

Issue 29

www.cambridge-arthritis.org.uk

2019

SUPPORTING PATIENT CARE AND RESEARCH IN RHEUMATIC DISEASES

Thank you to Sheila Smith



In January 2019, Sheila Smith, manager of the Rheumatology Research Unit/E6 and secretary of CARE retired following 31 years of service. Sheila began her career at Addenbrooke's hospital in 1969 at age 19, working for 6 years as a medical secretary in the Department of Surgery. In 1975, she got married and moved to the north west of the country, spending 3 years working for the Safety and Reliability Directorate of the Atomic Energy Authority. In 1984, Sheila returned to Cambridge with three young children in tow and returned to work at Addenbrooke's. Initially she worked as a locum medical secretary and then moved to the Department of Rheumatology working for Dr Jumbo Jenner. In 1987, Sheila was encouraged to go for promotion and moved to E6 working for many years with Professor Brian Hazelman. On Professor Hazelman's retirement, Sheila worked alongside Dr Andrew Ostor in E6 for several years. Following Andrew Ostor's return to Australia, Sheila worked tirelessly to smooth the transition to the new personnel on E6, Dr Deepak Jadon and Dr Natasha Jordan. Over the years, Sheila has seen many changes on E6 and says she has many happy memories of her 31 years working in the unit. Sheila will be greatly missed and on behalf of the Rheumatology Research Unit and CARE, we would like to express our gratitude for Sheila's hard work and dedication to Rheumatology research.

CLINICAL RESEARCH ON E6 - Dr Deepak Jadon - STUDIES OF INFLAMMATORY ARTHRITIS



Dr Deepak Jadon is a consultant rheumatologist and Director of the Rheumatology Research Unit (RRU) at Addenbrooke's Hospital. His major clinical and research interests relate to inflammatory arthritides such as psoriatic arthritis (PsA), ankylosing spondylitis (AS) and rheumatoid arthritis (RA).

We currently have 22 clinical studies active and three 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, a senior administrator (Mrs Katherine Hodges) and six research fellows (senior doctors undertaking a period of research, as described below).

Dr Mark Sapsford has now returned to a consultant post in New Zealand having in 2017/18 recruited 106 patients with PsA to his research study, **CLUE-PsA** that investigated the burden of enthesitis (inflammation where tendons, ligaments and joint capsules insert into bone) as measured by ultrasound versus clinical examination. The results of the study will be shared with you in due course.

Dr Jobie Evans has started to recruit to his 2-year study (**ProSpA-CD**) investigating how MRI scans of the abdomen in patients with Crohn's disease can be used to screen for patients with spondyloarthritis (inflammation of the spine). He will aim to recruit 200 patients over the coming year.

Dr Joseph Hutton is developing a PhD research study investigating extreme forms of PsA, including PsA-mutilans and enthesitis using imaging (x-rays, MRI, ultrasound) and immunology related to macrophage (a type of white cell) trafficking.

Dr Hannah Jethwa is about to start a 2-year study investigating how blood tests may be added to a questionnaire (PEST) to improve the detection of arthritis (PsA) amongst patients with skin psoriasis in the dermatology clinic.

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 has recruited 11 patients to date, with a target of 30 patients over the coming year.

Dr Tania Gudu is the fellow dedicated to the clinical trials on the RRU. In PsA she 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; we have recruited 22 patients to date; **SPEED study** where patients with PsA will be randomised to receive adalimumab anti-TNF therapy immediately after diagnosis; **POISE study** where patients with PsA will be randomised to receive NSAIDs only immediately after diagnosis if they have good prognosis (outlook) markers; British Society of Rheumatology **PsA Registry** assessing the safety of biologic treatments in clinical practice; **COSMOS trial** assessing the effectiveness of guselkumab (IL-23i) in patients with PsA; and the **PROPER study** in which patients with either PsA or AS switching from originator (Humira) to biosimilar (Imraldi) adalimumab will be closely monitored for effectiveness and safety.

