News Rheum

Edition 4: Childhood & Rare Diseases Spring 2019

WORKING TOWARDS BETTER RHEUMATIC AND ARTHRITIS RESEARCH - **TOGETHER**

Welcome to the fourth News Rheum Newsletter! The theme of this edition is CHILDHOOD ARTHRITIS & RARE RHEUMATIC DISEASES

February 28th was international Rare Disease Day and March 18th was the inaugural World Young Rheumatic Disease Day (WORD Day).

Members of the Rare Disease Research Partnership RAinDRoP, at the Rare Disease Research Priority Setting Day.

We hope you enjoy News Rheum. If you would like to get involved, please contact us at:

patientvoicearthritis@ucd.ie

IN THIS ISSUE

WORD Day 2019

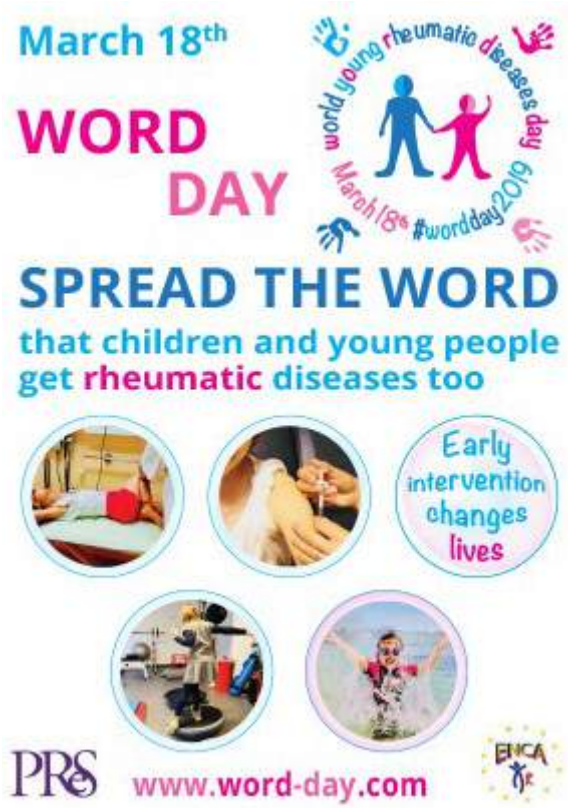
March 18th 2019 saw the first annual **WO**rld young **R**heumatic **D**iseases Day (WORD Day). The event's purpose is to raise international awareness of young people living with rheumatic diseases such as lupus erythematosus and juvenile arthritis.

Beyond spreading the word that young adults and even children do get rheumatic diseases, the main take-away was the importance of early intervention. The audience was broad - parents, doctors, primary practitioners, educators and the public - and the message to everyone involved with rheumatic care was: diagnose as early as possible and, where appropriate, arrange for quick referral to specialist paediatric rheumatologists.

Internationally, WORD Day was organized by ENCA (European Network for Children with Arthritis) and PReS (Peadiatric Rheumatology, European Association). In Ireland, sessions were arranged by iCAN Ireland (Irish Children's Arthritis Network) and the UCD Centre for Arthritis Research; these included:

- Workshop to help young patients make animated videos about their experiences of rheumatic disease
- A seminar for patients aged 10-20 to meet researchers investigating rheumatic diseases and their treatment
- Information sessions on strengthening activities, smart treatments for arthritis, rare diseases, juvenile idiopathic arthritis and the role of the immune system.

The animated videos are now online; go to icanireland.ie/blog, or search "iCAN Ireland" on Youtube. The video *But You Don't Look Sick* was viewed more than 23,000 times.



