Lupus Academy Roadshow Meeting

Abstract Book

University College Hospital
Education Centre, London, UK
8th April 2018

LupusAcademy
Communicate. Educate. Treat.

Continuing Professional Development (CPD) Approval

The Lupus Academy Roadshow, London, UK, has been approved by the Federation of the Royal Colleges of Physicians of the United Kingdom for 6 category 1 (external) CPD credits.

Dear Friends and Colleagues,

We are delighted to welcome you to the Lupus Academy† Roadshow Meeting here in London, which we hope you will find engaging, informative and rewarding for your clinical practice.

The Lupus Academy is committed to continuing the development of high quality educational programmes, focused on providing insightful and clinically relevant content through both live meetings and eLearning environments. With this, we aim will support you as you strive to provide best-in-class patient care and improve patient outcomes in lupus.

CPD approval for this meeting has been applied for through the Federation of the Royal Colleges of Physicians of the United Kingdom. This programme aims to provide latest insights into advances in global research and clinical practice in lupus and allied diseases.

The scientific component of this programme, developed by our Steering Committee of 12 international experts in lupus, is designed to create a highly interactive forum through which we can all develop a logical approach to the management of lupus worldwide.

This meeting will give you the opportunity to meet like-minded clinicians and scientists and, through the sharing of clinical and scientific experience, develop your knowledge in this complex and multidisciplinary therapeutic area.

We sincerely hope that this meeting will provide you with new ideas for your clinical work, enriched enthusiasm for collaborative research, and fruitful discussions with your colleagues who care for patients with lupus.

We look forward to meeting and talking with you here in London.

With kind regards,

On behalf of the Lupus Academy Steering Committee

Professor David Isenberg
Course Chair, London

Professor Zahir Amoura
Professor Thomas Dörner
Professor Munther Khamashta
Professor Ronald van Vollenhoven
Professor Ricard Cervera
Professor Richard Furie
Professor Sandra Navarra
Professor Murray Urowitz
Professor Andrea Doria
Professor Bevra Hahn
Professor Bernardo Pons-Estel

†The Lupus Academy is a long-term initiative dedicated to improving patient outcomes in SLE through an interactive educational forum dedicated to sharing best clinical practice through the dissemination and discussion of clinical and basic scientific research about SLE and allied diseases.

Meeting Learning Objectives

- Recognise disease complications in patients with lupus and atherosclerosis and those patients with lupus who are pregnant
- Discuss the roles and significance of B cells, complement and, metabolomics in improving our understanding of the lupus disease process
- Explain the importance of compliance in the management of lupus as well as the challenges of managing both renal and non-renal lupus
- Describe the role of biologics in the management of lupus, present and future

Supporters

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The Lupus Academy receives financial support by means of independent educational grants or other "hands off" mechanisms whereby the Lupus Academy maintains full control over the planning, content, speaker selection and execution of all the educational activities it develops and presents.

Information about the supporters for previous years can be found at the relevant meeting pages on our website www.lupus-academy.org.

There are various opportunities to support the Lupus Academy. Please contact us for further information secretariat@lupus-academy.org.

Contents

Programme

Sunday 8th April			Page
Welcome and Registration			
10:00	Opening address	David Isenberg *(UCL)*	
Some Lupus Complications		*Moderators:* David Isenberg *(UCL)* & Marina Botto *(Imperial College London)*	
10:15-10:45	SLE and atherosclerosis	Anisur Rahman *(UCL)*	12
10-45-11:15	SLE and pregnancy	Ian Giles *(UCL)*	14
11:15-11:25	**Break**		
The Science of Lupus		*Moderators:* Nathalie Costedoat-Chalumeau *(Université René Descartes, Paris)* & Caroline Gordon *(University of Birmingham)*	
11:25–11:55	What's wrong with B cells in SLE?	Claudia Mauri *(UCL)*	16
11:55–12:25	Complement and lupus—unravelling the mysteries	Marina Botto *(Imperial College London)*	18
12:25–12:55	Metabolomics—a guide to the perplexed and what does it have to do with lupus anyway?	Liz Jury *(UCL)*	20
12:55–13:25	**Lunch**		
Treatment Issues I		*Moderators:* Alan Salama *(UCL)* & Ian Giles *(UCL)*	
13:25–13:55	Compliance matters	Nathalie Costedoat-Chalumeau *(Université René Descartes, Paris)*	22
13:55–14:25	Managing non-renal lupus	Caroline Gordon *(University of Birmingham)*	24
14:25-14:30	**Break**		
Problem Cases			
14:30–15:15	Group 1	Nathalie Costedoat-Chalumeau *(Université René Descartes, Paris)* & David Isenberg *(UCL)*	
	Group 2	Anisur Rahman *(UCL)* & Ian Giles *(UCL)*	
	Group 3	Alan Salama *(UCL)* & Caroline Gordon *(University of Birmingham)*	
Treatment Issues II		*Moderators:* Anisur Rahman *(UCL)* & Claudia Mauri *(UCL)*	
15:15–15:45	Managing renal lupus	Alan Salama *(UCL)*	26
15:45–16:45	Biologics for lupus—what's coming?	David Isenberg *(UCL)*	28
16:45	**Close**		

