Expert Forum

Immune-Mediated Inflammatory Disease (IMID) Conference

Making Education Easy

Nelson, NZ, September 2012

In this review:

Welcome to this review of the inaugural Immune-Mediated Inflammatory Disease (IMID) conference, held in Nelson 5-6th September 2012.

The IMID conference bridged multiple specialties (dermatology, gastroenterology and rheumatology) and provided an excellent forum to facilitate a better understanding of immune-mediated inflammatory diseases and their management. The IMID Steering Committee (Assoc. Prof. Richard Gearry, Dr Julia Martin and Dr Nicholas Birchall) together with AbbVie, brought together an impressive line-up of local and international speakers, including eminent experts Professor Walter P. Maksymowych (Canadian rheumatologist), Dr Cory A. Siegel (US gastroenterologist) and Dr Stephen Tyring (US dermatologist). The conference took the format of combined and breakout sessions covering all three specialties. Dr Nicholas Birchall, Dr Michael Corkill, Assoc. Prof. Richard Gearry, Dr Melissa Haines, Dr Julia Martin, Dr David Rowbotham, Dr Michael Schultz and Dr Ravi Suppiah chaired individual sessions. This review summarises the presentations made at the meeting.

SpA: What can we learn from the rheumatology experience?

Presenter: Dr Katey Jenks

Classification

The spondyloarthropathies are generally considered as five individual diseases (AS, PsA, reactive arthritis, arthritis associated with IBD and undifferentiated SpA) with overlapping features such as HLA-B27 positivity, sacroiliitis, psoriasis, gut inflammation and enthesitis. Recently, the ASAS published new classification criteria separating SpA into predominantly axial or peripheral disease. To meet the criteria for axial SpA, an individual must have >3 months of back pain and age of onset <45 years, and either sacroiliitis on imaging plus ≥1 SpA feature or HLA-B27 plus ≥2 SpA features. SpA features include: inflammatory back pain, arthritis, enthesitis (heel), uveitis, dactylitis, psoriasis, CD/UC, good response to NSAIDs, family history of SpA, HLA-B27, elevated CRP.[1] These criteria enable the classification of patients at an earlier stage of disease, mainly by using MRI to diagnose sacroiliitis. To meet the criteria for peripheral SpA, an individual must have arthritis or enthesitis or dactylitis plus ≥1 SpA feature (uveitis, psoriasis, CD/UC, preceding infection, HLA-B27, sacroiliitis on imaging) or ≥2 other SpA features (arthritis, enthesitis, dactylitis, inflammatory back pain [ever], family history of SpA).[2]

Monitoring disease activity

Monitoring SpA relies on regular clinical assessment and the ASAS and GRAPPA have identified the following core domains: joint count, inflammatory markers, patient global/pain scores, spinal mobility, enthesitis score, dactylitis score, BASDAI, BASFI, skin and nail scores, ASQoL and DISQ. The BASDAI has been well validated, and forms part of the Pharmac criteria for starting and continuing anti-TNF therapy.[3] Composite outcome measures include ASAS20/40 improvement criteria, ASAS partial remission criteria, ASDAS, ACR20, PsARC and PASDAS.

Abbreviations used in this issue

ACR = American College of Rheumatology
ADEPT = Adalimumab Effectiveness in Psoriatic Arthritis Trial
ADR = adverse drug reaction
ANCA = antineutrophil cytoplasmic antibody
AS = ankylosing spondylitis
ASAS = Assessment of SpA International Society
ASCA = anti-saccharomyces cerevisiae antibody
ASDAS = Ankylosing Spondylitis Disease Activity Score
ASQoL = Ankylosing Spondylitis Quality of Life
BASDAI = Bath Ankylosing Spondylitis Disease Activity Index
BASFI = Bath Ankylosing Spondylitis Functional Index
BASMI = Bath Ankylosing Spondylitis Metrology Index
BMI = body mass index
BSA = body surface area
CASPAR = Classification Criteria for Psoriatic Arthritis
CCP = cyclic citrullinated peptide
CD = Crohn's disease
CDAI = Crohn's Disease Activity Index
CRP = C-reactive protein
CT = computed tomography
DISQ = Dudley Inflammatory Bowel Questionnaire
DLQI = Dermatology Life Quality Index
DMARDs = disease-modifying antirheumatic drugs
EAM = extra-articular manifestation
EIMs = extra-intestinal manifestations
Eow = every other week
ESR = erythrocyte sedimentation rate
ESSG = European Spondyloarthropathy Study Group
EULAR = European League Against Rheumatism
FDA = Food and Drug Administration
GRAPPA = Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
HIV = human immunodeficiency virus
HLA = human leukocyte antigen
HR = hazard ratio
IBD = inflammatory bowel disease
IBS = irritable bowel syndrome
IL-23R = interleukin 23 receptor
IRR = incidence rate ratio
IMID = immune-mediated inflammatory disease
IVF = in vitro fertilisation
MHAQ = Modified Health Assessment Questionnaire
MHC = major histocompatibility complex
MRI = magnetic resonance imaging
NMSC = non-melanoma skin cancer
NSAIDs = non-steroidal anti-inflammatory drugs
OmpC = *Escherichia coli* outer membrane porin C
OR = odds ratio
PASDAS = Psoriatic Arthritis Disease Activity Score
PASI = Psoriasis Area and Severity Index
PsA = psoriatic arthritis
PsARC = Psoriatic Arthritis Response Criteria
PTPN22 = protein tyrosine phosphatase non-receptor type 22
RA = rheumatoid arthritis
RF = rheumatoid factor
RR = relative risk
SAE = serious adverse event
SC = subcutaneous
SDAI = Simplified Disease Activity Index
SIR = standardised incidence ratio
SLE = systemic lupus erythematosus
SpA = spondyloarthropathy/spondyloarthritis
SPARCC = Spondyloarthritis Research Consortium of Canada
TB = tuberculosis
TNF = tumour necrosis factor
TNFAIP3 = tumour necrosis factor alpha-induced protein 3
TPMT = thiopurine methyltransferase
UC = ulcerative colitis
WCC = white cell count

Treatment

Trials of TNF-α blockers (adalimumab, etanercept, golimumab and infliximab) in AS have shown an ASAS40 response rate of ~40-50% (compared to 10-15% with placebo) and improvements in spinal mobility, enthesitis scores, sleep and function, with efficacy up to 8 years.[4-7] In the adalimumab trial, responses were seen as early as 2 weeks and this is often observed in clinical practice.[4]

Conventional disease-modifying therapy (methotrexate, sulfasalazine and leflunomide) is effective in peripheral arthritis, but not axial SpA and these agents are used as first-line therapy in patients with PsA. TNF-α blockers are used in PsA patients who have had an incomplete response to conventional disease-modifying therapy and trials of adalimumab, etanercept, golimumab and infliximab have shown ACR20 response rates at 12 weeks of ~50-60% (compared to 10-15% with placebo) and significant improvements in psoriasis, enthesitis and quality of life, with extension trials showing persisting efficacy.[8-11]

Ongoing trials for SpA are investigating certolizumab (anti-TNF-α), secukinumab (anti-*IL17A*) and ustekinumab (anti- *IL12/23*). Studies of anti-TNF-α in early SpA are also being undertaken (these patients may have the most to gain) along with studies to evaluate dose reduction for patients in remission.

Local experience

In NZ, anti-TNF therapy has been available for 3 years for patients with SpA (835 adalimumab Pharmac approvals, 204 etanercept approvals and 80 approvals for both agents) and 35 serious adverse reactions have been reported.

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IBD: What can we learn from the gastroenterology experience?

Presenter: Associate Professor Richard Gearry

Disease assessment

Gastroenterologists assess disease by looking at symptoms and signs, blood and faecal tests, imaging, endoscopy and white cell scans. The problem with diagnosing IBD is that unlike a skin or rheumatological condition that can be visualised, it is hidden away. Endoscopy allows for the visualisation of the disease, but may not be particularly pleasant for patients. The procedure is also expensive and resource intensive, and it is not possible to use this modality as often as gastroenterologists would like. Instead, they are left with having to use the CDAI, a disease activity tool developed in the early 1970s, used by the FDA and other agencies to licence drugs, and a requirement for access to drugs such as adalimumab in NZ. Gastroenterologists often despise using the CDAI, which requires patients to keep a 7-day diary recording stool frequency, abdominal pain and general wellbeing. These scores are then multiplied, with the general wellbeing score being multiplied by seven. This does not necessarily give an accurate representation of disease, because how well an individual feels on a day-to-day basis does not necessarily reflect their underlying disease activity. The overall accuracy of a CDAI ≥150 for predicting endoscopically active disease is only 40%.[1] Furthermore, the CDAI does not differentiate accurately between inactive and mild or moderate disease.[1]

Clinical tools are poor at assessing IBD because the gut is a simple organ with limited means of expressing itself (diarrhoea, constipation, urgency/frequency, abdominal pain, rectal bleeding) and because there is often confusion between IBD and IBS. IBS affects 1/6 women and 1/9 men, but is even more common in those with IBD, affecting 1/2 patients with CD and 1/3 patients with UC. Functional symptoms in IBS are not generated by inflammation, but rather by bowel sensitivity and these patients can score a CDAI of 200-300, which is not particularly helpful if one is trying to measure inflammatory activity. Biomarkers (faecal calprotectin and CRP) are increasingly being used in IBD and these correlate more closely than the CDAI with endoscopic activity.[1] These markers are helpful, but endoscopy is still the best determinant of inflammation. Implications of poor disease assessment tools are high placebo and low drug response rates in trials, and hence more accurate disease assessment tools are needed in order to obtain better results, for better decision-making and, therefore, better patient outcomes.[2]

Clearance of biologics

Immunoglobulins are cleared by proteases and an understanding of antibodies in IBD is evolving. IBD-specific clearance issues are also emerging. One is that IBD and other IMIDs can exhibit changes in gut permeability, which can result in significant protein loss. Because biologic drugs are proteins, they may be lost through the intestine and this loss may be greater in those with more severe disease. In such patients, higher rates of both primary and secondary non-response may be seen. These patients may require double induction doses or reduced dose intervals.

