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因運動損傷而到急症室求診是非常普遍。不同的運動會有自己獨特的受傷模式。在"運動急症系列"中，將討論六種時下流行運動的受傷種類及緊急情況。在這課程中您將學習到與該運動相關的具體緊急情況，預防措施和應急處理。這方面的知識是從事這些運動的人士所必需的。

Date	Topics	Speakers
9 Oct	A Skier and Snowboarder 雪嶺雄峰 - Skiing related injuries and their management	Dr. Elvis Ying-Leung MAK FHKCEM 麥應良醫生 香港急症科醫學院院士
16 Oct	A Rugby Player 短兵相接 - Contact Sports related injuries and their management	Dr. Kenneth Wing-Cheung WU FHKCEM 胡永祥醫生 香港急症科醫學院院士
23 Oct	A Trail Walker and Marathon Runner 毅行耐走 - Endurance Sports injuries and their management	Dr. Kam-Leung LAW FHKCEM 羅金亮醫生 香港急症科醫學院院士
30 Oct	A Bicycle Rider 千里單騎 - Cycling related injuries and their management	Dr. Francis Yip-Kwong LAU FHKCOS 劉業光醫生 香港骨科醫學院院士
6 Nov	A Sudden Collapsed Field Player 球場上的最後戰士 - Medical Emergency in Sports, their recognition and management	Dr. Willis Wing-Hong KWOK FHKCEM 郭永康醫生 香港急症科醫學院院士
13 Nov	A Scuba Diver 活在水世界 - Diving related injuries and their management	Dr. Man-Kam HO FHKCEM 何文錦醫生 香港急症科醫學院院士

Dates : 9, 16, 23, 30 October & 6, 13 November 2017 (Every Monday)
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The Cover Shot

UNKAI (Sea of clouds), taken this year in early June at the UNKAI Terrace, situated on the Hoshino Resorts Tomamu, Hokkaido at a 1088m mountain. Every year from May to October, there is a 30%-50% chance to see this breathtaking sea of clouds in hand reaching distance. A 13 minutes gondola ride at 4 am in the morning takes you to the top of the mountain. A "Cloud Walk" at the UNKAI Terrace feels like you are walking in the fluffy clouds. In the picture, with the warmth from the sun, the UNKAI starts vanishing and you can see the top of the two resort towers emerging from the sea of clouds. This astonishing moment is definitely for early birds only as it won't last for long.

Dr Man-leung KWOK
MBChB, MRCP, FHKCP, FHKAM, FRCP
Specialist in Rheumatology, Private Practice

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Editorial

Dr Temy Mo-yin MOK

MBBS, MD, HKCP, HKAM, FRCP, FRCPA

Associate Professor, Department of Biomedical Sciences, City University of Hong Kong
Consultant Rheumatologist, North District Hospital, New Territories

Editor

Dr Temy Mo-yin MOK

The theme of this issue of the Hong Kong Medical Diary is Treat-to-Target in Rheumatology. With the success in improvement of clinical outcomes from treating-to-target in diabetes mellitus, hypertension and hyperlipidaemia, initiatives in establishing this target driven approach are looming in the field of Rheumatology and are expected to replace the traditional symptom-based approach in the management of various rheumatic diseases in the near future. Treating-to-target in the management of rheumatoid arthritis has taken the lead in this regard with well-defined instruments for measurement of disease activity, achievable therapeutic targets and effective treatment options including combination of disease modifying anti-rheumatic drugs (DMARDs) and biological agents. By close monitoring of the disease activity in patients with rheumatoid arthritis, titrating the treatment regimen to a realistic and achievable clinical target towards treating to a state of absence or low disease activity, these patients are shown to have retardation of erosive joint damage, improved functional status and quality of life.

Task forces from international collaborative efforts have been set up and are working towards the notion of treat-to-target in other rheumatic diseases including systemic lupus erythematosus, spondyloarthritis, psoriatic arthropathy, etc. A number of challenges shall be met in this pursuit as you will read from this issue.

In this issue, Dr Ronald Yip has nicely illustrated the current state-of-the-art approach in the management of patients with rheumatoid arthritis accompanied by a treatment algorithm for your reference. Dr Eugene Fung is providing a comprehensive overview on the approach to treat gouty arthritis to a targeted low serum uric acid level using existing and novel therapeutic regimens. I will reveal the challenges in treating-to-target in the management of systemic lupus erythematosus, a complicated multisystemic autoimmune disease. Dr James Wei sets the scene revealing the effort of an international task force on the recommendations of treating spondyloarthritis and the treat-to-target algorithm based on conventional DMARDs and biologic agents. You will also read the very nicely written treat-to-target approach in psoriatic arthropathy and the outline of pharmacological agents by Dr Lucia Chau. In the lifestyle column, Dr ML Kwok has shared with us his lovely interest and hobby of playing saxophone and his wonderful travel experience viewing Unkai on the top of a mountain in Hokkaido.

I am sure you will enjoy reading this issue and be fascinated about the treat-to-target concept extending into the rheumatology field in clinical medicine.

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Treat-to-Target in Rheumatoid Arthritis

Dr Ronald Man-lung YIP

MBChB (CUHK), FHKCP, FHKAM(Med), FRCP(Edin)

Clinical Services Director, Integrated Diagnostic and Medical Centre, Tung Wah Group of Hospitals
Vice President, the Hong Kong Society of Rheumatology
Honorary Clinical Associate Professor, Department of Medicine and Therapeutics, the Chinese University of Hong Kong

Dr Ronald Man-lung YIP

Introduction

Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder which is characterised by diarthrodial joint involvement with synovitis and pannus formation. It carries high mortality and morbidity. In general, a decrease of 5-9 years of life expectancy occurs in RA. Extra-articular manifestations or comorbidities such as cardiovascular complications, osteoporosis, infection, malignancy and immune related manifestations also affect long term morbidity and quality of life. Over the past 20 years, advances made in the understanding of pathogenesis of RA have resulted in the development of new treatments, making remissions a possibility for RA.

Disease modifying anti-Rheumatic Drugs (DMARDs) are cornerstone drug therapies to reduce the joint inflammation and progression of RA. DMARDs are heterogeneous groups of compounds with different biochemical and pharmacokinetic properties that have positive impacts on the radiological outcome of joint damages (erosions and joint space narrowing). Examples of commonly used conventional DMARDs in RA include methotrexate, lefluominde, sulphasalazine, gold and antimalarials such as hydroxychloroquine. In the recent decade, biological DMARDs with different modalities of actions and synthetic targeted DMARDs have become available for the treatment of refractory cases.

Biological DMARDs are agents that target inflammatory cytokines and cells within the synovium and immune system. Biological DMARDs that are available in Hong Kong include anti-tumour necrosis factor (TNF) agents such as infliximab, adalimumab, golimumab, certolizumab and etanercept, anti-IL6 receptor agents such as Tocilizumab, anti-B cell therapy such as Rituximab, and costimulation blockade agents such as abatacept. Recently, a targeted synthetic DMARD inhibiting the Janus Kinase pathway, tofacitinib, has also been approved for the treatment of RA.

In addition to the development of new therapeutic agents for the treatment of RA, there is also a revolutionised approach in management strategy--using the traditional step up (symptom alleviating) approach by changing dosage or addition of medications only if the symptom progress has become obsolete. To attain maximal efficacy and disease control, international guidelines and standards of care recommend a treat-to-target approach.

Concept of Treat-to-Target

The treat-to-target concept is not new in the management of some chronic medical conditions such as diabetes, hypertension and hyperlipidaemia. The success in reducing long term complications and overall mortality by focusing on a specific target such as HbA1C in diabetes, LDL cholesterol level in hyperlipidaemia and blood pressure target in hypertension has attracted clinical researchers in using a treat-to-target approach in RA. A treat-to-target concept is generally defined as a treatment strategy in which a clinician treats the patient aggressively enough to reach and maintain a specific and measurable goal. In the case of RA, the measured goal is the absence of inflammation, as the presence of persistent inflammation/ disease activity at the joint level will predict joint damage, which is irreversible and will contribute to functional impairment.

To make this concept feasible, a few components are essential. The first requisite is to diagnose RA early. Joint damages that occur in RA are not reversible. It is important to institute treatment relatively early in the disease course so that damage can be prevented or minimised. The old 1987 American College of Rheumatology (ACR) criteria, which included features of long term damages such as rheumatoid nodules or X-ray changes, were not sensitive enough to detect RA early. Therefore a new classification scheme was proposed in 2010 for early diagnosis. Another essential component in the treat-to-target concept is the regular assessment of disease activity by using a measurement which reflects the activity of the disease. Therapies can be adapted accordingly if the measured goal is not achieved.

Due to the complexity of the signs and symptoms of RA, there is no single laboratory value that reflects the disease activity. Inflammatory markers such as CRP (C–reactive protein) or ESR (erythrocyte sedimentation rate) can be normal at presentation and may not change with clinical improvement. On the other hand, they can also be affected by other causes of inflammation such as infection or fever. Therefore a composite scoring system which incorporates quantitative joint count, patient self-report multifaceted questionnaires and laboratory markers has been applied to determine activity status and its changes in RA.

Many clinical trials have confirmed benefits on treat-to-target approach in RA. The earlier TICORA (Tight Control of Rheumatoid Arthritis) trial and CAMERA

(Computer Assisted Management in Early Rheumatoid Arthritis) trial compared treatment strategy with tight regular treatment adaptations with routine care. Both of these trials together with many subsequent strategy-based trials showed significant clinical reduction in RA activity, higher proportion of patients achieving remission, and significantly fewer radiographic changes in the strategy-based group than the routine care group. Even in studies using just conventional DMARD plus glucocorticoid regimen without biological agents, strategic approaches showed higher response rates than routine therapy. These showed that strategy is more important than particular agents and that biological agents could be reserved for patients who do not response to traditional conventional DMARDs or those with poor prognostic factors.

Importance of Early identification/ Early Diagnosis of RA

In RA, a biological " window of opportunity " exists. There were studies showing that irreversible radiographic erosions occurred as early as 2 years. Functional loss also occurs early in RA. The earlier the treatment, the higher rate of success in getting the disease in remission. Therefore the ACR/European League of Rheumatism (ACR/EULAR) has published a classification criterion in 2010 to replace the old criterion aiming to capture the disease in early phase to tailor treatment. In the 2010 criterion, the number of joint counts, inflammatory markers and rheumatoid factor (RF) and anti-CCP antibodies are included to aid early identification of RA for early institution of treatment.

Disease activity monitoring and Assessment

Apart from early identification of RA, disease assessment is another important aspect in the treat-to-target approach. With a composite measure of disease activity, one can monitor the activity of RA more accurately and adapt and change therapies if the target is not reached. Several validated instruments are used to measure disease activity in RA. Most of them comprise multidimensional assessment of a patient's current disease activity. Core measurements include the number of tender joint counts/ swollen joint counts, patient and physician assessments of disease activity on a visual analogue scale and the acute phase reactants such as ESR and CRP. Some commonly used examples of the assessment tools are DAS 28 (disease activity Score in 28 joints), SDAI (simplified disease activity index), CDAI (clinical disease activity index) and RAPID3 (Routine Assessment of patient index data). Each scoring system would have its own cut off point for their classifications into high, moderate or low disease activity and disease remission.

The calculations of some of the disease activity indices are as follows:

DAS 28= $0.56\sqrt{(TJC28)} + 0.28\sqrt{(SJC28)} + 0.36Ln(CRP10 + 1) + 0.014PtGA$ (0-100 scale)+ 0.96

SDAI = (28TJC) + (28SJC) + PhGA(0-10scale) + PtGA(0-10 scale) + CRP(mg/dl)

CDAI = (28TJC) + (28SJC) + PhGA (0-10scale)+ PtGA(0-10 scale)

PhGA = physician's global assessment
PtGA = patient's global assessment
28 TJC = number of tender joints in a total of 28 joints
28 SJC= number of swollen joints in a total of 28 joints

Although the choice of assessment tools may be different in different clinical trials or vary according to the practice of different rheumatologists, the key message is that measurements of disease activity must be obtained and documented every time and regularly to enable an adaptation of therapy to be made in case the treatment target is not reached.

Treatment Target

Now we have tools for early diagnosis and assessment, but what is our treatment target? In RA, the optimal target should be the threshold of disease activity at which progression of joint damage is halted and the maximal functional impairment is recovered. Studies have suggested that only a remission is associated with the cessation of progression. Therefore, the main treatment target should be remission. Different assessment tools and clinical trials vary slightly in their own remission criteria, while some are more stringent than the others. In some strategy-based trials, outcome measurements would also include physical function, work disability and imaging changes such as absence of subclinical synovitis in ultrasound or MRI to define remission. In general, clinical remission remains the most commonly accepted remission criterion.