Biographies

Professor Marina Botto, MD, FMedSci

Imperial College London

Disclosures

None.

Marina Botto is Professor of Rheumatology, Head of the Division of Immunology and Inflammation and Director of Bioservices at Imperial College London. She is also an Honorary Consultant Rheumatologist at Imperial College Academic Health Science Centre.

Professor Botto received her medical degree and qualification in rheumatology in Italy. She then moved to the UK where she completed her academic training. She is a member of the American College of Rheumatology. In 2009 she was elected Fellow of the UK Academy of Medical Sciences. She has authored over 150 original publications on the complement system and the pathogenesis of systemic lupus erythematosus (SLE). She is a member and/or Chair of several grant committees in the UK and in Europe.

Professor Botto research focuses on complement biology and systemic autoimmunity. Over the years she has developed several animal models of complement deficiency that have helped understanding the role of complement in SLE, renal diseases and more recently in cancer. She has also pioneered the idea that the complement component C1q can act outside the complement system and has roles in ageing, angiogenesis and cancer. Her work, using a variety of experimental models, has opened the way to the design of targeted complement inhibitor strategies that will have the potential to treat individuals suffering from a wide range of chronic inflammatory conditions. She has supervised more than 40 students.

Professor Nathalie Costedoat-Chalumeau, MD, PhD

Cochin Hospital, Paris

Disclosures

None.

Nathalie Costedoat-Chalumeau is a Professor of internal medicine at Cochin Hospital, Paris, one of the five national reference centres in France for rare autoimmune and systemic diseases.

Professor Costedoat-Chalumeau a member of the Systemic Lupus International Collaborating Clinics (SLICC) group. She is involved with several cohorts and databases, collaborating with another French group to develop a French database of clinical data from patients with systemic lupus erythematosus (SLE) and/or antiphospholipid syndrome (APS), 500 of whom are followed in her center. In addition, she is responsible for a cohort of neonatal lupus patients that includes more than 250 families and has several collaborations with Jill Buyon's group at New York University.

Professor Costedoat-Chalumeau's clinical research deals primarily with: (1) hydroxychloroquine and its measurement in blood; (2) Adherence to treatment; and (3) Pregnancy in women with SLE and APS. She has designed and successfully led several national and international prospective studies on SLE including: (1) The PLUS study (and 10 ancillary studies), a randomized prospective study at 36 French centers that included 573 patients with SLE;[1] (2) The Adherence study, an international prospective study that included 305 patients;[2] and the GR2 study (since 2015), a French prospective study on pregnancy and rare diseases that currently includes 980 patients.[3]

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2. Costedoat-Chalumeau N, Houssiau F, Izmirly P, *et al*. A Prospective International Study on Adherence to Treatment in 305 Patients With Flaring SLE: Assessment by Drug Levels and Self-Administered Questionnaires. *Clin Pharmacol Ther.* 2017.
3. https://clinicaltrials.gov/ct2/show/NCT02450396.

Biographies

Dr Ian Giles, PhD, FRCP

University College London Hospital

Disclosures

None.

Ian Giles qualified from the Royal London Hospital and carried out general medical and rheumatology clinical training in various London hospitals. He then carried out Arthritis Research UK funded clinical research (PhD) and Clinical Scientist Fellowships at University College London. He is now Reader and Honorary Consultant Rheumatologist at University College London Hospital. His specialist clinical and research interests focus upon the diagnosis and long-term management of patients with autoimmune rheumatic diseases, particularly lupus, and the management of these conditions in pregnancy. One of his long term translational research interests, through an Arthritis Research UK programme grant and now Medical research Council developmental pathway funding scheme, has been development of a first-in-class product to prevent thrombosis in patients with antiphospholipid syndrome. Through his interest in pregnancy in rheumatic disease he chaired the recent British Society for Rheumatology guidelines on prescribing anti-rheumatic drugs in pregnancy.