IBD references:

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Psoriasis: What can we learn from the dermatology experience?

Presenter: Dr Nicholas Birchall

The evolution of treatment

Psoriasis can engender a significant burden on sufferers and the incidence of the condition has increased nearly 2-fold over the last three decades.[1] When Dr Birchall started his medical career, a lot of patients with the condition spent a significant amount of time in hospital and he was frustrated in their management, as treatments were very limited. This period was followed by slight hope when etretinate and acitretin became available, but these agents had a 2-year pregnancy stand-down period. New hope came with cyclosporin, cytokines and colony-stimulating factors. Subsequently, there was a phase of despondence when patients with major infections died after being treated with these agents. Newer agents are effective, but also have associated concerns.

How is psoriasis diagnosed?

In most cases the diagnosis of psoriasis is clinical and undertaken by looking at typical morphology, typical distribution, family history and biopsy. It is possible that the various forms of psoriasis are not one disorder, but rather the skin's manifestation of several different processes. Before the PASI was developed there were no real criteria for monitoring patients. However, the PASI, which is required for access to biologics in NZ, tends to group patients and doesn't really identify those at the very severe end of the spectrum. Another important tool for assessing patients is the DLQI, but unfortunately this is not part of the Pharmac criteria for managing patients.[2] If a patient scores more than 10 on the PASI or the DLQI, they have severe disease and these are the patients who should be treated with oral systemic agents or biologics.

What have we learnt from therapy?

It takes ~6 months before 90% of the steady state concentration of methotrexate polyglutamate is reached and elimination is slow (mean half-life of 3.1 weeks).[3] It is also evident that responses are maximised when the patient is folate replete, that oral absorption of methotrexate is highly variable and that SC injection and split dosing are more effective.[4] These observations correlate with findings in the CHAMPION study where the PASI 75 response with methotrexate was slow to start with, but had reached 36% by week 16, peaking at week 26.[5] A study in RA confirmed that SC administration of methotrexate was more effective than oral administration.[6]

Skin Cancer

Patients with psoriasis have an increased risk of NMSC and lymphoproliferative disease (non-Hodgkin's lymphoma, Hodgkin's disease) at baseline.[7-10] Trials of biologics often exclude patients with a history of skin cancer and do not necessarily represent those typically treated in clinical practice. A large observational US study revealed a 1.5-fold risk of NMSC in RA patients treated with biologics, and a study of CD patients using biologics revealed a 2-fold increase.[11,12] Clinicians must be sure to educate their patients on the risk of skin cancer.

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PANEL DISCUSSION: **Chair:** Dr Julia Martin; **Panel:** Dr Nicholas Birchall, Assoc. Prof. Richard Gearry, Prof. John Highton, Dr Katey Jenks

Biologics and skin cancer: At Auckland City Hospital, patients receiving biologics go through a biologics clinic. They are warned about the increased risk of skin cancers with these agents and sign a consent form detailing risks. Patients are informed that they are responsible for organising their own annual skin checks. Assoc. Prof. Gearry informs patients on biologics of the risks of skin, cervical and other types of cancers and advises them to have regular skin checks. Dr Birchall believes that there is no necessity to stop biologics if a patient develops skin cancer while on one of these agents, but monitoring should be increased.

Faecal calprotectin: Assoc. Prof. Gearry explained that a negative faecal calprotectin is very useful in AS patients with equivocal symptoms of IBD, as it indicates an absence of gut inflammation. However, when faecal calprotectin is positive, an endoscopy needs to be undertaken for a definitive answer.

Biologics and pregnancy: Dr Jenks advises patients to not become pregnant while taking anti-TNF therapy; however, in Australia, anti-TNF therapy is used during pregnancy. Dr Martin commented that in rheumatology, it is uncommon for patients with active disease to aim to get pregnant. She pointed out that data are emerging indicating that pregnancy on biologics is safe. In fact, some IVF clinics are using anti-TNFs to improve pregnancy rates. Assoc. Prof. Gearry added that in IBD, the overriding factor is keeping disease in remission during pregnancy. He is seeing increasing numbers of patients on biologics who are becoming pregnant. Some patients choose to stop taking biologics during pregnancy as they feel the risk to their pregnancy is greater than the risk of their disease, but he would argue that the risk in pregnancy of a flare in disease is highly significant and he is becoming increasingly comfortable about keeping pregnant patients on biologics.

Patient follow-up: Dr Jenks commented that she would never discharge a patient on biologics back to their GP (she is also not happy discharging patients on methotrexate). There was agreement that nurses are key to effectively managing these patients. Assoc. Prof. Gearry and colleagues would also generally not discharge a patient on biologics back to their GP.

PLENARY: Overlap between SpA, Crohn's disease and psoriasis – how to optimise treatment

Presenter: Professor Walter Maksymowych, University of Alberta, Canada

Classification criteria

The ASAS group developed a new concept of SpA in an attempt to more broadly capture the overlap between SpA and related diseases, and to capture patients with early, pre-radiologic disease. The ASAS classification criteria separate SpA into predominantly axial or peripheral disease and minimise the necessity to use the term `undifferentiated' SpA. Critics have argued that the criteria are too broad (capturing patients with polyarticular PsA, for example).

Incidence and prevalence of extra-articular manifestations

In a Belgian epidemiological study of 847 patients with AS, 42% exhibited ≥1 EAM, including acute anterior uveitis (27%), IBD (10%) and psoriasis (11%).[1] A US claims database of 3888 patients with SpA showed the 2-year prevalence of EAMs to be 31.9%, with an incidence of 11.9% and surprisingly low rates of anti-TNF therapy use.[2] Prof. Maksymowych commented that in his clinic, the presence of an EAM is what tips the scales towards the use of anti-TNF therapy.

EAMs were found to be present early in disease in 708 patients with early SpA (mean symptom duration 18 months), with approximate rates of uveitis, IBD, psoriasis, enthesitis and peripheral arthritis of 9%, 3%, 16%, 49% and 21%, respectively.[3]

EIMS are frequently seen in patients with IBD. A Swiss cohort of 950 IBD patients (43% with CD and 31% with UC) exhibited between one and five EIMs per patient.[4] A cohort from Norway revealed an overall SpA prevalence of 22% (ESSG criteria) and an AS rate of 6% in those with CD and 2.6% in those with UC, 6 years after IBD diagnosis (AS predated UC in 100% and predated CD in 50%).[5]

A recent study involving 174,476 women revealed a significantly increased risk of CD (but not UC) in those with psoriasis (RR 3.86; 95% CI 2.23-6.67); this risk was especially pronounced for those with concomitant PsA (RR 6.43; 95% CI 2.04-20.32).[6] While there is no question of an overlap between these diseases, the extent of the overlap depends on how extensively the patient is investigated. MRI assessment in 44 patients with IBD and non-radiographic SpA revealed evidence of sacroiliitis in 17 (39%) patients.[7] Only 5 of the 44 patients fulfilled the modified NY criteria for AS and there was little correlation between symptoms and MRI evidence of inflammation. This finding is consistent with data showing CT evidence of sacroiliitis in 30% of non-radiographic SpA cases.[8] Similarly in PsA, ~40% of patients have been shown to exhibit MRI features of sacroiliitis, with the BASDAI, BASFI and HLA-B27 not correlating well with MRI evidence of inflammation.[9]

In 1995, Mielants et al documented an association between asymptomatic gut lesions and SpA.[10] Chronic gut lesions were found to be a risk factor for CD, with 20% of patients exhibiting such lesions developing clinically overt IBD over a 5-year period. More recent data show that subclinical gut inflammation is common in all types of SpA, with an overall prevalence of 46.2%, and such inflammation may be present in the early stages of disease.[11]

Disease aetiology: genetics and pathophysiology

Genetic studies have demonstrated an association between *IL-23R* variants and AS, and implicate a distinct single-nucleotide polymorphism (SNP; Arg381Gln), which is also associated with psoriasis and IBD, and appears to protect against the development of CD.[12-14] *IL-23* is an important factor regulating the production of *IL-17* (a major pro-inflammatory cytokine), which has been shown to be over-expressed in the colon of B27-transgenic rats.[16] Serum *IL-17* has also been found to be increased in undifferentiated SpA/reactive arthritis, AS and PsA, but not RA.[15-18] *IL-23* has been shown to be strongly overexpressed in AS patients with subclinical intestinal disease and over-representation of *IL-17A* and *IL-22*-producing CD8T cells has been observed in lesional skin of patients with psoriasis.[19,20]

While elevated levels of serum *IL-17* and peripheral blood Th17 cells have been identified in AS, Th17 cells have not been detected in the axial and peripheral joints in AS. [21-23] Studies have shown that innate immune cells such as mast cells, neutrophils and innate lymphoid cells are the major producers of *IL-17* at the sites of inflammation in SpA, psoriasis and IBD.[22,24-26] These findings suggest that Th17 may not be the primary cell driving inflammation in AS, and account for the fact that abatacept is not effective in AS or CD. Further evidence for this comes from a study showing that *IL-23* promotes highly specific entheseal inflammation by acting on a previously unidentified population of $CD3^+CD4^-CD8^-$ entheseal resident lymphocytes.[27] *IL-23*-driven disease is not substantially ameliorated by the neutralisation of TNF or *IL-6*.[27]