Updates from PARE 2019 Conference

by Stacey Gerealis

The 22nd EULAR Annual European Conference of was held in the Czech Republic on the 5th-7th of April 2019. The conference theme was ***Time2Work***

Johannes W. J. Bijlsma, *President of EULAR* opened the conference with **Adam Vojtěch, *Minister of Health*, Jiří Vencovský, *President of the Czech Society of Rheumatology*** and **Edita Müllerová, *President of the Czech League*.**

Safety and Health at Work (EU OSHA) gave the keynote presentation. She presented findings from the European Parliament project – *Safer and Healthier Work at Any Age* in the context of an aging workforce and the return to work. Here are some of the key findings:

- You don't have to be 100% fit to work
- Early intervention is the focus to staying in work
- Returning to work should be a clinical treatment outcome
- Multidisciplinary programmes should support companies and employees.
- Policy, interventions and budgets should be aligned.
- Access to occupational health services is crucial for early detection and for promoting workplace health.
- Clinicians and employers should focus on workers' capabilities, not their disabilities.
- Financial and technical support should be provided for employers to help people return to work.
- Governments need to have a greater public health focus on prevention and early intervention measures for chronic diseases.

"Too often having a chronic MSD leads to early exit" from work. With the right attitude from an employer and the right support from public health systems, "many can continue to work".

During 2020-2022 under the *Health Works* campaigns, OSHA will be focussing on Musculoskeletal Disorders .

Jakub Závada, *Institute of Rheumatology, Prague* presented *The Effect of Anti-TNF Therapy on Work Productivity and Activity Impairment in Patients with RA, AS and PSA over One Year from Real Life Data* from the Czech Biologics Registry.

Sarah Copsey, *European Agency for*

Updates from PARE 2019 (continued)

Workshops were held on the Value of Work, Occupational Rehabilitation, Finding the Right Job at the Right Time and Working with Policy-Makers, Employers and Trades Unions. **Professor Anthony Woolf - *Chair of the Arthritis and Musculoskeletal Alliance (ARMA)*** highlighted a best-practice case study in engaging with policy-makers from a UK perspective while **Gráinne O'Leary, *CEO of Arthritis Ireland*** presented the Fit for Work Ireland Coalition and discussed the work done to improve job-related problems for people in Ireland from an employee and employer perspective. For more information see www.fitforwork.ie

The Campaign's six main messages:

- MSDs are preventable and manageable
- Preventive measures can be simple and low cost
- Early intervention and rehabilitation of workers with MSDs is possible, needed and desired
- Staying physically active even in periods of musculoskeletal pain is important
- MSDs can be influenced by stress; tackle MSDs and work-related stress together
- Promote good musculoskeletal health among the future generation of workers.

Ms Copsey's key message was that health and safety measures which make work easier for whole the workforce can enable an individual with reduced work capacity to remain in employment and simple measures to support an individual can benefit the whole workforce.

Updates from PARE 2019 (continued)

Finally, Arthritis Ireland presented two patient-led projects in the best practice fair; *Fibromyalgia Health and Wellbeing Summit* and *Under 50 and Living with Arthritis National Conference 2018* presented by **Gloria Shannon (above) from *Young Arthritis Network,*** which won the overall prize for the best in the *Public, Policy-Makers & Health Professionals* category.

Rare Rheumatic Diseases:

One Researcher's Reasons for Addressing This Side of Rheumatology

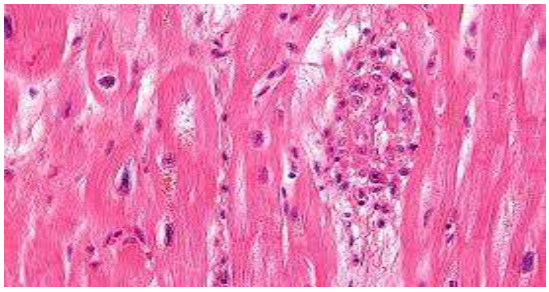
by Stephanie Skeffington

After ten years of working in one of the best rheumatology centres in the world, in Leeds, Dr Alexander Fraser became the first rheumatologist in University Hospital Limerick (UHL) 13 years ago. Dr Fraser and his team are also clinical partners on a UCD research project into a Behçets-like disease.

Dr Fraser's keen interest in rare rheumatic diseases stems from his time running a Behçets clinic in Leeds but, faced with running his own clinic in UHL, it would have been easy to forget this or at least put rare rheumatic diseases on the back burner.

