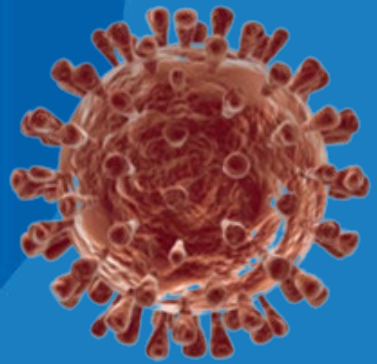
What have we learned from COVID? A Rheumatology Perspective

Prof David Kane,
National Lead, HSE Clinical Programme for Rheumatology



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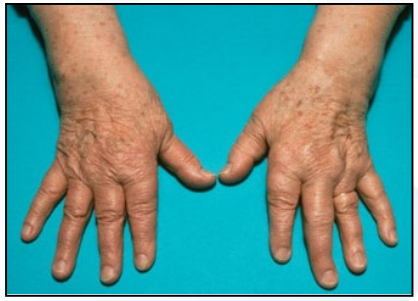
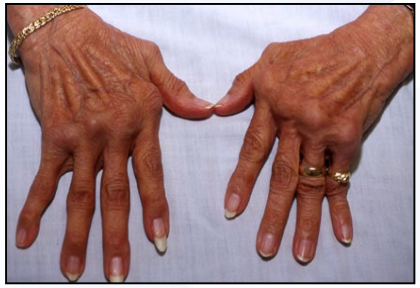
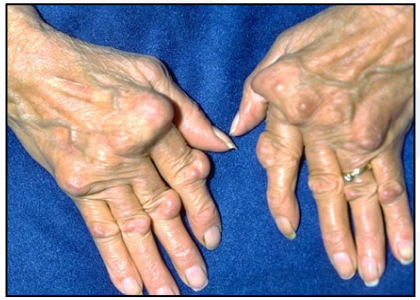
Rheumatoid arthritis and biologics



47,700 people in IRL
Peak onset 30's

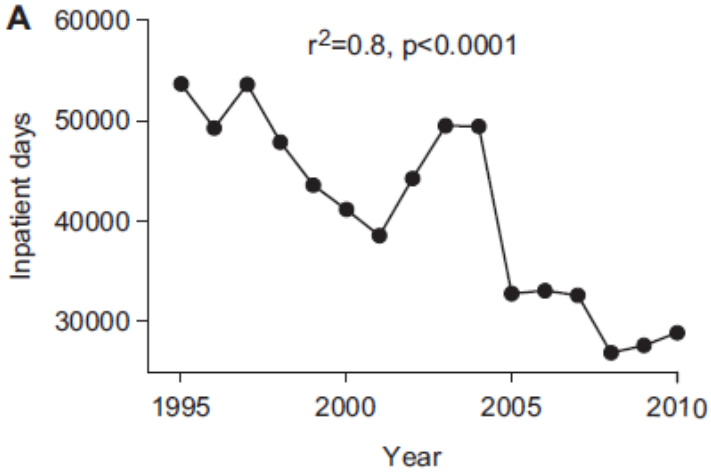


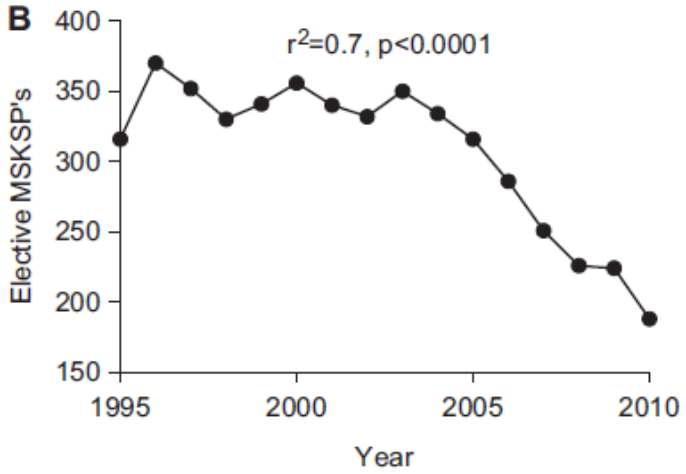
- Without treatment
- 50% UE @ 5 years



- With treatment
- 50% less admissions
- 50% less surgeries

Harty et al, Rheumatology 2015





Rheumatology Therapies 2020 (**in bold late 1990's**)