Disease management

A preliminary study investigating the use of the anti-*IL-17A* monoclonal antibody secukinumab for AS has shown 30-60% of patients to respond to treatment

with the agent.[28] Likewise, the anti-*IL-17* antibody ixekizumab has been shown to be effective in psoriasis with very high PASI 75 response rates.[29] A recent Phase III study has shown ustekinumab (a monoclonal antibody directed against *IL-12* and *IL-23*) to be effective for skin and musculoskeletal inflammation in PsA.[30] However, ustekinumab does not appear to be effective in CD.[31] The efficacy of TNF inhibitors in CD has been clearly demonstrated.[32,33] Furthermore, adalimumab has been shown to improve psoriasis in patients with AS.[34] A retrospective study investigating the efficacy of TNF inhibitors in reducing uveitis flares in patients with spondyloarthropathy has shown adalimumab and infliximab to be effective, but not etanercept.[35] Data from nine studies investigating IBD flares and new-onset IBD in AS patients receiving anti-TNF showed that IBD flares are infrequent events and that infliximab, but not etanercept, largely prevents IBD activity.[36]

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Predicting outcomes and personalising treatment decisions for patients with Crohn's disease

Presenter: Dr Corey Siegel

Risk factors for an aggressive disease course in CD

The disease course varies between patients with CD and not all require early intensive therapy.[1] Evidence suggests that ~30% of patients with CD progress to penetrating or stricturing disease within 2 years, with the rate increased to ~50% by 6 years and ~85% by 20 years.[1] At CD diagnosis, features predictive of early complicated disease include: age at onset < 40 years; small bowel and colonic disease; smoking; perianal lesion at diagnosis; requirement for steroids at first flare.[2] Predictors of rapid progression to surgery in CD include: oral corticosteroid use in first 6 months; smoking; ileal localisation only; nausea/vomiting; abdominal pain.[3] Specific serological markers have also been identified that may help to predict IBD course.[4,5] Furthermore, genetics likely play a role in the development of complicated CD and a number of genes have been implicated, including NOD2 and CARD15.[6,7]

Predicting a response to anti-TNF therapy

The serological markers ANCA and ASCA have been shown to predict response to infliximab, while a number of genetic markers have been identified that predict a better or worse response to anti-TNF therapy in RA and CD.[8-10] Other factors predictive of a better anti-TNF response in CD include short disease duration, younger age, elevated CRP and high apoptotic response rate.[11,15] Stricture has been shown to be associated with a worse response.[12]

Statistical modelling - determining when early anti-TNF is most beneficial

At their first presentation, or first colonoscopy, it is often possible to get a feel for which patients will have worse IBD, but sometimes it is difficult to define and relay this information to patients. To this end, Dr Siegel and colleagues have developed a prediction tool to help children with CD and their parents understand individualised risks of disease complications and response to therapy.[13] The model was developed using prospective and retrospective data on 579 well-characterised paediatric CD patients (median age at diagnosis = 12 yrs) enrolled at 21 centres in North America, and employed system dynamics analysis, a methodology that addresses the inherent dynamic complexity of interactions between variables.

The model is adaptable and additional variables can be added as more data become available. Following individual patients over time will determine the accuracy of the predictive model. Dr Siegel explained that it is more important than ever to risk-stratify patients, not only because we know that some patients are going to do well when treated early, but because we know that medications have potential toxicities.

A model to guide post-operative management in adults

Approximately 70% of patients with CD require surgery within 15 years of diagnosis, with the majority requiring multiple surgeries.[14,15] Endoscopic recurrence occurs early, at rates of ~80% 1 year after resection; however, early medical therapy can prevent both endoscopic and clinical recurrence of disease.[15] Dr Siegel and colleagues developed a tool for predicting adult CD post-operative recurrence using clinical, endoscopic, serologic and genetic factors gathered using prospective data from 150 patients with CD (median age 53 yrs), all of whom had undergone ≥1 abdominal surgery by a single surgeon. The rates of endoscopic and clinical recurrence were 70% and 37%, respectively, during a median follow-up of 15 months. Variables included in the model were age at first surgery, history of prior surgery, smoking history, Rutgeert's score, anti-OmpC quartile; anti-I2 titre, and five genetic loci with some predictive value.

Personalising treatment references:

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Expert Forum publications are designed to encapsulate the essence of a local meeting of health professionals who have a keen interest in a condition or disease state. These meetings are typically a day in duration, and will include presentations of local research and discussion of guidelines and management strategies.

Even for local events it is not always possible for everyone with a similar therapeutic interest to attend. Expert Forum publications capture what was said and allows it to be made available to a wider audience through the Research Review membership or through physical distribution.

PLENARY: Interpreting safety data from trials and registries – implications for daily clinical practice

Presenter: Dr Stephen Tyring, University of Texas Health Science Center, Houston, Tx

Adalimumab safety data

Adalimumab [Humira®] safety and mortality rates were investigated in an analysis of 19,041 patients exposed to the agent in 36 global clinical trials over 10 years to 2007 in RA (19 trials), PsA (3), AS (3), CD (5), psoriasis (5) and juvenile idiopathic arthritis (1).[1] Across the trials, the rates of concomitant immunosuppressant use ranged from 61.8% (RA trials) to 0.3% (psoriasis trials); rates of concomitant systemic steroid use ranged from 58.6% (RA) to 1.2% (psoriasis).[1] SAEs were defined as follows: fatal or life threatening; requiring inpatient hospitalisation or prolongation of existing hospitalisation; resulting in persistent or significant disability or requiring medical/surgical intervention to prevent another serious outcome; birth of a child with a congenital anomaly or birth defect; miscarriage; elective abortion. Two US data sources were used to determine the expected number of cancers in the general population.

SAEs of interest across the trials and the number of such events per 100 patient-years are shown in the table below. The number of SAEs varied across trials, possibly due to the different rates of concomitant medication use, with the rates being lowest in psoriasis trials.[1] SAEs were relatively stable over time. The rates of serious infection were highest in RA and CD, and lowest in AS and psoriasis. TB rates for each of the six diseases were similar. With regard to opportunistic infections, the most commonly reported was oral candidiasis. Demyelinating disorders and lupus-like syndrome were reported infrequently.

The SIR for malignancies for all of the trials combined was 0.83. While more cases of malignancies have been observed among patients receiving TNF antagonists compared to controls in clinical trials, such malignancies (other than lymphoma and NMSC) were similar in type and number to those expected in the general population. Lymphoma was reported in four of the six indications; the SIR for lymphoma in RA was 2.98. The SIRs for NMSC varied depending on which comparator database was employed. Based on the US National Cancer Institute database, the SIRs for basal cell carcinoma and squamous cell carcinoma for RA and squamous cell carcinoma for CD and psoriasis were significantly greater than 1.0 (range1.24–6.27). Dr Tyring pointed out that in some cases, a dysplastic or neoplastic skin lesion may go unnoticed underneath a psoriatic lesion, and only be obvious after the skin has cleared during therapy. In such cases, the cancer may mistakenly be attributed to the therapy.

Pooled data on serious adverse events of interest (events/100 patient-years) among 36 global clinical trials of adalimumab. (Adapted from Burmester et al.)[1]

	RA	PsA	AS	JIA	Ps	CD
N	12,345	837	1641	171	1819	2228
Exposure (patient years)	18,284.3	997.5	1255.2	398.4	2424.7	2373.7
Serious infections	4.65	2.81	1.11	2.76	1.32	5.18
Tuberculosis	0.29	0.30	0	0	0.12	0.13
Opportunistic infections	0.09	0	0	0	0	0.08
Histoplasmosis	0.03	0	0	0	0	0
Malignancies (excluding lymphoma and NMSC)	0.76	0.30	0.08	0	0.49	0.46
Lymphoma	0.12	0.20	0.08	0	0	0.08
NMSC	0.17	0	0.08	0	0.12	0
Demyelinating disorder	0.05	0	0.08	0	0	0.13
Lupus-like syndrome	0.07	0	0	0	0	0.04
CHF	0.23	0	0.16	0	0	0

AS = ankylosing spondylitis; CD = Crohn's disease; CHF = congestive heart failure; JIA = juvenile idiopathic arthritis; NMSC = non-melanoma skin cancer; Ps = psoriasis; PsA = psoriatic arthritis; RA = rheumatoid arthritis

Findings from the 24-week ADEPT revealed that the agent was generally well tolerated with a similar incidence of adverse events compared with placebo.[2] SAEs occurred in 5/151 (3.3%) adalimumab recipients and 7/162 (4.3%) placebo recipients. One adverse event of statistical significance between the two groups in the ADEPT study was injection site reactions; adalimumab 6.6% vs placebo 3.1%. However, such reactions do not generally cause patients to discontinue therapy.

Dr Tyring and colleagues investigated the long-term safety of adalimumab in moderate-to-severe psoriasis by analysing data from 13 clinical trials involving 3010 patients (4845 patient-years).[3] Safety data up to five years revealed no evidence of cumulative toxicity of adalimumab and showed generally stable adverse event rates. Another recent publication compared the risk of SAEs during treatment with biologic and non-biologic systemic therapy in patients (n = 310) who would not have been eligible for inclusion in RCTs.[4] Overall, this group of patients had an increased risk of SAEs (IRR 2.7; 95% CI 1.5-4.7), while the 161 patients exposed to biologics exhibited an IRR of 2.3 (95% CI 1.1-4.8), a rate similar to that in patients eligible for RCTs.

A Cochrane meta-analysis of 160 RCTs (n = 48,676; median duration 6 months) and 46 extension studies (n = 11,954; median duration 13 months) investigating biologics for any indication found that compared with controls, biologics were associated with a statistically significantly higher rate of total adverse events (OR 1.28), SAEs (OR 1.37) and TB reactivation (OR 4.68).[5] The meta-analysis also revealed that the rates of lymphoma and congestive heart failure were not different between biologic recipients and controls. More adverse events were seen with anti-*IL1*, anti-*IL6*, anti-CD28 and anti-B agents than with anti-TNFs. Among all anti-TNF agents, infliximab exhibited a higher rate of adverse events, SAEs and serious infections than etanercept, golimumab and certolizumab, all of which had higher rates than adalimumab.

