Highlights on the 67th ACR Meeting

This year, the ACR meeting was held at the Orange Convention Center of Orlando between 23rd and 28th October. Orlando is situated at Florida and is famous for the Disneyland and the Mickey Mouse. There were more than 7500 international delegates attending the meeting, which was organized perfectly well in a cool and nice weather.

In contrast to previous ACR meetings, the morning plenary sessions were replaced this year by basic immunology lectures for the clinical rheumatologists. Topics included cytokines in rheumatoid arthritis (RA), role of dendritic cells and interferon-α in the pathogenesis of systemic lupus erythematosus (SLE) and mechanisms of autoimmunity. Notes were provided and the lectures were conducted in a way that clinicians who did not have a background of basic scientific researches were able to follow. A series of ACR basic science symposia were also conducted by leading immunologists and scientists. Topics covered included cell adhesion molecules, antigen presenting cells and T cell memory in health and disease. On the other hand, sessions of oral abstract presentation (both clinical and basic scientific studies) were available each morning and critical comments were made by experts in the corresponding fields.

Regarding individual rheumatic diseases, there were no new data on the TNF antagonists in RA, except for the TEMPO study, which is a randomized controlled trial in Europe comparing the efficacy and tolerability of etanercept alone, methotrexate (MTX) alone, and combination of the two in MTX-naive RA patients with active arthritis. It was demonstrated that combination of etanercept with MTX was superior to either agent alone in terms of ACR responses. The combination arm was associated with an improvement in erosion scores. There is a revival of interest in the pathogenetic role of B cells in RA. A whole symposium was devoted to this topic and the use of rituximab, a chimeric anti-CD20 monoclonal antibody, in the treatment of active RA. Besides RA, the TNF antagonists are increasingly used in the treatment of ankylosing spondylitis (AS) and psoriatic arthropathy. A morning clinical session on the treatment update of AS and the use of magnetic resonance imaging (MRI) in the early diagnosis of AS was also presented on the second day of the meeting.

The survival of SLE patients has improved considerably in the past few decades. The focus of current clinical research is on the morbidity of the condition. More than 20 abstracts were presented on the risk factors and incidence of vascular disorders in patients with long standing disease. Early diagnosis of coronary atherosclerosis by spiral CT scanning for calcification of the coronary arteries was performed by several groups. Clinical trials on the efficacy of aspirin and the statins in primary and secondary prevention of atherosclerotic vascular disease in SLE are underway. Longitudinal studies on the changes in bone mineral density (BMD) of chronically corticosteroid-treated SLE patients of different ethnicities were also the main area of interest in the field.

An exciting abstract regarding therapeutics of SLE was presented by Dr. Ellen Ginzler, the convener of the US multicenter randomized controlled trial of mycophenolic mofetil (MMF) (3 g/day) versus intravenous pulse cyclophosphamide (IV CYC) in the treatment of lupus nephritis. In this study which involved 19 centers, 140 patients were randomized to receive either MMF or IV CYC and patients were allowed to change over to the other regimen for non-response after 3 months. Results at 24 weeks essentially showed that MMF was superior to CYC in terms of efficacy, withdrawal rates and toxicities. Besides certain flaws in the study design as pointed out by experts, a longer follow-up of the patients is needed for the ultimate outcome of interest.

Depleting B cells is becoming a new therapeutic option in autoimmune diseases refractory to conventional regimens. Besides RA, rituximab has also been tried with success in SLE, immune thrombocytopenia, immune hemolytic anemia, dermatomyositis, ANCA-related vasculitis and idiopathic membranous glomerulonephropathy. However, the major problem of these studies is their uncontrolled nature. Moreover, the optimal dosing of rituximab and whether combination with other cytotoxic agents is synergistic is still unclear.
Interestingly, there was a clinical session on geriatric rheumatology and geropharmacology. The focus was on the treatment of RA in elderly patients, with special consideration with regard to concurrent comorbidities, medications and the differences in pharmacokinetics in old people. The differences in the clinical presentation and prognosis of younger onset and elderly onset RA were discussed by Dr. Stephan Paget. Finally, sessions on cost-effectiveness of the TNF antagonists in the management of RA and medical ethics regarding clinical studies in patients with rheumatic diseases were also available for those attendees who were interested in these areas.

Chi-Chiu Mok
It was a precious and memorable experience to attend the 67th Annual Scientific Meeting of the American College of Rheumatology (ACR). The meeting was held in Orlando, Florida, a city that combines both tropical weather and beautiful scenery. Orlando is also a home of many theme parks that are synonymous with excitement and fun.