Clinical Remission is defined as the absence of signs and symptoms of significant inflammatory disease activity. In 2011, ACR and EULAR have come up with two remission criteria: the Boolean based definition and the Index based definition, with high validity and predictability for better long term outcome.

Boolean based definition :
Tender joint count ≤1. Swollen joint count ≤1. C reactive protein ≤ 1mg /dl. Patient's global assessment ≤1 (0-10 scale)

Index based definition :
Simplified Disease Activity Index Score ≤3.3 or CDAI score≤2.8

In patients who have long-standing disease with pre-existing damages, complete remission may not be realistic or achievable. Some patients may also have comorbidities that preclude the intensification of therapy to target remission. For these patients, a more realistic and acceptable target would be a state of low disease activity. A low disease activity state also retards damage accrual and improves functions when compared with high or moderate disease activity. Low disease activity will be defined according to any of the validated composite disease activity measures that include joint counts. Furthermore, continuous assessment is also important, as the target reached should be maintained and sustained in order to ensure good outcome and lack of adverse events.

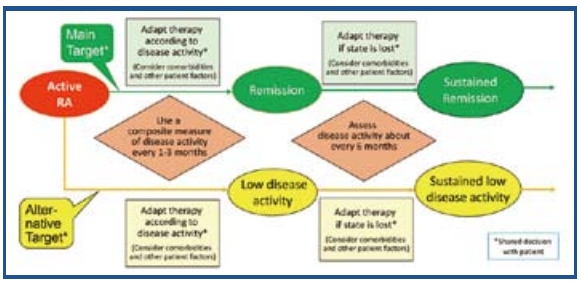
Recommendations from the international Treat-to-Target Task Force

In 2010, an international Task force has formulated consensus recommendation aimed at improving the management of RA in clinical practice. These were later updated based on evidence and expert opinion in 2014.

1. The primary target should be a state of clinical remission
2. Clinical remission is defined as the absence of signs and symptoms of significant inflammatory disease activity
3. Remission is the therapeutic target, and low disease activity as an alternative where remission is not feasible
4. Routine use of validated composite measures of disease activity
5. Treatment target should be influenced by comorbidities, patient factors and drug related risks
6. Regular measurements and documentation of disease activity e.g. monthly for high/moderate disease activity, 6-monthly for sustainable low disease activity
7. Structural changes, functional impairment and comorbidity also contribute to clinical decision making
8. Drug therapy should be adjusted at least 3 months until the desired target is reached
9. The desired treatment target should be maintained throughout the remaining course of the disease
10. Patient contribution to decision on treatment target and strategy

Here is a schematic representation of the treatment algorithm of Treat-to-Target approach in RA recommended by the international task force

Treatment algorithm for RA



Practical issues to achieve the Treat-to-Target Approach

Although treat-to-target approach is noted to have significant positive impact in the management of RA, there are many challenges limiting the adherence of this approach in real practice. Accessibility to rheumatologists early in the course of disease, cost of the drug treatment, inability of busy rheumatologists to schedule frequent visits and conducting structured RA disease activity measures, worries about side effects on stepping up therapies and patients' own perspectives of their disease control all contribute to potential failures of treat-to-target approach. Therefore, an important principle is that the treatment should be based on a shared decision between the patient and the rheumatologist. These would involve patient education on the disease nature and characteristics, risks and progression, modalities of assessment; shared decision on treatment targets, and discussions on the benefits and side effects of different therapeutic choices.

In 2016, an EULAR recommendation provided practical guidelines on the choice of different DMARDs in the overall management. It stated that therapy with DMARDs should be started as soon as the diagnosis of RA is made. Methotrexate should be part of the first treatment strategy unless contraindicated or intolerant, in which cases lefunomide or sulphasalazine should be considered as the first part of treatment strategy. Short-term glucocorticoids should be considered when initiating or changing conventional synthetic DMARDs, but should be tapered off as rapidly as clinically feasible. Poor prognostic factors which include moderate to high disease activity, high acute phase reactant levels, high swollen joint counts, presence of RF and/ or anti-CCP Ab at high levels, presence of early erosions and failures of ≥2 conventional DMARDs should be taken into consideration in the next step when the first treatment strategy failed to show improvement in 3 months' time. When poor prognostic factors are present, addition of biological DMARDs or targeted synthetic DMARDs should be considered. In those without poor prognostic factors, addition of other conventional DMARDs can be considered. If the patient still fails to achieve clinical remission, change of biological DMARDs or targeted synthetic DMARDs would be considered. On the other hand, when a patient is able to achieve sustained and persistent remission, tapering of biological DMARDs or even conventional DMARDs may be considered. This would certainly be based on the duration of disease, depth of improvement, and duration of remission, and such decision should be discussed with the patient.

Conclusions

Treat-to-target approach in RA is clearly an important strategy in modern management of RA based on substantial evidence in the literature. It will definitely reduce joint damage and radiographic erosions, improve clinical outcome, physical function and quality of life in RA patients. Implementation of this strategies is not without challenges. More researches are undergoing to develop new drugs, predictive markers in RA, and refining many of the concepts in the treat-to-target approach. The whole medical community, rheumatologists and patients are key stakeholders in contributing to the success in this management strategy.

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"The argument for treat-to-target in gout" 2017

Dr Eugene FUNG

MD, FRCPC, FACR

Director, Research Center of Central Texas Little River Arthritis & Osteoporosis;
Clinical Assistant Professor, University of Texas Southwestern Medical Center Family and Community Health Residency Program

Dr Eugene FUNG

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 October 2017.

When to and Why Treat Gout? Physiological and Pathological Background

There are two sources of uric acid production, 70% endogenic from body cell nucleotide break down and 30% exogenic from food. The net effect of resorption and secretion in the kidneys (70%) and guts (30%) will determine our serum level of uric acid load. Humans are under-excretors; our kidneys are more effective in uric acid reabsorption (90%) than excretion (<10%).

Uric acid solubility maximises at 404.5 μmol/L (6.8 mg/dL), with precipitation occurs above that level. It is also dependent on the hydration status and local body temperature; clinically we propose to set the target control level at 360 μmol/L, even lower at 300 μmol/L for tophaceous gout, when there is obvious expanded uric acid pool or increased burden.

Shedding or deposition of uric acid, in crystalline form of sodium mono-urate which is poorly soluble in the joints or other structures, can induce inflammation: through the processes of pattern recognition by innate immune system, internalised by the NLRP3 inflammasome, Toll Like Receptor (TLR) stimulation, Capase 1- cleavage to active interleukin-1 beta (IL-1β) release, signal transduction and gene activation that lead to secretion of proinflammatory cytokines and chemokines, which recruit leukocytes and further amplify the inflammatory cascade, until it is finally halted by NETosis[1].

Gout tophus is a granuloma comprises of monocytes, neutrophils and sodium mono-urate crystals interaction. As a consequence, the generation of IL-1β and activation of the RANKL pathway result in bone resorption or destruction, and that leads to the familiar "punch-out" bone lesion and osteolysis[2].

Is Treatment Worthwhile? Prognosis and Outcome

Hyperuricaemia is an independent factor of hypertension in adults, male and female, including children. Hyperuricaemia increases the odds for reduced eGFR and albuminuria. The hyperuricaemia-induced oxidative stress, chronic inflammation, and endothelial dysfunction might contribute to further metabolic consequences. One recent study shows reducing the hyperuricaemia does improve associated cardiovascular morbidities[3,4].

Is This Gout? Arriving at the Diagnosis

For decades, in acute case, the gold standard for making a diagnosis of gout is the demonstration of intracellular sodium mono-urate crystals from the joint fluid. While it is still true, the reality is that it is not always practical, or even possible. The 2015 American College of Rheumatology/European League Against Rheumatism (ACR/ EULAR) classification has made it practice friendly; its scores are based on clinical history (episode onset maximised at <24hr, lasted no more than 14 days, and eventual complete resolution), symptoms (specific activities affected and joints dysfunction) and signs (erythema, tophus clinically or by image, and typical bone change), while the absence of Urate actually will score negatively towards the diagnosis; the diagnosis scores are also boosted by the serum level[5]. The uric acid level is sometimes considered non-diagnostic during an acute attack, due to the cytokines effect on its excretion. Repeating the serum uric acid, at least 4 weeks after the acute onset, might yield a more accurate baseline serum level.

Once gouty arthritis becomes chronic with secondary ongoing inflammatory or degenerative changes, one would have more difficulty to diagnose clinically; in this setting the finding of typical tophus, the ultrasonic which is more sensitive (rather than specific) than Dual Energy (DE)-CT scan in finding tophus are helpful[6], and the demonstration of Uric Acid crystal in the tissue or joint fluid of course makes the diagnosis indisputable.

How To Treat? Management principles

The aim for treating acute gout attack or critical gout is to abolish attack or the acute inflammation. Beware of the acute spell early in the course can be self-limited and only lasts for days.

While not all gout patients will have repeat attacks, the ones who have more than one spell, or uric acid level higher than 400, will likely have recurrence. The aim

for proper uric acid reduction should be lower than saturation point: hence the most accepted target is 360, but preferably 300 if documented tophus or many co-morbidities are present. Lowering uric acid can resolve tophi and reduce cardiovascular morbidities as well[3]. Preventing exacerbations with colchicine or NSAID is needed and preferably should start before the uric acid lowering therapy.

The presence of uric acid deposition perpetuates the inflammation, which can be interpolated with intermittent critical spells. Lowering the uric acid level reduces or eventually depletes the uric acid pool and resolves tophi. Polygout or gouty arthritis is primarily driven by interleukin 1β (IL-1β) and is also implicated in bone destruction[2]. By uric acid lowering we actually control inflammation, prevent recurrent attacks, reduce uric acid load and damage.

What Is The Target?

The Outcome Measures in Rheumatology (OMERACT) Preliminary Remission Criteria consensus in 2016 are: (1) Ideal uric acid level < 360 μmol/L (2) Free of recurrent acute spells = 0 for 6 months (3) Resolution of tophi = 0 for 6 months (4) Pain by VAS from gout < 2/ 10 in 1 year (5) Patient VAS Global <2/10 in 1 year. There are debates, however, as to 4 & 5 as they are patient's subjectivity dependent[7].

Modification of Uric Acid Production

Since body mass is related to endogenous source of uric acid, efforts to maintain control or to lose weight, even if it does not control the gout directly, would still help other coexisting morbidities.

For unexplained reasons, the purine-content of the foodstuff does not always parallel the risk of gout, especially in the context of tea. Green tea can raise uric acid level in normal persons, but paradoxically reduces it in hyperuricaemic individuals; so far there is no proof of increased gout in green tea drinkers[8]. The well-established triggering agents are alcohol, especially beer and spirit, fructose enriched sweet drink, seafood especially shellfish, meat and internal organs like liver and kidney. Fructose, besides being a cardiometabolic risk, is also known to increase uric acid production. Soy or beans are not uniform offender: and as a matter of fact, soymilk and low fat dairy products are favourable for gout sufferers[9].

It is out of our scope to review all arthritis medication for acute gout attacks:

For NSAID, the dose has to be in the higher range, such as Indomethacin 50mg tid, to be effective. It has been proposed to use a proton-pump inhibitor concomitantly; but the recently reported multiple long-term side effects, like osteoporosis, increased infection and renal dysfunction would only justify their short term use, in acute gout patients with high gastrointestinal risks.

The usage of colchicine for prevention and to abolish an acute attack needs to be prompt and early: the best timing is as soon as the patient feels the symptom, or witnesses the first sign of inflammation. The oral dose is 0.5-0.6 mg 2 tablets at the very early sign, and follows by another tablet an hour later. For prophylactic use, one tab bid has been replaced often by one daily dose; and every other day can also be tried, especially if the side effect of abdominal distress and diarrhoea cannot be tolerated on daily usage. The interaction of colchicine and statins resulting in rhabdomyolysis has been reported infrequently, but with caution to the patient and vigilance of muscle symptom one can still use it safely. A recent 10-year 202,999 patients study from Hong Kong confirms its short term safety, outsides of rare neutropenia which can be life-threatening and caution of drug interaction suggested[10].

As to Glucocorticoids – in moderate oral dose, such as Prednisone 30-35mg daily for 5-7 days, or intra-articular injection can be quite effective. Chronic usage should be avoided because the high incidence of coexistent metabolic risks, indeed diabetes exacerbations if present is a concern. Paradoxically, there have also been reports of increased tophi formation in chronic usage of steroid.

Medication for long term gout management

In subnormal renal function, <30ml/min or 0.5 ml/s, the Uricosuric agent is generally not effective. For all Uricosurics, proper hydration, urine alkalinisation, and monitoring renal uric acid excretion are suggested in order to limit adverse renal events, urolithiasis included.