Professor Caroline Gordon, MA, MD, FRCP

University of Birmingham

Disclosures

Grants/Research Support: UCB
Consultant/Advisor: EMD Serono; GSK; UCB

Caroline Gordon is Professor of Rheumatology at the University of Birmingham since 2007, having previously been a Reader, Senior Lecturer and Lecturer from 1989. She is Consultant Rheumatologist at Sandwell and West Birmingham Hospitals NHS Trust. Professor Gordon undertakes clinics at Birmingham Women's Hospital for patients with rheumatic diseases that require pre-pregnancy counselling and combined antenatal care. Her previous training included Rheumatology and Immunology at the University of California, San Francisco, and medical training in Bristol and Brighton, UK. Her first degree was from the University of Cambridge (Immunology and Virology) and her medical degree was from the University of London.

Professor Gordon is a member of the British Isles Lupus Assessment Group (BILAG), the Systemic Lupus International Collaborating Clinics (SLICC), co-Chair of the European League Against Rheumatism (EULAR) Task Force for Systemic Lupus Erythematosus (SLE) and she has been a member of several American College of Rheumatology (ACR) and Lupus Foundation of America committees. She is a consultant to the Centers for Disease Control and Prevention on epidemiological studies of lupus. In 2013 she gave the prestigious Heberden Round at the British Society for Rheumatology (BSR) meeting. She actively contributed to the BSR Guidelines on Prescribing Drugs in Pregnancy and Breast-feeding and led the BSR Guidelines on the Management of SLE published in 2017.

Much of Professor Gordon's research work has focused on disease assessment for trials and outcome studies, particularly the development of the BILAG disease activity index. She has been involved in the development of the SLICC/ACR damage index and the Lupus QoL survey. She led the initiative producing EULAR points to consider for conducting clinical trials in SLE, advises the pharmaceutical industry and has been involved in organising five investigator-led clinical trials. She is interested in both clinical and laboratory markers of disease flare, the genetic susceptibility to lupus, predictors of response to treatment, and the health of children born to mothers with lupus. She is a co-Investigator on the Medical Research Council funded Strategic Medicine Consortium "Masterplans".

Professor David Isenberg, MD, FRCP, FAMS

University College London

Disclosures

Professor Isenberg is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the Lupus Academy's 2018 London Roadshow Meeting programme and materials.

David Isenberg is the Arthritis Research UK Diamond Jubilee Professor of Rheumatology at University College London (UCL). He graduated from St. Bartholomew's Hospital, London, in 1973, and trained in general medicine, rheumatology, neurology, psychiatry and gastroenterology, becoming a Research Fellow at UCL/The Middlesex Hospital in 1979. He was awarded his MD in 1984, based on his studies of myositis. During a year of research at Tufts University, Boston, he became interested in autoantibody structure/function and origin. He was appointed Consultant Rheumatologist in 1984, Professor in 1991 and became the arc Diamond Jubilee Chair of Rheumatology at UCL in 1996. He has fellowships of both the Royal College of Physicians and the Academy of Medical Sciences.

Professor Isenberg is on the Editorial Boards of five journals, including the *Journal of Rheumatology*. He is Chair of the British Isles Lupus Assessment Group and Lupus UK's Research Committee and was Chair of the Systemic Lupus International Collaborating Clinics group (1998–2003). During the past 20 years, Professor Isenberg has undertaken many roles at Arthritis Research UK and currently sits on the Executive Board. He is past-President of the British Society for Rheumatology (2004–2006) and he chaired the Society's Biologics Register Committee for 5 years (2006–2011). Professor Isenberg was the 2010 recipient of the Evelyn V. Hess Prize from the Lupus Foundation of America for his contribution to lupus research and treatment. He has authored over 550 original articles, 275 reviews/chapters and 20 books, many on topics related to lupus.

Professor Isenberg's principal clinical interests are the development of disease activity and damage assessment tools in patients with lupus. His specialist interest is autoimmune rheumatic diseases, notably systemic lupus erythematosus, Sjogren's syndrome, myositis and antiphospholipid antibody syndrome. In 2016 he became a Master of the American College of Rheumatology.

Dr Liz Jury, PhD

University College London

Disclosures

None.

Liz Jury is Reader in Experimental Rheumatology and Deputy Graduate Tutor at the Centre for Rheumatology Research, University College London.