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Exploring the link between IBD and the skin

Presenter: Dr Amanda Oakley

Dermatoses associated with IBD

Evidence suggests that bowel disease may lead to skin disease via a reaction to an allergen in the bowel, via infection, due to debility or malabsorption, or as a consequence of a reaction to treatment. Dermatoses associated with IBD include: local skin disease (granulomatous plaques, fistulae, fissures and aphthous ulcers); reactive dermatoses or neutrophilic dermatoses (pyoderma gangrenosum, Sweet syndrome, bowel-associated dermatosis, pyodermatitis/pyostomatitis vegetans, hypersensitivity vasculitis and erythema nodosum); nutritional deficiency (pellagra); adverse reactions to drugs (skin infections, inflammatory dermatoses [acne, psoriasis, eczema etc.]); and associated conditions (psoriasis, hidradenitis, alopecia areata, vitiligo and lichen planus). While pyoderma gangrenosum and erythema nodosum have a well-established association with IBD, they occur infrequently.[1] Mucocutaneous disease is associated with more severe IBD.

Aphthous ulcers: Oral aphthous ulcers are present in 10% of CD cases and in 4% of UC cases.[1] A proportion of young patients presenting with severe recurrent aphthae may progress to IBD.

Orofacial granulomatosis: In a study of 207 patients with orofacial granulomatosis, 22% had CD.[2] Dr Oakley presented the case of a 7-year-old boy with angular chelitis, swollen, cracked lips, oral sores and lumps, gingival hyperplasia, anal abscess and fissures. Within 12-month's of presentation, he was diagnosed with CD. Other symptoms of this condition include cobblestone mucosa, oral aphthous ulcers and mucosal tags.

Pyoderma gangrenosum: IBD is present in 10-30% of patients with pyoderma gangrenosum.[3,4] Dr Oakley presented the case of a 42-year-old woman with a history of well-controlled long-standing CD and a 6-week history of a painful ulcer on her right forearm. She had a history of leg ulcers x 3, which had healed on oral steroids. Her current ulcer worsened when her oral steroid dose was reduced. Cyclosporin was started and her ulcer improved, but removing her plaster induced another ulcer (this is a common feature of pyoderma gangrenosum, and even a minor injury may koebnerise).

Sweet syndrome (acute febrile neutrophilic dermatosis)**:** This condition is more common in women than in men and presents as painful erythematous plaques, mucosal lesions, fever and neutrophil leukocytosis. Prednisone is beneficial in most.

Bowel-associated dermatosis-arthritis syndrome: This condition is associated with IBD and bowel bypass surgery. Symptoms include recurrent episodes of fever, malaise, myalgia, small-joint arthralgia and rash.

Cutaneous vasculitis: IBD is also associated with cutaneous vasculitis. This can take the form of small vessel disease (leukocytoclastic/hypersensitivity vasculitis) or large vessel disease (cutaneous polyarteritis nodosa), or granulomatous perivasculitis.

Pellagra: This condition is due to a niacin deficiency resulting from prolonged diarrhoea or anorexia. A bilateral, symmetrical, peeling rash occurs on photo-exposed areas. It improves rapidly with niacin supplementation.

Cutaneous adverse drug reactions: The most common skin reaction is the morbilliform rash; another type is urticaria. Systemic steroids may cause cutaneous atrophy, purpura, striae, steroid acne, hypertrichosis and facial plethora. TNF-α inhibitors may cause new-onset plaque psoriasis, palmoplantar pustulosis, discoid eczema, generalised granuloma annulare and vitiligo.

Hidradenitis suppurativa: This painful, smelly, deforming comorbidity of CD is very difficult to treat. Severe disease may be granulomatous and ulcerate. For many patients there is no satisfactory on-licence drug treatment and surgery may be required.

IBD/Skin references:

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IBD and the skin

Presenter: Dr John Wyeth

Dr Wyeth presented three cases of skin disease associated with IBD.

Case 1: A 10-year-old girl presented in 2004 with abdominal pain, constipation, anismus and a dilated colon. Blood tests revealed an elevated WCC, low albumin and elevated CRP. Following colonoscopy she was diagnosed with CD and treated with 5-ASA, prednisone and azathioprine, but her progress was poor. A year later, symptoms were ongoing with rectal and labial abscesses and she underwent a defunctioning colostomy. Recurrence of perirectal and rectovaginal abscess required surgical drainage and prolonged doses of antibiotics. She subsequently underwent a distal colon resection and proctectomy with a gracilis flap. There was no evidence of active CD, but deep ulceration was present around her vagina. Skin biopsy revealed granuloma. She was diagnosed with metastatic CD. She is now 18 years of age, has no fistulae, but continues to have severe genital inflammation. She is continuing on adalimumab and methotrexate has been initiated. She has been referred to a surgeon.

Case 2: A 36-year-old female lawyer presented in 2011 with acute-onset diarrhoea, slight fever and elevated CRP. A colonoscopy revealed CD. She rapidly improved with prednisone. However, erythema nodosum had developed with the onset of her CD and did not settle with prednisone. Azathioprine was started, but after 6 weeks was not tolerated and was discontinued. Adalimumab was initiated and her symptoms (including erythema nodosum) completely resolved. She was also taking mesalazine. After 6 months, her CRP had increased and her painful erythema nodosum recurred. Treatment options include adding steroids, optimising the dose of adalimumab by administering it weekly, switching to another anti-TNF or adding methotrexate.

Case 3: A 57-year-old man, with a 20-year history of complicated CD, presented for a second opinion and consideration for inclusion in a clinical trial of vedolizumab. He was currently taking adalimumab 40mg every 2 weeks, azathioprine and long-term prednisone. He reported a 12-month history of a nodular, tender, growing tumour on his vertex. Following resection, a moderately differentiated squamous cell carcinoma was diagnosed. There was no perineural or vascular invasion, and excision appeared complete.

Dinner plenary: Case presentations for panel discussion

Chair: Dr David Rowbotham; **Panel:** Professor Walter Maksymowych, Dr Corey Siegel, Dr Stephen Tyring

Case 1: Presented by Dr Sutharshan Kannuthurai
A 42-year-old male smoker with a family history of CD and a 2-year history of arthralgia (mainly confined to his lower limbs) and spontaneously occurring painful skin lesions on his ankle and dorsal surface of his foot, was referred to rheumatology. The skin lesions developed as a purple patch or pustule and subsequently ulcerated, healing over 2-3 months. He experienced malaise, weight loss (12kg) and a change in his bowel habits during the previous year (4-6 bowel motions per day without blood, mucous or pain). He exhibited erythema of both hands, erythematous nodular lesions on his feet, cold/dusky extremities and an absent right dorsalis pedis pulse. He was taking ibuprofen for pain. Tests revealed an elevated ESR and CRP, slight lymphocytopenia, and absence of HLA-B27, RF, Hepatitis B and C, syphilis and HIV. Pyoderma gangrenosum was suspected. Skin biopsy revealed marked suppuration with an intense neutrophilic infiltrate and abscess formation, absence of vasculitis away from areas of abscess formation, no bacterial or fungal organisms and relative sparing of the epidermis and superficial dermis. Findings were most consistent with erythema nodosum. Colonoscopy findings were consistent with CD. His symptoms minimally improved with two courses of oral prednisone. He then received IV methylprednisolone then tapering oral prednisone, doxycline, azathioprine and Pentasa. His skin, bowel and other symptoms started to improve. Intra-articular steroids into both knees gave short-term (2 months) benefit.

Discussion: Patients with IBD should avoid NSAIDs. The extent of CD should be determined. Capsule endoscopy was suggested, but debated. Good radiographic imaging often provides enough information. CD has multiple phenotypes and the way it is classified in the future will no doubt change.

Case 2: Presented by Professor Walter Maksymowych
An 18-year-old man with a 6-year history of AS, a 2-year history of CD (currently inactive) and painful knees and neck, was receiving celecoxib, Pentasa and prednisone when he was referred. Physical examination revealed active synovitis, plantar fasciitis, patellar enthesitis, restricted rotation of his neck and hip, and restricted spinal mobility. He was HLA-B27 positive, had a CRP of 69 mg/L, bilateral Grade 2 sacroiliitis and new bone formation in his neck. Sulfasalazine was started but discontinued due to rash and nausea. Methotrexate was ineffective. SC infliximab 3 mg/kg resulted in substantial improvement within 2 months. Prednisone and celecoxib were subsequently discontinued. After 1 year, bilateral knee synovitis developed along with a flare of CD.

Intra-articular steroids into each knee were given and the infliximab dose increased to 5 mg/kg every 6 weeks. After 6 months, there was modest improvement in synovitis and CD. Infliximab was subsequently replaced with adalimumab and he experienced remission of both CD and peripheral synovitis within 3 months.

Discussion: Approx. half of the audience acknowledged that NSAIDs shouldn't be used in IBD. Prof. Maksymowych commented that the presence of inactive IBD in a patient with SpA prompts him to move towards anti-TNF therapy. Sulfasalazine is not effective in early SpA. Canadian recommendations (SPARCC) call for the use of methotrexate in peripheral SpA, however, there is no evidence that the agent is effective in peripheral or axial SpA. Most rheumatologists in NZ would have trialled methotrexate in this patient. Dr Siegel commented that he would investigate the patient's trough infliximab and antibody levels. He added that risk-stratifying patients with IBD is important and allows for identification of those who will benefit from early anti-TNF therapy.