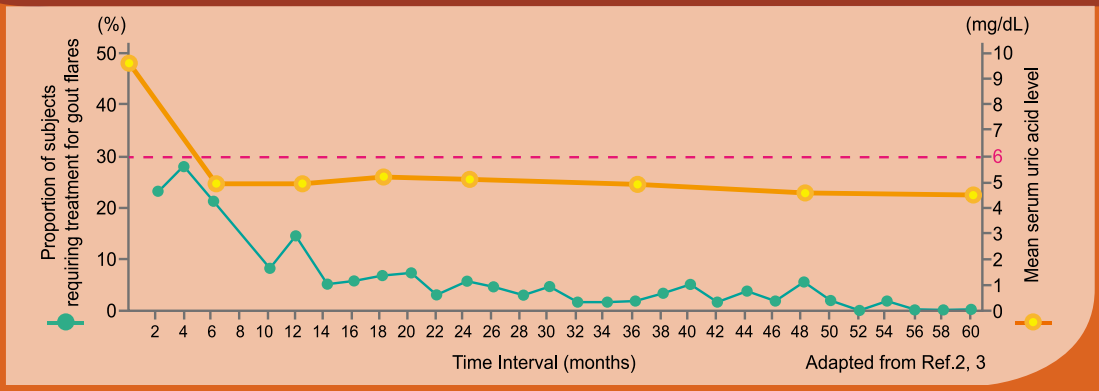
Probenecid: first week 250mg bid to titrate up to 500mg bid, with the increase as 500mg every 4 weeks, until 2000mg is reached. Do beware of the possibility of many drug interactions.

Benzbromarone: 50-300mg daily. This agent has been used in many other parts of the world, but has never received approval in USA due to hepatotoxicity, including liver necrosis and cirrhosis, presumptively due to autoimmune process. A recent New Zealand study nevertheless confirms that liver function test changes tend to be uncommon and mild, and none of the deaths related to the drug[11].

Lesinurad: 200mg daily, to be used in combination with Xanthine Oxidase Inhibitor (XOI). This medication has the unique action of inhibiting URAT 1 and OAT 4, the major tubular transporters for uric acid. In combination of XOI, it has achieved lower level <300 (<5) of uric acid and does better than XOI only in over 12 months usage. A new preparation to combine with allopurinol is in the work[12,13].

Xanthine oxidase inhibitor is a time-honoured therapeutic. **Allopurinol** is still a very important part of modern days gout management. It is recommended to start with 100mg, increase every 2-4 weeks; the approved upper limit 800mg is considered low. Many clinicians, including myself, do go to the higher range of 900-1200 mg if no significant renal dysfunction. It has to be adjusted to the renal function, due to toxicity especially its metabolite oxypurinol. Severe cutaneous adverse drug reactions (SCARs) or allopurinol

Potent urate-lowering effect in achieving serum uric acid (sUA) levels of 6.0 mg/dL[1], which can reduce gout flares eventually to zero on long-term treatment.[2]



Mean sUA Level and % of Subjects Requiring Treatment of Gout Flares in FOCUS STUDY [2, 3]

Reference :
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hypersensitivity syndrome (AHS), including drug reactions with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), are particularly important for south or east Asian populations; there have been several studies which advocate testing allele HLA-B5801 before using allopurinol in those Asian groups, especially the Hans (Mainland and Taiwan), Koreans, and Thais[14,15].

The second XOI, **Febuxostat**, in contrast to allopurinol has the advantage of safety with even moderate renal dysfunction. The starting dose is 40mg, but the effective dose often is 80-120 mg; studies show best effect with 120mg. Like allopurinol, the usage of prophylactic medication, while lowering uric acid in the first 6 months is very important, as that would prevent or reduce the frequency of increased attacks. The reported higher cardiovascular events with this medication, comparing to Allopurinol, are of some concern and need to be further followed[16,17].

Humans are one of the primate species that have no intrinsic enzyme, uricase, to break down uric acid "de novo" and convert to the more soluble allantoin; in the meantime the ineffective excretion mechanism further increases the uric acid burden and therefore tophaceous gout can occur. The adoption of porcine uricase does work except the drawback of the foreign protein can be allergenic.

Pegloticase, at 8 mg i.v. 2 hours infusion every 2 weeks is the current approved therapy[18]. It is so effective that the serum uric acid sometimes is just too low to be measured. Its frequency of severe infusion reactions has been reduced, by screening out the G6PD deficiency and testing the uric acid level before the next infusion to check for neutralising antibody presence. Allergy and high cost make it more suitable for a bridge, or gap, therapy for 6-12 months, and we can transfer to the usual oral medication afterwards. It enables us to reach the target a lot faster and resolves the tophi rapidly, and it is not contraindicated even in situations when XOI cannot be used: such as post transplantation on chronic immunosuppression drugs, like azathioprine and mercaptopurine[19,20].

Rasburicase has been used in the past for treating cell lysis crisis during cancer therapy, It is bound to be replaced by Pegloticase with time.

Other uricase like Pegsiticase is another uricase in phase 3 trial and it has been used along with i.v. Rapamycin and earlier results seem to be encouraging. Oral uricase is still experimental, but it can break down the uric acid in the gut and prevent its resorption in early animal studies. Its clinical efficacy remains to be seen.

Education and Adherence

Studies have shown favourable outcomes rely on adherence of the treatment programme, and there is general poor patient understanding; we should therefore emphasise as to the followings[21]: (1) avoid food and drink that can increase uric acid production, or even trigger attacks such as meat and shellfish, beer and spirit, (2) aware of the possibility of frequent early flares upon the initiation of uric acid lowering therapy, and prophylactic drugs until attack free for 3-6 months (3) use the acute attack controlling medication at the very first sign or symptom of acute recurrence (4) uric acid lowering therapy is a lifetime commitment at this time (5) once the uric acid target achieved, one can relax the dietary restrictions, with moderation, to match patient life style and enhance treatment adherence.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled ""The argument for treat-to-target in gout" 2017" by Dr Eugene FUNG and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 October 2017. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. **In diagnosing gout, a repeat uric acid testing is worthwhile only after 4 weeks.**
2. **At the level 404.5 umol/L (6.8 mg/dL) uric acid will never precipitate.**
3. **We can be reassured of non-tophaceous gout if there is no palpable and visible tophus after careful examination.**
4. **Hyperuricaemia or gout affects the kidney through the direct effect on renal deposition only.**
5. **Sweet drinks enriched with corn syrup or fructose are alright for gout patient to consume.**
6. **Chinese diet like Green tea and soymilk are not acceptable for gout.**
7. **Allopurinol is better not be used at the time of an acute attack.**
8. **Testing of the presence of the HLA-B5801 allele before prescribing allopurinol is cost effective for Han Chinese, Koreans and Vietnamese.**
9. **Uricosuric agent is probably contraindicated with a history of renal stone.**
10. **Adherence or compliance to gout treatment is not difficult to achieve, if we educate our patients properly.**

ANSWER SHEET FOR OCTOBER 2017

Please return the completed answer sheet to the Federation Secretariat on or before 31 October 2017 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

"The argument for treat-to-target in gout" 2017

Dr Eugene FUNG

MD, FRCPC

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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Answers to September 2017 Issue

Depression in children and adolescents

1. T 2. F 3. F 4. T 5. T 6. T 7. F 8. F 9. T 10. T

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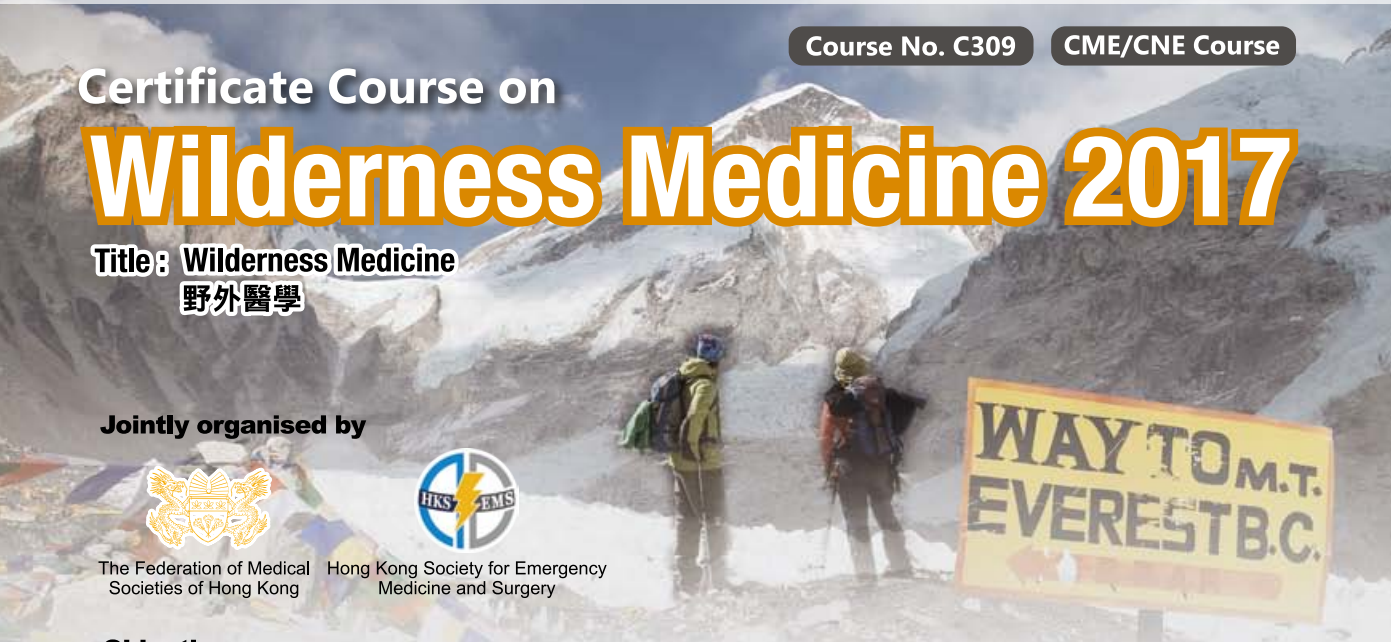

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Objectives:

Wilderness activities have rapidly grained an increase in popularity in recent years. However the exotic environment possesses totally different and unpredictable threats and dangers to the participants who are involved in wilderness activities. Wilderness Medicine is practiced by those who have specially interest in wilderness emergency medical management. In this course, we use six file series to illustrate practical information and management in six medical problems commonly encountered in wilderness.

野外活動在過去幾年迅速普及。但野外環境對於野外活動的參與者，會造成完全不同類型及不可預料的威脅和危險。野外醫學是對於野外緊急醫療治理有特殊興趣練的實踐。在這課程中，我們透過六個檔案以說明六種在野外環境中最常可能出現的醫療問題及其相關實用之處理技巧。

Date	Topics	Speakers
3 Nov	A hiker bitten by deathful venomous creature. (Poisonous stings and bites in wilderness) 一個被致命毒物咬傷的徒步旅行者 (野外被毒物蜇咬)	Dr. Ng Wah Shan 伍華山醫生 香港急症科醫學院院士
10 Nov	A hiking trip to Everest Basecamp (High altitude related wilderness problems) 前往珠峰大本營的徒步行程 (野外高海拔的相關問題)	Dr. Ho Man Kam 何文錦醫生 香港急症科醫學院院士
17 Nov	A hiker facing thunderstorm in wilderness (Wilderness survival and lightening related injuries) 徒步旅行者在荒野面對雷雨 (野外生存及雷擊相關的傷害)	Dr. Chee Pay Yun, Peter 池丕恩醫生 香港急症科醫學院院士
24 Nov	A hiking trip to extreme climate zone (Heat and cold related problem in wilderness) 一個前往極端氣候區的徒步行程 (野外高溫及低溫所引致的問題)	Dr. Law Kam Leung 羅金亮醫生 香港急症科醫學院院士
1 Dec	A hiker fall from cliff with multiple injuries (Trauma and wound management in wilderness) 從懸崖墮下而多處受傷的徒步旅行者 (野外意外創傷及傷口的處理)	Dr. Siu Yuet Chung, Axel 蕭粵中醫生 香港急症科醫學院院士
8 Dec	A hiker fall into a stream in Sai Kung (Helicopter Search And Rescue in HK) 一個在西貢墮落山澗的徒步旅行者 (香港的直升機搜尋及救援)	Mr. Kwok Shing Lam 郭成霖先生 政府飛行服務隊 航空醫療護士/急症室護士長

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Challenges in treating-to-target in systemic lupus erythematosus

Dr Temy Mo-yin MOK

MBBS, MD, HKCP, HKAM, FRCP, FRCPA

Associate Professor, Department of Biomedical Sciences, City University of Hong Kong
Consultant Rheumatologist, North District Hospital, New Territories

Dr Temy Mo-yin MOK

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that is prevalent among Asians compared to Caucasian populations. This disease affects predominantly women in their reproductive age and is associated with significant morbidity and mortality[1]. It is a multisystemic disease and can affect major body organs such as the kidneys and brain leading to inflammation and damage. Although the survival rate of these patients has dramatically improved with corticosteroids and immunosuppressive use over the past few decades, the current treatment is associated with significant adverse effects. Both disease activity and side effects from treatment are associated with cumulative damage accrual leading to morbidities and poor health-related quality of life. Patients with SLE also have higher a standardised mortality rate with increased deaths from cardiovascular diseases and infective complications[2].