methotrexate, leflunomide, **hydroxychloroquine**, **sulfasalazine**, **gold**, **azathioprine**, **ciclosporin**, **cyclophosphamide**, mycophenolate, minocycline, **penicillamine**, tacrolimus, anakinra, infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, rituximab, abatacept, tocilizumab, sarilumab, sirukumab, olokizumab, ixekizumab, guselkumab, ustekinumab, mavrilimumab, tofacitinib, baricitinib, peficitinib, filgotinib, upadacitinib or fostamatinib

csDMARD – the old tablets

bDMARD – IV/SC … TNFi, IL1i, IL6i, IL17i, IL23i, T-cell, B-cell

tsDMARD – the new tablets

What is the Downside of Immunotherapy?

Increased infection:

- Serious Infection: mitigate with patient selection, monitoring, prompt treatment, vaccination (annual flu, 5 year pneumococcal, shingles over 65)
- Opportunistic (eg TB with TNFi) – pre treatment screening and Rx.
- Exacerbation (Hep B and C) – pre treatment screening and Rx.
- HSV – JAKi and steroids

Cancer: Non Melanoma Skin Cancer may be increased – sun protection

MACE: No increase – monitor and treat lipids and BP

Lower Intestinal Perforation (LIP): IL-6i therapy only - exclude if diverticulitis

VTE: JAKi – exclude if VTE risks

Annals of the Rheumatic Diseases

Safety of synthetic and biological DMARDs: a systematic literature review informing the 2019 update of the EULAR recommendations for the management of rheumatoid arthritis

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Timeline of a Pandemic

RTÉ NEWS

16 Jan 2020

BBC NEWS

Home | War in Ukraine | Coronavirus | Climate | Video | World | UK | Business | Tech | Science | Stories

World | Africa | Asia | Australia | Europe | Latin America | Middle East | US & Canada

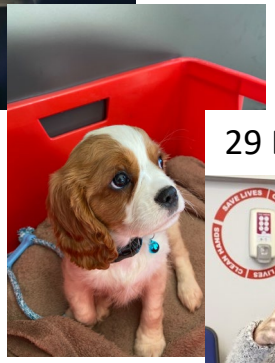
29 Feb 2020

Coronavirus: First case confirmed in Republic of Ireland

29 February 2020

Trump Says He's Taking Hydroxychloroquine, Prompting Warning From Health Experts

His announcement drew immediate criticism from a range of medical experts, who warned not just of the dangers it posed for the president's health but also of the example it set.



29 Dec 2020

Annie Lynch (79) who was the first person in the Republic of Ireland to receive the Covid-19 vaccine.

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Key Issues in Rheumatology?

Immunotherapy and the risk of contracting /dying from COVID-19
Anxiety / Fake news / Infodemic
Occupational Health

Immunotherapy in treatment of COVID

- Hydroxychloroquine
- Dexamethasone
- Tocilizumab

Vaccination

- Prioritization
- Interaction with immunotherapy

COVID-19 Global Rheumatology Alliance

The Global Rheumatology Community's Response to the Worldwide COVID-19 Pandemic

Clinician and Patient driven
Rapid development following pandemic
Irish Lead – Dr Richard Conway

9193 patients
Ireland - Largest contributor per capita
N=130 (Wave 1 - N=105)

Characteristics	N=105
Age , years, median (IQR)	59 (48, 76)
Female	64 (61%)
Hospitalised	47 (45%)
Required oxygen	25 (24%)
AIRVO/NIV	3 (3%)
Ventilated	4 (4%)
Deceased	10 (10%)

eular

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Multivariate model – Hospitalisation in Ireland

- Female OR 0.34 (95% CI 0.09, 1.36) p=0.128
- Age OR 1.06 (95% CI 1.01, 1.10) p=0.01
- Inflammatory arthritis (vs CTD) OR 0.09 (0.02, 0.32) p<0.001
- Number comorbidities OR 1.93 (1.11, 3.35) p=0.02
- Glucocorticoids OR 15.01 (1.77, 127.16) p=0.013

Trinity Rheumatology and Covid-19 Registry - TRACR

Dr Rachael Flood, Dr Richard Conway, Dr Colm Kirby,
Prof David Kane, Prof Ronan Mullan

Tallaght University Hospital | Ospidéal Ollscoile Thamhlachta

An Academic Partner of Trinity College Dublin

The Meath Foundation
Fondúireacht Na Mí

ST. JAMES'S HOSPITAL
DUBLIN . IRELAND

TRACR Study

A total of 7,500 patients comprising 4,524 with IRDs and 2,976 with non-inflammatory disease (nIRDs) were contacted.