Same as last year, the meeting started with a series of immunology update lectures covering advances in laboratory researches. From the excellent lectures given by Professors Virginia Pascual (Texas), Brian L. Kotzin (Colorado) and David A. Fox (Michigan), the emerging roles of dendritic cell in autoimmunity were discussed. Dendritic cells are able to decide when to implement self-tolerance or immune response. The process starts early at the stage of T cell selection, immature dendritic cells allows self-tolerance by giving no costimulation signals while presenting antigens in lymphoid organ, resulting in either T cell deletion or circulatory non-autoreactive T cell. However, once dendritic cells get matured and migrated to draining lymph node, they can present antigens professionally with strong costimulation signals and hence T and B cell activation. Several costimulatory pathways on dendritic cell were identified includes CTLA-4/B7, CD28/B7, 4-1BB/4-1BBL, OX-40/OX-40L, CD40/CD40L. Amazingly, when the dendritic cell presents antigens to T cell, it can also influence the development of either the Th1 or Th2 response by differential cytokine production. For instance, both IL-12 and IL 23 producing dendritic cell promotes Th1 response while IL-4 dendritic cell promotes production of Th2 cytokine. IL-23, a new cytokine secreted by dendritic cells, works very similarly to IL-12; in fact they share the same subunit in their receptors.

Going back to lupus pathogenesis, dendritic cells are also involved. It was found that interferon-α, mainly released by a subset of dendritic cell called plasmacytoid dendritic cell, can drive the monocyte differentiation into cells which behave like dendritic cell in lupus patients. This results in over-presentation of apoptotic bodies to autoreactive T and B cells. Loss of T cell tolerance is another mechanism. It is observed that systemic autoimmune disease is mainly caused by loss of peripheral T cell tolerance. Other possible mechanisms include abnormal availability of self antigen, aberrant expression of MHC class II molecule, increased effectiveness of antigen presentation, enhanced costimulation signals as well as epitope spreading.

The clinical symposia covered several hot topics in rheumatology this year, namely rational management of fibromyalgia, ankylosing spondylitis, treatment of hypertension in rheumatic diseases and estrogen replacement therapy. Of particular interest is B cell depletion therapy in autoimmune diseases. Professor R. John Looney (New York) has updated the data regarding rituximab. Besides its role in methotrexate-refractory rheumatoid arthritis (RA), preliminary data also suggests that it is effective in many different autoimmune diseases such as adult chronic ITP, refractory autoimmune hemolytic anemia in children, IgM Ab-associated polynuropathy, resistant dermatomyositis and ANCA related vasculitis. For SLE, rituximab has proven success in a small open study of 6 lupus patients resistant to conventional immunosuppressive therapy. Another novel agent worth mentioning is B cell toleragen, which is now in phase II/III study. LJP394 can reduce flares in SLE patients who have high affinity to the agent.

In the context of ankylosing spondylitis (AS), Robert BM Landewe (Netherlands) has highlighted its unfavorable outcome because of delay in diagnosis and treatment. The International ASAS Consensus Statement for the use of anti-TNFα in AS is recently published. Juergen Braun (Germany) explained that anti-TNF agent should be reserved for those with persistent disease which is refractory to conventional treatment. Stringent screening program for tuberculosis and heart failure should be offered to all patients before TNF antagonist treatment.

As osteoporosis is an important area in rheumatology, a few sessions were devoted to discuss the management issue. Nelson B. Watts (Ohio) gave a review on the use of antiresorptive and anabolic agents in osteoporosis. Alendronate, risedronate and raloxifene have already been approved by FDA for both prevention and treatment of osteoporosis. Teriparatide is the only anabolic agent that is approved for treatment of postmenopausal osteoporosis recently. But only the former 2 agents have been shown to reduce the risk of vertebral as well as hip fractures.

The plenary sessions this year consist of abstract presentations on a broad range of topics. From one abstract concerning lupus nephritis, the efficacy of mycophenolic mofetil (MMF) is an impressive agent for induction therapy. In this multicenter open randomized study, 140 patients were randomized into standard NIH 6 monthly pulse of CYC or MMF 3 g/day for 6 months. Preliminary data showed that MMF was superior to CYC in inducing complete remission and was associated with a lower withdrawal rate, better toxicity profile and patient acceptance. MMF seems to be an attractive alternative to CYC as induction therapy of lupus nephritis. However, its routine use as first line is hindered by the cost and the lack of long term data.