Unmet need in the management of SLE

Despite a relapsing-remitting pattern of clinical course for lupus, a significant proportion (46%-52%) of SLE patients suffered from persistently active disease[3]. About one-fourth (24.5%) of patients had refractory SLE during their disease course[4]. Refractory diseases are frequently observed with the manifestations of discoid lupus, lupus nephritis and neuropsychiatric lupus despite current treatment armamentarium. Patients with active lupus nephritis who do not respond to induction therapy have worse long-term renal response and damage compared to those who show early complete or partial response. Organ damage in SLE patients predicts higher damage accrual and mortality in the future[5]. The only approved biologic agent, Belimumab, for the treatment of active SLE is indicated for patients with mild to moderate disease activity. Therefore, there is a pressing need to develop strategies for better disease management and therapeutic regimens with higher clinical efficacy and fewer side effects.

Treat-to-target approach is associated with good clinical outcomes

Medical treatment of chronic diseases including diabetes mellitus, hypertension and hyperlipidaemia showcases a benefit of a treat-to-target approach in disease management. There are ample clinical evidences to show superior clinical outcomes in disease control towards well-defined treatment targets. In recent years, disease control in the rheumatology field has also evolved from a symptom-based approach to the treat-to-target approach[6]. This is best fulfilled in the management of rheumatoid arthritis (RA), which has in place, well-established instruments for measurement of disease activity, effective treatment options including combination of disease modifying anti-rheumatic drugs (DMARDs) and biological agents and a realistic and achievable therapeutic target. In addition to treating to a target of absence of disease activity i.e. remission, or to a state of low disease activity where remission may not be achieved, close follow up and monitoring with target-driven titration of medications at a reasonable time period adds to the benefit of better control of symptoms and disease activity, retardation of radiographic erosive changes of the joints, functional status and improved quality of life[7].

Challenges faced in treat-to-target for SLE

It is appealing for management of SLE to take on the same approach with the goal to improve clinical outcomes. In the pursuit to this end, there are a few issues and challenges that need to be addressed.

1. What is an achievable therapeutic target in SLE?

Clinical remission has been shown to be a realistic and achievable treatment target for the treat-to-target approach in RA. In the past two decades, biologic agents of higher clinical efficacy and of different modes of action are available for treatment of this chronic deforming joint disease. The proportion of RA patients achieving remissions has significantly increased, particularly those with early disease. Treating to remission in early RA and to low disease activity, where the remission may not be achieved in patients with chronic established RA, has been shown to be associated with superior clinical outcomes.

Moderate-to-severe lupus manifestations, particularly renal, neuropsychiatric and haematological systems are associated with significant damage accrual and mortality. Remission and low disease activity have been shown to predict favourable long-term clinical outcomes. In active lupus nephritis, complete or partial response to treatment is associated with significant reduction in risk of end-stage renal disease[8]. Depending on the observation period of SLE cohorts, complete remissions have been reported to be present in only

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6.5% of patients for at least a year[9] to 14.5% for 3 years[10]. Relapses are common and occur despite sustained quiescent disease for 10 years[11]. Thus, a complete remission appears to be an ideal treatment target for SLE. On the other hand, achieving low disease activity in SLE has also been shown to be associated with better health related-quality of life[12]. However, it is of note that the reported frequencies of remission, low disease activity and relapses in different cohorts vary widely, partly as a result of lack of consensus in the definition of these different state of disease activity.

2. Prevention of flares and damage are surrogates of improved disease outcomes

Disease flares or exacerbations are common in SLE. Depending on the definitions of flare and the follow up period, flare rates are reported to be 50%-74% with severe flares in 13%-38%[3]. Exacerbations of major organ involvement including lupus nephritis and neuropsychiatric lupus are associated with increased risk of irreversible damage and death. Damage accrual in both of these organs predicts further damage in these organs and increased risk of mortality[5]. Thus, prevention of flares is also an important therapeutic goal in SLE. As damage accrual is a collective result from disease activity and side effects from corticosteroids and immunosuppressive drugs, efforts should involve better control of disease activity, prevention of flares and reducing side effects of medications.

3. Current disease activity instruments do not fully capture all disease activity in SLE

Several major instruments are commonly used in the monitoring of disease activity of SLE in the research setting. These include the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), a modified SLEDAI-2000 (SLEDAI-2k) and British Isles Lupus Activity Group (BILAG), which are validated reliable instruments to measure disease activity in SLE and have been applied as monitoring tools in recent clinical trials[13]. Diversity of these different instruments is apparently related to the heterogeneity nature of the SLE syndrome, which manifests with different clinical and serological profiles for individual patients. The SLEDAI is a composite index generated from summation of scores attributed to the presence of activity in various internal organs and serological markers. The BILAG evaluates changes in organ-specific activity based on the physician's intention to treat. A single score is assigned to each organ system including the manifestations and serological tests. In addition to clinical scoring, changes in the levels of anti-double stranded (ds) DNA antibodies and C3/C4 are common serological markers used to monitor changes in disease activity in SLE.

Despite the high face validity of these instruments, there are caveats and deficiencies. Although the disease activity scores generated from these instruments correlate with response rates in observational studies, they have not been validated by randomised clinical trials and lack a threshold of clinically meaningful change[14]. Furthermore, revisions of the original versions of these scores[15] are required to capture disease activity in the gastrointestinal tract and ophthalmological system that are less commonly involved in SLE. Physician global assessment (PGA) may capture subtle disease activity not included in current disease activity instruments but is subjective and has significant inter-observer variations. Most important, these organ-specific scoring systems lack verification from associated changes in biomarkers and histological features specific to the involved organs.

4. Difficulty in defining activity for organ-specific manifestations

In addition to defining different disease activity status according to common disease activity instruments in RA, ultrasound scan of peripheral joints offers non-invasive detection of subclinical disease with higher sensitivity. In various internal organ involvement by SLE, invasiveness of investigative modalities limits accessibility of tissues and biomarkers for evaluation of disease activity at the organ level. As an invasive procedure not without risk, renal biopsy is "restricted to" diagnosis and scoring of severity in active lupus nephritis in clinical practice. A repeat renal biopsy after induction therapy to measure disease activity at the organ level can be difficult to justify. Likewise, detection of activity of neuropsychiatric disease relies on imaging modalities such as MRI scan of brain that may not be feasible for serial monitoring too frequently. Thus, there is lack of validated scores for evaluation of organ-specific disease activity to help define the therapeutic targets of remission and low disease activity. Despite this, the criteria of complete and partial remissions involving evaluation of proteinuria, active urinary sediments and renal function post induction therapy in active lupus nephritis are better defined and is the most applied organ-specific disease activity scoring system in clinical trials. As expected, organ-specific outcome may be applicable only to some but not all types of SLE manifestations. There is a need for development of non-invasive organ-specific biomarkers validated for different levels of disease activity.

5.Ambiguous serological activity without clinical manifestation

Indeed, the definition of clinical remission can be obscure in the SLE syndrome. There are patients who show absence of both clinical and serological activity, and those who show absence of clinical activity but have elevated anti-dsDNA antibody and/or low C3/C4[16]. Furthermore, the absence of clinical and/or serological activity in these patients may occur while the patients are receiving corticosteroid and immunosuppressive drugs or while they are not receiving any medication with the exception of anti-malarials (hydroxychloroquine). Although changes in serological markers commonly precede clinical activity of lupus, many patients who have active serology alone can stay without any flare for a number of years and have less cumulative damage[17]. The predictive value of sole serological activity for clinical flare is low. The number of patients with serological activity alone needed to be treated with medium dose corticosteroids to prevent one major flare was estimated to be 3 to 4, and was not without side effects[18]. Thus, treatment of patients with only serological but no clinical activity may carry a risk of overtreatment. These patients are recommended to be closely monitored instead.

6. Co-morbidities of SLE are also key contributory factors to poor disease outcome

Other SLE associated manifestations such as antiphospholipid syndrome may also contribute to damage accrual. While antiphospholipid antibodies are present in one-third of patients, around 8% of SLE patients develop secondary antiphospholipid syndrome[19]. These patients are prone to recurrent arterial or venous thrombosis and recurrent miscarriages and the development of neuropsychiatric damage[20]. Furthermore, chronic SLE patients also have co-morbidities such as hypertension, diabetes and hyperlipidaemia. Thus, treat-to-target approach in SLE should also be accompanied by efforts in the management of other co-morbidities that would not be reflected in disease activity instruments.

European League Against Rheumatism criteria for treat-to-target for SLE

An international task force on treat-to-target in SLE has formulated recommendations with the goals to yield superior outcomes in terms of clinical course, long-term damage and functional status. The working group established four overarching principles for management of SLE emphasising the importance of (1) contribution of the patient in the decision making, (2) multidisciplinary approach, (3) regular monitoring and adjustment of therapy with (4) the goals towards ensuring long-term survival, preventing organ damage, optimising health-related quality of life by controlling disease activity, minimising comorbidities and drug toxicity. Box 1 shows a simplified version of the recommendations by this task force:

Box 1. Recommendations:	
1.	Remission as therapeutic target, or lowest possible disease activity where remission cannot be reached, as measured by validated lupus activity index
2.	Prevention of flares
3.	Treatment of serological activity without clinical activity is not recommended
4.	Prevention of damage accrual
5.	Address factors negatively influencing health-related quality of life such as fatigue, pain and depression
6.	Early recognition and treatment of lupus nephritis
7.	Keep at least 3 years of immunosuppressive maintenance following induction therapy for lupus nephritis
8.	Lowest corticosteroid dosage needed and if possible, should be withdrawn completely
9.	Prevention and treatment of antiphospholipid syndrome-related morbidity
10.	Antimalarials for all patients if feasible
11.	Co-morbidity control

Conclusion

In conclusion, continuous efforts are needed to work towards the establishment of a treat-to-target approach in the management of SLE for better patient care. With the development of better instruments for measurement of organ-specific disease activity that are user-friendly in clinical practice, better defined realistic and achievable therapeutic targets, organ-specific outcome criteria to guide appropriate use of immunosuppressive regimen, close monitoring of patients with active serological activity, and biologic agents of higher efficacy, it is foreseen that the goals of preventing disease flare and damage with avoidance of overtreatment, and ultimately better health-related quality of life and reduced mortality can be achieved.

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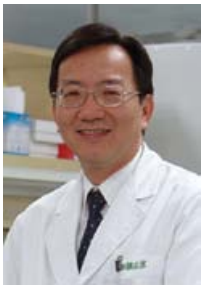
Treat-to-Target in Spondyloarthritis

Prof James Cheng-chung WEI

MD, PhD.

Institute of Medicine, Chung Shan Medical University;
Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital;
Graduate Institute of Integrated Medicine, China Medical University, Taichung, Taiwan



Prof James Cheng-chung WEI

Introduction

The spectrum of spondyloarthritis (SpA) can be classified into ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), inflammatory bowel disease-associated arthritis, and undifferentiated spondyloarthritis (USpA). Common clinical features of SpA are chronic inflammatory arthritis over the spine, sacroiliac joints, peripheral joints and extra-articular manifestations, such as uveitis, psoriasis, and bowel inflammation. The ASAS (Assessment in Spondyloarthritis International Society) working group generated new ASAS criteria for axial and peripheral spondyloarthritis by predominant pattern of clinical manifestations in 2009 and 2011. Non-radiographic axial spondyloarthritis (nr-axSpA) was a new term introduced to describe patients who fulfilled the 2009 ASAS criteria for axial SpA, but not the 1984 modified New York criteria for AS. This article aims to address the unmet needs of treat-to-target (T2T) concepts and strategy in the treatment of spondyloarthritis.

T2T in Rheumatoid Arthritis (RA)

Treat-to-target (T2T) is a well-known concept of aggressive treatment to prevent end-organ damage and preserve function. The T2T concept has been validated in many chronic diseases such as hyperuricaemia, hyperlipidaemia, diabetes and hypertension. In rheumatoid arthritis, a treatment goal has been targeted by clinical remissions defined by the Disease activity score (DAS)-28 less than 2.6 or, if the remission is unlikely to be achievable, at least a low disease activity (LDA) defined by DAS-28 less than 3.2.

