

Lupus Academy Roadshow Meeting

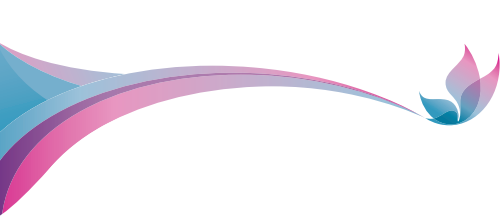
Abstract Book

Bourbon Asunción
Convention Hotel,
Paraguay
14th April 2018



LupusAcademy

Communicate. Educate. Treat.



Continuing Medical Education (CME) accreditation

The Lupus Academy Roadshow Asunción, Paraguay is designated for a maximum of 7 Continuing Medical Education credits from the Paraguayan Society of Rheumatology and 4 credits from the Paraguayan Society of Internal Medicine. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

Dear Friends and Colleagues,

We are delighted to welcome you to the Lupus Academy[†] Roadshow Meeting here in Asunción, 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.

This Roadshow Meeting is CME accredited by the Paraguayan Society of Rheumatology and 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 Asunción.

With kind regards,

On behalf of the Lupus Academy Steering Committee

Professor Ricard Cervera

Course Chair, Asunción

Professor Zahir Amoura
Professor Richard Furie
Professor Munther Khamashta
Professor Ronald van Vollenhoven

Professor Andrea Doria
Professor Bevra Hahn
Professor Sandra Navarra
Professor Murray Urowitz

Professor Thomas Dörner
Professor David Isenberg
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

- Explain the GLADEL experience of lupus in Latin America and lessons from the EURO LUPUS Study
- Describe treatment challenges of managing catastrophic APS, severe flares in pregnancy and persistent cytopenias in patients with SLE
- Discuss the role of new oral anticoagulants in SLE and the importance of steroid sparing regimens and reduction of damage
- Discuss cases focusing on lupus nephritis, CNS lupus and cardiovascular risk in patients with SLE
- Discuss the role of vitamin D in lupus and therapeutic perspectives in SLE
- Explain the value and relevance of laboratory tests in the management of APS

Supporters (Institutions)



UNIVERSITAT DE
BARCELONA

Supporters (Societies)



Supporters (In-kind)

In-kind support has been provided by:



Industry Supporters

We are grateful to the following companies for supporting the Lupus Academy Paraguay Roadshow: Abbott, Laboratorio Curie and Saval. The annual Lupus Academy education programme has been supported by independent educational grants from: GSK, Bristol-Myers Squibb and Celgene

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	6
Biographies.....	8
Abstracts.....	16
Case Study Workshops.....	31

Saturday 14th April			Page
Welcome and Registration			
08:30–08:45	Opening address	Ricard Cervera (<i>Barcelona, Catalonia, Spain</i>) Bernardo Pons-Estel (<i>Rosario, Argentina</i>)	
Plenary I: We are not all equal			<i>Moderator: Isabel Acosta-Colman (Asunción, Paraguay)</i>
08:45–09:15	Lupus in Latin America: GLADEL experience	Bernardo Pons-Estel (<i>Rosario, Argentina</i>)	16
09:15–09:45	SLE epidemiology: Lessons from the EURO LUPUS Study	Ricard Cervera (<i>Barcelona, Catalonia, Spain</i>)	18
09:45–10:00	Questions		
10:00–10:30 Coffee Break			
Plenary II: S.O.S. in Lupus: Caught between a rock and a hard place			<i>Moderator: Marcia Melo-Martins (Asunción, Paraguay)</i>
10:30–11:00	Catastrophic APS	Ricard Cervera (<i>Barcelona, Catalonia, Spain</i>)	20
11:00–11:30	Severe flares during pregnancy	Josep Ordi-Ros (<i>Barcelona, Catalonia, Spain</i>)	22
11:30–12:00	Persistent cytopenias in SLE	Claudio Galarza-Maldonado (<i>Cuenca, Ecuador</i>)	24
12:00–12:15	Questions		
12:15–13:15 Lunch			
Plenary III: Myths and truths			<i>Moderator: Ricard Cervera (Barcelona, Catalonia, Spain)</i>
13:15–13:45	Lupus Academy video presentation: Where do new oral anticoagulants fit in SLE?	Hannah Cohen (<i>London, United Kingdom</i>)	26
13:45–14:15	Lupus Academy video presentation: Using lower doses of glucocorticoids in SLE: Less toxicity, same efficacy	Guillermo Ruiz-Irastorza (<i>Bilbao, Basque Country, Spain</i>)	28

Parallel case study workshops: I			
14:30–15:45	<i>Moderator: Josep Ordi-Ros (Barcelona, Catalonia, Spain)</i> Lupus nephritis	Isabel Acosta-Colman (Asunción, Paraguay) Guillermo Pons-Estel (Rosario, Argentina)	32
	<i>Moderator: Claudio Galarza-Maldonado (Cuenca, Ecuador)</i> Neuro lupus	Ernesto Cairoli (Montevideo, Uruguay) Gabriel Elizaur (Asunción, Paraguay)	34
	<i>Moderator: Bernardo Pons-Estel (Rosario, Argentina)</i> Cardiovascular risk in SLE	Sonia Cabrera-Villalba (Asunción, Paraguay) Gabriela Avila-Pedretti (Asunción, Paraguay)	38
Parallel case study workshops: II			
15:45–17:00	<i>Moderator: Josep Ordi-Ros (Barcelona, Catalonia, Spain)</i> Lupus nephritis	Isabel Acosta-Colman (Asunción, Paraguay) Guillermo Pons-Estel (Rosario, Argentina)	32
	<i>Moderator: Claudio Galarza-Maldonado (Cuenca, Ecuador)</i> Neuro lupus	Ernesto Cairoli (Montevideo, Uruguay) Gabriel Elizaur (Asunción, Paraguay)	34
	<i>Moderator: Bernardo Pons-Estel (Rosario, Argentina)</i> Cardiovascular risk in SLE	Sonia Cabrera-Villalba (Asunción, Paraguay) Gabriela Avila-Pedretti (Asunción, Paraguay)	38
17:00–17:30	Coffee Break		
Plenary IV: Miscellaneous		<i>Moderator: Guillermo Pons-Estel (Rosario, Argentina)</i>	
17:30–18:00	Controversies in lupus and vitamin D	Margarita Duarte (Asunción, Paraguay)	40
18:00–18:30	Therapeutic perspectives in SLE	Claudio Galarza-Maldonado (Cuenca, Ecuador)	42
18:30–19:00	APS: What clinicians should know about laboratory tests	Josép Ordi-Ros (Barcelona, Catalonia, Spain)	44
19:00–19:10	Questions		
19:10–19:25	Closing Address	Marcia Melo-Martins (Asunción, Paraguay)	

Biographies



Disclosures

None.

Dr Isabel Acosta-Colman, MD, MSc, PhD
National University of Asunción, Paraguay

Isabel Acosta-Colman is a Rheumatologist and Researcher at the National University of Asunción, (UNA), Paraguay. She graduated in internal medicine from UNA and specialised in rheumatology at the Autonomous University of Barcelona (UAB), Catalonia, Spain. She received her master's degree in autoimmune diseases from the University of Barcelona in 2011 and her PhD in internal medicine from the UAB in 2012. Beginning her training in lupus at the UAB, she continued this in the Department of Rheumatology and Immunology at the University of Alabama, Birmingham, USA.

Dr Acosta-Colman is currently leader of the Research Team on Systemic Autoimmune Diseases at the Department of Rheumatology, Hospital Clinics of Asunción. She has actively led several research projects, such as the immune-mediated inflammatory diseases Paraguay (IMID PY) project—the first clinical registry and biobank

of patients with immune-mediated diseases in Paraguay. Within the framework of this project, she has developed a research-line focused on the study of clinical and genetic biomarkers of susceptibility and severity in patients with IMIDs, especially patients with systemic lupus erythematosus. Some of Dr Acosta-Colman's work has been published in recognised journals such as *Pharmacogenomics*. She is also a collaborating researcher with the Latin American Lupus Group (GLADEL).

In recent years Dr Acosta-Colman has taken part in the Academic Committee of the Masters Course on Autoimmune Diseases that is held at the UNA, with the support of the University of Barcelona. In addition, she has been the tutor of numerous students undertaking their degree/master's theses and is Editorial Director of the *Revista Paraguaya de Reumatología*.



Disclosures

None.

Dr Gabriela Avila-Pedretti, MD, Ms, PhD
Central Hospital of the Institute of Social Security, Asunción, Paraguay

Gabriela Avila is a Consultant Doctor at the Rheumatology Department of the Central Hospital of the Institute of Social Security and works at the Research Department of the Faculty of Medical Sciences of the National University of Asunción in Paraguay.

She received her MD degree from the Faculty of Medical Sciences of the National University of Asunción, where she also finished her internal medicine fellowship. She completed her postgraduate training in rheumatology at the Vall d'Hebron University Hospital in Barcelona, Catalonia, Spain and received her master's degree in Autoimmune Diseases from the University of Barcelona. After that, she was a Predoctoral Fellow at the Rheumatology Research Group of the Vall d'Hebron Research Institute and received a *cum laude* award for her PhD project from the University of Barcelona.

She is an Associate Editor of the *Paraguayan Journal of Rheumatology*. Her research interests include clinical and epidemiological aspects of rheumatological diseases and detection of biomarkers for precision medicine.

Currently, she is working on research projects related to susceptibility to autoimmune diseases, predictors of response to biological therapies and cardiovascular risk associated with traditional and non-traditional risk factors in rheumatic diseases.



Dr Sonia Cabrera-Villalba, MD, Ms, PhD
Hospital Clinics of Asunción, Paraguay

Disclosures

None.

Sonia Cabrera-Villalba is a Rheumatologist, currently working in the Rheumatology Department at Hospital Clinics of Asunción, Paraguay and at the Rheumatology Service from the Central Hospital of the Institute of Social Security, Asunción, Paraguay. She is also a Teaching Assistant of the Postgraduate Course in Rheumatology in both hospitals.