Case 3: Presented by Professor Walter Maksymowych
A 24-year-old man with a 2-year history of inflammatory back pain and a 6-year history of IBD (currently inactive) was treated with prednisone. He was HLA-B27 negative. A pelvic x-ray found minimal bilateral sacroiliitis and no evidence to suggest seronegative spondyloarthropathy. An MRI showed erosion of the right iliac bow and subchondral fat infiltration.

Discussion: In Prof. Maksymowych's view, this patient clearly has axial SpA, however, they would not have met the new ASAS classification criteria for the condition because they did not have active (acute) inflammation on MRI. Diagnosis of non-radiographic axial SpA is important because patients may be highly symptomatic and effective therapy is available.

PLENARY: Communicating the risks and benefits of IBD therapy to patients

Presenter: Dr Corey Siegel, Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, New Hampshire, US

There is good evidence that `top down' therapy is superior for CD and combination therapy (infliximab + azathioprine) is superior to either agent alone.[1,2] While we know which medications we should be using for treating our patients, doctors and patients alike have concerns about the risks of these agents.

Risks of immunomodulators and biologics

The most important side-effects of 6-mercaptopurine and azathioprine are serious infection (5%), pancreatitis (3%), hepatitis (2%), nausea (2%), allergic reactions (2%) and non-Hodgkin's lymphoma (0.04%), and it is estimated that 11% of patients stop therapy due to adverse events.[3,4] A study of 19,486 IBD patients found an increased risk of lymphoproliferative disorders in those taking thiopurines compared with thiopurine-naïve patients (HR 5.28; 95% CI 2.01-13.9).[5] The rates of lymphoma per 10,000 patient-years were: current users 9, discontinued 2, never exposed 2.6. There appears to be no data indicating an increased risk of solid tumours associated with thiopurines in IBD. A large study looking at skin cancer associated with thiopurines revealed a rate of ~6 cases per 1000 patients.[6] Dr Siegel pointed out that this is a fairly low rate and not a reason to back off on therapy, rather, he advocates recommending that patients wear sunscreen and receive regular skin checks. Data is sparse on the risk of non-Hodgkin's lymphoma associated with methotrexate for IBD, and two studies in RA indicate varying rates (5-fold increase in risk in an Australian study, but no increased risk in a US study).[7,8]

Approximately 10% of patients are unable to tolerate anti-TNF therapy. The most important side-effects are infusion or injection-site reactions (3-20%), serious infection (3%), drug-related lupus-like reaction (1%), TB (0.05%) and non-Hodgkin's lymphoma (0.06%).[9] A systematic review investigating the risk of death from sepsis with infliximab revealed a rate of 1 in 250 patients, but these patients were predominantly older (average age 63 years), had long-standing disease, multiple co-morbidities and were on concomitant steroids and/or narcotics.[10] Data is also limited on the risk of solid tumours associated with anti-TNF therapy for IBD, but there appears to be no increased risk in RA patients.[8] A recent analysis of a large claims database revealed an increased risk of melanoma associated with anti-TNF therapy for IBD (OR 1.88; 95% CI 1.08-3.29).[11] In RA, risk of lymphoma does not seem to be increased with use of anti-TNF therapy alone or with methotrexate.[12] A meta-analysis investigating the risk of non-Hodgkin's lymphoma with anti-TNF therapy for CD in 8905 patients revealed a rate of 6.1 per 10,000 patient-years.[4] The mean age of those developing lymphoma was 52 years, 62% were male and 10 of the 13 patients with lymphoma were receiving combination therapy. Dr Siegel pointed out that while the risk of lymphoma was 3-fold higher than in the general population, the numbers are still low (6 patients out of 10,000 patient-years compared with 2 patients per 10,000 patient-years). Hepatosplenic T-cell lymphoma, which is incurable, is very infrequent in anti-TNF therapy recipients (~30 reported cases, mostly young men) and world wide, only two cases have been reported during the first 2 years of therapy.[13] Dr Siegel suggests that rather than worrying about the consequences of these drugs first up, we should be using the best therapy (thiopurine + anti-TNF) and then discontinuing one of the agents after 6-12 months when the patient is in `deep' remission.

The FDA has 147 post-marketing reports of leukaemia in patients receiving anti-TNF medications, but most patients were also receiving other immunosuppressive therapy. The average time to onset of leukaemia was 1-2 years and there does not seem to be a cumulative risk of using these agents.

What puts patients at most risk? Treatment or the disease itself?

The alternative to taking thiopurines and biologics is prednisone. The risks associated with the use of this agent are well documented and adverse effects have been reported in ~55% of patients.[14] A UK study investigating the risk of mortality in CD revealed that patients with severe disease and current prednisone use have the highest risk; HR 2.44 (95% CI 1.84-3.25) and HR 2.48 (95% CI 1.85-3.31), respectively. Therefore, from a mortality angle, the best things that we can do for patients is to take them off prednisone and treat to improve their disease severity.

Are two drugs better than one?

The SONIC trial demonstrated an 11% therapeutic gain when infliximab + azathioprine was compared with infliximab alone.[2] While a study investigating the use of prednisone, 6-mercaptopurine/azathioprine and infliximab suggested that the risk of opportunistic infection is significantly increased the more concomitant medications are taken; most of the infections were non-serious and all but one was associated with the use of concomitant steroids.[15] Hence, further evidence that the best approach may be to avoid steroids first up. Other studies have shown similar infection rates between infliximab monotherapy and infliximab in combination with azathioprine or methotrexate.[2,16]

Who should get combination therapy?

Dr Siegel and colleagues formed a panel to assess the appropriateness of combination anti-TNF in different types of patients.[17] The general consensus was that combination therapy is generally appropriate. An algorithm was also developed to aid treatment decision-making regarding the use of combination therapy in CD (available from: www.BRIDGeIBD.com).

Communicating risk

Patients are afraid of newer drugs, such as biologics, with reported side effects. The job of the clinician is to inform patients of these risks, putting them in perspective and to inform them that more is now understood about these agents. Dr Siegel advises against using vague terms such as `rare' or `common', as individuals have very different interpretations of their meaning. He suggests reporting absolute risks rather than relative risks, avoiding decimals, keeping common denominators consistent (i.e. risk per 10,000), using visual aids and giving perspective to other diseases and life risks.

Decision aids

One of the aids Dr Siegel uses for communicating risk to patients is a drawing of 10,000 schematic people on which he can highlight the estimated number in the general population who will develop a particular disease (e.g. non-Hodgkin's lymphoma) and the number who are predicted to develop

such an illness as a consequence of a particular drug therapy (such Palettes are available from: http://www.riskcomm.com/).

Dr Siegel and colleagues have also developed an option grid for patients to help them, together with their clinicians, decide on the best initial treatment for their CD and have created a web-based decision aid tool for patients.

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Small-intestinal injury in patients with SpA – cause or consequence?

Presenter: Dr Michael Schultz

Intestinal inflammation in SpA

The SpAs have variably strong association with HLA-B27 (mainly AS). Evidence suggests that between 25% and 75% of patients with SpA have asymptomatic ileitis and approximately 6% to 10% may develop IBD.[1,2,3] Early studies of HLA-B27 transgenic rats showed that germ-free rats did not develop gastroduodenitis, colitis or arthritis, while those colonised with defined bacterial cocktails containing Bacteroides spp. developed colitis and gastritis.[4]

Dr Schultz and colleagues altered the intestinal composition of the HLA-B27 transgenic rat model using an inulin-containing probiotic preparation and found that this induced an attenuation of colitis.[5] Probiotics were then trialed in an RCT involving 63 patients with SpA, but there was no significant benefit over placebo.[6]

There appears to be a high prevalence (41%) of subclinical intestinal inflammation among first-degree relatives of patients with AS, irrespective of HLA genotype.[7] It should also be noted that while ileitis is often caused by CD, it may be caused by a variety of other diseases and may often be subclinical.

Dr Schultz and colleagues have shown that SpA patients report a significant incidence (31%) of bowel symptoms (DISQ), and that such symptoms correlate with disease activity (CDAI); when their abdominal symptoms flare their joint symptoms flare and vice versa.[8] In the investigation, a significant number of SpA patients experienced loose stools and 7.8% (6/77) had symptoms consistent with active IBD; 4/6 had elevated faecal calprotectin levels. Furthermore, the BASDAI and DISQ were found to correlate well with each other, but faecal calprotectin did not correlate with symptoms. In nine patients with SpA who underwent capsule endoscopy, findings did not necessarily correlate with faecal calprotectin levels or symptoms. Colonoscopy findings were normal in most of these patients.

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The IBD Connect Programme - enhancing patient and physician communication in IBD

Presenter: Dr David Rowbotham

IBD Connect is a communication tool aimed at guiding patients towards disease control. Dr Rowbotham believes it to be an excellent resource to help patients become engaged and empowered with regard to their IBD treatment. Specifically, IBD Connect aims to improve disease understanding, align expectations, improved benefit/risk communication, improve patient preference, improve outcomes and improve adherence.

Extensive gaps exist between which IBD-related issues patients and gastroenterologists consider important. For example, while patients often have a significantly reduced quality of life, gastroenterologists often don't ask patients about this aspect of their disease and other issues that may be affecting them. Often the clinic interview takes a clinical focus with a tick-box approach, whereas patients just want to be treated like a human and receive some empathy for the fact that issues like toileting rule their daily life. To this end, patients often want time to talk, want answers to their questions and solutions to their disease, along with hope for a cure.