Dr Jury started her career at St Bartholomew's Hospital, London developing the Immunopathology service specialising in the diagnosis of autoimmunity in general and lupus in particular. She established the detection of complex anti-nuclear antibodies and anti-phospholipid antibodies into the routine service at Barts and was involved with setting up UK-wide standards and training for these assays. In 2000, she joined Professor David Isenberg's team and now leads her own research group performing research into the causes of adult and juvenile-onset lupus. Her main focus is to understand how immune cell function is influenced by fats in the blood and fats in the immune cell plasma membrane and she was awarded the Garrod Prize by the British Society for Rheumatology for this work in 2014. In 2016 she successfully obtained the Athena Swann Award as Professor Dame Carol Black Senior Lecturer. She continues to investigate defects in fat metabolism in lupus patients and is currently exploring ways to control fat biosynthesis as a novel therapeutic strategy. You can follow Dr Jury's research on twitter @Jury_Lab.

Biographies

Professor Claudia Mauri, PhD

University College London

Disclosures

None.

Claudia Mauri is Professor of Immunology and Vice-Dean International Faculty Medical Science at University College London. She received her Doctor of Biology with *magna cum laude* in 1989 and PhD equivalent in 1996 from the University La Sapienza in Rome, Italy. She performed postdoctoral work in London at The Kennedy Institute of Rheumatology, Imperial College, UK. She moved to University College London in 2002 where she established her group. Professor Mauri's research interest lies in understanding the mechanisms driving autoimmunity, with a particular interest in unravelling the function of regulatory B-cells in experimental models of rheumatic disease and in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Professor Mauri's group was amongst the first to identify a novel subset of B cells with a powerful immunosuppressive capacity. Her work was seminal in the identification of CD40 activation for regulatory B-cell activation and how the adoptive transfer of this B-cell subset can efficiently prevent disease development and ameliorates established arthritis (*Nature Medicine* 2000, *JEM*, 2003). More recently, she has shown that inflammation, driven by gut-microflora composition, is a primary requisite for Breg development (*Nature Medicine* 2014).

Professor Mauri's group has translated the results obtained from experimental models to humans, and showed that in healthy Bregs directly suppress pro-inflammatory cytokine production by T cells, whilst supporting the differentiation of regulatory T-cells. However, in autoimmune diseases such as RA or SLE, Bregs have lost their capacity to suppress pro-inflammatory T-cell responses (*Immunity* 2000, 2010, 2016).

Professor Anisur Rahman, PhD, FRCP

University College London

Disclosures

Meeting Honorarium/ Expenses: Chugai
Clinical Trial Adjudication Committee Member: Neovacs SA

Anisur Rahman is Professor of Rheumatology at University College London, UK. He qualified from Oxford University in 1988 after which he trained in rheumatology in London. He obtained his PhD for research into the molecular properties of autoantibodies that cause tissue damage in systemic lupus erythematosus and antiphospholipid syndrome (APS). In 2000, Professor Rahman began to build up his own research group and was appointed as a Senior Lecturer at University College London. He was awarded the Michael Mason Prize for this research by the British Society of Rheumatology in 2004 and was promoted to a personal Chair in rheumatology in 2008. As well as continuing his basic science research Professor Rahman has developed clinical research programmes in autoimmune rheumatic disease and chronic pain. As a member of both the British Isles Lupus Assessment Group (BILAG) and the Systemic Lupus International Collaborative Clinics (SLICC) he is involved in large multicentre research projects in the field of lupus. Professor Rahman's basic science group is developing a potential new therapeutic agent for APS.

Professor Rahman has forged a successful collaboration with researchers in primary care at Barts and The London School of Medicine and Dentistry and together they are working on studies of beliefs and expectations about chronic pain in different ethnic groups. This collaboration has also carried out National Institute for Health Research (NIHR)-funded research into development of a self-management programme for people with chronic pain in the community.

Professor Alan Salama, MBBS, PhD, FRCP
University College London Centre for Nephrology

Alan Salama is a Professor and Consultant Nephrologist at the University College London Centre for Nephrology, at the Royal Free Hospital. He is the Clinic Lead for Vasculitis and co-founded the first national vasculitis database (UKIVAS), for which he is the renal lead.

Professor Salama qualified from Oxford and at the Royal London Hospital, and trained at Guy's and The Hammersmith Hospitals. He received his PhD from the Royal Postgraduate Medical School and was a post-doctoral Fellow at The Brigham and Women's Hospital, Harvard Medical School in Boston, Massachusetts.

Professor Salama runs a busy vasculitis and lupus service, is involved in clinical trials and runs a laboratory focusing on understanding why the immune system is perturbed in systemic autoimmune disease and how this may be restored more effectively back to health. More recently, his laboratory has begun work on novel methods of preventing acute kidney injury. He is desperate to run a marathon in less than 3 hours 15 minutes.

Disclosures
None.