Dr Cabrera-Villalba received her medical degree and graduated in Internal Medicine from the National University of Asunción (UNA), Paraguay and qualification in Rheumatology from Hospital Clinic, Barcelona, Spain. She received her master's degree in Advanced Medical Competences, Specialty in Autoimmune Diseases, from the University of Barcelona in 2012, after which she became a fellow of the Arthritis Unit, Hospital Clinic, Barcelona. Dr Cabrera-Villalba received her PhD (*cum laude*) in Medicine from the University of Barcelona in 2014.

Dr Cabrera-Villalba is currently working on several autoimmune disease research projects, and her work has been published in several international journals including *Rheumatology (Oxford)*, *The Journal of Rheumatology*, *Arthritis Research and Therapy*, *Clinical Rheumatology* and *Reumatología Clínica*.

Dr Cabrera-Villalba currently is a council member of the Paraguayan Society of Rheumatology (PSR) and the Spanish Society of Rheumatology (SER), and is on the Editorial Board of *Paraguayan Journal of Rheumatology*.



Dr Ernesto Cairoli, MD, MSc, PhD
Hospital Clinic, University of the Republic, Montevideo, Uruguay

Disclosures

None.

Ernesto Cairoli is a specialist in internal medicine, Associate Professor and Head of the Systemic Autoimmune Diseases Unit at the Hospital Clinic, Faculty of Medicine, University of the Republic (UDELAR), Montevideo, Uruguay.

Dr Cairoli is a member of National System of Research, categorized as Level 1 researcher, and has been part of GLADEL 2.0 (Latin American Group for the Study of Systemic Lupus Erythematosus) since 2015. He undertook basic research training at the Pasteur Institute in Paris, France (2004–2005) and completed his masters and PhD in PROINBIO–UDELAR programme in Uruguay. Dr Cairoli undertook his clinical training at the Department of Autoimmune Diseases in the Hospital Clinic in Barcelona, Spain, with Professor Ricard Cervera in 2009, and at the Louise Coote Lupus Unit, Guy's and St Thomas Hospital, London, UK, with Professor David D'Cruz in 2016.

Biographies



Professor Ricard Cervera, MD, PhD, FRCP
Hospital Clinic, Barcelona, Catalonia, Spain

Disclosures

Consultant/Advisor:

AstraZeneca; Celgene;
GSK; Pfizer; UCB.

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

Ricard Cervera is co-Founder and Head of the Department of Autoimmune Diseases at Hospital Clinic, Barcelona. He is also leader of the Research Team on Systemic Autoimmune Diseases at the Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS) and Professor at the University of Barcelona where he coordinates the Masters Course on Autoimmune Diseases. He qualified in medicine in 1983 from the University of Barcelona and received his PhD in 1988 for his thesis on anticardiolipin antibodies. He spent 2 years at the Lupus Research Unit at The Rayne Institute, St Thomas' Hospital, London, UK.

Professor Cervera is an Associate Editor of the journal *Lupus Science & Medicine* and is on the Editorial Boards of 20 medical journals. He is Founder and Member of the Board of the European Lupus Society and past-coordinator of the European Working Party on Systemic Lupus Erythematosus (Euro-Lupus Group) (1991–2008) and of the European Forum on Antiphospholipid Antibodies (2009–2017). He is Chairman of the Medical Advisory Board of the Catalan Association

of Lupus Patients and Medical Advisor to Lupus Europe. He chaired the 6th, 8th and 11th International Congresses on Autoimmunity, the 1st, 2nd and 5th Latin-American Congresses on Autoimmunity, the 5th Meeting of the European Forum on Antiphospholipid Antibodies and the 8th European Lupus Congress.

Professor Cervera's research interests include clinical and epidemiological aspects of systemic autoimmune diseases, particularly SLE and antiphospholipid syndrome, with special focus on its 'catastrophic' variant. He has presented over 300 invited lectures and published more than 800 scientific papers (H-factor, 67), including original articles in the *New England Journal of Medicine*, *The Lancet*, *Annals of Rheumatic Diseases*, *Arthritis & Rheumatism*, *American Journal of Medicine* and *Medicine (Baltimore)*. He is co-Editor of 25 books, including 'The Antiphospholipid Syndrome', 'Vascular Manifestations of Systemic Autoimmune Diseases' and 'Diagnostic Criteria in Autoimmune Diseases'.



Dr Hannah Cohen, MBChB, MD, FRCP, FRCPath
University College London, UK

Disclosures

Grants/Research

Support: Bayer

Consultant/Advisor: Bayer

Hannah Cohen is Consultant and Honorary Reader in Haematology at University College London (UCL) Hospitals NHS Foundation Trust and University College London, UK. She is Trust Clinical Lead in anticoagulation and venous thromboembolism, leads the thrombosis and haemostasis service for Women's Health, and is Haematology Lead for the UCL undergraduate curriculum. She studied medicine at the University of Manchester, trained in haematology at the Middlesex and UCL Hospitals, and was awarded her MD degree for studies on haemostasis in renal allograft recipients.

In the first randomised controlled trial (RCT) in women with antiphospholipid antibodies and recurrent miscarriage, Dr Cohen established a regimen that has become standard treatment internationally. She led the Rivaroxaban in Antiphospholipid Syndrome (RAPS) trial, the first RCT of a direct oral anticoagulant in thrombotic APS. She is a co-Investigator in the prospective RCT on Hydroxychloroquine versus placebo

during Pregnancy in women with Antiphospholipid Antibodies (HYPATIA) and in the study of the Clinical Relevance of Brain Microbleeds in Stroke (CROMIS-2). She is also leading the RISAPS (Rivaroxaban in Stroke Patients with APS) trial.

She is a Founder member, Executive Committee member, and UK Core Laboratory Director of APS ACTION. She co-Chairs the International Society of Thrombosis and Haemostasis (ISTH) Women's Health Scientific Subcommittee, where she has led ISTH guidance on the management of direct oral anticoagulants in relation to pregnancy. She has published over 200 peer-reviewed articles.

As a founder member and Steering Group Chair of the Serious Hazards of Transfusion (SHOT) UK confidential enquiry into transfusion risks, Dr Cohen established SHOT as an international gold standard in haemovigilance. SHOT recommendations underpinned initiatives that have led to improved patient safety in the UK.



Professor Margarita Duarte, MD, PhD
 National University of Asunción, Asunción, Paraguay

Margarita Duarte is currently Professor and Chief of Rheumatology at the Department of Internal Medicine at the National University of Asunción (UNA), where she is also Professor of Physiology.

Professor Duarte received her medical degree and her training in internal medicine from the School of Medicine from the UNA, Paraguay. She completed her fellowship in Rheumatology at Goethe University, Frankfurt, Germany. Dr Duarte received her PhD from the Autonomous University of Barcelona in Spain.

Professor Duarte's clinical expertise is focused on systemic lupus erythematosus (SLE), antiphospholipid syndrome and systemic vasculitis. She has led a lupus clinic since 1999, and developed a biobank for autoimmune disease (IMID) project in 2013.

Professor Duarte's research interest includes genetic background and cardiovascular risks associated with systemic autoimmune diseases such as SLE, rheumatoid arthritis and systemic sclerosis. She is also interested in the association between levels of vitamin D and autoimmune diseases in population studies, which she is currently pioneering in Paraguay.

Disclosures

None.



Dr Gabriel Elizaur, MD, MSc
 Catholic University of Asunción, Paraguay
 Central Hospital of the Institute of Social Security, Asunción, Paraguay

Gabriel Elizaur is coordinator of the Systemic Autoimmune Diseases Unit of Rheumatology Service, Internal Medicine Department, Central Hospital of the Institute of Social Security, Asunción,

Dr Elizaur received his medical degree and qualification in Internal Medicine and Rheumatology from the Catholic University of Asunción, Paraguay. He received his MSc Advanced Medical Skills in Systemic Autoimmune Diseases from Hospital Clinic, University of Barcelona, Spain. He is an Associate Professor in the Rheumatology Service fellowship programme at the Catholic University of Asunción, Paraguay.

He is a member of the Paraguayan and Spanish Society of Rheumatology and also a member of the Paraguayan Society of Internal Medicine.

Disclosures

None.

Biographies



Disclosures

None.

Dr Claudio Galarza-Maldonado, MD, PhD

Monte Sinai and Hospital del Rio, Cuenca, Ecuador

Claudio Galarza-Maldonado is Head of the Autoimmune and Rheumatic Diseases Unit (UNERA) at the Medical Corporation Monte Sinai and Hospital del Rio, Cuenca, Ecuador.

Dr Galarza-Maldonado received his medical degree and qualification in Rheumatology from the Medical State University of Minsk, Belarus and has a PhD degree in the management of systemic lupus erythematosus (SLE). He has a certificate on Shared Value in Healthcare from the London School of Economics and Political Science and is also a member of American College of Rheumatology (ACR).

Dr Galarza-Maldonado is on the Editorial Boards of *Revista Colombiana de Reumatologia* and *Revista Brasileira de Reumatologia*. He has authored several books and publications on SLE, rheumatoid arthritis, rheumatology and autoimmunity. He was co-winner of the 2011 International League of Associations for Rheumatology (ILAR) award.

Dr Galarza-Maldonado organised and was co-Chairman of the 5th Latin American Congress of Autoimmunity. He was also involved as expert in some guideline and position papers by Latin American Group for the Study of Systemic Lupus Erythematosus (GLADEL), Latin American Study Group Rheumatoid Arthritis (GLADAR) and Pan-American League of Rheumatology (PANLAR). He is also coordinator of the PANLAR Consensus on Biosimilars.

Dr Galarza has more than 20 years' experience of the clinical management and follow-up of patients with SLE, rheumatoid arthritis and obstetric antiphospholipid syndrome.



Disclosures

None.

Dr Melo Martins, MD, PhD

National University of Asunción, Asunción, Paraguay

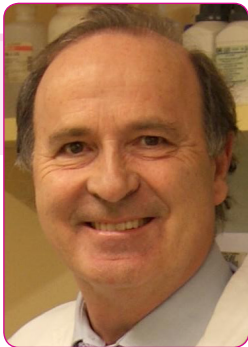
Dr Melo Martins is a Rheumatologist and specialist in internal medicine at the National University of Asunción (UNA), Paraguay.