"Why do I do it? It's purely selfish really, I find it really interesting, I love the buzz of treating someone with anything potentially dangerous, damaging or life threatening and getting miraculous results particularly with the new biologic medications available. It's great for me and it's great for my team."

He then went on to explain the challenges that today's rare rheumatic patients face. "The big issue is that pharma have no incentive to create new treatments as they don't get back any financial input for researching treatments as by definition they are rare. When you think of the fact that 6-7% of all adults in Europe have a rare disease, it's actually more common than you think and every week five new diseases are discovered. How do we incentivize both research and research into treatments? The licensing bodies in America and Europe have taken action to require pharma to fulfil fewer steps than normal but this has not had a great uptake."



Many rare rheumatic diseases are treated with drugs used 'off-licence'; this is where the drug is used outside of the use it was actually licensed for by the national regulatory bodies such as the HPRA or the EMA. "There are about six anti-TNF drugs that we use against autoimmune and auto-inflammatory targets off-licence for those with no alternative. For instance, we have 5-6 patients with a rare skin disease (morphoe prophunda) who went on Orcenia (Licensed for RA) and they all improved dramatically when no previous treatment had been shown to be effective."

Due to his past experience working with Behçets patients in Leeds, Dr Fraser estimated that, due to the disease being most common in those of African, Asian and Mediterranean ethnicity, in Limerick he should be seeing very few patients. "Due to the ethnicity of the population in Limerick I should have had one maybe two but I had thirty. Why do I have so many? Is it because I like it, I know about it and keep diagnosing it?"

"I looked into it further and discovered they weren't typical Behçets; while they satisfied the criteria, there is no blood test for Behçets – it is a clinical presentation. They had non-typical features such as nearly all being young females and no eye features."

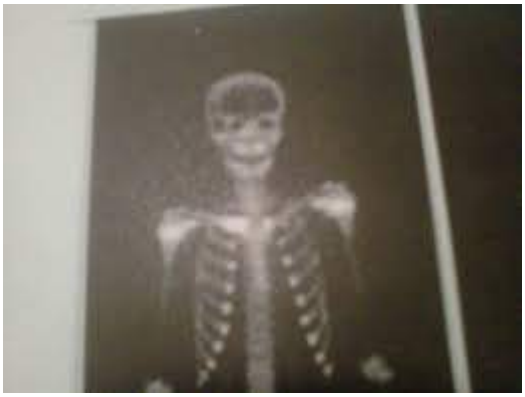
Rare Rheumatic Diseases (continued)

Realising that his patients had a Behçets-like disease, Dr Fraser had to decide what to tell his patients, taking into account the mental health implications. "You can't tell people you have something but we don't know what it is. So they satisfy the criteria for Behçets so that's their diagnosis, even though they know it's not; it's a similar mucocutaneous disorder"

Dr Fraser and his team identified and carried out clinical research and are clinical partners on a project with UCD's Centre for Arthritis Research on a Behçets-like disease project (www.ucd.ie/car/research/behcets). Dr Fraser explains how this research began by a chance discovery; "there was a patient, a girl and one of the nurses said to me: 'do you know we treat her half-sister, also with Behçets?' One sister with neuromyelitis optica (looks like multiple sclerosis but isn't), her full sister with Behçets and a half-sister to these two also with Behçets. We then sent their blood to Dr Emma Dorris and Dr Gerry Wilson in UCD for genetic screening. We tested all three parents, all of the brothers and sisters on one side and all of the brothers and sisters on the other side. We found that the father, all three of the sisters and a ten-year old child of one of the girls had a never previously seen deletion of the NF-kB gene."

"We looked quickly at the larger population to see if they had the same deletion; they don't but we are sure they'll have some other similar deletion. It's exciting"

In order to address the emotional and mental health implications of this type of discovery can have on his patients, Dr Fraser explained



that they "keep them tightly involved and up-to-date of what is happening."