Cross-referencing with test-centre positive PCR results and mortality data

750,000 pop
Feb- June 2020

210 email/phone responses.

78 cases met the criteria for PCR or physician diagnosed COVID-19

68 were community acquired

10 hospital acquired.

Annals of the
Rheumatic Diseases

R Flood, R Conway, C Kirby, D Gheta, D Kane, R Mullan.

on Hospital

Results

- 68 community acquired
- 40 inflammatory and 28 non-inflammatory
- Cumulative incidence/100,000
  inflammatory 884
  non-inflammatory 940
  general population Dublin 887
- Hospitalisation rates for community Covid-19
  - Inflammatory rheumatic disease 15%
  - General population 13%
- 8/78 deaths

DRUG	N	%
CSDMARD	18	45
BDMARD	16	40
MTX	9	22.5
HCQ	9	22.5
GC	2	5
TSDMARD	0	0

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Results

- Hospitalisation rates for community acquired Covid-19 in IRD (15%)

- In community acquired COVID-19, hospitalisation was more likely to occur
  - glucocorticoids (n=2 (33%) v n= 0 $p<0.01$)
  - type 2 diabetes (IRD n = 2 (33%) v n = 1 (2.9%) $p< 0.05$
  - nIRD (n = 3 (20%) v n = 1 (1.9%) $p<0.05$).

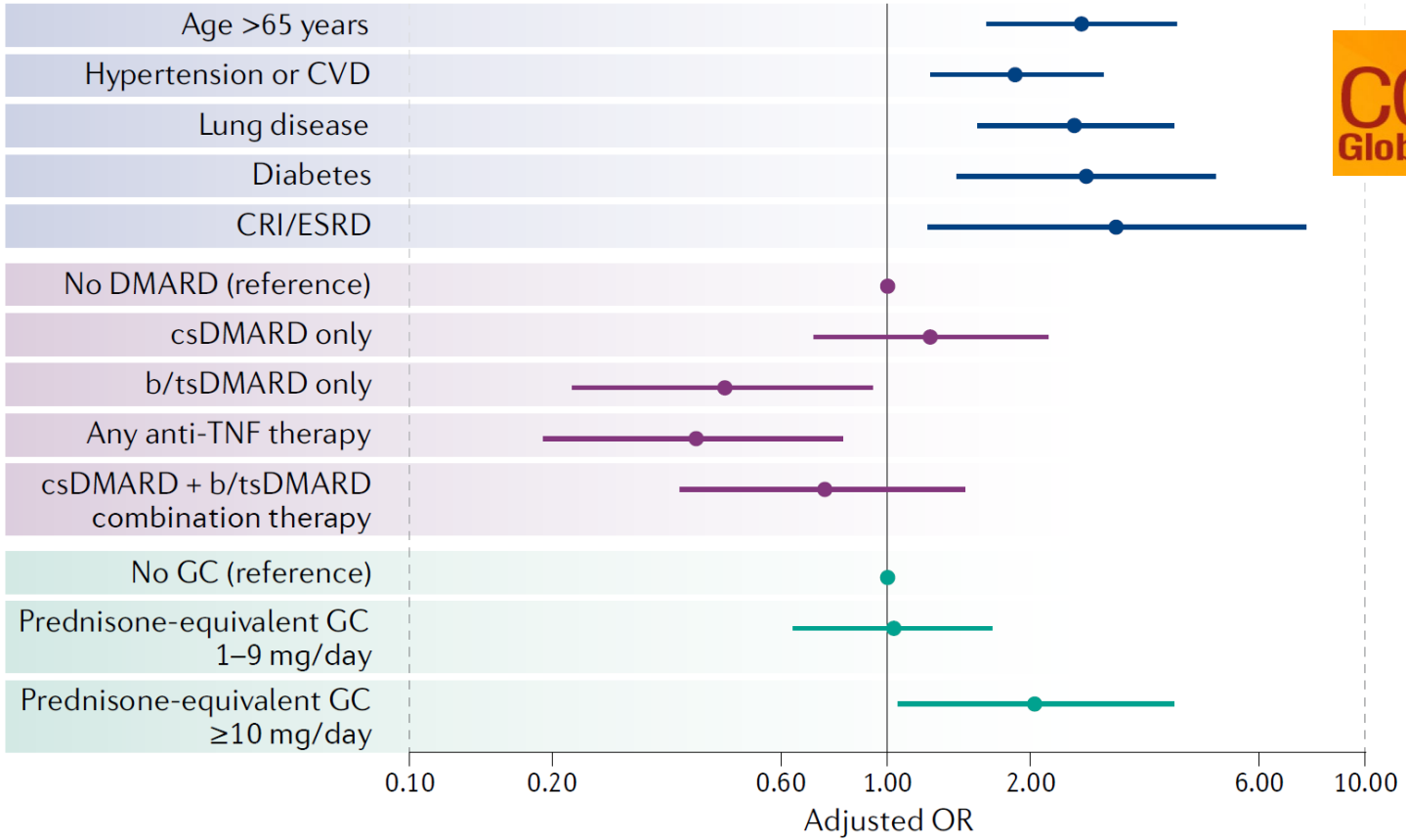
- No significant increase in mortality (5 IRD v 3 nIRD).