Dr Martins graduated in internal medicine from the UNA and specialised in rheumatology at the University of Chile, Santiago. She received her masters in medicine, from the UNA on 2015 and postgraduate certificate in bioethics in 2011.

Dr Martins is also an Adjunct Professor of Internal Medicine and Assistant Professor of Bioethics at the Faculty of Medical Sciences at UNA. She is a founding member of the Paraguayan Rheumatology Society and one of the creators of the first training centre in rheumatology, Hospital Clinics of Asunción. She is a pioneer of disease

modifying treatment in rheumatoid arthritis and integral management of systemic lupus erythematosus (SLE) in Paraguay. Dr Martins is currently an active member of the lupus clinical and leader of the lupus pregnancy clinical at the Department of Rheumatology, Hospital Clinics of Asunción in Paraguay.

Dr Martins has participated in several research projects, which principally relate to SLE, including the immune mediated inflammatory diseases Paraguay (IMID PY) project, the first clinical registry and biobank of patients with immune-mediated diseases in Paraguay. She is currently the Academic Secretary of the Masters course on Autoimmune Diseases at the UNA with the support of the University of Barcelona.



Dr Jose Ordi-Ros, MD, PhD

Hospital Vall d'Hebron, Barcelona, Catalonia, Spain

Disclosures

None.

Jose Ordi-Ros is a Senior Consultant in the Internal Medicine–Autoimmune Systemic Diseases department of Hospital Vall d'Hebron in Barcelona, Associate Professor at the Autonomous University of Barcelona, Member of the Scientific Committee of the Vall d'Hebron Research Institute and Head of the Laboratory of Research in Autoimmune and Systemic Diseases.

Dr Jose Ordi-Ros obtained a Licentiate in Surgery and Medicine from the Autonomous University of Barcelona in 1978. In 1979 he undertook the National Examination of Medical Specialties, MIR, and undertook the specialty in Internal Medicine at the Hospital Vall d'Hebrón which concluded in 1982. From 1981 to 1984 he carried out his Doctoral Thesis "Clinical Value of the Lupico Anticoagulant", which received a *cum laude* award from the Autonomous University of Barcelona. He has been part of the Internal Medicine Service of Hospital Vall d'Hebron since 1982.

From 1981 to 2017 Dr Ordi-Ros has been involved in the development of 184 publications in major scientific journals including, *New Engl J Med*, *Lancet*, *J Clin Investigation*, *Baltimore Medicine*,

Ann Intern Med, *Arthritis and Rheumatism*, and *Am J Medicine*. He has given more than 120 presentations to National and International Congresses of Internal Medicine on the subjects of rheumatology, systemic lupus erythematosus (SLE), haematology and antiphospholipid syndrome (APS). He has directed 16 Doctoral Theses related to SLE and APS. He has written 24 chapters of books related to SLE or APS.

Dr Ordi-Ros has been Principal Investigator of 12 national projects of the Health Research Fund and collaborator of 16 other projects. Tutor of pre-doctoral FIS Fellows and of the CSIC. He has made multiple presentations related to SLE, APS and hypercoagulation states at national and international congresses and he has been a reviewer of multiple articles on SLE in national and international journals. He has participated as a Principal Investigator of 54 international trials on SLE and several national trials as a promoter of them.

Dr Jose Ordi-Ros is the Founder and President of the Catalan Foundation for Generalized Erythematosus Lupus.

Biographies



Professor Bernardo A. Pons-Estel, MD

Regional Center for Autoimmune and Rheumatic Diseases (CREAR) and the Cardiovascular Institute of Rosario, Argentina

Disclosures

Professor Pons-Estel is a member of the Lupus Academy Steering Committee and has been involved in the planning and development of the Lupus Academy's Paraguay Roadshow Meeting programme and materials.

Bernardo A. Pons-Estel is Head of the Regional Center for Autoimmune and Rheumatic Diseases (CREAR), and the Cardiovascular Institute of Rosario (ICR), Argentina. He received his medical degree from the National University of Rosario and went on to train in Rheumatology, first in Argentina (Rosario) and thereafter the USA, where he was a fellow at New York University (Bellevue Hospital and the Irvington House Institute, New York) and at the University of Missouri Cancer Research Center, Columbia.

Professor Pons-Estel is the main coordinator for the Latin American Group for the Study of Systemic Lupus Erythematosus (GLADEL), the Genomic Study of Latin-American Patients with SLE (GLA-GENLES) and the Latin American Group for the Study of Rheumatic Diseases in Indigenous People (GLADERPO).

He is past-President of the Argentinean Rheumatology Society (2011–2013). In 2013, he chaired the 10th International Congress on SLE, which took place under GLADEL sponsorship in Buenos Aires, Argentina, and in 2018, he chaired the Pan-American League of Rheumatology Associations (PANLAR) Congress in Buenos Aires.

Professor Pons-Estel is a council member of the Science and Educational Committee of the Pan-American League of Association for Rheumatology (PANLAR). He is also an active member of the Systemic Lupus International Collaborating Clinics (SLICC), member of the Collaborative Initiatives Working Group (COIN) of the American College of Rheumatology (ACR), member of the Lupus Academy Steering Committee, and an International Member of the ACR. Recently, a collaboration between GLADEL and PANLAR materialised, the aim being the development of guidelines for the management of SLE patients in the South American subcontinent; Bernardo is integral part of this collaboration.



Dr Guillermo J. Pons-Estel, MD, MSc, PhD

Hospital Provincial de Rosario and Regional Center for Autoimmune and Rheumatic Diseases (CREAR), Rosario, Argentina

Disclosures

None.

Guillermo J. Pons-Estel is an Internist and Rheumatologist at the Rheumatology Division, Department of Internal Medicine, Hospital Provincial de Rosario and Regional Center for Autoimmune and Rheumatic Diseases (CREAR), Rosario, Argentina.

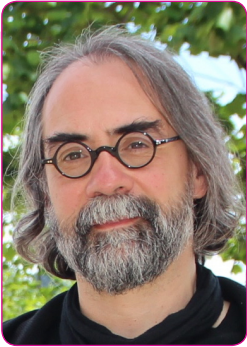
Dr Pons-Estel received his MD from the University of Rosario, Argentina in 2003 and was awarded his PhD in Medicine "International Doctor" (*cum laude*) by the University of Barcelona in 2011. He also finished the Masters Course in Autoimmune Diseases at the University of Barcelona and continued as Post-Doctoral Research Fellow at Department of Autoimmune Diseases, Clinical Institute of Medicine and Dermatology, Hospital Clinic, Barcelona, Catalonia, Spain (2011–2017).

Dr Pons-Estel received further training in the Department of Medicine. Division of Clinical Immunology and Rheumatology, Schools of Medicine and Public Health, University of Alabama,

Birmingham, USA, under the mentorship of Dr Graciela S. Alarcón.

Dr Pons-Estel is a member of the Spanish and Argentinean Societies of Rheumatology and Study Group on Autoimmune Diseases (GEAS). He has been member of Latin American Group for the Study of Systemic Lupus Erythematosus (GLADEL) and AntiPhospholipid Syndrome Alliance For Clinical Trials and International Networking (APS ACTION) since 2008 and 2010, respectively. Finally, he is the coordinator of the project: Urinary and Serological biomarkers of Lupus Nephritis in Latin American patients with systemic lupus erythematosus (SLE) that involves 42 centres from 10 Latin American countries.

Dr Pons-Estel's work has focused on the study of autoimmune diseases, with special interest on SLE and APS. He is author of 38 peer-reviewed publications, 15 book chapters and over 60 communications.



Professor Guillermo Ruiz-Irastorza, MD, PhD

Autoimmune Research Unit, Cruces University Hospital, Bizkaia, Spain

Disclosures

None.

Guillermo Ruiz-Irastorza is Head of the Autoimmune Research Unit at Cruces University Hospital, Bizkaia, Spain, where he has been since 2001.

Professor Ruiz-Irastorza received his MD from the Universidad Autonoma de Madrid, Spain in 1990 and became a specialist in internal medicine in 1996. Following his PhD from the University of the Basque Country, Spain in 1999, he spent a year as a Research Fellow at the Lupus Research Unit, St Thomas' Hospital, London, UK, before returning to the Hospital Universitario Cruces as Consultant Physician in Internal Medicine. He became Professor of Medicine at the University of the Basque Country, Spain in 2004.

Professor Ruiz-Irastorza is a member of the Editorial Board of the journal *Lupus*, and a reviewer of several other journals in the fields of rheumatology and autoimmune diseases, including *Annals of Rheumatic Diseases*, *Arthritis & Rheumatology*, *Rheumatology*, *Journal of Rheumatology* and *Lupus Science & Medicine*.

He is a member of the Grupo de Estudio de las Enfermedades Autoinmunes Sistemicas (GEAS), and coordinator of the first Spanish national lupus inception cohort study. He has been member of the Systemic Lupus International Collaborating Clinics since 2008.

Professor Ruiz-Irastorza's clinical and research interests focus on systemic lupus erythematosus, antiphospholipid syndrome, and pregnancy and autoimmune diseases. He is author of 151 peerreviewed publications and 20 book chapters.



Plenary I: We are not all equal

Moderator: Isabel Acosta-Colman (Asunción, Paraguay)

Professor Bernardo A. Pons-Estel, MD

Regional Center for Autoimmune and Rheumatic Diseases (CREAR) and the Cardiovascular Institute of Rosario, Argentina

Lupus in Latin America: GLADEL experience

References

1. Pons-Estel BA, Catoggio LJ, Cardiel MH, et al. The GLADEL multinational Latin American prospective inception cohort of 1,214 patients with systemic lupus erythematosus: ethnic and disease heterogeneity among "Hispanics". *Medicine (Baltimore)*. 2004;83(1):1–17.
2. Pons-Estel GJ, Alarcon GS, Burgos PI, et al. Mestizos with systemic lupus erythematosus develop renal disease early while antimalarials retard its appearance: data from a Latin American cohort. *Lupus*. 2013;22(9):899–907.
3. Alarcon GS, McGwin G, Jr., Sanchez ML, et al. Systemic lupus erythematosus in three ethnic groups. XIV. Poverty, wealth, and their influence on disease activity. *Arthritis Rheum*. 2004;51(1):73–7.
4. Ugarte-Gil MF, Pons-Estel GJ, Molineros J, et al. Disease features and outcomes in United States lupus patients of Hispanic origin and their Mestizo counterparts in Latin America: a commentary. *Rheumatology (Oxford)*. 2016;55(3):436–40.