In patients with RA we are recruiting to the: British Society of Rheumatology **RA Registry** assessing the safety of biologic treatments in clinical practice; and the IMRABIOME study assessing the microbiome of patients with RA (Dr Andra Negoescu, consultant, is leading the study in Cambridge).

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 & Reader at the University of Cambridge) is leading two clinical studies relating to osteoporosis and osteogenesis imperfecta (**ToPAZ** and **Asteroid** studies) as well as other studies in his university department.

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 AUROIMMUE 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 disappointingly 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.

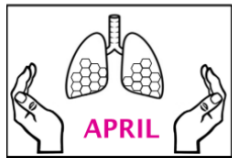
Finally, let us not forget patients who suffer with rheumatoid arthritis and chronic pain and fatigue. In collaboration with Dr Mike Lee in the Academic Division of Anaesthetics, brain scans are being performed to try and understand why some patients feel fatigued with rheumatoid arthritis and others 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

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, which aims to demonstrate that intravenous Rituximab is more effective than the current best treatment (intravenous Cyclophosphamide) for interstitial lung disease in CTD. This is important because treatment of inflammatory interstitial lung disease is currently limited to corticosteroids (which have many side-effects), mycophenolate mofetil, cyclophosphamide and tacrolimus. The latter three are all more difficult to use in patients who have frequent chest infections. We have recruited 3 patients to RECITAL so far and hope to be able to recruit a further 2-3.



Safety of abatacept in rheumatoid arthritis associated interstitial lung disease: A feasibility trial (APRIL)

This trial is investigating the safety of abatacept in patients whose rheumatoid arthritis is complicated by interstitial lung disease – abatacept is already known to be very effective in treating the arthritis in many patients, but some drugs which are effective for arthritis may not be safe when lung disease is present. The study is also measuring whether the lung disease responds to the drug with improved lung function, changes on CT chest and decreased breathlessness. The project is funded by an unrestricted grant from Bristol Myers Squibb with some bridging funding from CARE.

Thank you to all the patients who are participating in this study. You will all have noticed that the clinical fellow initially running the project, Dr Maeve Fifield is on maternity leave for a year. Baby Orla arrived 5th April 2019. In Dr Fifield's absence study visits are being run by Dr Hall, Dr Parfrey (Chest Physician) and Dr Stober. There are now 11 patients recruited to the APRIL study, three of whom have completed. We hope to have finished recruiting in spring 2020.



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

Cambridge is participating this multicentre study, which is run from Manchester. The purpose of the study is to 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 (a rarer form of systemic sclerosis with widespread skin involvement). This study is recruiting much more slowly than predicted – a problem across all centres and not just in Cambridge. We have recruited 1 patient (compared to our prediction of 3 at this point in time). So we are on the lookout for patients with early disease (within 3 years of onset of any non-Raynaud's manifestations of systemic sclerosis)



In May 2016, CARE Trustee Dr Hall arranged a meeting in Sidney Sussex College Cambridge and invited clinicians with interest and expertise in connective tissue disease and vasculitis (CTDV) across the East of England (EoE). This was the birth of the **Eastern Network for Rare Autoimmune Disease (ENRAD)**. The mission statement of the network is to improve the quality, value and sustainability of services for

patients with CTDV in the region. A high priority for the network was to set up a virtual case conference, to enable discussion of complex cases for the following reasons:

- To assist with diagnosis when this was unclear
- To discuss management of rare or resistant-to-treatment problems
- To provide regional governance for the use of high-cost drugs in patients with CTDV
- To identify if there are relevant clinical trials for patients with conditions with inadequate current treatment options

- To identify training and education needs for clinicians with an interest in CTDV in the region



The **ENRAD Video Case Conference (ENRAD VCC)** has run twice monthly from **Cambridge University NHS Foundation Trust (CUHFT)** since August 2016. Our work has been recognised nationally by the British Society for Rheumatology Best Practice Award 2018 (The photo shows network members, together with BSR President Dr Elizabeth Price (far right) receiving the award).

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. This year we have banked **£59.00**. We understand that as we move further towards a cashless society we need to provide alternative ways to donate and are launching a new website through which you will be able to donate online.

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