- Hospitalisation was not increased in patients receiving long-term anticytokine biological therapies.

Annals of the
Rheumatic Diseases

CLINICAL SCIENCE

Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry



COVID-19
Global Rheumatology Alliance

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Annals of the
Rheumatic Diseases

EPIDEMIOLOGICAL SCIENCE

Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry

What are COVID 19 related risks in people with rheumatic diseases?

COVID-19
Global Rheumatology Alliance

- Moderate/High Disease Activity – OR 1.87 (95%CI 1.27, 2.77)
- Steroids >10mg/day – OR 1.69 (95%CI 1.18, 2.41)
- Rituximab – OR 4.04 (95%CI 2.32, 7.03)
- CYC/AZA/MMF/TAC/CIC – OR 2.22 (95%CI 1.43, 3.46)
- No DMARD – OR 2.11 (95%CI 1.48, 3.01)

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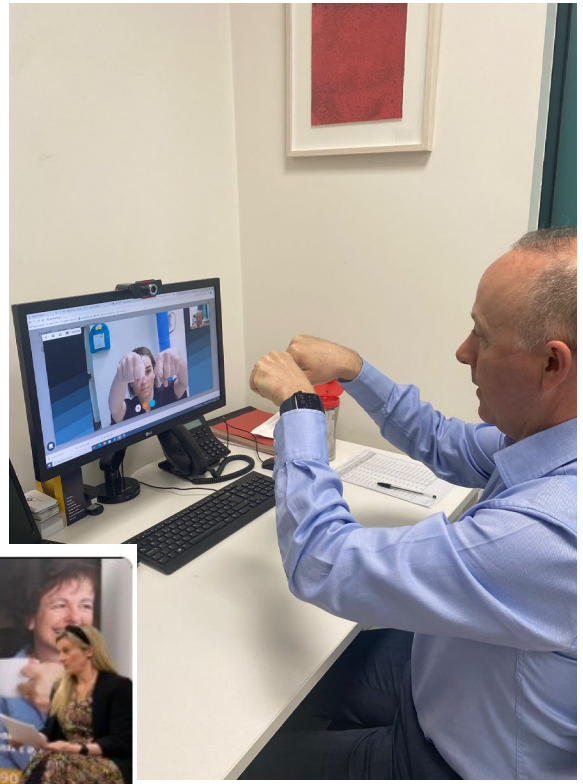
Digital Transformation

- Telehealth
- Videoconsultation.. **TPro**, Hashealth, Doxyme, Zoom
- E-prescription
- Social Media for rapid communication
- Rheumatology Patient App
- Patient Reported Outcome Measures (PROMs)
- Fitbit / Iwatch…. For monitoring



Covid-19 and arthritis
Arthritis Ireland
117 views · 25 March 2020

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Covid Vaccination in Rheumatology

EULAR (Ireland)

Immunotherapies may impair vaccine response

rituximab – vaccinate at end of 6 month cycle

methotrexate – short pause of 1-2 weeks may be beneficial, unlikely to cause flare

other DMARDs – theoretical risk, no evidence for pausing

don't stop steroids

aim to optimize boosters – all immunotherapies listed for 4th dose in Ireland

ACR

Advise pauses for multiple agents of variable duration based on expert opinion but very limited evidence

Managing Infections in Immunotherapy?