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterised by an array of laboratory abnormalities and clinical manifestations. It has been recognised that ethnicity and socioeconomic factors have a major impact on the incidence, disease activity, damage and mortality of this disease.

The need for comprehensive published epidemiologic and clinical data from Latin American SLE patients resulted in the creation of the Grupo Latino Americano De Estudio del Lupus (GLADEL) cohort in 1997. This inception cohort recruited a total of 1480 multi-ethnic [Mestizo, African-Latin American (ALA), Caucasian and other] SLE patients diagnosed within 2 years from the time of enrolment from 34 Latin American centres with expertise in the diagnosis and management of this disease.¹ GLADEL has shown that ALA and Mestizo patients, in comparison with Caucasians, experienced early age at onset, more severe disease, higher frequency of renal disease, hypertension, pericarditis and polyadenopathy and a higher maximum disease activity and damage. Furthermore, GLADEL showed that Mestizo SLE patients are at an increased risk not only of developing renal involvement overall but of doing so earlier.²

GLADEL is creating strategic partnerships with other lupus study groups around the world. In this sense, the close relationship with LUMINA has allowed to compare Latin American Mestizos with their counterpart "Hispanics" in the US, showing that USA-based Hispanic patients seemed to have a poorer prognosis than their counterparts from Latin America, despite having a comparable genetic background. Socioeconomic factors may account for these observations.^{3,4} Similarly, GLADEL and new partner institutions, through a multicentre collaboration within Latin America, the Genome Network Systemic Lupus Erythematosus Consortium (GLA-GENLES), are aiming to identify genome-wide associations and to examine the relationship between genetic ancestry, sociodemographic characteristics and clinical features in a large cohort of Mestizos/Hispanics SLE patients.⁵

GLADEL has contributed to improving our knowledge about the course and outcome of lupus in patients from this part of the Americas.

Learning Objectives

- Describe epidemiologic and clinical SLE data in Latin American cohorts
- Discuss the genetic predisposition for SLE data in Latin American cohorts
- Explain the need for and collaborations in improving understanding of the clinical course and improving outcomes for patients with SLE

Notes

5. Alarcon-Riquelme ME, Ziegler JT, Molineros J, et al. Genome-Wide Association Study in an Amerindian Ancestry Population Reveals Novel Systemic Lupus Erythematosus Risk Loci and the Role of European Admixture. *Arthritis Rheumatol*. 2016;68(4):932–43.



Plenary I: We are not all equal

Moderator: Isabel Acosta-Colman (Asunción, Paraguay)

Professor Ricard Cervera, MD, PhD, FRCP
Hospital Clinic, Barcelona, Catalonia, Spain

SLE epidemiology: Lessons from the EURO-LUPUS Study

References

1. Cervera R, Khamashta MA, Font J, et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. *Medicine (Baltimore)*. 1993;72(2):113–24.
2. Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 5-year period. A multicenter prospective study of 1,000 patients. European Working Party on Systemic Lupus Erythematosus. *Medicine (Baltimore)*. 1999;78(3):167–75.
3. Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. *Medicine (Baltimore)*. 2003;82(5):299–308.

Systemic lupus erythematosus (SLE) may affect any organ of the body and display a broad spectrum of clinical and immunological manifestations. Its natural history is characterised by episodes of relapse or flare, interchanging with remission, and the outcome is highly variable ranging from permanent remission to death. In recent years, both morbidity and mortality in SLE have been modified due to a number of possible reasons, including improved knowledge of its pathogenetic mechanisms and prognostic factors, as well as the use of immunosuppressive regimes. Additionally, it has been suggested that the spectrum of clinical manifestations, as well as the causes of death, are different depending on the time of evolution of the disease. Furthermore, it has been postulated that SLE tends to enter into remission in many patients after a long time of evolution. However, other studies have shown that patients with a long disease duration (more than 10 years) still have active disease.

In an attempt to clarify the long-term evolution of patients with SLE, a multicentre observational study of 1,000 European patients was started in 1990. The clinical and immunological characteristics of these patients when entered in the study¹ as well as after 5-year² and 10-year³ periods of follow-up have been recorded. In this lecture we will present the frequency and characteristics of the main causes of morbidity and mortality after a 10-year follow-up period as well as compare the frequency of the early manifestations in this cohort with the frequency of the manifestations that appeared later in the evolution of the disease.

Learning Objectives

- Recognise the main causes of morbidity and mortality in the short and long-term in the European SLE patient population
- Identify the predictive factors with prognostic value for morbidity and mortality in SLE
- Discuss the hypothesis that SLE is a syndrome with different forms of presentation

[illegible]



Professor Ricard Cervera, MD, PhD, FRCP
Hospital Clinic, Barcelona, Catalonia, Spain

Catastrophic APS

References

1. Espinosa G, Rodríguez-Pinto I, Cervera R. Catastrophic antiphospholipid syndrome: an update. *Panminerva Med.* 2017;59(3):254–68.
2. Rodríguez-Pinto I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: The current management approach. *Best Pract Res Clin Rheumatol.* 2016;30(2):239–49.
3. Rodríguez-Pinto I, Moitinho M, Santacreu I, et al. Catastrophic antiphospholipid syndrome (CAPS): Descriptive analysis of 500 patients from the International CAPS Registry. *Autoimmun Rev.* 2016;15(12):1120–4.
4. Rodríguez-Pintó I, Espinosa G, Erkan D, Shoenfeld Y, Cervera R. On behalf of the CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies). The effect of “triple therapy” with anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins on the mortality of catastrophic antiphospholipid syndrome (CAPS) patients. *Ann Rheum Dis.* 2017;76(Suppl 2):150.

Patients with catastrophic antiphospholipid syndrome (CAPS) have in common: a) Clinical evidence of multiple organ involvement developing over a very short period of time; b) Histopathological evidence of multiple small vessel occlusions, and c) Laboratory confirmation of the presence of antiphospholipid antibodies (aPL), usually in high titre.^{1,2}

The CAPS Registry documents the entire clinical, laboratory and therapeutic data of all published cases with CAPS as well as of many additional patients whose data has been fully registered. The periodic analysis of this registry has allowed increased knowledge of this condition. In the most recent analysis, including 500 patients, precipitating factors were identified in 65% of the episodes.³ The most frequent factors were infections (49% of episodes), mainly in the respiratory tract (33%), followed by the urinary tract (19%) and the skin (13%). The clinical

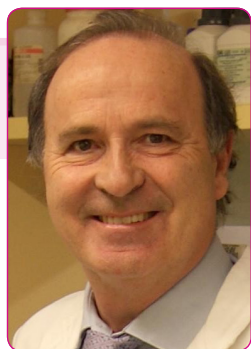
picture was characterised by renal involvement (73%), with variable degree of renal failure, and lung involvement (60%), in the form of acute respiratory distress syndrome or pulmonary embolism (26%). Up to 56% of patients showed central nervous system manifestations because of stroke or encephalopathy. The heart was affected in half of the episodes, mainly due to myocardial infarction or valvulopathy. Death occurred in 37% of episodes.

Management of CAPS is challenging. Early diagnosis and aggressive therapies are essential. The evidence-based information about the current treatment also comes from the CAPS Registry where the higher recovery rate was achieved by the combination of anticoagulation plus glucocorticoids plus plasma exchange and/or intravenous immunoglobulins. Additionally, there are few data supporting new therapeutic approaches, including rituximab and eculizumab.⁴

Learning Objectives

- Recognise the main clinical and laboratory features of the CAPS
- Identify the predisposing factors for the development of a catastrophic event in the APS
- Analyse the therapeutic options for the CAPS

[illegible]



Dr Jose Ordi-Ros, MD, PhD

Hospital Vall d'Hebron, Barcelona, Catalonia, Spain

Severe flares during pregnancy

References

1. Jara LJ, Medina G, Cruz-Dominguez P, et al. Risk factors of systemic lupus erythematosus flares during pregnancy. *Immunol Res.* 2014;60(2-3):184–92.
2. Knight C, Nelson-Percy C. Management of systemic lupus erythematosus during pregnancy: challenges and solutions. *Open Access Rheumatol.* 2017;10:37–53.
3. de Jesus GR, Mendoza-Pinto C, de Jesus NR, et al. Understanding and Managing Pregnancy in Patients with Lupus. *Autoimmune Dis.* 2015;2015:943490.
4. Lightstone L, Hladunewich MA. Lupus Nephritis and Pregnancy: Concerns and Management. *Semin Nephrol.* 2017;37(4):347–53.
5. Bramham K, Hunt BJ, Bewley S, et al. Pregnancy outcomes in systemic lupus erythematosus with and without previous nephritis. *J Rheumatol.* 2011;38(9):1906–13.
6. Lateef A, Petri M. Systemic Lupus Erythematosus and Pregnancy. *Rheum Dis Clin North Am.* 2017;43(2):215–26.