Comparative studies have been done to compare the T2T regimen with standard practice and have demonstrated clinical benefit in preventing structural damage and preserving physical function in patients with rheumatoid arthritis. In the Tight Control in RA (TICORA) study, the tight control group substantially improved disease activity, radiographic progression, physical function and quality of life at no additional costs after an 18 month study period. Meta-analysis also showed that tight control in RA resulted in significantly better clinical outcomes than usual care. It is suggested that tight control with protocolised treatment adjustments is more beneficial than if no such protocol is used.

There are some controversies in T2T RA development such as optimal treatment target and treatment approach. Nowadays, T2T concepts have been successfully implemented and became guidance for daily practice in management of RA. The importance of tight control in RA has been stressed by the European League Against Rheumatism (EULAR) Guidelines and the National Institute for Health and Care Excellence (NICE) guideline. These recommendations are widely used by rheumatologists to reach optimal outcomes of RA.

T2T in AS

Unlike RA, the concept of T2T in SpA just started a few years ago and the evidence of T2T in SpA is still very limited. In 2013, an international task force on recommendations of treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target had been organised[1]. Based on a systematic literature review and expert opinion in a Delphi-like process, level of evidence, grade and strength of the recommendations were derived. The task force defined the treatment target as remission or, alternatively, low disease activity[2].

Validated assessment tools to evaluate disease activity of SpA are now available. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used for measuring disease activity and the Bath Ankylosing Spondylitis Functional Index (BASFI) for function. ASAS20 and ASAS40 are well-accepted endpoints to measure response rates in clinical trials. An ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis has been developed[3]. The ASDAS indices seemed to perform better than BASDAI with good face and construct validity, and high discriminant capacity. The ASDAS performed similarly in AS, early forms of SpA, non-radiographic axial SpA and peripheral SpA. The ASAS had defined inactive disease, moderate, high and very high disease activity by three ASDAS cut-offs (1.3, 2.1 and 3.5 units). A cut-off of >/=1.1 units change was chosen to define clinically important improvement and change >/=2.0 units for major improvement[4]. By experts' consensus, ASDAS no more than 2.1 is the current treatment target[5]. A treatment algorithm for axial SpA had been proposed (Fig. 1). However, there are no head-to-head comparison trials to prove this concept right now.

T2T in PsA

In PsA, several studies have been done to develop composite disease activity measures. The DAPSA (Disease Activity index for PSoriatic Arthritis) or formal name DAREA (Disease Activity Index for Reactive Arthritis) and PASDAS (psoriatic arthritis disease activity score) had been validated to assess disease activity in PsA[7]. PASDAS, AMDF (Arithmetic

Mean of the Desirability Function) and modified CPDAI (Composite Psoriatic Disease Activity Index) better reflected domains such as skin, enthesitis, and dactylitis[6]. Clinical trials have used disease activity measurements to guide treatment decision. ACR-20/50/70 and joint counts were used to describe response rate in peripheral PsA. Current consensus for T2T in PsA is the minimal disease activity (MDA)[7,8].

The TICOPA study was the first randomised controlled trial comparing tight control of early psoriatic arthritis with standard care in psoriatic arthritis[9]. Patients assigned to the intensive management group followed a strict treatment protocol whereby dose continuation/escalation was determined through the objective assessment of the minimal disease activity (MDA) criteria. Patients assigned to the standard care group had treatment prescribed as felt appropriate by the treating clinician, with no set protocol. After 48 weeks of follow up, the tight control group clearly improved clinical outcome by ACR-20/50/70 and PASI-75. There were no changes seen in radiographs over 48 wks. However, evidence on the effect of T2T on long-term SpA outcome, such as structural damage, is still lacking. More adverse events were seen in the tight control group, possibly due to more use of biological agents. There were debates that this trial was merely a comparative study of biologics versus standard care.

In 2017 the T2T in SpA recommendations was updated. In principle, the treatment target is remission or inactive disease of musculoskeletal and extra-articular manifestations, and the target should be individualised. It is important that remission/inactive disease should be based on a combination of clinical and laboratory parameters, and disease activity should be measured on the basis of clinical signs and symptoms as well as acute phase reactants [10].

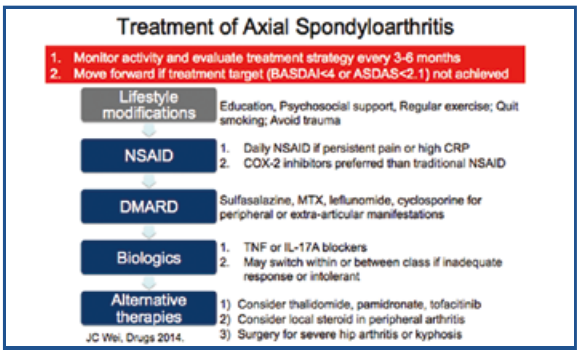


Fig. 1. Treat-to-target (T2T) algorithm for spondyloarthritis. NSAID, non-steroidal anti-inflammatory drugs; DMARD, disease-modifying anti-rheumatic drugs; TNF, tumour necrosis factor. Revised from JC Wei. Drugs, 2014 Jul;74(10)

Conclusions

The evidence of T2T in the treatment of SpA is still very limited. To develop recommendations of T2T in SpA needs a consensus on treatment goals and a T2T treatment algorithm to monitor disease activity and adjust therapies. Comparative clinical trials to compare T2T treatment strategy with standard treatment are warranted. Clinical trial designs in such comparative studies should have clear disease definition for patient enrollment. Short-term endpoints such as ASAS20/40 in AS and long-term endpoints such as X ray progression and MRI score are necessary.

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APLAR: Asia Pacific League of Associations for Rheumatology; **DMARDs:** disease-modifying antirheumatic drugs; **EULAR:** European League Against Rheumatism; **IV:** intravenous; **RA:** rheumatoid arthritis; **SC:** subcutaneous; **TNF:** tumor necrosis factor.

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Abbreviated Prescribing Information

Actemra® (tocilizumab)

Indications: Treatment of severe, active and progressive RA in adults not previously treated with MTX. Treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who had an inadequate response or were intolerant to previous disease-modifying anti-rheumatic drugs (DMARDs) or TNF antagonists. Actemra has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with methotrexate. Actemra can be given in combination with methotrexate (MTX), or can be given as monotherapy in case of intolerance to MTX or if continued treatment with MTX is inappropriate. *Concentrate for Solution for Infusion (80 mg/4 ml, 200 mg/10 ml, 400 mg/ 20 ml)* is also indicated for treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids, and polyarthritis juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older who have responded inadequately to previous therapy with MTX. **Dosage & administration:** Concentrate for Solution for Infusion 80 mg/4 ml, 200 mg/10 ml, 400 mg/ 20 ml: *RA (Adults):* Recommended dosage is 8 mg/kg diluted to a final volume of 100 ml given once every 4 weeks by iv infusion over 1 hour. Doses above 800 mg per infusion are not recommended in patients >100 kg. Doses above 1.2 g have not been evaluated in clinical studies. *sJIA (Children):* Recommended dosage is 8 mg/kg diluted to 100 ml for patients ≥ 30 kg; and 12 mg/kg diluted to 50mL for patients < 30 kg given once every 2 weeks. *pJIA (Children):* Recommend 8 mg/kg diluted to a final volume of 100ml for patients ≥ 30 kg given once every 4 weeks; and 10 mg/kg diluted to a final volume of 50 ml for patients <30 kg given once every 4 weeks. 162mg solution for injection: Recommended dosage is subcutaneous 162mg once every week. The safety and efficacy in children from birth to less than 18 years have not been established. All dosage formulation: No dose adjustment is required in elderly patients, or in patients with mild renal impairment. Actemra has not been studied in patients with hepatic impairment. Dose adjustments or interruptions are recommended in the event of liver enzyme abnormalities, low absolute neutrophil count or low platelet count (see full Prescribing Information for details). **Contraindications:** Hypersensitivity to tocilizumab or to any of the excipients, active, severe infections. **Warnings & Precautions:** *Infections:* If serious infection develops interrupt therapy until infection is controlled. Exercise caution in patients with a history of recurring infection or other underlying conditions which may predispose to infection. *Complications of Diverticulitis:* Use with caution in patients with a history of intestinal ulceration or diverticulitis. Patients with symptoms of complicated diverticulitis should be evaluated promptly. *Tuberculosis:* Screen for latent TB prior to starting therapy; treat latent TB with standard therapy before initiating Actemra. *Vaccination:* Live and live attenuated vaccines should not be given concurrently. Patients, particularly those with sJIA or pJIA should be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating tocilizumab therapy. *Hypersensitivity reactions:* Stop infusion immediately, initiate appropriate treatment and discontinue permanently if anaphylactic reaction or serious hypersensitivity reaction occurs. *Active hepatic disease/impairment:* Use with caution in patients with active hepatic disease or hepatic impairment. *Viral reactivation:* Viral reactivation has been reported. *Neurological disorders:* Physicians to be vigilant for indicative symptoms. *Haematological abnormalities:* Not recommended in patients with ANC < 0.5 x 109/l or platelet count < 50 x 103/ml. Use with caution in patients with low neutrophil or platelet count; monitor neutrophils and platelets according to Prescribing Information. If reduced, follow recommendations for dose modification. *Hepatic transaminase elevations:* Not recommended in patients with baseline ALT or AST > 5xULN; use with caution in patients with ALT or AST > 1.5xULN. Monitor ALT/AST levels according to Prescribing Information, if raised follow recommendations for dose modification. *Lipid parameters:* Lipid parameters should be assessed according to Prescribing Information, if elevated, patients should be managed according to local guidelines for hyperlipidaemia. *Macrophage activation syndrome (MAS):* MAS is a serious life-threatening disorder that may develop in patients with sJIA. In clinical trials, tocilizumab has not been studied in patients during an episode of active MAS. *Malignancy:* The risk of malignancy is increased in patients with RA. Immunomodulatory medicinal products may increase the risk of malignancy. *Cardiovascular risk:* RA patients have an increased risk for cardiovascular disorders and should have risk factors managed as part of usual standard of care. **Interactions:** MTX, NSAIDs or corticosteroids had no effect on tocilizumab clearance. Co-administration with MTX had no significant effect on MTX exposure. Tocilizumab has not been studied in combination with other biological DMARDs. Patients taking medicines which are individually adjusted and metabolized via CYP450 3A4, 1A2 or 2C9 should be monitored when starting or stopping Actemra, as doses of these products may need to be adjusted. Given its long elimination half-life (t1/2), the effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy. **Use in Pregnancy & Lactation:** No adequate data from use in pregnant women. Animal study showed a higher number of spontaneous abortion/ embryo-foetal death at high dose. Actemra should not be used during pregnancy unless clearly indicated by medical need. It is unknown whether tocilizumab is excreted in human breast milk. A decision on whether to continue/discontinue breast-feeding or Actemra therapy should be made taking into account the relative benefits to mother and child. **Adverse effects:** RA - *Common adverse reactions:* Most commonly reported ADRs were URTI. Other events listed as common were cellulitis, oral herpes simplex, herpes zoster, abdominal pain, mouth ulceration, gastritis, rash, pruritus, urticaria, headache, dizziness, hepatic transaminases increased, weight increased, hypertension, leucopenia, neutropenia, hypercholesterolaemia, peripheral oedema, hypersensitivity reaction, cough, dyspnea, conjunctivitis and total bilirubin increased. *Infections:* Rate of serious infections was 5.3 per 100 patient years with tocilizumab + DMARDs, and 3.6 per 100 patient years with tocilizumab monotherapy. In the all exposure population, serious infection rate was 4.7 per 100 patient years. Some of the reported serious infections were fatal. Opportunistic infections have been reported. *Infusion reactions:* Adverse events associated with infusion were reported in 6.9% of patients receiving IV tocilizumab + DMARDs; these events were not treatment limiting. Hypersensitivity reactions requiring treatment discontinuation occurred in 0.3% of patients treated with IV tocilizumab. *Injection site reaction:* Common. Injection site reactions in patients receiving SC tocilizumab were mild to moderate in severity. The majority was resolved without any treatment and none necessitated drug discontinuation. Immunogenicity: Anti-tocilizumab antibodies have been observed. sJIA – ADRs were similar in type to those seen in RA patients. *Infections:* Rate of serious infections in the tocilizumab group was 11.5 per 100 patient years. *Infusion reactions:* 16% of patients in the tocilizumab group experienced an event within 24 hours of infusion. In the tocilizumab group, the events included, but not limited to rash, urticaria, diarrhea, epigastric discomfort, arthralgia and headache. *Immunogenicity:* Anti-tocilizumab antibodies were reported. pJIA – ADRs were similar to those seen in RA and sJIA patients. *Infections:* Rate of infections in all exposure population was 163.7 patient years. *Infusion reactions:* 20.2% of all exposure population experienced an event within 24 hours of infusion and the most common events were dizziness and hypotension. Immunogenicity: A case of positive anti-tocilizumab antibodies was reported. RA, sJIA & pJIA - *Other:* decreased neutrophil count, decreased platelet count, transient elevation of AST/ALT, lipid parameter increases. Prescriber should consult the Prescribing Information in relation to other side effects. The safety observed for Actemra SC was consistent with the known safety profile of Actemra IV with a higher frequency of injection site reactions observed with Actemra SC.