Motivational interviewing

Motivational interviewing centres on understanding and affirming patient's needs and freedom of choice, monitoring the degree of readiness to change and engaging patients in a non-authoritative manner.[1] When communicating with patients, eye contact, facial expression, body language, tone of voice and choice of words are important. Also be mindful to not interrupt, have no external interruption, be non-judgmental, talk less than the patient and listen as much as you inform. It is very important to acknowledge what the patient wants to talk about before moving on to items on your agenda. Patient ambivalence is normal and must be explored rather than confronted. Often when health care professionals are met with ambivalence, they tend to use direct persuasion and argue for change in order to fix problems for their patients (the righting reflex), but unfortunately the more ambivalent the patient, the less likely is direct persuasion to be effective. Also, the less empathetic the clinician, the more likely the patient is to be resistant.

Motivational conversation is collaborative and evocative and has four principles: listening (and hearing), avoiding the righting reflex, supporting the patient and exploring and understanding the patient's motivation. Communication can go wrong in many ways, but motivational communication and reflective listening can help avoid confusion by verifying what each participant has said and meant.

Change talk centres around helping patients to develop and verbalise their positive thoughts on change, which increases the likelihood of change. Change involves contemplation, preparation and action. Preparatory change talk for patents involves them expressing a desire to change then expressing the ability to change, then reasons for change and the need for change. Mobilising change talk involves commitment, activation and taking steps. Dr Rowbotham pointed out that clinicians must listen carefully for the `change talk' and not let the opportunity pass to engage with the patient at that point.

Communication reference:

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Adalimumab for Crohn's disease in NZ – results from four hospitals

Presenter: Dr Richard Gearry

In order to determine the patterns of use of adalimumab in NZ, the effect on hospital admissions and the clinical efficacy of the agent, Dr Gearry and colleagues undertook a retrospective case note review of patients at four centres: Christchurch (n = 117), Auckland City (30), Hutt/Wairarapa (28) and Dunedin (19). For the majority of patients, the indication for starting adalimumab was a CDAI >300. The adalimumab continuation rates were: 92% at 6 months; 87% at 12 months; 75% at 24 months (these rates were significantly higher than those seen in clinical trials). Overall, 38/166 (23%) patients discontinued adalimumab. Reasons for discontinuation included: loss of response (n= 28); pregnancy (3); ADR (7); patient decision (2). Continuation rates were not significantly different between the four centres, between

males and females, between disease locations (ileocolonic, colonic or ileal), between non-perianal and perianal disease or between disease duration (< or > 2 years). However, patients with penetrating disease were less likely to discontinue adalimumab than those with stricturing or inflammatory disease. During treatment with adalimumab, the median CDAI decreased from 357 to 110 ($p < 0.0001$). There was also a significant difference in the number of days in hospital before and after the use of adalimumab; mean reduction ~1.5 days.

In Christchurch, Dr Gearry and colleagues managed 14 patients (8 female) who failed adalimumab eow by switching them to adalimumab weekly for a maximum of 3 months (then adalimumab eow). Nine were receiving concomitant azathioprine and two were taking methotrexate. Weekly adalimumab induced remission in nine of the 14 patients and this was maintained on eow therapy. Overall, there was a significant reduction in CDAI 3 months after reverting back to adalimumab eow. ADRs were: injection site reaction (n = 1); ethmoid sinusitis (1); osteomyelitis great toe (1); pneumonia (1).

Ten Topics in Rheumatology GP Training Programme

Presenter: Associate Professor Andrew Harrison

In the Wellington region, demand exceeds rheumatology service capacity and there is a need to integrate primary and secondary sectors in order to address this mismatch. To this end, Assoc. Prof. Harrison organised a GP training programme in the region, which was attended by 60 GPs. The programme was sponsored by AbbVie and was incentivised with CME points and social contact with peers. Feedback was extremely positive and attendees expressed interest in applying the format to other specialties.

In developing the programme, Assoc. Prof. Harrison designed a rheumatology seminar for GPs that provided information of interest to them. Topic selection was based on feedback forms distributed at a previous seminar on AS, consultation with the liaison GPs at Capital Coast and Hutt Valley District Health Boards, and feedback from a focus group at a GP peer session.

The seminar took the following format: 10 topics, seven speakers, 45-minute talks and 5 minutes of case discussion. Topics covered were: Referring to and communicating with the rheumatology unit; Investigating, treating and referring suspected inflammatory arthritis; Monitoring patients on DMARDs; Biologics in primary care; Managing osteoarthritis and musculoskeletal pain; Management of a flare (RA, SLE, SpA); Joint injections; Polymyalgia and giant cell arteritis; Gout; SpA (AS, PsA). A booklet summarising the presentations and case studies was distributed.

GPs were asked which topics they would like to have covered in future training programmes. They suggested travel medicine, dermatology, gastroenterology, endocrinology, cardiology, respiratory medicine, orthopaedics, geriatrics, paediatric cases, hands-on joint injections and psychological factors. They also suggested looking at chronic pain management across a spectrum of general practice.

Rheumatologists and Dermatologists collaborating for optimal treatment outcomes in PsA and psoriasis, focussing on Special Authority Criteria

Presenters: Dr Daniel Ching (rheumatologist) and Dr Nicholas Birchall (dermatologist)

PsA cases

Dr Ching presented two cases demonstrating that PsA is not always easy to diagnose.

Case 1: A 37-year-old woman presented with painful, swollen left sternoclavicular joint arthritis, but no other symptoms. Four months later, her knees had also become swollen. Examination at that time revealed scalp psoriasis and the diagnosis of PsA was made.

Case 2: A 22-year-old woman with a 3-year history of reactive arthritis affecting her left knee, which occurred after an episode of viral gastroenteritis, had received three knee aspirations and injections for the condition. She subsequently presented to Dr Ching with recurrent arthritis in her left knee and pain and swelling in her left foot. She had a 12-year history of scalp psoriasis. Dr Ching diagnosed this patient with PsA.

Dr Ching explained that he looks for psoriasis in patients with undifferentiated inflammatory arthritis, persistent `reactive' arthritis and HLA-B27-related arthritis. The following regions should be investigted for `hidden' psoriasis: the scalp, the natal cleft, the umbilicus, in and behind the ears, the genital region and the nails (pitting, onycholysis, hyperkeratosis and ridging).

Clinical measures of disease severity and outcome in psoriasis

Dr Birchall explained that the PASI is a poor tool for scoring psoriasis and that objective measures are needed. He pointed out that most dermatologists worldwide consider a PASI score of >10 and/or a DLQI >10 to equate to moderately severe psoriasis, or worse. However, in NZ, Pharmac requires a PASI of >15 for access to biologics and does not take into account nail or genital skin involvement. Another problem with the Pharmac criteria is that a patient with a baseline PASI score of 16, for example, may have their PASI reduced to 7 with biologics, but not be eligible to continue therapy, whereas a patient with a baseline score of 36 and a reduction to 7 after treatment is eligible to continue on biologics.

The CASPAR criteria for PsA is not a relevant tool for the dermatologist. A consensus group has recently developed recommendations for the treatment of nail psoriasis in patients with moderate-to-severe disease.[1] Dr Birchall pointed out that nail psoriasis has a big impact on patients lives and is often resistant to treatment. He explained that there is increasing awareness that nail disease parallels joint problems and that treatment often needs to be more aggressive. He suggests referring to dermNet NZ for examples of the different types of nail psoriasis (http://dermnetnz.org/).

Methotrexate treatment for PsA

Dr Ching explained that the following baseline investigations should be undertaken before starting a patient on methotrexate: full blood count; creatinine; liver function; hepatitis B and C serology; chest x-rays. He advises his patients to be immunised against pneumococcal disease and influenza. With regard to monitoring for adverse effects of methotrexate, Dr Ching undertakes a full blood count and liver function tests every 2 weeks for 6 weeks, then monthly (3-monthly in long-term stable patients). Common dose schedules for methotrexate in PsA include: 7.5 mg/week, increasing to 15 mg/week after 1 month (up to 25-30 mg/week); 10 mg/week, increasing up to 20 mg/week after 1 month; 7.5 mg/week, increasing by 2.5 mg/week up to 20-25 mg/week.

Liver fibrosis and methotrexate

Dr Birchall pointed out that dermatologists unlike rheumatologists have had an ongoing concern about methotrexate-induced liver fibrosis, with this adverse event being more common in patients with psoriasis than those with RA. US guidelines recommend performing a liver biopsy at each cumulative interval of 1.5g of methotrexate. While liver biopsy is perceived as the gold standard, it is associated with high error, morbidity and mortality rates.[2] Monitoring procollagen (P3NP) level has been shown to be useful for monitoring hepatic change and is being used in NZ in dermatology patients on methotrexate.[3] Liver scans are also being used to monitor such patients.

In 2003, the NZ Dermatological Society undertook an audit of methotrexate use in NZ and revealed very close concordance with use of the agent and that only 16% of dermatologists ever used a dose greater than 15 mg/week (more recent evidence suggests that increasing the dose beyond 15 mg/week in psoriasis is of no significant clinical benefit). Dr Birchall starts patients on methotrexate 15 mg/week (often 7.5mg morning and evening on the same day). He also prescribes folic acid, performs standard blood checks, scores the PASI at each visit, monitors P3NP levels, informs patients with verbal, written and DermNet information, and addresses lifestyle issues.

Collaboration in treating PsA patients

Dr Ching stressed the importance of good communication between rheumatologists and dermatologists. Rheumatologists should promptly refer patients to a dermatologist if they have severe psoriasis or psoriasis affecting the face, palm of hand, or sole of the foot. Likewise, dermatologists should promptly refer patients to a rheumatologist if they have painful and swollen joints, with or without a raised ESR or CRP.

Rheumatology and dermatology references:

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Comorbidities associated with psoriasis and implications for treatment

Presenter: Dr Stephen Tyring

PsA, a chronic immune-mediated inflammatory arthritis involving elevated levels of TNF-α, is present in ~30% of patients with psoriasis and can be as debilitating as RA. While the majority of patients with this comorbidity develop skin lesions first, ~15% of patients present initially with joint symptoms. Clinicians should enquire about symptoms of joint pain in those presenting with psoriasis, because early intervention with anti-TNF agents may be beneficial.