Maternal complications in patients with systemic lupus erythematosus (SLE) include SLE activity, preeclampsia and arterial hypertension, especially in patients with renal involvement. Recently, efforts have been made to create a “pregnancy-version” of existing activity indexes, such as the ECLAM, SLEDAI, SLAM, and LAI, aimed at making studies more comparable. The British Isles Lupus Assessment Group (BILAG) 2004-Pregnancy index has been shown to be reliable for the assessment of disease activity in pregnant SLE patients. The results of prospective, controlled observational studies show some discordance: some studies found that women are at increased risk of lupus flares when pregnant, while other studies found the rate of flares was unchanged as compared to non-pregnant SLE patients.¹ This discrepancy may be explained by disease heterogeneity, the limited number of patients enrolled in SLE-pregnancy studies, the lack of homogeneous criteria for defining lupus flares, and the different SLE treatments used during pregnancy. In addition, several manifestations secondary to pregnancy may be wrongly attributed to lupus flares, including arthralgias, myalgias, facial and palmar rash, hearing loss, and oedema in the face, hands and lower limbs. Likewise, serological abnormalities used to define lupus flares may be physiologically altered during pregnancy, that is, complement and erythrocyte sedimentation rate.² There seems to be a consensus that the risk of flares depends on the level of maternal disease activity in the 6–12 months before conception and is higher in women with repeated flares before conception, in those who discontinue useful medications and, in particular, in women with active glomerulonephritis at conception. A study showed that disease activity in the 6 months before conception was associated with an increase in the rate of pregnancy loss. The same features of previous manifestations were the best predictors of further manifestations: dermatological flares by previous skin rash, renal flares by previous nephritis, and haematological flares by previous haematological abnormalities. Thrombocytopaenia in SLE during pregnancy indicates higher disease activity, severe organ damage, early onset preeclampsia and

higher pregnancy loss. Central nervous system (CNS) lupus in pregnancy represents an especially severe manifestation of SLE and may involve great maternal and fetal risks.³ Compared with non-pregnant active female patients with SLE, active pregnancy-related lupus, including new-onset lupus and flare lupus, had a higher incidence of renal and haematological involvement but less mucocutaneous and musculoskeletal involvement.³ Distinguishing clinical indicators of lupus nephritis (LN) activity from pregnancy physiological manifestations and those related to preeclampsia can be a challenge. Therefore, during pregnancy, patients with LN may have isolated elevation of proteinuria that is not necessarily indicative of active nephritis. The patients with LN have 2–3 times higher chance of flare when compared to patients without LN, both systemic and renal disease activity.⁴ A disease flare may occur at any time, but there may be a trend towards flares in the third trimester. In fact, patients who started a pregnancy in a stable remission period and continued on medications experienced fewer flares, which were mostly mild and generally well managed with a temporary increase in prednisone dose. Therefore, during pregnancy patients with LN may have isolated elevation of proteinuria that is not necessarily indicative of active nephritis. The patients with LN have 2–3 times higher chance of flare when compared to patients without LN, both systemic and renal disease activity. Furthermore, patients with LN tend to develop preeclampsia (PE) earlier compared with women with SLE without nephritis.⁵ One of the most complex and challenging aspects during a pregnancy patients with lupus is the precise characterisation of the LN activity and the differentiation of PE. In both complications hypertension, proteinuria and edema are present. Differential diagnosis is essential, as treatment varies significantly: in PE, delivery should be considered, while immunosuppressive drugs should be administered to patients with LN. Lupus nephritis is likely to be associated with positive anti-dsDNA antibodies (especially in high titers), serum complement consumption, and dysmorphic haematuria and/or red blood cell cylinders. In this scenario, the probable diagnosis is a proliferative

kidney disease. During clinical evaluation, the onset of fever, presence of discoid or subacute cutaneous lupus lesions, vasculitis, oral ulcers, polyserositis, lymphadenomegaly, positive direct Coombs, myocarditis and pneumonitis also indicate lupus flare. In contrast, if the gestational age is greater than 22 weeks, with no signs of SLE activity and hyperuricemia is present, we can state the diagnosis of PE with relative precision. Renal biopsy is a valuable research tool for accurate characterisation of LN, but it is usually avoided during pregnancy considering technical difficulties of this procedure in pregnant women.⁴ This is important as sepsis is a prominent cause of indirect maternal mortality, as well as mortality in non-pregnant SLE patients. If there is any diagnostic doubt, it may be worth using intravenous immunoglobulin (IVIg) for first-line treatment as this will dampen inflammation but not worsen infection (unlike high-dose steroids). Treatment of flares during pregnancy is guided by

the severity and organ involvement, similar to the non-pregnant state. However, the choice of agents is limited to safe drugs, as discussed above. Steroids in the lowest possible doses should be used, but short courses of high doses can be used for flares. Non-steroidal anti-inflammatory drugs can be used for mild symptoms in the first and second trimester; however, caution needs to be exercised in view of recent data associated with malformations. Hydroxychloroquine should be continued throughout the pregnancy. Other safe immunosuppressants that can be used include azathioprine and calcineurin inhibitors. Although developmental delays in offspring were recently reported with azathioprine, more studies are required to further evaluate this association. Intravenous immunoglobulin and plasmapheresis remain alternative options but the higher risk of thrombosis with IVIg and fluid overload have to be considered.⁶

Learning Objectives

- Evaluate and understand precipitating factors of SLE flare
- Discuss diagnostic possibilities: Lupus nephritis or eclampsia
- Explain the diagnosis and treatment of SLE flare

Notes

[illegible]

Abstracts

Plenary II: S.O.S in lupus: Caught between a rock and a hard place

Moderator: Marcia Melo-Martins
(Asunción, Paraguay)



Dr Claudio Galarza-Maldonado, MD, PhD
Monte Sinai and Hospital del Rio, Cuenca, Ecuador

Persistent cytopenias in SLE

References

1. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1997;40(9):1725.

Haematological manifestations in systemic lupus erythematosus (SLE) are commonly observed and include anaemia, leukopenia, lymphopenia and thrombocytopenia. The American College of Rheumatology (ACR) has included these as diagnostic markers for SLE.¹ Cytopenias in SLE could be due to the disease itself, another concomitant illness or drug toxicities. The treatment for these manifestations could be according to the cause; and is based on small retrospective clinical studies or case reports, and sometimes represents important challenge for doctors who treat patients in daily practice.

Biologic therapy could be an alternative for the patients with SLE in general and also for the control of autoimmune cytopenias. Better understanding of mechanisms leading to autoimmune disorders may improve stratified approaches to management and control of these clinical manifestations.

Learning Objectives

- Discuss the classification of cytopenias in SLE
- Discuss the autoimmune mechanisms of cytopenias
- Discuss the current therapeutic options

[illegible]



Plenary III: Myths and truths

Moderator: Ricard Cervera (Barcelona, Catalonia, Spain)

Dr Hannah Cohen, MBChB MD FRCP FRCPATH
University College London, UK

Lupus Academy video presentation: Where do new oral anticoagulants fit in SLE?

References

1. Summaries of Product Characteristics (SPCs) and Patient Information Leaflets (PILs): *electronic Medicines Compendium*: <https://www.medicines.org.uk/emc/>
2. Cohen H, Efthymiou M, Gates C, Isenberg D. Direct oral anticoagulants for thromboprophylaxis in patients with antiphospholipid syndrome. *Semin Thromb Hemost*. 2017 Feb 14. doi: 10.1055/s-0036-1597902.
3. Ruiz-Irastorza G, Egurbide MV, Ugalde J, Aguirre C. High impact of antiphospholipid syndrome on irreversible organ damage and survival of patients with systemic lupus erythematosus. *Arch Intern Med*. 2004;164:77–82.
4. Cohen H, Hunt BJ, Efthymiou M, et al. Rivaroxaban versus warfarin to treat patients with thrombotic antiphospholipid syndrome, with or without systemic lupus erythematosus (RAPS): a randomised, controlled, open-label, phase 2/3, non-inferiority trial. *The Lancet Haematology*. 2016;3:e426–e36.
5. Urbanus RT. Rivaroxaban to treat thrombotic antiphospholipid syndrome. *The Lancet Haematology*. 2016;3:e403–4.

The direct oral anticoagulants (DOACs) include dabigatran etexilate, a direct thrombin inhibitor, and apixaban, edoxaban, and rivaroxaban, direct factor Xa inhibitors. DOACs are established as therapeutic alternatives to warfarin and other vitamin K antagonists (VKAs), and becoming the standard of care for a wide range of indications. These include primary thromboprophylaxis for major lower limb orthopedic surgery, the treatment and secondary prevention of venous thromboembolism (VTE), the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation; and acute coronary syndromes.¹ DOACs, in contrast to VKAs, are prescribed at a fixed dose with a more predictable effect and, therefore, do not require regular anticoagulant monitoring in the majority of clinical settings. They also have a rapid onset of action, so bridging anticoagulation with low-molecular-weight heparin at the initiation of anticoagulation can often be eliminated. In addition, they are not affected by changes in diet and alcohol intake and have fewer drug interactions that affect anticoagulant intensity, which would be expected to result in improved quality of life for patients.

The main focus of studies of DOACs in systemic lupus erythematosus (SLE) is on comparison with warfarin in patients with thrombotic antiphospholipid syndrome (APS), in whom the current mainstay of treatment is anticoagulation with VKAs.² Approximately 15% of patients with SLE have thrombotic APS, which is a major adverse prognostic factor.³ Appropriate management of thrombotic APS is essential to minimise its deleterious impact. The RAPS (Rivaroxaban in Antiphospholipid Syndrome) trial randomised 116 APS patients, approximately 20%

of whom had SLE, on warfarin target INR 2.5 for previous VTE, to remain on warfarin, or switch to rivaroxaban 20 mg daily. The primary outcome was the percentage change in endogenous thrombin potential (ETP). When anticoagulation intensity was assessed by the ETP alone, rivaroxaban was inferior to warfarin. However, peak thrombin generation was lower with rivaroxaban and, therefore, the overall thrombogram indicated no difference in thrombotic risk. This conclusion was supported by concentrations of in-vivo coagulation activation markers being increased in only a few patients in both treatment groups, and the absence of new thrombotic events during 6 months of treatment. Quality-of-life assessment showed a significant improvement with rivaroxaban.^{4,5}

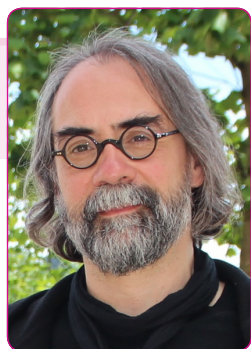
In summary, RAPS suggests that rivaroxaban offers an effective, safe and convenient alternative to warfarin in SLE patients with APS who have previous VTE and require standard intensity anticoagulation. Anecdotal clinical reports and case series suggest that recurrent thrombotic events with DOACs in APS/SLE patients mainly occur when DOACs are used for APS-related arterial thrombosis or in triple antiphospholipid antibody positive APS patients (of note, 28% of RAPS patients were triple positive). The RAPS results are not applicable to APS patients with VTE who require higher intensity anticoagulation (i.e. those with recurrent VTE while on standard intensity anticoagulation) or APS patients with stroke or other ischemic brain manifestations, or arterial thrombosis in other sites. Ongoing and future studies will clarify the role of DOACs in these APS patient subgroups with SLE, as well as in other SLE patients with or without antiphospholipid antibodies.