After being involved in treating patients with rare rheumatic diseases for many years, Dr Fraser is concerned with what the future holds when it comes to their treatment options, considering recent government proposals. The most recent is a 'preferred prescription list', which would state which biologics are to be used for which condition, meaning he effectively could no longer prescribe these drugs off licence to rare rheumatic disease patients. He routinely has to use drugs off-licence, explaining "you are exposing yourself treating off-licence as, if there are poor results or side effects, then legally you are exposed as a clinician. However we find that, if you keep the patients closely informed and part of the whole process, then they are on board with what you are doing. He explains why he would never stop doing this; "You use drugs off-licence in rare disease where there are no alternatives and I've had great success doing it and it's really rewarding. As long as you do the right thing for the right reasons. If someone is really stuck you have to do something and I don't believe it's ethical not to do something, particularly with the wonderful new treatments we have available to us in this modern era."

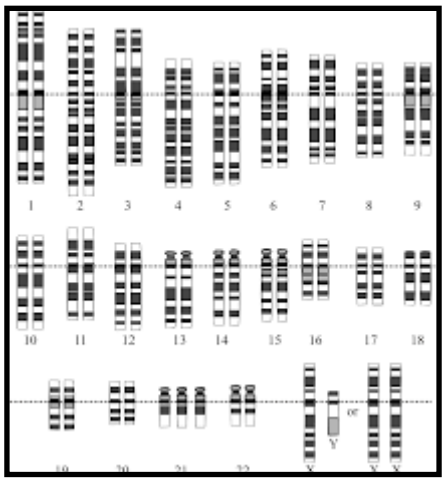
Do cells in the inflamed joint act differently in children with Down Syndrome and inflammatory arthritis compared to JIA?

by Sharon Ansboro & Ursula Fearon

Down Syndrome (DS) is a common chromosomal disorder characterized by the presence of a full or part of a third copy of chromosome 21. A variety of medical conditions are associated with DS, including autoimmune disorders such as diabetes mellitus, coeliac disease and thyroid dysfunction. Arthritis also occurs but has been largely under-reported in this population.

There is little data in the literature; the largest case series for reference is a retrospective chart review of nine children with Trisomy-21 (T-21) and arthritis. Over the last four years, through a National Musculoskeletal Screening Initiative led by Dr Orla Killeen and Dr Charlene Foley, the largest study worldwide of children with Down syndrome who have inflammatory Arthritis has been completed. This study demonstrated that Down's Arthritis (DA) in children is an under-recognised condition, occurring more frequently than with the general paediatric population. Indeed, we now estimate the prevalence of DA to be 18- to 21-fold greater than that of Juvenile Idiopathic Arthritis (JIA), therefore much higher than that previously reported. DA was also associated with a more erosive disease compared to JIA, with delayed diagnosis resulting in chronic disability and functional impairment.

The studies examining the underlying mechanisms that drive disease in children with DA are limited, with no studies to date examining cells at the site of inflammation. However the observed increase in erosive disease suggests that a key cell type, specifically 'synovial fibroblasts (SFC) that reside in the inflamed joint' may have a more pathogenic phenotype. These cells are specifically primed to invade cartilage and bone, so are the key drivers of joint destruction and thus disability. Based on the observed increase in erosive disease in children with DA compared to JIA, we decided to investigate if this specific invasive cell type differed between the two diseases. To do this, we obtained synovial tissue and synovial fibroblasts from the joints of children with DA and



JIA, who were undergoing routine steroid injection of their inflamed joints. The tissue was analysed for cellular inflammation and the synovial fibroblasts were then grown in the research labs, Molecular Rheumatology, TCD (Dr Sharon Ansboro/ Prof Ursula Fearon) and their pathogenic function was compared between DA and JIA, with a specific focus on their ability to migrate and invade the joint.

After growing these cells for a number of weeks in the lab, we observed an increase in the ability of DA synovial fibroblast to migrate compared to that of JIA. This effect was paralleled by a significant increase in the invasive capacity of DA synovial fibroblasts compared to JIA, which suggests they may have the ability to induce a more erosive disease. Furthermore, we identified that the DA synovial fibroblasts require more energy to function and observed that they switch the way they produce energy, allowing them to consume more glucose, to provide enough energy to carry out their invasive function in the joint. Supporting these findings, we also demonstrated an increase in specific genes associated with energy and cellular invasiveness in DA synovial fibroblasts compared to JIA. Finally, analysis of the joint tissue demonstrated a thickening of the invading layer of the synovium in DA compared JIA and it is in this layer where the invading synovial fibroblasts specifically reside.