Increased infection:

- Serious Infection
    - Increase risk can be mitigated with patient selection
    - Ensure regular clinical and lab monitoring
    - Prompt patient presentation and treatment of infection
    - Temporary pause of therapy usually advised except steroids/vasculitis
- Pre treatment screening and Rx for TB, Hep B, Hep C, HIV, varicella
- COVID-19
    - risk mainly in vasculitis / CTD (may be Rx bias)
    - Increased risk with steroids / rituximab / cyclophos / mycophenolate
- Vaccination
    - annual flu
    - 5 yearly pneumococcal
    - shingles over 65 – all when recombinant available
    - Additional (4th dose) for SarsCoV

Thank you

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Cases from the Covid-19 Pandemic

Dr Orla Ni Mhuircheartaigh
Consultant Rheumatologist

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Overview of Challenges in Rheumatology

- Vaccinations in immunosuppressed Rheumatology patients
- CV 19 infection in immunosuppressed Rheumatology patients
- Cytokine storms in CV 19 infection
- Immune mediated complications of CV 19
- Immunosuppressive treatment in CV 19 infection (Steroids , Toculizumab)
- CV 19 related anxiety in immunosuppressed Rheumatology Patients

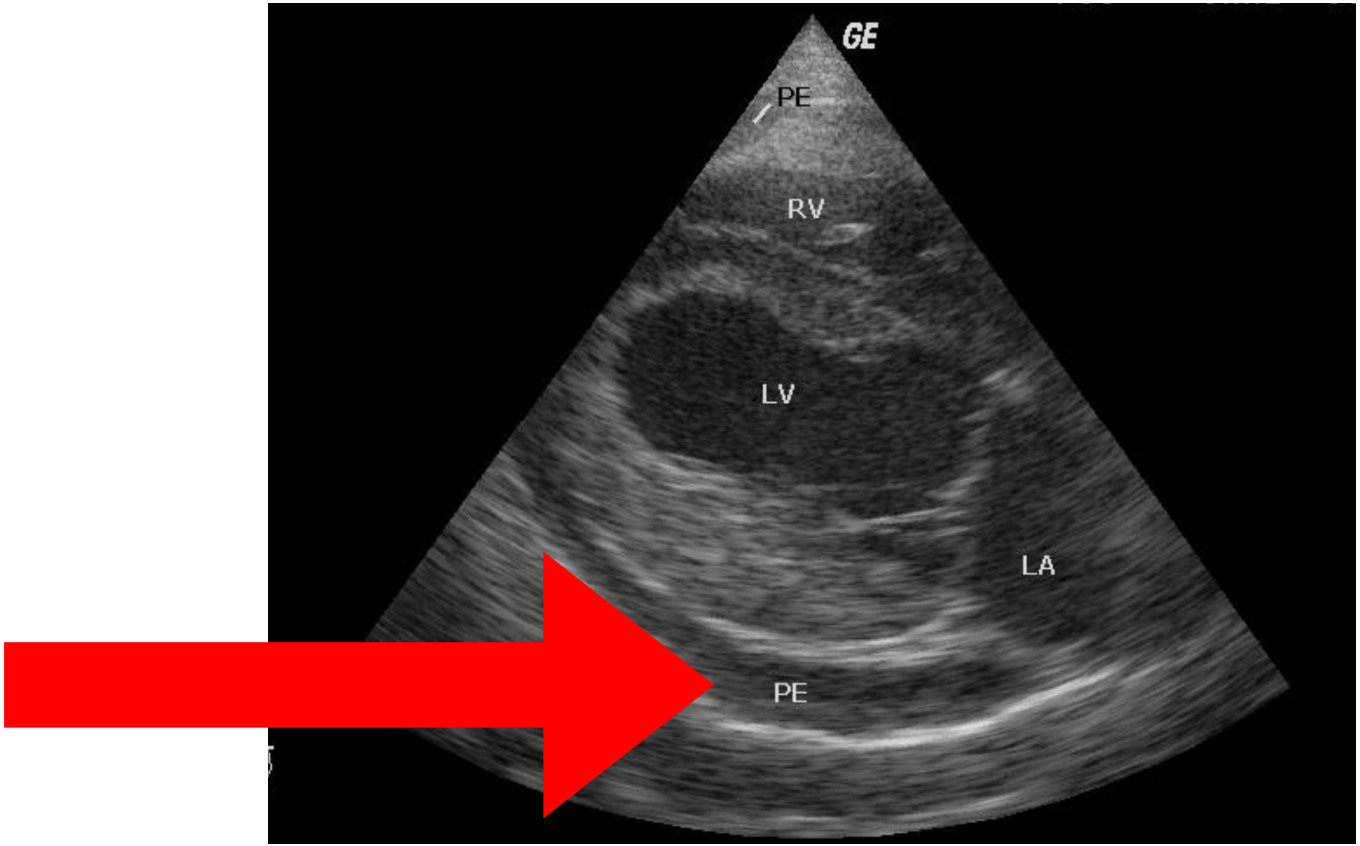
Case 1

- Case of DM, May 2021
- 83yr old lady, presented to Beacon ED weakness, fever, palpitations, Chest pain
- 10/7 days after receiving the 2nd dose of the Moderna Vaccine
- PMHx: HTN, IHD, OA, Dyslipidaemia, Depression, Breast Cancer (2001)
- Independent, lives alone, supportive family, non smoker, no alcohol

- Bloods: WCC 12.7 (Neut 9.1) CRP 162, ESR 65, Ferritin 895, HB 13.5,
- MSU (Negative), CXR (NAD), ECG (Sinus tachycardia)
- Vitals: HR 113, BP 95/68, O2 98%, RR 18, Temp 37.8
- Held off on antibiotics (No source of sepsis identified)
- Admitted for further investigations

- Blood cultures x 5- All negative
- Temp - 37.5 - 38.1
- CTTAP - Trace left pleural effusion, Moderate sized pericarial effusion , No source of infection, No malignancy
- Bloods: RF - CCP - ANA - ENA - ANCA - C3C4 normal, Immunoglobulins - IGG 7.3 (IGA, IGM, normal), LDH normal
- Additional bloods HIV - Hep B - Hep C - Quantiferon - , Trop normal, BNP normal

Echocardiogram



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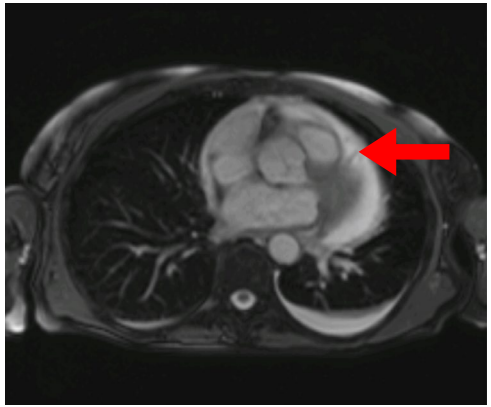
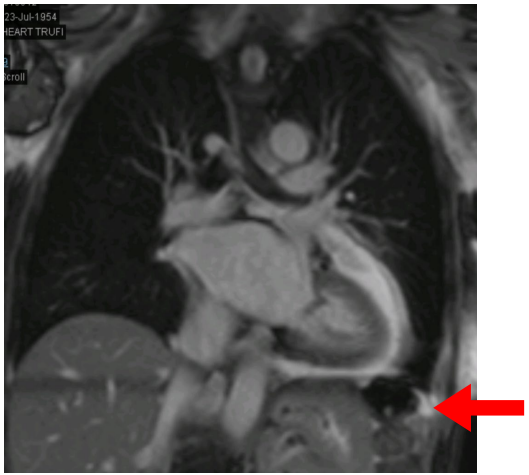
Cardiac MRI Findings

