt Orthopaedic Hospital in Oswestry and the University of York.

The clinical services at Addenbrooke's Hospital include the delivery of trauma and elective orthopaedic care, and a major trauma centre. The fractured neck of femur services has had significant success with the treatment and adherence to best practice for care. The results with elective hip and knee replacement surgery as evidenced by the national joint registry data are favourable, and we await a further **GIRFT** (Getting It Right First Time) visit to the Trust by Professor Tim Briggs.

Collecting Boxes - 'THANK YOU' to all those who are still holding CARE collecting boxes and also to those who are new holders. The collecting boxes are emptied into a large jar when they are returned. This year we have banked **£146.00**

Visit our [fundraising page](#) to request information or to donate now

Care is a registered Charity, number 802862, and exists to support patient care and research in rheumatic diseases in the region around Cambridge. It shares offices with the Rheumatology Clinical Research Unit.