Learning Objectives

- Describe the potential benefits of direct oral anticoagulants compared with VKAs and considerations with regard to their use
- Discuss the data on the use of direct oral anticoagulants in APS patients with SLE
- Explain appropriate current use of direct oral anticoagulants in patients with SLE

Notes

This image shows a single page of white paper with horizontal ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.



Plenary III: Myths and truths

Moderator: Ricard Cervera (Barcelona, Catalonia, Spain)

Professor Guillermo Ruiz-Irastorza, MD, PhD

Autoimmune Research Unit at Cruces University Hospital, Bizkaia, Spain

Lupus Academy video presentation: Using lower doses of glucocorticoids in SLE: less toxicity, same efficacy

References

1. Luijten RK, Fritsch-Stork RD, Bijlsma JW, Derksen RH. The use of glucocorticoids in systemic lupus erythematosus. After 60 years still more an art than science. *Autoimmun Rev.* 2013;12(5):617–28.
2. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res (Hoboken).* 2012;64(6):797–808.
3. Buttgerit F, Burmester GR, Lipworth BJ. Optimised glucocorticoid therapy: the sharpening of an old spear. *Lancet.* 2005;365(9461):801–3.
4. Zonana-Nacach A, Barr SG, Magder LS, Petri M. Damage in systemic lupus erythematosus and its association with corticosteroids. *Arthritis Rheum.* 2000;43(8):1801–8.
5. Ruiz-Arzuza I, Ugarte A, Cabezas-Rodriguez I, et al. Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus. *Rheumatology (Oxford).* 2014;53(8):1470–6.

Glucocorticoids have long been one of the cornerstones of the treatment of inflammatory conditions, including systemic lupus erythematosus (SLE). The use of high doses of oral prednisone/prednisolone is recommended by most guidelines in cases of moderate to high lupus activity.^{1,2} However, such recommendations are based more on custom than on true evidence.

According to the pharmacological basis of the effects of glucocorticoids, the genomic pathway is almost fully saturated at doses of prednisone over 30 mg/d, which means that toxicity associated with transactivation is close to maximum above those levels. On the contrary, the non-genomic pathway is responsible for a rapid and powerful anti-inflammatory response, mostly free from the secondary effects of the genomic pathway; this pathway is activated at doses over 100 mg/d, being fully active over 250 mg/d.³

Results from clinical studies corroborate these data. It has been consistently shown that glucocorticoid-related damage is dose-dependent, with doses below 5–7.5 mg/d being probably safe and doses >30 mg/d being associated with a sharp increase in the frequency of side effects. The use of pulses of methyl-prednisolone has been also free from secondary damage in most studies.^{4,5}

Moreover, recent data from observational studies and a small clinical trial support the fact that lower doses of oral prednisone are as effective as high doses in treating active lupus, particularly, but not only, renal disease.^{6–8} Thus, a door has been opened to a more rational use of glucocorticoids, taking advantage of their unquestionable anti-inflammatory and immunomodulatory properties whilst reducing the risks for the also unquestionable toxicity.

In our experience, combination therapy with hydroxychloroquine, immunosuppressive drugs and, especially, pulses of methylprednisolone (no need to exceed 500 mg per pulse; a 250 mg pulse is usually enough) help reduce the initial doses of prednisone to less than 30 mg/d with very rapid tapering, and offer high efficacy minimising short- and long-term secondary effects.

Learning Objectives

- Understand the role of the genomic and non-genomic pathways in the therapeutic and toxic effects of glucocorticoids
- Review published data in SLE patients showing the association of different doses of glucocorticoids with side effects including damage
- Discuss the results from recent studies on the efficacy and toxicity of therapeutic schemes using lower doses of prednisone in severe lupus
- Use practical guidelines for using lower doses of prednisone in the setting of active lupus

Notes

6. Zeher M, Doria A, Lan J, et al. Efficacy and safety of enteric-coated mycophenolate sodium in combination with two glucocorticoid regimens for the treatment of active lupus nephritis. *Lupus*. 2011;20(14):1484–93.
7. Ruiz-Irastorza G, Danza A, Perales I, et al. Prednisone in lupus nephritis: how much is enough? *Autoimmun Rev*. 2014;13(2):206–14.
8. Ruiz-Arruza I, Barbosa C, Ugarte A, Ruiz-Irastorza G. Comparison of high versus low-medium prednisone doses for the treatment of systemic lupus erythematosus patients with high activity at diagnosis. *Autoimmun Rev*. 2015;14(10):875–9.

[illegible]

Case Study Workshops

Saturday 14th April

Parallel case study workshops

Moderator: Josep Ordi-Ros (Barcelona, Catalonia, Spain)
Lupus nephritis

Isabel Acosta (*Asunción, Paraguay*)
Guillermo Pons-Estel (*Rosario, Argentina*)

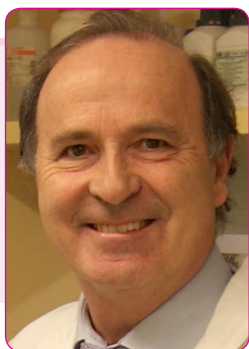
Moderator: Claudio Galarza-Maldonado (Cuenca, Ecuador)
Neurolupus

Gabriel Elizaur (*Asunción, Paraguay*)
Ernesto Cairoli (*Montevideo, Uruguay*)

Moderator: Bernardo Pons-Estel (Rosario, Argentina)
Cardiovascular risk in SLE

Sonia Cabrera (*Asunción, Paraguay*)
Gabriela Avila (*Asunción, Paraguay*)

Case Study Workshop



Moderator: Josep Ordi-Ros (Barcelona, Catalonia, Spain)

Presenters: Isabel Acosta-Colman (Asunción, Paraguay) & Guillermo Pons-Estel (Rosario, Argentina)

Lupus nephritis



The course of lupus nephritis (LN) is highly variable and multiple sociodemographic, clinical, serological and histopathological factors are responsible for its ultimate prognosis and outcome. Lupus nephritis may present silently but, even then, it can ultimately lead to severe renal insufficiency, which may occur in 50–70% of lupus patients depending on the population. Despite overall improvement in the care of patients with systemic lupus erythematosus (SLE), and an increase in the 5- and 10-year overall and renal survival rates, SLE prognosis remains unsatisfactory.

Understanding the factors that predispose poor renal outcomes is important to establish a prompt diagnosis and allow earlier treatment initiation. Patients from some ethnic groups such as Mestizos (Amerindian/European descendants), African Americans and Asians are more likely to develop renal involvement earlier and to experience less favorable outcomes compared with Caucasians.¹ Younger age at nephritis onset and male gender have also been reported as being poor prognostic indicators. Other socioeconomic factors such as poverty and smoking may also account for the progression of LN to renal damage. Within the laboratory and immunological domains, numerous predictors have all been shown to have poor prognostic significance. They include, elevation of serum creatinine and nephrotic syndrome at initial presentation, persistent arterial hypertension, low hematocrit, hypocomplementaemia, rising anti-dsDNA and anti-C1q antibodies titers, presence of antiphospholipid antibodies and failure to achieve clinical remission within the first year of treatment.¹⁻³

The relationship between histological features and the clinical course of LN has been well recognised. Proliferative lupus glomerulonephritis, presence of cellular crescents, fibrinoid necrosis, tubular atrophy, interstitial fibrosis, subendothelial immune deposits and capillary thrombosis have all been associated with a more aggressive course as evidenced by heavy proteinuria and renal function deterioration in a significant proportion of patients.²

Nevertheless, these markers for detecting and assessing LN are unsatisfactory for several reasons. They lack the ability to differentiate renal activity from renal damage, which is cardinal for planning a treatment strategy. The pathogenic processes underlying LN may begin well before renal function becomes impaired and abnormal urinary findings and other laboratory parameters are found to be abnormal. A number of urine protein biomarker candidates, including chemokines, cytokines, growth factors, proinflammatory factors and adhesion molecules, have been evaluated as potential SLE biomarkers, but their validation is still in progress.^{4, 5}

Dr Isabel Acosta-Colman, MD, Msc, PhD

Case 1: 21-year-old female with oedema and fatigue

A 21-year-old patient from Asunción is admitted to the Hospital de Clinicas for generalised oedema and fatigue. She has no previous medical or family history. Physical examination revealed blood pressure of 160/90, oedema of the lower limbs up to 1/3 bilateral medium and pallor of skin and mucous membranes. Routine laboratory analyses showed Hg 10 g/dL, Hto 32%, creatinine 2.1 mg/dL, pathological sediment, proteinuria: 7240 mg/24 hrs, ANA 1:320, anti-DNA +, anti Ro and anti La -, anti Sm +, Coombs test -, C3: 39 mg/dL (89–187), C4: 6.1 mg/dL (16.5–38).

Discussion points:

Should we perform a renal biopsy in this case?

How would you treat her?

References

1. Mavragani CP, Fragoulis GE, Somarakis G, *et al.* Clinical and laboratory predictors of distinct histopathological features of lupus nephritis. *Medicine (Baltimore)*. 2015;94(21):e829.
2. Mok CC. Prognostic factors in lupus nephritis. *Lupus*. 2005;14(1):39–44.
3. Pons-Estel GJ, Alarcon GS, Hachuel L, *et al.* Anti-malarials exert a protective effect while Mestizo patients are at increased risk of developing SLE renal disease: data from a Latin-American cohort. *Rheumatology (Oxford)*. 2012;51(7):1293–8.