In a large UK cohort, the relative risk of myocardial infarction was increased for those with psoriasis, revealing the following incidences per 1000 patients-years: controls 3.58; mild psoriasis 4.04; severe psoriasis 5.13. The RR was greatest in young patients with severe psoriasis.[1]

Another comorbidity, the metabolic syndrome (which appears to be linked to increased inflammation), involves the presence of at least three of the following: increased waist circumference or abdominal obesity; hypertension; hypertriglyceridaemia; reduced HDL; insulin resistance.[2] These symptoms lead to a chronic inflammatory state associated with markedly increased cardiovascular mortality.[2] The prevalence of the metabolic syndrome is significantly increased in patients with moderate-to-severe psoriasis compared with controls (OR 5.29: 95% CI 2.78-12.8) and a significant variability exists between genders; men OR 10.6 (95% CI 3.2-34.7), women OR 3.4 (95% CI 1.2-9.5).[3] Furthermore, analysis of data from the US Nurses Health Study II found an increased risk of psoriasis in women associated with an increasing BMI, when compared to a BMI of 21-22.9 kg/m^2; multivariate RRs of 1.40 (95% CI 1.13-1.73) with a BMI = 25-29.9 kg/m^2, 1.48 (95% CI 1.15-1.91) with a BMI = 30-34.9 kg/m^2 and 2.69 (95% CI 2.12-3.40) with a BMI ≥ 35.0 kg/m^2.[4] Hip circumference, waist circumference, and waist-hip ratio were all associated with a higher risk of incident psoriasis ($p < 0.001$). Another study has shown a higher incidence of obesity in patients with psoriasis compared with the general population (34% vs 18%; $p < 0.001$).[5]

There is also evidence for an increased risk of chronic pulmonary disease, carotid atherosclerosis, angina, peripheral vascular disease and stroke in patients with psoriasis/PsA.[6-8] A number of studies have demonstrated the efficacy of anti-TNF agents for treating various comorbidities, and a study investigating methotrexate has found that the agent reduces the incidence of vascular disease in patients with psoriasis or RA.[9-13]

Evidence for an increased risk of type 2 diabetes in patients with psoriasis comes from a large study showing that the adjusted attributable risk of developing the condition is 0.9 cases/1000 patients per year (0.7 cases/1000 mild psoriasis patients per year and 3.0 cases/1000 severe psoriasis patients per year).[14] The study also revealed that patients with psoriasis and incident type 2 diabetes were more likely to require pharmacotherapy for their diabetes than those with incident diabetes alone (adjusted risk 1.55; 95% CI 1.15-2.10).

Considerations prior to starting and during anti-TNF therapy

Dr Tyring prefers not to start biological therapy on a patient with a recent (<5 years) history of solid tumour malignancy. He pointed out that, overall, the risk of cancer does not appear to be increased with the use of adalimumab.[15] Of concern are bacterial, fungal, protozoan and viral infections (including hepatitis B and C) and these should also be screened for and treated prior to starting anti-TNF therapy. TB testing is recommended for those starting anti-TNF therapy, and if present, this should be treated prior to initiating therapy (QuantiFERON-TB testing is useful for detecting latent TB). Dr Tyring commented that it is usually not necessary to stop anti-TNF therapy if a patient develops herpes zoster virus, human papillomavirus or herpes simplex virus infection during treatment.

Demyelination has been reported with all TNF-α inhibitors, although it is uncommon. In such a circumstance, treatment would be discontinued and not be restarted. The use of TNF-α inhibitors should be avoided in those with pre-existing demyelinating diseases or those with first-degree relatives with such conditions. New-onset congestive heart failure has rarely been reported during anti-TNF therapy. It has been suggested that anti-TNF therapy may worsen pre-existing congestive heart failure and such therapy should be avoided in patients with this condition.

Who should receive anti-TNF therapy?

- Patients with >10% BSA involvement
- Patients with PsA
- Patients with <10% BSA involvement, if palmar, plantar, face or genital involvement
- Patients with contraindications to other systemic therapies

What if anti-TNF therapy doesn't clear the psoriasis?

- Increase frequency of SC injections
- Add methotrexate
- Add topical therapy/phototherapy/other systemic therapy?

Comorbidities references:

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Fit for work and work productivity

Presenters: Dr David Gardner and Dr John Petrie

Effects of RA on work productivity

Dr Gardner explained that the effects of RA on work productivity begin early and without intervention are progressive and sustained. Approximately 20-30% of individuals with RA have reduced work capacity within 2-3 years, with the rate increasing to 50% after 10 years. Furthermore, patients with RA on average have 20-80 days off work per year due to their disease, experience an associated loss of income and high indirect costs (which may be 2-4 times greater than the cost of treating the condition), and 15-35% of these individuals are on a disability allowance. RA patients in employment tend to exhibit a 5-10% reduction in productivity and career advancement may be lost. Mancuso et al. found that all individuals with RA had to make adjustments to their day-to-day practice at work, but <10% received assistance from their employers.[1]

The effects of RA treatment on work productivity were investigated in a review by Birnbaum et al., who showed no effect of DMARD therapy on this measure.[2] However, studies included in their analysis were undertaken in patients with long-standing RA. Subsequent studies, including the PREMIER study, have shown TNF antagonists to improve work productivity in RA, with adalimumab therapy resulting in a significant improvement in work-related issues (loss of job, inability to work and difficulty working) compared with DMARDs.[3,4] A health-economic companion study with the PREMIER study, evaluating household and work-place outcomes for patients with RA who were homemakers or employed workers, revealed a significant improvement over a 2-year period in both groups (less presenteeism [reduced ability to do the tasks required] and greater likelihood of gaining/retaining employment) when patients used adalimumab.[5] The study also revealed that baseline radiographic progression was an independent predictor of employment status. A study investigating the effect of adalimumab in combination with methotrexate on job loss in patients with RA showed approximately 50% fewer jobs lost at 52 weeks in those receiving combination therapy compared with those treated with methotrexate alone.[6] A Canadian study evaluating the short-term effect of adalimumab on work productivity in moderate-to-severe RA revealed that while the overall changes were small, levels of absenteeism and unpaid help were improved.[7] This study confirmed the findings that patients with longer-standing disease exhibit less of an improvement in these parameters.

Fit for work?

Dr Petrie discussed The Work Foundation, which was established in 2002. The Foundation, whose global ambassador is Lech Walesa, has undertaken a number of projects (including the Fit for Work project) in the UK and Europe, looking at aspects of work (socioeconomic, innovation and workforce effectiveness). The Fit for Work project, which has now become global, has examined the impact of musculoskeletal disorders on individuals' ability to work and the impact of this on economies and society as a whole. A Fit for Work project in NZ has been undertaken with grant support from AbbVie. Local commentators on the project included: Dr David Beaumont, Sandra Kirby (Arthritis NZ),

Chris Polaczuk (ACC), Janice Reagan (OT Waitemata DHB) and David Tappin (Massey University). Specific components of musculoskeletal disorders were investigated (back pain, work-related upper limb disorders and inflammatory arthritis [RA and SpA]). Findings from local literature revealed that musculoskeletal disorders affect nearly 1 in 4 adults, comprise 25% of total annual health costs ($5,570 million per annum) and account for 11.7% of sickness and 14.5% of invalids benefit claims. Estimated annual costs (NZ$ million) of musculoskeletal disorder in NZ are as follows: arthritis 2,089; osteoporosis 1,133; sickness benefits 320; joint replacement 191; pharmaceutical 61; pathology 19; imaging 49.[8]

What can be done about the economic burden of musculoskeletal disorders?

Dr Petrie outlined the following recommendations and focus areas derived from the NZ Fit For Work report: early diagnosis and intervention, identifying where work is good (early return to work can be beneficial), employing the biopsychosocial paradigm and focussing on capacity (not incapacity). The report identified the following stakeholders to whom the aforementioned recommendations should be addressed: the NZ Government and policymakers, employers, health professionals and individuals. The policymakers should be informed of the following: musculoskeletal disorders should be incorporated into the National Health Strategy, health care pathways with physiotherapy and OTs in addition to specialists should be accessible to patients, awareness should be raised amongst employers of the impact of musculoskeletal disorders and awareness raised on the benefits of their proactive management. Employers should focus on capacity (not incapacity), should assist employees early, involve occupational health professionals, establish return to work plans, undertake workplace-based rehabilitation and provide retraining and workplace modifications. Health care professionals should aim for early diagnosis and intervention, focus on capacity (not incapacity), encourage self-management and be aware of the psychosocial components of patient's beliefs, attitudes and behaviour. The concept that work is good for patients with arthritis has been reiterated by the Royal Australasian College of Physicians.

Communication and management for better health outcomes

Dr Petrie pointed out that miscommunication between doctors and patients can have a negative impact on patient outcome. He explained that clinicians often use the terms `degeneration', `wear and tear', `no cure', `learn to live with it' and `take your painkillers only when necessary'. When patients hear these terms, they interpret them as `disintegrating', `continuing damage', `nothing can help me', `I'll wind up in a wheelchair' and `I must just suffer the pain'. He added that in his clinic, he does not use the term `painkillers', but rather refers to these agents as `mobility enhancers'.

Evidence suggests that 80% of individuals will at some stage over the course of the next two years suffer an episode of back pain sufficient to stop them performing their normal daily activities.[9] The question arises as to why do some people with common health problems never recover as expected. It may be, as quoted by Dr Wilbert Fordyce, `people with something better to do, don't suffer as much'.