This is the first study to demonstrate differences in the joint tissue of children with DA compared to JIA. It also demonstrates that the synovial fibroblast display a more aggressive invasive phenotype in DA which relies on their ability to produce energy. This capacity to invade may underlie the observed increase in erosive disease in children with DA. Whether this is due to delayed diagnoses or is a distinct feature of the disease is unclear. However, it highlights the need for increased awareness of the condition in children with DS, which will lead to earlier diagnoses and treatment and should in turn lead to significant improvements in their clinical care and management.

RAinDRoP:
The Rare Disease Partnership
by Suja Somanadhan & Emma Dorris

The UCD Centre for Arthritis Research is involved in a new partnership with colleagues from across UCD, the HSE and carers and people living with rare diseases across Ireland.

RAinDRoP
Rare Disease Research Partnership

The Rare Disease Research Partnership (RAinDRoP) aims to bring together our individual skills, knowledge and experience, to prioritize and progress research into rare diseases in Ireland. Led by Dr Suja Somanadhan (UCD School of Nursing, Midwifery and Health Systems), this is an exciting opportunity to bring the community of people focussed on rare disease together, to make our research better, more relevant and more likely to improve the lives of those living with rare diseases.

Rare Disease Event:

4th April 2019,

UCD Student Centre

The RAinDRoP Workshop was a unique opportunity to influence future research into rare diseases. The workshop sessions were chosen with a life-course perspective in mind. Sessions focussed on three key areas of important, but currently under-researched, shared challenges in the rare disease community:

1) Pathway to diagnosis, focussing on early, accurate diagnosis and the communication challenges associated with a rare disease diagnosis

2) Supporting management and self-management of rare disease

3) Integrated care pathways and palliative care needs of individuals with advanced rare diseases.

The RAinDRop workshop stimulated the development of a rare diseases research consensus group, which will include national and international experts from the clinical, academic, professional disciplines, patients and caregivers.

This workshop enabled research priorities based on the patients living with rare diseases rather than their specific diagnoses. The event featured contributions from national and international patients and caregivers and from clinical and academic professionals.

Attendees at the workshop consolidated the rare disease research questions down to the top 15 priorities for rare disease research in Ireland. This will be further reduced to the top 10 priorities by way of a public survey. If you are a person living with a rare disease or a parent, family member, carer or friend of someone who does, or if you are a health care professional or researcher interested in rare disease research, please go to www.surveymonkey.com/r/RAinDRoP19 to take the survey and be part of determining the rare disease research priorities for Ireland for the next seven years.

Involvement Opportunities

by Emma Dorris

Chronic Pain

Dr Emma Dorris (UCD) and Matt McCann (Access Earth) are working together on a technical solution to help social isolation that can be caused by sensory overload associated with chronic pain. The North-East Fibromyalgia Support Group has helped us design a survey so that we can understand the environmental triggers that can cause sensory overload. If you can help us further, please take our survey here: www.surveymonkey.com/r/88PN3L2

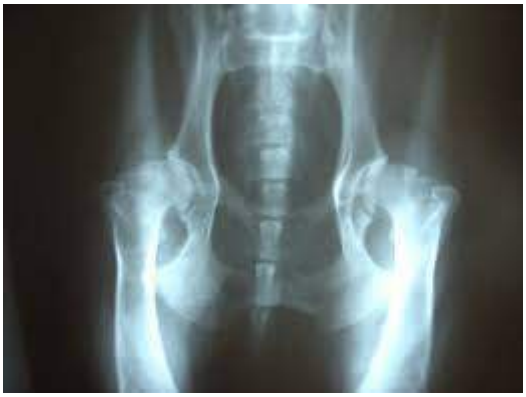
This information will go towards the development of an app. If you would like to test-drive and review the app , while it is being developed, please contact patientvoicearthritis@ucd.ie

Fibromyalgia

We are currently advertising for a research Master's student for a fibromyalgia project. If you would like to be involved in mentoring this student from September, so that they can better understand life with fibromyalgia; for more information, please contact patientvoicearthritis@ucd.ie.