Abstracts

Some Lupus Complications **Moderators:** David Isenberg (UCL) & Marina Botto (Imperial College London)

Professor Anisur Rahman, PhD, FRCP
University College London

SLE and atherosclerosis

There is strong evidence for an increased risk of cardiovascular disease (CVD) and subclinical atherosclerosis in patients with systemic lupus erythematosus (SLE). The overall increase in CVD risk is 5–10 fold and cannot be explained fully by standard risk factors such as smoking, hypertension and diabetes.[1] Therefore, standard risk scores are not useful for identifying which patients with SLE are likely to develop CVD. In the large SLICC study, including a multinational inception cohort of 1,249 patients, only older age and male gender were independently associated with CVD risk.[2]

So how can we monitor and address CVD risk factors appropriately in our patients? One possibility is to pick up atherosclerosis early by vascular ultrasound. Baseline carotid intima-media thickness and presence of plaque both predict development of CVD over the next 8 years.[3] However, this technique is not available everywhere and may be operator-dependent.

Serological markers include antibodies, microparticles and invariant natural killer T cells (iNKT cells), but none have been associated with CVD consistently enough to be used in clinical management. IgG anti-apolipoprotein A1 antibodies are associated with the development of CVD in patients with rheumatoid arthritis and with disease activity in SLE, but have not been shown to associate with CVD in patients with SLE.4 Endothelial microparticles are released from active or damaged endothelium, and their levels have been associated with abnormal endothelial function in active SLE. iNKT cells are stimulated by lipids. In a study comparing 36 SLE patients with atherosclerotic plaque and 64 with no plaque, the plaque group had and altered number and phenotype of iNKT cells. However, this complex assay is currently not useful as a clinical test.[5]

Overall, we are still searching for the right test or combination of tests to enable us to manage atherosclerosis in SLE.

Learning Objectives

- Discuss the increased risk of atherosclerosis and CVD in patients with SLE and understand that this risk is not fully explained by conventional risk factors
- Determine that vascular ultrasound identifies plaque, which predicts future CVD
- Describe why antibodies, microparticles and invariant natural killer T cells are possible serological biomarkers for atherosclerosis in SLE
- Recognise that no test or combination of tests currently predicts atherosclerosis in SLE accurately enough for clinical use

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5. Smith E, Croca S, Waddington KE, et al. Cross-talk between iNKT cells and monocytes triggers an atheroprotective immune response in SLE patients with asymptomatic plaque. *Science Immunology*. 2016;1(6).

Notes

Abstracts

Some Lupus Complications **Moderators:** David Isenberg (UCL) & Marina Botto (Imperial College London)

Dr Ian Giles, PhD, FRCP
University College London Hospital

SLE and pregnancy

Systemic lupus erythematosus (SLE) has a predilection for women of child-bearing age, with a UK prevalence of ~80/100,000 in women aged 20–49 years.[1] Pregnancy in SLE is associated with higher maternal and foetal morbidity compared to the general population. SLE may be associated with antiphospholipid syndrome (APS), that is characterised by vascular thrombosis and/or obstetric morbidity in the context of persistently positive antiphospholipid antibodies (aPL), namely lupus anticoagulant (LA), anticardiolipin (aCL) and anti-β2 glycoprotein 1 (aβ2GP1). APS may also occur in the absence of another autoimmune rheumatic disease and although the overall prevalence of APS is unknown, estimates of aPL prevalence are 6% in pregnancy morbidity, 9.5% in deep vein thromboses, 11% in myocardial infarctions and up to 17% in stroke in individuals less than 50 years of age.[2]

Consequently, healthcare professionals within rheumatology and other medical specialities will encounter patients with SLE and/or APS who are planning and/or become pregnant. These patients require careful preconception planning as well as vigilant medical and obstetric monitoring of their disease to reduce the incidence of potential adverse maternal-foetal outcomes. Various challenges in managing SLE and/or APS pregnancies shall be discussed in this lecture, particularly regarding: parity and/or fertility; maternal disease; adverse pregnancy outcomes and management.

Learning Objectives

- Explain the prevalence of SLE in pregnancy and its association with APS
- Discuss the prevalence of aPL and associated morbidities
- Describe the importance of preconception planning and vigilant disease monitoring in pregnant patients with SLE and/or APS to improve patient and foetal outcomes

References

1. Rees F, Doherty M, Grainge M, et al. The incidence and prevalence of systemic lupus erythematosus in the UK, 1999-2012. *Ann Rheum Dis.* 2016;75(1):136–41.