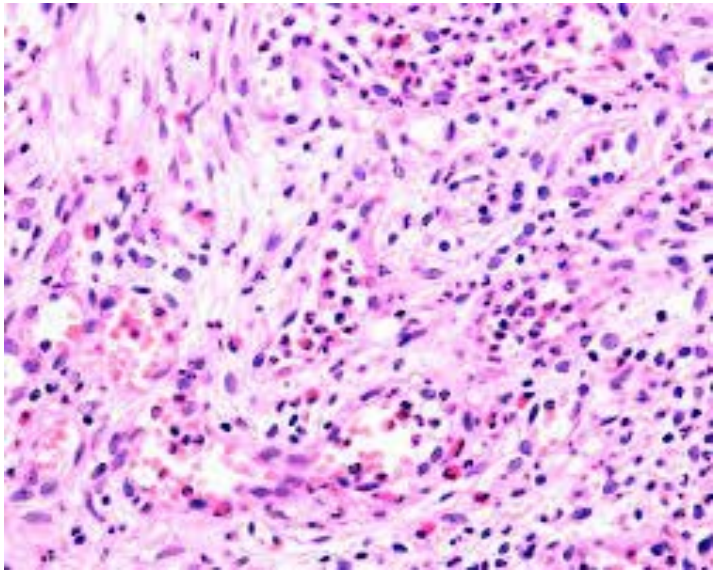




- Normal LV size and function EF 56%
- Normal RV size and function EF 50%
- Left Pleural enhancement with atelectasis and small pleural effusion
- Circumferential pericardial enhancement with moderate pericardial effusion
- No evidence of pericardial constriction or tamponade

Diagnostic Pericardiocenthesis

- 5ml inflammatory serous fluid
- Inflammatory infiltrate
- Culture and gram stain -ve
- Acid Fast Bacilli -ve
- Glucose normal
- Cytology negative



Immune Mediated Pericarditis

- Started on Colchicine , NSAIDS -> modest improvement x 3/7 (CRP 160-112)
- Prednisolone 40mg started , PPI cover CD3F -> Dramatic improvement 48 hrs (CRP 112-23)
- DC , Tapering steroids over 8/52
- Follow up , 6 weeks Fully resolved , CRP 7
- 3/12 and 6/12 follow up - No recurrence

Serositis

- Common Causes of serositis: Infection, TB, Malignancy, Autoimmune disease
- Cases post CV 19 infection , CV 19 vaccination
- Very rare, most common mRNA
- Most common, within 14/7, after 2nd dose, younger males
- Mild, respond to conservative measures
- Confirmed cases of myocarditis - not receive another dose of mRNA vaccine
- Over 18 yrs- non mRNA vaccine after 28 days
- Cases of pericarditis - Decision left at the discretion of cardiologist, patient other physicians involved in care
- Report HSE: Communication to Heathcare professionals: Report of myocarditis/ pericarditis post mRNA Covid-19 vaccination (28/2/22)

Case 2

- Case of CW, 63 yr old male, Connemara
- Dx with sero-positive RA, Dx December 2020
- PMHx: DM Type 2, Elevated BMI, Gout, Gold stage 3 COPD, HTN
- Farmer (Cattle and Sheep), Widowed, 3 children, Good social support, Smoker (40 pk yr hx), Alcohol 40U/wk
- Despite strong encouragement, declined to receive the CV 19 vaccination
- Started on MTX ->20mg (Dec-March), Adalidumab added in (April 2021)
- June 2021- In remission

- Sept 2021: Cough, fever, myalgia, pharyngitis, -> CV 19 Positive
- Day 4 CV19 illness, Admitted through Emergency Dept, Beacon Hospital- (CV 19 Isolation Pathway)
- Bloods: WCC 15.2 (Lymph 5.1) CRP 189 ESR 83, IL-6 54, Ferritin 1542, HB 12.1, ALT 230, AST 156, LDH 336, Trop < 14
- Vitals: HR 130, BP 143/89, O2 81%, RR 26, Temp 39.5
- CXR : Bibasal infiltrates , No effusions, Hyperinflation
- ECG (Sinus tachycardia)
- CVS: HSI/II , Nil added, tachycardic
- Resp: Clear lung fields, Mild diffuse wheeze, crepitations
- MSK: No synovitis

- ABG: PH: 7.15, PCO2: 11.3, PO2 9.1, HCO3 26
- Treatment: MTX and Adalidumab stopped
- Dexamethasone 6mg OD
- Started on AIRVO
- Partial Clinical Response, Day 4
- Administered IV Toculizumab (8mg/ KG)
- Continued on AIRVO , Supportive measures
- Day 7 , signs of clinical improvement, Weaned off AIRVO
- DC from hospital on Day 14

Follow Up

- MTX and Adalidumab both continued to be held on DC
- F/UP at 4 weeks: RA stable, Fatigue++, ALT 89, AST 65, CRP 13, Resp Exam clear
- Restarted Adalidumab at 6 weeks
- 8 weeks: LFT normal, MTX restarted
- Further discussion around Vaccination: Vaccinated - January 2022

Questions

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Thank you

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