Inflammatory Arthritis of Down Syndrome

As you may know, UCD, Trinity and Crumlin Children's hospital have been working together on research into Inflammatory Arthritis of Down Syndrome in childhood. We have a summer project to create physician information leaflets to get the information about Inflammatory Arthritis of Down Syndrome out to GPs and primary care workers. We are looking for patients, parents, family members or carers to help us with this project starting in June. For more information, please contact patientvoicearthritis@ucd.ie.



Training Opportunity

If you are a patient or part of a patient group who uses surveys or qualitative research (such as interviews and patient experience pieces) and would like some training on how best to develop your questions and analyse "open field" or text responses, we have a training opportunity for you. The Patient Voice in Arthritis Research, in association with the UCD Conway Patient Voice in Health Research have asked QUESTS (Qualitative Research in Trials Centre, Galway) to develop a half-day training course just for research-active patients (which encompasses people living with disease, family members, careers or patient advocates).

The training focusses on developing questions and looking at how the data is used and will touch on how the analytic techniques are applicable to other forms of data collection (e.g. focus groups and interviews). This will take place in UCD on June 7th at 11am-3pm. Lunch will be provided.

Places are extremely limited and preference is given to patients who have been involved with either (1) a Patient Voice research project or researcher, (2) involved with a research project or researcher within UCD Conway or (3) involved with clinical trial research (at any stage of clinical trial including, concept, design, development outcome, or if part of a patient group: deciding whether your group should be involved in assisting with clinical trials nationally or internationally). Remaining places will be allocated on a first- come, first-served basis. To receive a registration link for the training course, email patientvoicearthritis@ucd.ie.

Self-Managing Rheumatoid Arthritis: A Photovoice Study

Do you want to use photography to share your experience of living with RA?

This is an opportunity to take part in a study which uses photography to show everyday life with Rheumatoid Arthritis (RA).

You will be part of a small group working with a researcher to identify the challenges and solutions to living with the condition. This study uses a "photovoice" method to reveal the hidden experience of RA and create social action and change within our communities.

Participants must be over 18

"This is a very simple device I use to open bottles as I don't have the strength to open bottle tops"

To REGISTER your interest contact:

Susie Donnelly, Researcher at University College Dublin

Email: susie.donnelly@ucd.ie **Tel:** (01) 716 6462 (direct line)

For more details, visit www.ucd.ie/CAR

Update from the UCD CAR Steering Committee

by Wendy Costello

The first I knew of the UCD CAR was when Dr Emma Dorris put a call out for patients and carers to come to a meeting in Dublin. I am chair of iCAN and I thought I would go along to make sure paediatric rheumatology was represented at this. From this meeting, I knew Emma and I were going to get on. Her passion to involve patients and carers in the work was delighted to do a small part by co-chairing a session and this was the first time for me to meet Professor Gerry Wilson. I didn't get time to chat to him on the day as it was so busy. Following this, a call was put out for participants to join the newly formed Steering Committee. I applied and was absolutely delighted to be accepted. We arrived for quiet amazed at the work being done there. Patients and carers form a third of the group and I feel this is very important. My voice is important and I feel part of a team that I would never of imagined I would be part of, fourteen years ago, as I arrived at Crumlin Children's Hospital with a very sick three-year-old. Emma would not like to be singled out but

of the Centre was clear and she broke down the walls of this institute we knew little about. So the Patient Voice in rheumatology was born. The first big job of this initiative was a research conference open to the public. I our first meeting and I was quite nervous. Gerry made me feel so welcome straight away and I was so thrilled to find they are actually all human! We have had two meetings so far and I already feel part of the team and am she has made this possible and PPI and funding have made it possible. We are in our infancy but I look forward to developing this group and being an integral part of it.

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