2. Cervera R. Antiphospholipid syndrome. *Thromb Res.* 2017;151 Suppl 1:S43–s7.

Notes

Abstracts

The Science of Lupus **Moderators:** Nathalie Costedoat-Chalumeau (Université René Descartes, Paris) & Caroline Gordon (University of Birmingham)

Professor Claudia Mauri, PhD
University College London

What's wrong with B cells in SLE?

References

1. Crow MK. Type I interferon in the pathogenesis of lupus. *J Immunol*. 2014;192(12):5459–68.

B cells are central to the pathogenesis of systemic lupus erythematosus (SLE), thus providing the rational for the use of rituximab (B cell depletion) therapy. However, not all SLE-patients respond to rituximab, and upon B-cell repopulation some patients relapse. In addition to B-cell abnormalities, an upregulation of interferon-I (IFN-I) induced genes in the blood (IFN-I signature) has been identified in 60–80% of SLE-patients.[1] This talk will present our recent findings showing how the maturation and dysfunction of B cells is orchestrated by the concentration of IFNβ and discuss how we could take advantage of IFN-gene signature to predict response to rituximab.

Learning Objectives

- Discuss how we may use type 1 IFN signature to predict response to rituximab
- Describe the role of regulatory B cells in the maintenance of immunotolerance in healthy individuals
- Discuss why SLE patients do not have regulatory B cells
- Discuss the potential for personalised therapy for SLE patients

Notes

Abstracts

The Science of Lupus

Moderators: Nathalie Costedoat-Chalumeau (Université René Descartes, Paris) & Caroline Gordon (University of Birmingham)

Professor Marina Botto, MD, FMedSci
Imperial College London

Complement and lupus – unravelling the mysteries

In humans, homozygous deficiency of the first component of the complement system, C1q, is the most powerful susceptibility genetic factor for the development of systemic lupus erythematosus (SLE).1 The vast majority of patients with C1q deficiency develop a syndrome closely related to SLE. The disease is typically of early onset and is often very severe. Although the phenotype of disease varies between patients, the fact that C1q deficiency is sufficient to cause SLE in almost all humans identifies a pivotal role for this molecule. The challenge is to identify the relevant physiological activity that can explain this strong association.[1, 2]

One of the hypotheses to explain the heightened susceptibility to the development of SLE in the absence of C1q invokes an important role for complement in the physiological waste-disposal mechanisms of dying cells.[3] However, impaired clearance of such cells is, on its own, insufficient to produce autoimmunity. The data available from knockout mice emphasize that susceptibility to an autoimmune disease might depend on many factors in addition to the defective removal of dying cells.

Recently, in vivo models have provided insights into the manner by which C1q and C3 act to modulate both adaptive and innate immune responses. Specifically, they have demonstrated that C1q may not only act as initiator of the classical complement pathway, but can also mediate multiple immune responses in a complement activation independent manner.[4]

In summary, it is clear that the traditional view of the role of complement in SLE needs revision. Complement activation in SLE has been viewed as a major cause of tissue injury. Instead, evidence is emerging that complement may play a protective role rather than an exclusively pro-inflammatory role in tissue injury.

Learning Objectives

- Describe the paradoxical role of complement in SLE
- Review the current hypotheses of why C1q-deficiency predisposes to the development of SLE
- Discuss new roles of C1q outside the complement system

References

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Notes

Abstracts

Dr Liz Jury, PhD
University College London

Metabolomics—a guide to the perplexed and what does it have to do with lupus anyway?

Burgeoning evidence shows that defects in lipid (fat) metabolism contribute to lupus pathogenesis. Changes in both serum and cellular fats can influence immune responses but the mechanisms remain uncertain, particularly in human health and autoimmunity.[1] Our work in juvenile- and adult-onset lupus, both associated with an increased cardiovascular risk, link immune cell dysregulation and defects in fat metabolism.[2]

The plasma membrane of immune cells is a flexible fat-rich interface where functional cell surface receptors become activated and produce signals leading to immune responses such as release of pro- or anti-inflammatory cytokines; changes in the fat composition of the plasma membrane can influence immune cell signaling and function.[3] We have identified previously that the plasma membrane fat composition differs in immune cells from lupus patients compared to healthy donors and that this is associated with changes in the levels of blood fats and expression of enzymes implicated in the regulation of fat synthesis and metabolism.[4]

Blood fats are transported by lipoproteins, which are made up of many different types and sizes of fat. Using metabolomic analyses over 200 different types of blood fat can be detected.5 This includes measuring the size and lipid composition of very low, intermediate and low density lipoproteins (VLDL, IDL and LDL), which can deposit fats in arterial walls and peripheral cells and are considered pro-atherogenic, and high density lipoproteins (HDL) that transport fats back to the liver for excretion. This presentation will discuss (1) How changes in blood fats can influence immune cell fats and immune cell function; (2) How, based on their circulating blood fats, patients with juvenile-onset lupus can be stratified into three distinct groups each with a unique immunophenotype and clinical presentation; and (3) Potential strategies for changing blood fat profiles to combat immune cell dysregulation and reduce cardiovascular risk in lupus patients.