Date of preparation: March 2017

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Treat-to-Target in Psoriatic Arthritis

Dr Lucia Shuk-yi CHAU

MBBS (HK), MRCP (UK), FRCP (Edin), FHKCP, FHKAM (Medicine), DPD (Cardiff)
Specialist in Rheumatology

Introduction

The last decade saw breakthroughs in the treatment of rheumatoid arthritis (RA). The development of biologic therapy and the finding of a "window of opportunity" are among the few. A study on tight treatment of early rheumatoid arthritis has found that with a rigorous treatment protocol aiming to bring down the disease activity to a preset target can result not only in good symptomatic control but also retardation of radiographic changes[1]. The success of the "Treat-to-target" (T2T) approach in RA has prompted extrapolation of T2T in treatment of other rheumatic diseases. A large international task force has published in 2014 recommendations on the treatment of spondyloarthritis, including psoriatic arthritis (PsA), using T2T approach[2].

Psoriasis affects 0.09% - 11.4% of the population globally[3]. The prevalence in China is estimated to be 0.35 – 2.14%. Among patients with psoriasis, up to 30% may develop PsA, in whom progressive joint damage[4], disability, reduced quality of life[5] and life expectancy[6] are observed. Should tight and targeted approach of treatment be beneficial to lessen the burden of the disease, the benefit is not only to the suffering individuals but also to society.

Target of Treatment in Psoriatic Arthritis

In contrast to RA, PsA is a more diversified clinical syndrome. Its manifestations include skin disease, peripheral arthritis, axial spondylitis, enthesitis, dactylitis and nail disease. Besides the management of these symptoms, a comprehensive treatment should also take care of fatigue, pain, physical function and quality of life among others[7]. Setting a target for treatment therefore poses a significant challenge. An all-rounded assessment would be ideal to allow a full picture of the disease status and progress, but would be demanding and time-consuming to apply in daily clinical practice. A number of composite measurements of disease activity are proposed by different research groups, in which various aspects of PsA are assessed in different combinations. Most of them involve complicated equations that computation of the score would usually require computer software.

The simplest composite measurement is the Minimal Disease Activity (MDA)[8]. It is said to be satisfied if 5 of the 7 criteria are met (Box 1). Patient pain VAS, patient global VAS and HAQ can be obtained by asking the patients to fill in simple questionnaires while they are in the waiting room. For swollen / tender joint counts as well as tender enthesial points, it is relatively easy to check if at most one site is involved without the need to actually count all the inflamed joints / enthesitis. Similarly, assessment of skin involvement to be less than 3% of BSA (1% = 1 palm size of the patient) would be quick to complete.

Box 1. A patient is classified as in MDA when he meets 5 of 7 of the following criteria:

1.	Tender joint count ≤ 1
2.	Swollen joint count ≤ 1
3.	PASI ≤ 1 or BSA ≤ 3%
4.	Patient pain VAS ≤ 15 (0-100mm scale)
5.	Patient global activity VAS ≤ 20 (0-100mm scale)
6.	HAQ ≤ 0.5
7.	Tender enthesial points ≤ 1

* PASI = Psoriatic Area and Severity Index; BSA = body surface area; VAS = visual analog scale; HAQ = Health assessment questionnaire

While achieving a remission is perceived to be difficult, a minimal disease activity is accepted by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) as a useful target of treatment. The MDA criteria have been shown to be discriminative and to have prognostic value in terms of long term joint damage[9]. The criteria were also used in a randomised controlled trial, the TICOPA study, to address if a tight control algorithm can benefit patients with PsA.

The TICOPA Study

The concept of tight control of disease activity in PsA was tested in the TICOPA study , in which 206 patients with early psoriatic arthritis (< 24 months symptom duration) were randomised into tight control (n=101) or standard care (n=105). In the tight control group, patients were reviewed every 4 weeks with escalation of treatment if minimal disease activity (MDA) criteria was not met. The ladder of treatment escalation was: methotrexate → methotrexate + sulphasalazine → methotrexate + ciclosporin A or methotrexate + leflunomide → first-line anti-TNFα therapy → second-line anti-TNFα therapy. Patients in the standard care group were reviewed every 12 weeks, and treated according to clinical decision of the consultant rheumatologist without the use of any formal disease activity measurement.

At the end of 48 weeks, patients in the tight control group were more likely to achieve an American College of Rheumatology (ACR) 20% (ACR20) response than patients in the standard care group (odds ratio 1.91).

Besides, patients in the tight control group are more likely to achieve ACR 50% response (ACR50), ACR 70% response (ACR70) and 75% improvement in psoriasis area severity index (PASI75). Radiographic progression did not differ between the two treatment groups at 48 weeks. This was attributed to the fact that all study patients had very early disease, and that both groups received active treatment.

Adverse events were reported more frequently in the tight control group than in the standard care group, and comprised nausea, fatigue, common cold, headache, musculoskeletal pain and gastrointestinal upset. Abnormalities in liver function tests were reported equally in both groups. Serious adverse events were more common in the tight control group (14%) vs standard care group (6%), which required hospital admission but none were judged to be life-threatening. The TICOPA study demonstrated that a protocol-driven tight control treatment algorithm for early PsA is feasible and beneficial to patients in the sense that greater improvements in joint and skin disease, as well as physical function and quality of life can be achieved when compared with usual standard of care.

Pharmacological Treatment for Psoriatic Arthritis

Any target in treatment would be meaningless if there is no effective therapy. The efficacy of synthetic disease-modifying anti-rheumatic drugs (DMARD) including methotrexate, sulphasalazine, ciclosporine A and leflunomide was shown by clinical trials[11]. Head to head trials of DMARDs showed that methotrexate and ciclosporine A were equally effective in treatment of peripheral arthritis and skin disease[12], while ciclosporin A appeared more effective than sulphasalazine[13]. In general, DMARDs are not useful for axial disease and enthesitis. The choice of DMARD should put into consideration the co-morbidity of the patients. Careful monitoring of liver enzymes should be offered regularly especially in cases of alcohol consumption, obesity, type II diabetes and non-alcoholic steatohepatitis or concurrent treatment with other potentially hepatotoxic drugs.

Biologic Treatment for Psoriatic Arthritis

The treatment of PsA has been revolutionised since the emergence of anti-TNFα therapy. Meta-analysis showed that for all kinds of anti-TNFα therapy, treatment was effective in achievement of ACR20, ACR50, ACR70, PsA Response Criteria (PsARC), and 50% improvement in PASI (PASI50) responses[10]. There were 2 new non-TNF biologics – ustekinumab and secukinumab – joining the armamentarium of effective pharmacological therapy in the past few years. The mechanism of action was via inhibition of IL12/IL23 pathway and the IL-17 pathway, respectively. The efficacy of these new biologics had been extensively studied for use in patients who did not respond adequately to synthetic disease modifying anti-rheumatic drugs (DMARDs) or to anti-TNFα biologics. In both of these groups of patients, these 2 new biologics demonstrated efficacy in terms of improvement in joint symptoms, skin disease, functional outcome as well as retardation of radiological progression when compared with placebo [14,15,16,17,18].

With respect to safety of biologic therapies, recent data suggest that they have a similar and acceptable risk profile in PsA as in psoriasis or RA. The most common side effects of anti-TNFα therapy were upper respiratory tract infection, injection site reactions, pharyngitis and headache[19]. Although severe infections are uncommon, the risk of tuberculosis (TB) reactivation and hepatitis reactivation should not be overlooked. Patients should be carefully screened for latent TB with chest radiographs, tuberculin skin tests and/or interferon gamma release essays (IGRAs), and treated before and during anti-TNFα therapy if found positive for it. Reactivation of hepatitis B was not only seen in patients who were positive for HBsAg, but also in patients negative for HBsAg but positive for anti-HBc (HBV occult carriers)[20]. Antiviral prophylaxis should be prescribed during and 6-12 months after the end of anti-TNFα therapy. Concerning the risk of malignancy, data from the British Society of Rheumatology Biologics Register did not show any increase in the incidence of cancer when compared to patients on DMARD[21]. For the non-TNF biologics, ustekinumab and secukinumab, the side effect profile is more or less the same as anti-TNFαtherapies, with slightly more incidence of candidiasis for secukinumab.

EULAR Recommendations for Management of Psoriatic Arthritis

The European League Against Rheumatism has published guidelines for management of psoriatic arthritis in 2011 and 2015[22,23]. The main recommendations were to treat PsA with the aim to achieve remission or minimal disease activity, using DMARD, local steroid injection, or biologic therapy. Patients should be reviewed regularly and the treatment regime adjusted according to disease activity and/or drug toxicity. Earlier considerations for biologic therapy are appropriate for manifestations which do not usually respond to DMARD, e.g. enthesitis, dactylitis and axial disease. Extra-articular manifestations, metabolic syndrome, cardiovascular disease and other co-morbidities should also be taken care of.

Future Research Agenda

Despite the success of treatment of PsA with DMARD and biologic therapies, some questions are still unanswered. First is the efficacy of biologic therapy in axial disease. Currently there are no clinical trials addressing this subgroup of patients. Efficacy is presumed based on the results of biologics in spondyloarthritis. Second is whether a "window of opportunity" exists for PsA in which long-term disease activity, radiographic progression, and complications including cardiovascular events can be reduced by a tight control algorithm in early PsA. Extended observation of the patients in the TICOPA study or other cohort studies may shed light to this in future.

Conclusion

Psoriatic arthritis is a potentially debilitating disease causing joint damage, reduction in functional ability, compromised quality of life and reduced life expectancy. A tight, targeted approach to treatment has

been shown to be beneficial and should be adopted in clinical practice. The use of DMARD, the development of anti-TNFα and new non-TNF biologics have made it possible to achieve remission or low disease activity in psoriatic arthritis.

References

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Radiology Quiz

Dr Grace HT NG

MBChB, FRCR

Department of Radiology, Queen Mary Hospital

Dr Grace HT NG

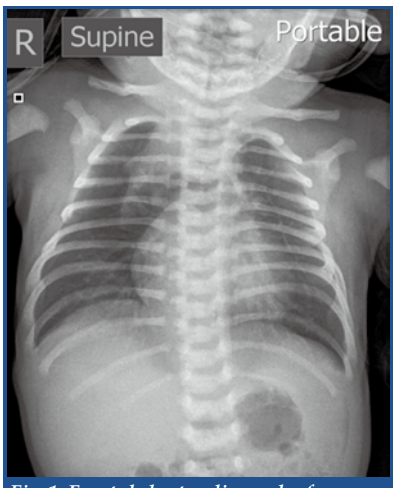

Fig. 1. Frontal chest radiograph of neonate (A).

Infant (A), born at 36 weeks of gestation, developed respiratory distress shortly after birth. Chest x-ray (CXR) taken and shown below.

Questions

What are the most significant abnormality and possible causes?

(See P.33 for answers)

Life Style

Dr Man-leung KWOK

MBChB, MRCP, FHKCP, FHKAM, FRCP

Specialist in Rheumatology, Private Practice

Dr Man-leung KWOK

Lifestyle—"LIFE" to me is family, friends and work. These three elements play an important role in my life. My life won't be complete if any one of the elements is missing. To live my "LIFE" with "STYLE", sports, music, art appreciation and travel are the ingredients of it. I don't have a "fixed style", I love it to be "freestyle"…

Badminton

Sports is definitely an important part of my life. I love badminton and golf. Recently I started running and cycling as well. I was one of the members of the school badminton team in my secondary school. Since then, I have been playing badminton all the time. I enjoy playing in a team and compete in competitions. With heavy workload, I am glad that I can still manage to get every Sunday as my badminton day. I train with my coach in the afternoon and play with different doctors in the evening. It is a big challenge to maintain and improve in speed, accuracy and being competitive. Years ago, I got the 2nd Runner-up in the HKMA badminton Tournament! It was a hard game to fight against the young fellows. I am so pleased that I can arouse the awareness of the importance of exercise and being active in daily life through patient group activities. I was introduced to running and cycling for about a year. I find running extremely good in helping me to keep fit! It doesn't take me such long hours as golf does. I can easily let go of my mind and relax during running. Being active in daily life brings many benefits to me and I am ready to try different new sports in the future.