In the next few months, with the treatment chosen, the patient does not improve, proteinuria remains in the nephrotic range and activity parameters remain altered.

Discussion points:

What treatment alternatives should be considered for this patient?

In the following months the patient presents with improved activity parameters and initiates maintenance treatment. Months later, the patient marries and expresses the desire for pregnancy.

When would you advise her to get pregnant?

Learning Objectives

- Explain the importance of performing a renal biopsy for the diagnosis of lupus nephritis
- Describe the recommended induction and maintenance treatment for patients with lupus nephritis
- Explain the importance of pregnancy counseling in patients with SLE

Dr Guillermo Pons-Estel, MD, MSc, PhD

Case study 1

An 18-year-old Mestizo male, presents with swelling of the distal aspect of both lower extremities and headaches. He is of low socioeconomic status, lives in a rural area of Northern Argentina and is currently in between unskilled jobs. He has a family history of lupus (three brothers with autoimmune disease: one died from SLE aged 20 years, another brother has haematological and cutaneous SLE, and the last one developed deep vein thrombosis, fever, lymphadenopathy, polyarthritis and mild thrombocytopaenia about a year ago and was diagnosed with antiphospholipid syndrome).

He is found to have persistent hypertension (150/95 mmHg) as well as pericardial and pleural effusions. Laboratory tests reveal: NC anemia, hypoalbuminaemia (2.8 g/dL), elevated serum creatinine (2.0 mg/dL). Urinary sediment showed haematuria (20 RBCs/hpf) and cellular casts (5/hpf); a morning spot urine protein-to-creatinine ratio of 4, which was confirmed with a 24hs proteinuria of 4 g/24 hrs. Immunoserology showed hypocomplementemia with anti-dsDNA and anti-C1q positivity. IgG ACA: 80 GPL, IgG anti-β2GP1: 60 and lupus anticoagulant was also positive.

Case study 2

A 42-year-old Caucasian female, CEO of a coffee company, whose symptoms started 3 year ago with inflammatory plaques (2x3 cm) that healed leaving central scars, atrophy and dyspigmentation; clinical diagnosis of discoid lupus erythematosus was confirmed by skin biopsy. One year before presenting to the office she developed malar rash, photosensitivity, oral ulcers, arthritis and sicca manifestations. She comes periodically for follow up, feeling overall well. Physical examination reveals: Normal blood pressure; typical scarring discoid lesions over her skull and arms; no oedema or any other sign of active disease. Laboratory tests reveal: Normal CBC, serum creatinine of 0.9 mg/dL and eGFR 77mL/min; a urinary analysis shows 5 RBCs/hpf, <5 WBCs/hpf; and proteinuria 0.7 g/24 hrs. Immunoserology was either negative or normal except for positive anti-Ro/SSA and Sm antibodies.

Discussion points:

- Which are the predictors of good and poor lupus nephritis outcome in patient n° 1 and n° 2?
- What novel biomarkers should be considered for these patients?

Learning Objectives

- Describe the sociodemographic predictors of poor lupus nephritis outcomes
- Describe the clinical predictors of poor lupus nephritis outcomes
- Describe the serological predictors of poor lupus nephritis outcomes
- Describe the histopathological predictors of poor lupus nephritis outcomes
- Describe novel urinary biomarkers of lupus nephritis

4. Soliman S, Mohan C. Lupus nephritis biomarkers. *Clin Immunol.* 2017;185:10–20.

5. Wolf BJ, Spainhour JC, Arthur JM, et al. Development of Biomarker Models to Predict Outcomes in Lupus Nephritis. *Arthritis Rheumatol.* 2016;68(8):1955–63.

Additional Reading

1. Tourna Z, Gladman DD. Current and future therapies for SLE: obstacles and recommendations for the development of novel treatments. *Lupus Sci Med.* 2017;4(1):e000239.

2. La Paglia GMC, Leone MC, Lepri G, et al. One year in review 2017: systemic lupus erythematosus. *Clin Exp Rheumatol.* 2017;35(4):551–61.

3. Mubarak M, Nasri H. ISN/RPS 2003 classification of lupus nephritis: time to take a look on the achievements and limitations of the schema. *J Nephropathol.* 2014;3(3):87–90.

4. Colla L, Diena D, Rossetti M, et al. Immunosuppression in pregnant women with renal disease: review of the latest evidence in the biologics era. *J Nephrol.* 2018.

5. Yu F, Haas M, Glasscock R, Zhao MH. Redefining lupus nephritis: clinical implications of pathophysiologic subtypes. *Nat Rev Nephrol.* 2017;13(8):483–95.

Case Study Workshop



Moderator: Claudio Galarza-Maldonado (Cuenca, Ecuador)

Presenters: Ernesto Cairoli (Montevideo, Uruguay) & Gabriel Elizaur (Asunción, Paraguay)

Neuro lupus



Dr Ernesto Cairoli, MD, MSc, PhD

Case 1: 35-year-old Mestizo female

A 35-year-old Mestizo female was diagnosed with systemic lupus erythematosus (SLE) 16 years ago (characterised by cutaneous and joint involvement and membranous nephropathy). One year after diagnosis, lupus psychosis was diagnosed and then a major depression reverted 2 years later.

Six months ago, a planned cesarean section was performed due to twin pregnancy with a good development of newborns, but the patient developed a puerperal depression, remaining in treatment with sertraline and clonazepam as well as hydroxychloroquine 200 mg/day, prednisone 15 mg/day and azathioprine 150 mg/day.

Now she presents to the emergency department with 3-day history of altered attention, spatial and time disorientation, amimia, akinesia and progressive decreasing speech until reaching mutism.

In the emergency department, inappropriate behaviours and abnormal buco-linguofacial movements were observed as well as a waxy flexibility of upper limbs were observed suggesting a catatonic state diagnosis. Family members denied use of recreational or psychotropic drugs (except for the prescribed treatment).

Physical examination: 37°C axillar temperature, normal blood pressure and no alterations in skin or joints were observed. In the neurological examination, the described mutism and waxy rigidity of the four limbs were the only positive findings.

Laboratory tests: Glycaemia, creatinine, electrolytes, thyroid-stimulating hormone, hepatogram, coagulation test and chest radiography were normal. Blood tests: 900 lymphocytes and normal haemoglobin and platelets. Immunology tests: ANA 1/320 homogeneous pattern, anti-dsDNA positive, normal complement and negative antiphospholipid antibodies. Urine tests: Proteinuria 0.38 g/24 hrs.

No structural or vascular alterations were detected in CT and MRI brain studies.

CSF: Biochemistry and cellularity within normal values. Bacteriological test: Direct and cultivation without germs detection. Specific studies in CSF for tuberculosis and cryptococcus and PCR for herpes virus were negative. Blood and urine cultures were negative. Serology for VDRL, HIV, HBV and HCV negatives. EEG reported no epileptogenic activity.

Discussion points:

Initial diagnostic approach of neurological involvement in a patient with SLE

Initial evaluation of neuropsychiatric lupus: focal vs diffuse; inflammatory vs thrombotic

Therapeutic strategies in the SLE patient with CNS involvement

Dr Gabriel Elizaur, MD, MSc

Case 2: 26-year-old pregnant female

A 26-year-old female, 14 weeks pregnant, with history of preeclampsia is admitted after 2 weeks of headache, lumbar pain and lower extremities weakness. She also reported nausea, vomiting and fever (38.5%).

Physical examination reveals: She is awake and alert and has a normal respiratory rate; anesthesia of both lower extremities and dermatomes at the D4–D5 level that eventually progressed to the D12 level over the next 3 days following admission; acute urinary retention without sensory control of the bladder; normal cranial nerves; deep tendon reflexes absent in both knees; absent plantar cutaneous reflex; marked rigidity in the neck; and no arthritis or rash.

Laboratory examination reveals: Haemoglobin 9.2 g/dL; WBC 6300/mm³; N 80%; L 20%; platelets 220.000/mm³; GOT 39 U/L; GPT 37 U/L. Tbili 0.24 mg/dL; Urea 7 mg/dL; Cr 0.7mg/dL; Na: 136 mEq/L; K: 3.6 mEq/L; VDRL negative; HIV negative; CRP: 92 mg/dL; TORCHSV negatives; normal urinary sediment; proteinuria: 250 mg/dL; creatinine clearance 152 ml/min; normal vitamin B12 and homocysteinaemia.

Immunology tests reveal: ANA 1:320 fine speckled pattern, anti dsDNA 1/20, hypocomplementaemia, anti SM +. ANCA, anti acuaporin 4 IgG, anti Ro and anti La were negative. Antiphospholipid panel triple negative. CSF: negative GRAM stain, cultures negative, PCR viral panel (HSV1; HSV2; CMV, enterovirus, Epstein Barr) negative; AFB negative, VDRL negative, WBC: 328/mm³; PMN 80%; MN 20%; CSF glucose 20 mg/dL (glycaemia 120mg/dL); CSF protein: 88 mg/dL (plasma total protein 6.8 mg/dL).

Bilateral pleural effusions. No pericardial effusion. No abdominal serositis. EMG pure motor polyneuropathy, axonal type of lower extremities. On MRI: posterolateral inflammatory demyelinating lesions of 54 mm that included medulla up to C2 and 46 mm from C6 to D2. There were also other central inflammatory lesions of 115 mm from D8 to D12 that enhanced with gadolinium contrast. Gynecological ultrasound was concordant with gestational age.

Discussion points:

Clinical and radiological characteristics of myelitis related to SLE

Therapeutic choices in myelitis related to SLE

When to consider biologic therapies in CNS lupus?

Dr Ernesto Cairolí, MD, MSc, PhD

Case 3: 16-year-old Caucasian female

A 16-year-old Caucasian female presents with a family history of SLE (father) and whose mother had experienced four miscarriages.

The patient was in puerperium period, after delivery of her first pregnancy, born in term by vaginal delivery, 30 days ago.

Two days ago she began to experience involuntary movements, fast, brief, and sometimes stereotyped, present in face and limbs (mostly in upper limbs), suggesting the chorea diagnosis.