Learning Objectives

- Describe the complexity of blood fats–beyond the standard measures of total HDL, LDL and triglycerides
- Discuss how changes in blood fats can influence immune cell function
- Describe how blood fats can be used to stratify lupus patients into three distinct groups with unique clinical characteristics
- Describe how the blood fat profile of lupus patients could be used to identify patients that would benefit from fat modifying interventions

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1. Waddington KE, Jury EC. Manipulating membrane lipid profiles to restore T-cell function in autoimmunity. *Biochem Soc Trans.* 2015;43(4):745–51.

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Notes

Abstracts

Treatment Issues (I)

Moderators: Alan Salama (UCL) & Ian Giles (UCL)

Professor Nathalie Costedoat-Chalumeau, MD, PhD
Cochin Hospital, Paris

Compliance matters

Adherence is defined as "the extent to which a person's behaviour coincides with medical or health advice". Non-adherence to therapeutic regimens is a common and expensive problem in patients with chronic diseases, including systemic lupus erythematosus (SLE), and is associated with a higher risk of flares, morbidity, hospitalisations and poor renal outcome;[1, 2] it is also very difficult to evaluate.[3] The rates of non-adherence in SLE patients range from 3% to 76% depending on the assessment methods, which are all subject to limitations.

Hydroxychloroquine (HCQ), a major medication in systemic lupus erythematosus (SLE) with an excellent benefit/risk ratio, a long half-life and can be quantified by high-performance liquid chromatography. Studies have shown that undetectable or very low levels of blood HCQ may be a simple, objective and reliable marker of non-adherence in SLE patients.[1, 4, 5] The accurate diagnosis of non-adherence may prevent to incorrectly interpret it, as a lack of response. It may then avoid an unnecessary or even dangerous treatment escalation.

Learning Objectives

- Describe the frequency and consequences of non-adherence
- Describe the methods to evaluate non-adherence
- Analyse blood hydroxychloroquine levels
- Effectively discuss non-adherence with patients

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Notes

Abstracts

Professor Caroline Gordon, MA, MD, FRCP
University of Birmingham

Management of non-renal lupus

Systemic lupus erythematosus (SLE) can present at almost any age, particularly in women in the reproductive age group, and may have a remitting-relapsing or more chronic course. It is associated with considerable morbidity due to flares of active lupus and accumulated damage. Death from active lupus is rare in the UK, but there is an increased risk of premature death mostly due to infection or cardiovascular disease.[1]

Initial assessment of lupus should include confirmation of the diagnosis and determination of the level of disease activity. Patients should have serological evidence supporting a diagnosis of lupus (see executive summary of the British Society for Rheumatology (BSR) guidelines for SLE).[2] It is important to determine whether clinical and laboratory features are due to inflammation and/or thrombosis, damage, drug toxicity or co-morbidity such as fibromyalgia or infection. Regular monitoring of lupus, drug toxicity and co-morbidities is needed indefinitely. Multidisciplinary care is recommended. Patients should be educated about the disease and its treatment including ultraviolet protection (see full BSR guidelines).[3] It is important to get patients to a low level of disease activity if not remission.[4]

The evidence for treatment of lupus has recently been reviewed in detail (see full BSR guideline).[3] There is good evidence to support the treatment of mild non-renal lupus with hydroxychloroquine and methotrexate, and less evidence for intermittent non-steroidal anti-inflammatory drugs. Moderate non-renal lupus usually requires unlicensed immunosuppressive agents (eg methotrexate, azathioprine, mycophenolate mofetil [MMF], ciclosporin) to reduce lupus activity, corticosteroid usage and the risk of developing chronic damage. Severe lupus requires initial high dose corticosteroids often combined with MMF or intravenous cyclophosphamide. Belimumab and rituximab may be used in patients with appropriate clinical disease activity that have failed at least two immunosuppressive drugs, hydroxychloroquine and corticosteroids according to NICE and NHS England guidance.[5,6] Intravenous immunoglobulin and plasma exchange should only be used in refractory disease or rare situations such as thrombotic thrombocytopenic purpura.