Saxophone

Playing Saxophone looks charm and attractive! The warmth and gentle of the music from the saxophone attracted me to start learning it 3 years ago. It is not easy to learn something new when we are grown up. It was a hard time for me in the first few months. I knew nothing about music. I had to start from zero. From identifying different notes to getting all the tempo right. From playing kindergarten nursey rhymes to classical and jazz music. It was yet a challenging but fun-filled journey. In the past year, I was able to stand on the stage and gave my first performance with a band! The sense of success brings me so much joy. It is hard to squeeze time to practise but once I start, I will be so into the music and don't even notice it is nearly midnight! It takes my mind away from the daily busy stressful clinical work. Luckily, I haven't received any complaint from my neighbours. Playing with a band is another challenge especially when playing jazz. You will never know what is going to happen next, the final production always brings excitement. One of my memorable performance was a duet with Dr ML Yip this year in a patient group's annual dinner. It was a surprise performance. Everyone enjoyed the music and it was a great success. To practise and prepare for the performance with good friends are fun. In the future, we are looking forward to have more chances and in one day we might have a Jazz band!

Travel

For the past few years, I went abroad for holiday more frequent than before. The more I travel, the more I love to travel. Most of the trips I made were to Japan. Hokkaido is one of my favourite destinations. Cherry blossoms, autumn foliage, summer lavender…Hokkaido has brought me breathtaking experience of its famous scenery. Recently, I went to Tomamu, Furano to try my luck on viewing the "Unkai"(sea of clouds). It was predicted to have only 30% of chance to view the "Unkai" on that day. The next morning at 4 am, there was fog peeking out from the window of the hotel room…. We decided to take the gondola up and try our luck. Reaching the top, I was amazed and over whelmed by the sea of cloud. I have never thought of seeing the "Unkai" on my first attempt. Every one was quiet, enjoying the wonderful moment. I felt so blessed, amazed and relaxed. I will never forget this amazing moment in my life. Food in Hokkaido is always attractive, from the wide selection of seafood to the Hokkaido grown vegetables and fruits are my all time favourite. Hokkaido is definitely a must return place for me. Sometimes I do travel to Europe, however the 13 hours of flight always hold me back. The mountains in Switzerland, The Lake District in UK, the historical castles and the Art treasures within the museums around Europe gave me wonderful memories. Going abroad brings me lots of great experiences and impact. I am in love with travel and always looking forward to the next trip.

To live the Life with Style is a difficult topic. I am trying my very best to make it a colourful one.

2nd meeting of Care for the Advanced Diseases Consortium

With the aim of fostering the development of care for advanced diseases in Hong Kong, the 'Care for the Advanced Disease Consortium' 「晚期病患」醫療及各界關顧聯盟 was established in March 2017. The 2nd meeting was held on 28 August.

The consortium was privileged to have Professors EK YEOH and Roger CHUNG sharing with members the Key Findings, Issues and Recommendations for End-of-life care for terminal illness and life-limiting conditions in older persons in Hong Kong. Our consortium member Prof Cecilia CHAN also kindly shared the blueprint of Australia Palliative & End of Life Care. The consortium will continue the momentum to consolidate suggestions and proposals for the much needed care for advanced diseases.

Care for Advanced Diseases: Joint CME Seminar

On 9 Sept 2017, a CME Seminar on Care for Advanced Diseases was held at the HKMA Club House (Wan Chai). The seminar was jointly organized by HKMA and HKFMS Foundation Care for Advanced Diseases Consortium and well attended by doctors. The event was oversubscribed and the seminar will be repeated in October or November. The second CME talk will be held in December. Details will be announced.

The topics shared were "Palliative care for advanced diseases: from principles to practice" and "Update on oncological palliation for advanced cancers". The consortium was glad to have Dr. Raymond LO, Convener of Care for Advanced Diseases Consortium and Dr Law Chun-key, Specialist in Clinical Oncology, as our speakers; with Dr. HO Chung Ping, Vice President of HKMA and Dr Douglas CHAN as the moderators. The lecture concluded with questions from participants with much fruitful discussion. The Federation would like to thank Mekim for sponsoring this meaningful event.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
1	2	★ HKMA Tai Po Community Network - The Right Treatment of Osteoarthritis ★ FMSHK Officers' Meeting ★ HKMA Council Meeting 3	4	5	6	7
8	9	★ HKMA Kowloon West Community Network - Management of Lung Cancer: Update in EGFR Targeted Treatment ★ HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors ★ HKMA Tai Po Community Network - MMRV: What do We Know Now? 10	★ Hong Kong Neurosurgical Society Monthly Academic Meeting –Updates in traumatic brain injury ★ HKMA Central, Western & Southern Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting 11	★ HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 1): Topic 1: Cardiac Emergencies & Use of Automatic External Defibrillator (AED); Topic 2: Respiratory Emergencies ★ HKMA Kowloon East Community Network - Common Nail Problems in Children ★ HKMA-HKS&H CME Programme 2017-2018 – "Update in Medical Practice" 12	★ HKMA Shatin Doctors Network - Cardiovascular Risk and Albuminuria 13	★ Refresher Course for Health Care Providers 2017/2018 14
15	16	★ HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors ★ HKMA-YTM Community Network - Diabetic Nephropathy ★ HKMA Tai Po Community Network - Common Skin Problems in Infants and Children ★ MPS Workshop - Mastering Shared Decision Making 17	★ HKMA Central, Western & Southern Community Network - Update on Management of Fatty Liver ★ MPS Workshop - Mastering Professional Interactions 18	★ FMSHK Executive Committee Meeting 19	20	★ HKMA Youth Forum ★ HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 2): Patients' Flow at A&E - What Private Practitioners Should Know (Q&A session included) Visiting tour to PYNEH ★ CME Lecture - Advances in the Management of hyponatremia and SIADH ★ MPS Workshop - Achieving Safer and Reliable Practice 21
22	23	★ HKMA Kowloon West Community Network - A Practical Approach to Managing Chronic Heart Failure ★ CME Lecture - Certificate Course in Psychiatry for Community Primary Care Doctors ★ HKMA Tai Po Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting 24	★ HKMA Central, Western & Southern Community Network - Advances in Drug Management for Diabesity Patients ★ MPS Workshop - Mastering Difficult Interactions with Patients 25	★ HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 3): Topic 1: CNS Emergencies & Acute Abdomen Topic 2: Other Office Emergencies ★ HKMA Kowloon East Community Network - Injectable Treatment for Osteoporsis and Hyperlipidemia ★ HKMA New Territories West Community Network - Modern End-of-Life Care ★ FMSHK Foundation Meeting 26	27	28
★ HKMA Swimming Gala 2017 29	30	★ Hong Kong Medical Association Hong Kong Society of Biological Psychiatry - Certificate Course in Psychiatry for Community Primary Care Doctors - Cases of Dementia and Treatment used 31				

Date / Time		Function	Enquiry / Remarks
3 TUE	1:45 PM	**HKMA Tai Po Community Network - The Right Treatment of Osteoarthritis** Organiser: HKMA Tai Po Community Network; Chairman: Dr. CHOW Chun Kwun, John; Speaker: Dr. YUEN Chi Pan; Venue: Chiuchow Garden Restaurant (潮江春), Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Candice TONG Tel: 2527 8285 1 CME Point
	8:00 PM	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
	9:00 PM	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association; Chairman: Dr. CHOI Kin; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Christine WONG Tel: 2527 8285
10 TUE	1:00 PM	**HKMA Kowloon West Community Network - Management of Lung Cancer: Update in EGFR Targeted Treatment** Organiser: HKMA Kowloon West Community Network; Chairman: Dr. MOK Kwan Yeung, Matthew; Speaker: Dr. AU Siu Kie; Venue: Crystal Room IV-V, 3/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
	1:00 PM	**HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors** Organiser: The Hong Kong Medical Association & The Hong Kong Society of Biological Psychaitry; Chairman: Prof. TANG Siu Wa; Speaker: Dr. YEUNG Ming Hong; Venue: PLAZA meeting room, Regus Conference Centre, 35/F, Central Plaza, 18 Harbour Road, Wanchai	HKMA CME Dept. Tel: 2527 8452 1.5 CME Points
	1:45 PM	**HKMA Tai Po Community Network - MMRV: What do We Know Now?** Organiser: HKMA Tai Po Community Network; Chairman: Dr. CHOW Chun Kwun, John; Speaker: Dr. HUNG Chi Wan, Emily; Venue: Chiuchow Garden Restaurant (潮江春), Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Iris SUM Tel: 3971 2929 1 CME Point
11 WED	7:30 AM	**Hong Kong Neurosurgical Society Monthly Academic Meeting –Updates in traumatic brain injury** Organiser: Hong Kong Neurosurgical Society; Chairman: Prof POON Wai Sang; Speaker: Dr SHAM Juan, Kevan; Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital	1.5 points College of Surgeons of Hong Kong Dr. LEE Wing Yan, Michael Tel: 2595 6456 Fax. No.: 2965 4061
	1:00 PM	**HKMA Central, Western & Southern Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting** Organiser: HKMA-Central, Western & Southern Community Network & DH-Primary Care Office; Chairman: Dr. POON Man Kay; Speaker: Prof. LAM Tai Pong; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
12 THU	1:00 PM	**HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 1): Topic 1: Cardiac Emergencies & Use of Automatic External Defibrillator (AED); Topic 2: Respiratory Emergencies** Organiser: HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA; Chairman: Dr. YIP Yuk Pang, Kenneth; Speaker: Dr. CHUNG Tong Shun; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai	Ms. Candice TONG Tel: 2527 8285 1 CME Point
	1:00 PM	**HKMA Kowloon East Community Network - Common Nail Problems in Children** Organiser: HKMA Kowloon East Community Network; Chairman: Dr. LEUNG Wing Hong; Speaker: Dr. FONG Chi Ming; Venue: Lei Garden Restaurant (利苑酒家), Shop no. L5-8, apm, Kwun Tong, No. 418 Kwun Tong Road, Kowloon	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
	1:00 PM	**HKMA-HKS&H CME Programme 2017-2018 – "Update in Medical Practice"** Organiser: The Hong Kong Medical Association & Hong Kong Sanatorium & Hospital; Speaker: Dr. TSOI Tak Hong; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 1 CME Point
13 FRI	1:00 PM	**HKMA Shatin Doctors Network - Cardiovascular Risk and Albuminuria** Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. LI Siu Lung, Steven; Venue: Jasmine Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin, Hong Kong	Mr. Billy SO Tel: 6329 7723 1 CME Point
14 SAT	2:15 PM	**Refresher Course for Health Care Providers 2017/2018** Organiser: Hong Kong Medical Association & HK College of Family Physicians & HA-Our Lady of Maryknoll Hospital; Speaker: Dr. HO Tsz Chung, Roy; Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara TSANG Tel: 2354 2440 2 CME Points
17 TUE	1:00 PM	**HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors** Organiser: The Hong Kong Medical Association & The Hong Kong Society of Biological Psychaitry; Chairman: Prof. TANG Siu Wa; Speaker: Dr. CHEUNG Hon Kee; Venue: PLAZA meeting room, Regus Conference Centre, 35/F, Central Plaza, 18 Harbour Road, Wanchai	HKMA CME Dept. Tel: 2527 8452 1.5 CME Points
	1:00 PM	**HKMA-YTM Community Network - Diabetic Nephropathy** Organiser: HKMA-YTM Community Network; Speaker: Dr. FUNG Lai Ming; Venue: Crystal Ballroom, 2/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
	1:45 PM	**HKMA Tai Po Community Network - Common Skin Problems in Infants and Children** Organiser: HKMA Tai Po Community Network; Chairman: Dr. CHOW Chun Kwun, John; Speaker: Dr. CHIU Lai Shan, Mona; Venue: Chiuchow Garden Restaurant (潮江春), Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Candice TONG Tel: 2527 8285 1 CME Point
	6:30 PM	**MPS Workshop - Mastering Shared Decision Making** Organiser: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. FUNG Shu Yan, Anthony; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
18 WED	1:00 PM	**HKMA Central, Western & Southern Community Network - Update on Management of Fatty Liver** Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. TSANG Chun Au; Speaker: Dr. CHAN Nor, Norman; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
	6:30 PM	**MPS Workshop - Mastering Professional Interactions** Organiser: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. LEE Wai Hung, Danny; Venue: The Cityview, Kowloon	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points