Dr Petrie explained that health outcome in chronic conditions depends on personal attributes, not disease processes and that recognition of an individual's health behaviour allows for more effective intervention. He pointed out that individuals diagnosed with a chronic condition initially experience a sense of loss, fear and uncertainty, followed a full awareness that everything as it was has changed and there is no going back. Dr Petrie explained that this is a critical stage because patients can either move into a sense of apathy and take on a disability persona, or they can have a more positive outlook. The biopsychosocial approach to management of these patients is critical and uses drug therapy, a psychological assessment, and manipulation of their work and leisure environment to enable a return to a more normal way of life.

Fit for work references:

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2. Birnbaum H et al. Expert Opin Pharmacother. 2009;10(2):255-69
3. St Clair EW et al. Arthritis Rheum. 2004;50(11):3432-43
4. Breedveld FC et al. Arthritis Rheum. 2006;54(1):26-37
5. van Vollenhoven RF et al. Arthritis Care Res. 2010;62(2):226-34
6. Bejarano V et al. Arthritis Rheum. 2008;59(10):1467-74
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9. The Back Pain Revolution. Gordon Waddell. Churchill Livingstone 1999

Aiming for treatment success in RA and PsA - how clinic tools can assist treat to target

Presenter: Dr Julia Martin

Recently, an international task force, chaired by J. Smolen (Austria), was established to review and summarise the evidence on tight control of RA, in order to formulate recommendations to enhance the implementation of treating to target in clinical practice. Seven core treat to target (T2T) studies were identified from the literature.[1] Most of the studies used low disease activity as the target, time frames for assessment varied from 1-4 months, and the majority were undertaken in early RA. Evaluation of all five studies that compared T2T with routine approaches showed significant clinical benefits of T2T. Recommendations developed by the T2T steering committee were discussed, amended and voted upon by >60 experts. From this, 10 recommendations and four overarching principles were derived.[2] T2T focuses on the principle that intensive management is more effective than routine care and that adherence to treatment guidelines improves outcomes. Subsequent studies have confirmed that a more targeted approach improves outcomes in RA, with one such study showing better clinical outcomes with DAS-driven therapy than routine care for those with recent-onset RA.[3]

Clinic tools for assessing RA and PsA

Clinic tools, including patient-reported outcome measures, biochemical markers, clinical assessment and imaging, can assist T2T. Patient-reported outcome measures include Pain Score and Patient Global, MHAQ, EuroQol and RAPID 3; Dr Martin recommends that at least the first three assessments be undertaken. Biochemical markers include: CRP, ESR, RF and CCP. Clinical assessment includes: 28 and 68 joint count, SDAI, CDAI, DAS28 and PASDAS (a composite score for PsA, which still needs to be validated). Dr Martin tends to just use the DAS28 (versions DAS28 3V CRP and DAS28 4V ESR), but commented that it doesn't really matter which of the outcome measures is used, as long as one of them is undertaken as studies clearly show that composite scores are more informative than just looking at the joints.

Clinical features include dactylitis, enthesitis, nail and skin disease. While outcome measures exist for all of these, Dr Martin does not use them in clinical practice, preferring to document the presence of such features, rather than grade them. She also asks her patients about fatigue and productivity.

Imaging in RA and PsA involves x-ray, musculoskeletal ultrasound and musculoskeletal MRI. Damage evident on x-ray correlates to disability (except in the earliest phases of RA) and there is some evidence that cartilage loss (measured as joint space narrowing) may be more significantly related to disability than erosions.[4,5] X-ray is inexpensive, is easy to interpret, is reproducible and can detect change. However, this imaging modality has poor sensitivity and emits ionising radiation. Musculoskeletal ultrasound can identify erosions, synovitis, tendon pathologies (tenosynovitis, tendon rupture, calcific tendonitis), cartilage loss, Bakers cysts and bursitis, and a number of studies have demonstrated this imaging modality to be an important clinical tool in RA.[6-9] Specifically, ultrasound is useful for picking up early erosions that are not seen on x-ray. Furthermore, Doppler informs of vascularity and a high Doppler signal on ultrasound predicts erosions and poor prognosis (Grade 3 Doppler is associated with a poorer outcome).[10] Dr Martin said that she undertakes joint examinations with ultrasound, but pointed out that recent studies suggests that not all joints need to be assessed this way, rather a subset may be evaluated.[11,12] Musculoskeletal ultrasound is inexpensive, safe (non ionising), portable, dynamic (real time), well accepted by patients and improves precision of intervention. Disadvantages of musculoskeletal ultrasound are reliability issues (depends on ultrasonographer), the presence of artefacts, the fact that it can be time consuming and that it cannot see into bone. The International Targeted Ultrasound Initiative (TUI), a network of rheumatologists dedicated to promoting ultrasound in the management of RA and its treatment outcomes, has useful resources for clinicians on its website: see http://www.targetedultrasound.net/.

Musculoskeletal MRI in RA identifies erosions, osteitis (bone marrow oedema), tendon pathologies and synovitis. However, this modality is not effective for characterising cartilage. MRI can detect erosions (and erosion progression) earlier than x-ray or ultrasound and osteitis is predictive of erosion development.[13] Furthermore, MRI detects synovitis in patients in clinical remission and MRI synovitis predicts the development of erosions.[13] This imaging modality has good joint capture, is sensitive to change and is reproducible. However, it is expensive, claustrophobic, time consuming and synovitis may be best evaluated with gadolinium.

What is treatment success?

A study has shown that 34% of patients will decline treatment despite active disease and that a DAS score of 4.05 is a patient-acceptable syndrome state.[14] Thus, patients appear to accept a much higher disease activity state than clinicians would want them to have. Ultrasound can be a useful tool to show patients that they do in fact have erosions forming in order to encourage them to be treated to prevent further damage to their joints. Low disease activity is at times accepted as treatment success, as there are some patients in whom treatment cannot be escalated due to their comorbidities. Clinical remission should be an aim in early disease activity. There is some emerging evidence that early aggressive treatment with biologics may in fact be a cure for RA, but at this stage this is debatable.

With regard to defining remission, the ACR/EULAR define remission in RA as follows: tender joint count, swollen joint count, CRP (in mg/dL) and the patient global assessment (0-10 scale) are all <1, or the SDAI is <3.3.[15] Dr Martin pointed out that this definition was derived for clinical trials and that in clinical practice if a patient has a DAS remission, but still has some synovitis on ultrasound, one needs to keep pushing on with treatment, dependent on their other comorbidities.

Dr Martin summarised the role of the dermatologist and pointed out that if the following four points are followed there is a high likelihood of treatment success.

- Define the target with the patient
- Direct the strategy chosen (e.g. rapid adjustment for tight control)
- Follow the patient over time
- Individualise the treatment

Treatment success references:

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Ankylosing spondylitis and axial spondyloarthritis: The challenge of early diagnosis

Presenters: Dr Simon Stebbings and Dr Douglas White

Studies suggest a mean of 8-11 years between the onset of AS and its diagnosis.[1] Early diagnosis of AS allows for early intervention and a number of studies have shown early intervention with NSAIDs or anti-TNFs to be beneficial in such patients.[2-4] Reasons for delayed diagnosis in AS include the fact that the onset of the disease is often insidious, there is a lack of awareness of this `rare' disease, and young patients may attribute symptoms to `part of life', especially in adolescence. Furthermore, GPs may be unaware of the characteristics of inflammatory back pain, clinical signs of AS may be subtle and AS accounts for only 5% of chronic lower back pain.

Achieving early diagnosis in AS

The modified NY criteria for AS has a requirement for evidence of radiographic change and this is known to take ~8 years to develop. The newer ASAS classification criteria for axial SpA have been shown to have a sensitivity of 82.9% and a specificity of 84.4%, and facilitate an earlier diagnosis of axial SpA than the NY criteria. Analysis of the individual sensitivities and specificities of the various SpA features of the ASAS criteria vary widely, with response to NSAIDs, for example, having less of an impact than the presence of HLA-B27 or MRI evidence of disease.[5] Looking at the likelihood product (mathematically derived from the likelihood ratios of the various SpA features), it is possible to determine the approximate post-test probability of AS; negative test findings are usually not incorporated into the calculation.

A NZ analysis of ~2000 GP referrals identified 143 patients with a rheumatologist-confirmed diagnosis of AS (sensitivity of 90.9% and a specificity of 78.0%). A review of symptoms in 300 GP referral letters for back pain showed much lower sensitivity and specificity for predicting AS. Dr White explained that early rheumatological referral by GPs of patients with inflammatory back pain is extremely important and to this end, referral guidelines have been developed.[6-7]

Dr White presented the following case:

Case: A 48-year-old Samoan man with a 12-year history of back pain, with both mechanical and inflammatory features, and occasional knee swelling and pain, had been treated with NSAIDs with only minimal response. His ESR and CRP levels were normal.

Dr White calculated this man's probability of AS to be 39.6%; at that time his HLA-B27 status was not known, but recalculation assuming it to be positive increased his probability to 85.5%. A subsequent x-ray revealed evidence of AS.

The Waikato AS Clinic

In the Waikato, Dr White and colleagues have set up an AS clinic to aid in the care of patients with this condition. The clinic, involving Dr White, a physiotherapist and a nurse specialist runs once a month and patient data are entered into a comprehensive database. In the past 18 months, 55 new patients (91% male) have been seen at the clinic and a large proportion have severe, long-standing disease. Feedback from patients attending the clinic has been positive.

Analysis has revealed that 60% of the clinic cohort fulfilled the NY criteria for AS, while 40% fulfilled the ASAS criteria, with each criteria picking up a different group of patients with regard to age and disease duration. Analysis of BASMI data against ASAS and NY criteria fulfilment has revealed that even if a patient has radiographic sacroiliitis they may still have good spinal mobility.

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