Patients should be counselled about the benefits and risks of any treatment, the expected time frame, dose-adjustments to minimise corticosteroid usage, as well as the need for contraception and issues related to planning pregnancy. Additional topics covered should include adequate vitamin D intake, weight control, exercise, not smoking and other measures to reduce atherosclerosis and osteoporosis, and to promote immunisations and cancer screening. Patients need personalised advice with written information from members of the multidisciplinary team including specialist nurses and an individual to contact in the event of new symptoms.

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Learning Objectives

- Discuss the importance of careful assessment of lupus patients to confirm diagnosis and assess disease activity, being mindful of differential diagnoses
- Ensure that patients receive appropriate education and monitoring of their disease and its drug treatment to reduce the risk of disease flare, side-effects of therapy and accrual of damage
- Describe which drugs are appropriate for mild, moderate and severe non-renal lupus and to aim for low disease activity or remission
- Promote multidisciplinary care and appropriate management of lupus patients to reduce the risk of complications, including the importance of pregnancy planning, reducing corticosteroid exposure and minimising the risk of premature death

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Abstracts

Treatment Issues (I)

Moderators: Alan Salama (UCL) & Ian Giles (UCL)

Professor Alan Salama, MBBS, PhD, FRCP
University College London Centre for Nephrology

Managing renal Lupus

Kidney involvement in systemic lupus erythematosus (SLE), termed lupus nephritis (LN) is common and portends a poorer outcome for patients, with reduced quality of life, increased risk of end stage renal disease (ESRD) requiring dialysis or a transplant and reduced overall patient survival. Although certain genetic associations are found in patients with LN, compared to those without, we remain unable to predict who will develop kidney disease and when. Diagnosis is still based on finding urinary or biochemical abnormalities and confirmed by renal biopsy, and the search for better biomarkers of disease activity and relapse risk continues. Most patients respond to therapy, traditionally based on targeting leucocyte activation and autoantibody production, with complete or partial remission, which is associated with better long-term outcome than in those who do not respond at all. This group of non-responders remain a significant minority with unmet clinical need, and appear to progress despite therapy, even taking into account lack of compliance, which is recognised by treating physicians as an issue, but not always by patients. Although there have been few new agents shown to improve outcome in LN over the last few years, novel therapeutic approaches have allowed some customisation of therapies for individual patients, in the aspiration of maintaining efficacy and reducing drug-related adverse events. Disappointingly, rates of progression to ESRD, which are 3–4%, have remained unchanged over the last 20 years, suggesting that current approaches are suitable for the majority but still failing an important minority. However, potential earlier introduction of novel targeting strategies, aimed at attenuating complement pathway activation, or other common final inflammatory pathway effectors may offer some hope in the future, and these will be discussed.

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Abstracts

Treatment Issues (I)

Moderators: Alan Salama (UCL) & Ian Giles (UCL)

Professor David Isenberg, MD, FRCP, FAMS
University College London

Biologics for lupus—what's coming?

Many double-blind control trials of biologic drugs given to patients with systemic lupus erythematosus (SLE) have failed to meet their primary and/or their secondary endpoints. To date only belimumab, which blocks the B-cell activating factor BAFF, has been officially approved and recommended for patients with skin and joint disease. In spite of its failure in large renal and non-renal trails, the success of B-cell depletion using rituximab in many open-label studies has led to its being recommended in the American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR) guidelines for the treatment of lupus nephritis. Nevertheless new approaches are clearly needed and there are encouraging signs that the use of fully humanized anti-CD20 monoclonals, inhibiting Bruton's tyrosine kinase (BTK), blocking the CD40 ligand, utilising a peptide approach to interfering with antigen presentation to autoreactive T-cells, utilising an analogue of the FC II , and more recently utilising an IL 12-23 blocker may also turn out to be of help in the treatment of patients with SLE.[1-3]

Learning Objectives

- Many previous biologic trials have failed in lupus and clinical trials design has clearly been a key issue
- Two biologics Benlysta and Rituximab clearly are effective and now recommended by various authorities
- Variations on an old 'theme' viz rituximab are now available, thus biosimilars and ofatumumab [fully humanized CD20]
- A plethora of new/newish ideas are in ongoing clinical trials eg atacicept blocks two B-cell activating factors and Anifrolumab and IFN, CD40L, FcIIR

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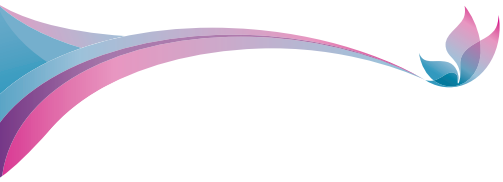

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