Date / Time	Function	Enquiry / Remarks
19 THU 8:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
21 SAT 10:00 AM	**HKMA Youth Forum** Organiser: The Hong Kong Medical Association; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, HK	Ms. Tracy GUO Tel: 2527 8285
1:00 PM	**HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 2): Patients' Flow at A&E - What Private Practitioners Should Know (Q&A session included) Visiting tour to PYNEH** Organiser: HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA; Chairman: Dr. LEUNG Kai Shing, Joe; Speaker: Dr. CHAN Nim Tak, Douglas; Venue: Seminar Room 1, HKEC Training Centre (Block B), Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	**CME Lecture - Advances in the Management of hyponatremia and SIADH** Organiser: The Hong Kong Medical Association; Speaker: Dr. Joseph G. VERBALIS, MD; Venue: 2/F, Royal Garden, 69 Mody Road, Tsim Sha Tsui East	HKMA CME Dept. Tel: 2527 8452 1 CME Point
2:30 PM	**MPS Workshop - Achieving Safer and Reliable Practice** Organiser: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. CHENG Ngai Shing, Justin; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
24 TUE 1:00 PM	**HKMA Kowloon West Community Network - A Practical Approach to Managing Chronic Heart Failure** Organiser: HKMA Kowloon West Community Network; Chairman: Dr. WONG Wai Hong, Bruce; Speaker: Dr. TSANG Kin Keung; Venue: Crystal Room IV-V, 3/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Mr. Ziv WONG Tel: 2527 8285
1:00 PM	**CME Lecture - Certificate Course in Psychiatry for Community Primary Care Doctors** Organiser: The Hong Kong Medical Association & The Hong Kong Society of Biological Psychaitry; Chairman: Prof. TANG Siu Wa; Speaker: Dr. LO Chun Wai; Venue: PLAZA meeting room, Regus Conference Centre, 35/F, Central Plaza, 18 Harbour Road, Wanchai	HKMA CME Dept. Tel: 2527 8452 1.5 CME Points
1:45 PM	**HKMA Tai Po Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting** Organiser: HKMA Tai Po Community Network; Chairman: Dr. CHOW Chun Kwan, John; Speaker: Dr. LUK Ka Hay, James; Venue: Chiuchow Garden Restaurant (潮江春), Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Candice TONG Tel: 2527 8285 1 CME Point
25 WED 1:00 PM	**HKMA Central, Western & Southern Community Network - Advances in Drug Management for Diabesity Patients** Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. CHAN Hau Ngai, Kingsley; Speaker: Dr. CHAN Chun Chung, Ray; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Mr. Ziv WONG Tel: 2527 8285 1 CME Point

Date / Time	Function	Enquiry / Remarks
25 WED 6:30 PM	**MPS Workshop - Mastering Difficult Interactions with Patients** Organiser: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. FUNG Shu Yan, Anthony; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
26 THU 1:00 PM	**HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA - Course on Emergency Medicine (Session 3): Topic 1: CNS Emergencies & Acute Abdomen Topic 2: Other Office Emergencies** Organiser: HKMA Hong Kong East Community Network & Hong Kong East Cluster, HA; Chairman: Dr. CHAN Hoi Chung, Samuel; Speaker: Dr. CHUNG Tong Shun; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA Kowloon East Community Network - Injectable Treatment for Osteoporsis and Hyperlipidemia** Organiser: HKMA Kowloon East Community Network; Chairman: Dr. MA Ping Kwan, Danny; Speaker: Dr. CHAN Chun Chung, Ray; Venue: V Cuisine, 6/F., Holiday Inn Express Hong Kong Kowloon East, 3 Tong Tak Street, Tseung Kwan O	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA New Territories West Community Network - Modern End-of-Life Care** Organiser: HKMA New Territories West Community Network; Chairman: Dr. TSANG Yat Fai; Speaker: Dr. LO Sing Hung; Venue: SB 1034, Special Block, Tuen Mun Hospital	Mr. Ziv WONG Tel: 2527 8285 1 CME Point
8:00 PM	**FMSHK Foundation Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Nancy CHAN Tel: 2527 8898
29 SUN 2:00 PM	**HKMA Swimming Gala 2017** Organiser: The Hong Kong Medical Association; Venue: Michael Clinton Swimming Pool, Hong Kong Polytechnic University, 30 Renfrew Rd, Kowloon Tong, Kowloon	Miss Ellie FU Tel: 2527 8285
31 TUE 1:00 PM	**Hong Kong Medical Association** **Hong Kong Society of Biological Psychiatry - Certificate Course in Psychiatry for Community Primary Care Doctors - Cases of Dementia and Treatment used** Organiser: The Hong Kong Medical Association & Hong Kong Society of Biological Psychiatry; Speaker: Prof. TANG Siu Wa; Venue: PLAZA meeting room, Regus Conference Centre, 35/F, Central Plaza, 18 Harbour Road, Wanchai	HKMA CME Dept. Tel: 2527 8452 1.5 CME Points

Upcoming Meeting

8 Nov	**HKMA Central, Western and Southern Community Network lecture** Organizer: HKMA Central, Western and Southern Community Network; Speaker: Dr. Chan Pak Hei, Michael (Cardiologist); Topic: Hyperuricemia and CV Risk; Venue: HKMA Central Premises	
18-19 Nov 2017	**The 7th Joint Scientific Meeting of The Royal College of Radiologists & Hong Kong College of Radiologists and 25th Annual Scientific Meeting of Hong Kong College of Radiologists** Venue: Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, HKSAR, China	HKCR Secretariat Tel: 2871 8788 Registration Secretariat Te: 8106 9878
22 Nov	**HKMA Central, Western and Southern Community Network lecture** Organizer: HKMA Central, Western and Southern Community Network; Speaker: Prof. Wong Ka Wing Lawrence (Neurology); Topic: Updates on LUTS and Neurological Diseases; Venue: HKMA Central Premises	

Certificate Course for health care workers working with patients suffering from advanced life-limiting diseases including cancer and non-cancer diseases

- **Course No. C305**
- **CME/CNE Course**

Certificate Course on

Palliative Medicine for Health Care Workers 2017

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Society of Palliative Medicine

Date	Topics	Speakers
3 Oct	Pain Management in Palliative Care (I)	Dr. Raymond Kam-wing WOO *Associate Consultant* *Department of Medicine & Geriatrics Caritas Medical Centre*
	Pain Management in Palliative Care (II)	Dr. Yin POON *Resident Specialist* *Department of Medicine & Geriatrics Caritas Medical Centre*
10 Oct	Symptom Management in Palliative Care Other Than Pain	Dr. Alice Ka-wai MOK *Associate Consultant* *Hospice & Palliative Care Unit* *Shatin Hospital*
17 Oct	Communication in Palliative Care	Dr. Rico K.Y. LIU, *Associate Director* *Comprehensive Oncology Centre* *Hong Kong Sanatorium & Hospital*
24 Oct	Palliative Care for Non-cancer Patients	Dr. Jeffrey S.C. NG *Associate Consultant* *Department of Medicine* *Haven of Hope Hospital*
31 Oct	(a) Management of Malignant Wound	Dr. Theresa T.K. LAI *Nurse Consultant* *Palliative Medical Unit* *Grantham Hospital*
	(b) Nutrition in Palliative Care	Ms. Penny CHOI *Dietitian* *Tuen Mun Hospital*
7 Nov	Palliative Radiotherapy, Chemotherapy and Targeted Therapy	Dr. Wong Kam Hung *Consultant* *Department of Clinical Oncology* *Queen Elizabeth Hospital*

Date : 3, 10, 17, 24, 31 October, 2017 & 7 November, 2017 (Every Tuesday)
Time : 7:00 p.m. – 8:30 p.m.
Venue : Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong
Course Fee : HK$750 (6 sessions)
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

Answers to Radiology Quiz

Answer:

This is a case of neonatal pneumomediastinum.

On CXR the thymus is displaced laterally and superiorly. It is abnormally well outlined by air within the mediastinum and is separated from the mediastinal and cardiac structures. This is the spinnaker sail sign (also known as the angel wing sign). An elevated thymic shadow can be appreciated on lateral CXR as well.

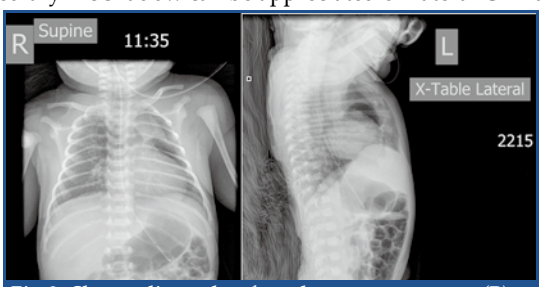

Fig. 2. Chest radiographs of another preterm neonate (B) with respiratory distress syndrome. Pneumomediastinum with an elevated thymus can be appreciated on both frontal and cross-table lateral views.

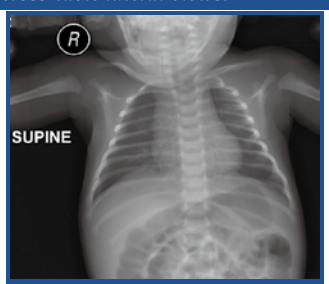

Fig. 3. Complete resolution of pneumomediastinum in neonate (B) after a few weeks.

It is different from the thymic sail sign, which is the normal thymic shadow on chest radiographs. Since the thymus is soft in consistency, it is easily indented by ribs and fissures, giving a lobulated outline. It does not displace the trachea nor separated from the mediastinum by air.

Neonatal pneumomediastinum is reported to occur in approximately 0.25% of live births, with most commonly reported causes include neonatal respiratory distress syndrome, meconium aspiration syndrome, pneumonia or exposure to positive pressure ventilation. However, its incidence is likely underestimated since affected neonates are often asymptomatic. Yet in some cases, neonates can also present with respiratory distress, tachypnoea, grunting or desaturation requiring respiratory support. Definitive diagnosis relies on frontal and lateral chest radiographs.

References

1. Daisuke Hatanaka, Mari Nakamura, Michiko Kusakari, Hidehiro Takahashi, Toshihiko Nakamura, Takashi Kamohara. Neonatal subcutaneous emphysema and pneumomediastinum soon after birth. Pediatrics International 58:6, 541-542
2. Iuri Corsini, Carlo Dani. (2015) Pneumomediastinum in term and late preterm newborns: what is the proper clinical approach? The Journal of Maternal-Fetal & Neonatal Medicine28, 1332-1335
3. C. Dani. Clinical management of the neonatal pneumomediastinum. Acta Biomed 2014;85:39-41
4. D. Hacking, M. Stewart. Neonatal pnemomediastinum. N Engl J Med 2001;344:1839
5. Dahnert. Radiology Review Manual 7th edition

Dr Grace HT NG
MBChB, FRCR
Department of Radiology, Queen Mary Hospital

50% of Gout Patients on ULT and 69% of Gout & CKD Patients Can't Meet sUA Target Level in the U.S.[6]

Abbreviations: CKD, chronic kidney disease; ULT, urate-lowering therapy;sUA, serum uric acid.

Reference :
1. Becker MA et al. N Engl J Med 2005;353(23):2450-2641 2. Schumacher HR Jr. et al. Rheumatology 2009;48:188-194 3. FEBURIC®HK packaging Insert Oct 2015 4. Sezai A et al. Circ J 2013; 77 (8):2043-2049 5. Tanaka K et al. Clin Exp Nephrol. 2015 Dec; 19(6):1044-53 6. Juraschek SP, et al. Arthritis Care Res. 2015;67(4):588-92.

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Version: 002
PI version: Oct 2015
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I: Feburic is indicated for the treatment of chronic hyperuricaemia in conditions where urate deposition has already occurred (including a history, or presence of, tophus and/or gouty arthritis). Feburic 120 mg is also indicated for the prevention and treatment of hyperuricaemia in adult patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis Syndrome (TLS). Feburic is indicated in adults. **D:** Gout 80 mg once daily. TLS 120mg once daily; start 2 days before the beginning of cytotoxic therapy and continue for a minimum of 7 days. **A:** May be taken w/o regard to food or antacid use. **CI:** Hypersensitivity. Pregnancy & lactation. **SP:** Ischaemic heart disease, congestive heart failure, rare serious hypersensitivity reactions, gout flare, malignant disease, Lesch-Nyhan syndrome. Concomitant mercaptopurine, azathioprine, theophylline. Altered thyroid function. Organ transplantation. Galactose intolerance, glucose-galactose malabsorption, Lapp lactase deficiency. Severe renal impairment. Moderate to severe hepatic impairment. Cardiac monitoring for patients at risk of TLS. May impair ability to drive or operate machinery. Childn & adolescents. **AR:** Gout flares, headache, diarrhoea, nausea, rash, oedema, liver function test abnormalities. **INT:** Mercaptopurine, azathioprine, NSAIDs, probenecid, glucuronidation inducer.

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