An exhaustive anamnesis was difficult due to the bucco-linguofacial dyskinesias present in the patient. The mother reported that the patient started with oral contraceptives 2 weeks ago and denied the use or abuse of drugs or psychotropic drugs. Additionally she reported the presence of hand arthritis and arthralgias in the last trimester of pregnancy.

Physical examination revealed: 37°C axillar temperature; normal blood pressure; and no alterations in skin or joints were observed. In the neurological examination, the described choreic movements were the highlighted features.

References

1. Bertsias GK, Ioannidis JP, Aringer M, et al. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis.* 2010;69(12):2074–82.
2. Toledano P, Sarbu N, Espinosa G, Bargallo N, Cervera R. Neuropsychiatric systemic lupus erythematosus: magnetic resonance imaging findings and correlation with clinical and immunological features. *Autoimmun Rev.* 2013;12(12):1166–70.
3. Cervera R, Asherson RA, Font J, et al. Chorea in the antiphospholipid syndrome. Clinical, radiologic, and immunologic characteristics of 50 patients from our clinics and the recent literature. *Medicine (Baltimore).* 1997;76(3):203–12.
4. Magro-Checa C, Zirkzee EJ, Huizinga TW, Steup-Beekman GM. Management of Neuropsychiatric Systemic Lupus Erythematosus: Current Approaches and Future Perspectives. *Drugs.* 2016;76(4):459–83.
5. Ye Y, Qian J, Gu Y, Chen X, Ye S. Rituximab in the treatment of severe lupus myelopathy. *Clin Rheumatol.* 2011;30(7):981–6.

continued



Case Study Workshop

Laboratory examination revealed: glycaemia, creatinine, electrolytes, TSH, hepatogram and chest radiography were normal. Blood test: 95,000 platelets, 720 lymphocytes. Immunology: ANA 1/160 homogeneous pattern, anti-dsDNA positive, significant decrease of C3 and C4 fraction complement and urine test without alterations. Antiphospholipid antibodies (lupus anticoagulant, anticardiolipin IgG and IgM and anti- β 2GP1) were positive. In emergency room, no structural alterations were detected in CT brain studies.

Discussion points:

Symptomatic vs immunosuppressive treatment in chorea related to SLE

Chorea and antiphospholipid syndrome

Therapeutic approach

Learning Objectives

At the end of the workshop, participants will be able to:

- Identify the clinical spectrum of serious CNS disease in SLE
- Identify the clinical and laboratory characteristics of neuropsychiatric lupus
- Identify the usefulness of MRI in diagnosis of neuropsychiatric lupus
- Describe the main therapeutic strategies in neuropsychiatric SLE with central compromise

[illegible]

Case Study Workshop



Moderator: Bernardo Pons-Estel (Rosario, Argentina)

Presenters: Sonia Cabrera-Villalba (Asunción, Paraguay) & Gabriela Avila-Pedretti (Asunción, Paraguay)

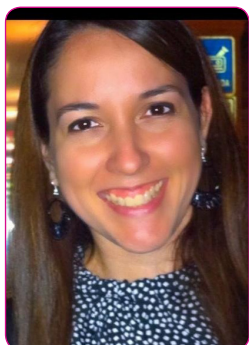
Cardiovascular risk in SLE



Dr Sonia Cabrera-Villalba, MD, Ms, PhD

Case 1: 25-year-old female

A 25-year-old female had been treated for systemic lupus erythematosus (SLE) for 6 years. She smokes 10 cigarettes a day. Her previous manifestations included photosensitive rash, pleuritis and pericarditis. Laboratory tests revealed +ANA (high titer) and +anti-dsDNA (high titer) and low complement C4. She was treated with antimalarials and prednisone. At age 35 years there was onset of proteinuria 4 g/24h, and lupus nephritis was confirmed with a renal biopsy Class IV, she was treated with IV methylprednisolone and cyclophosphamide, with preserved renal function. Six months later she developed dyspnoea, precordial pain with an electrocardiogram showing ST elevation, and was successfully treated at that point with thrombolytic therapy. Echocardiogram showed akinesia of the inferior wall of the left ventricle, with preserved ejection fraction. Valves were functional and pericardial effusion not been revealed. Corticosteroid therapy was been continued during this hospitalisation along with antimalarials, dual antiplatelet therapy (aspirin and clopidogrel), statins and beta blockers.



Learning Objectives

- Discuss risk factors for acute coronary syndrome
- Describe accelerated atherosclerosis in SLE patients
- Identify the enhanced cardiovascular risk associated with lupus nephritis

References

1. Tselios K, Sheane BJ, Gladman DD, Urowitz MB. Optimal Monitoring For Coronary Heart Disease Risk in Patients with Systemic Lupus Erythematosus: A Systematic Review. *J Rheumatol*. 2016;43(1):54–65.
2. Lopez P, Rodriguez-Carrio J, Martinez-Zapico A, et al. Serum Levels of Anti-PON1 and Anti-HDL Antibodies as Potential Biomarkers of Premature Atherosclerosis in Systemic Lupus Erythematosus. *Thromb Haemost*. 2017;117(11):2194–206.

Dr Gabriela Avila-Pedretti, MD, Ms, PhD

Case 2: 32-year-old female

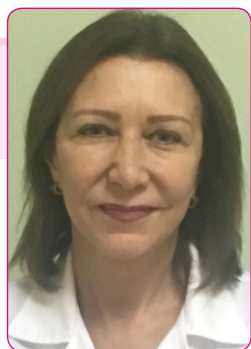
A 32-year-old female patient was first diagnosed with SLE based on polyarthritis, photosensitivity, malar rash, positive anti-nuclear antibody test and positive anti-dsDNA. She was obese and has had two pregnancies (with two live births and no miscarriage). Hydroxychloroquine and prednisone were started, but she discontinued the treatment. She returned 9 months later with alopecia, oral ulceration and polyarthritis. A complete routine laboratory was made and revealed positive anti-dsDNA, hypocomplementaemia and dyslipidemia (high levels of total cholesterol, triglycerides, low-density lipoprotein and low levels of high density lipoprotein). Renal function was preserved. Transthoracic echocardiography was normal, with a carotid intima-media thickness revealed in the vascular ultrasonography. Due to these findings homocysteine levels, CRP and apolipoprotein were requested and specific treatment was started.

Learning Objectives

- Discuss primary prevention of cardiovascular events in SLE patients
- Discuss the value of vascular ultrasound in cardiovascular assessment
- Describe molecular biomarkers of cardiovascular events in SLE patients

Notes

3. Wigen M, Svenugsson E, Mattiesson IY, et al. Cardiovascular disease in systemic lupus erythematosus is associated with increased levels of biomarkers reflecting receptor-activated apoptosis. *Atherosclerosis*. 2018;270:1–7.
4. Henrot P, Foret J, Barnetche T, et al. Assessment of subclinical atherosclerosis in systemic lupus erythematosus: A systematic review and meta-analysis. *Joint Bone Spine*. 2018;85(2):155–63.
5. Fasano S, Piero L, Pantano I, Iudici M, Valentini G. Longterm Hydroxychloroquine Therapy and Low-dose Aspirin May Have an Additive Effectiveness in the Primary Prevention of Cardiovascular Events in Patients with Systemic Lupus Erythematosus. *J Rheumatol*. 2017;44(7):1032–8.
6. Shama SK, Rathil M, Sahoo S, et al. Assessment of premature atherosclerosis in systemic lupus erythematosus patients with and without nephritis. *Lupus*. 2016;25(5):525–31.
7. Hallajzadeh J, Khoramdad M, Izadi N, et al. The association between metabolic syndrome and its components with systemic lupus erythematosus: a comprehensive systematic review and meta-analysis of observational studies. *Lupus*. 2018;961203317751047.
8. Giannelou M, Mavragani CP. Cardiovascular disease in systemic lupus erythematosus: A comprehensive update. *J Autoimmun*. 2017;82:1–12.
9. Gonzalez LA, Alarcon GS. The evolving concept of SLE comorbidities. *Expert Rev Clin Immunol*. 2017;13(8):753–68.



Plenary IV: Miscellaneous

Moderator: Guillermo Pons-Estel (Rosario, Argentina)

Professor Margarita Duarte, MD, PhD

National University of Asunción, Asunción, Paraguay

Controversies in lupus and vitamin D

References

1. Amson Y, Amital H, Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. *Ann Rheum Dis.* 2007;66(9):1137–42.
2. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357(3):266–81.
3. Ojeda A, Duarte M, Echeverría E, et al. Frequency of Vitamin D insufficiency in healthy young adults of Asunción. *Mem Inst Investig Cienc Salud.* 2014;12(1):26–32.
4. Aquino A, Ojeda A, Colman N, et al. Deficiency of vitamin D in postmenopausal patients and its relationship with calcium and phosphate metabolism and osteoporosis. *Mem Inst Investig Cienc Salud.* 2013;9(1):39–44.
5. Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. *Science.* 2006;311(5768):1770–3.
6. Roman L, Riquelme S, Losanto J, et al. Vitamin D prevalence in SLE patients at Rheumatology Department, Hospital de Clínicas, Asunción, Paraguay. *Rev Parag Reumatol.* 2016;2(1):24–8.

Vitamin D is a hormone, rather than a vitamin, the functions and mechanisms of action of which are currently under study. The discovery that receptors for vitamin D are present in all nucleated cells, and that their effects go far beyond phosphocalcic metabolism, force us to review the possible consequences of vitamin D deficiency in muscle tissue and the immune system, among other environments.^{1, 2}

In Paraguay, there is a high prevalence of vitamin D deficiency and insufficiency in patients with osteoporosis and, surprisingly, in healthy young people. In patients with systemic lupus erythematosus (SLE), who are photosensitive and should avoid exposure to the sun, it is logical to expect that there is also an inadequate level of vitamin D.^{3, 4}

The possibility that a vitamin D deficiency is associated with functional disorders of the immune system is inferred from several studies that demonstrate its effects on dendritic cells and response to infections.⁵

Although studies of vitamin D and disease activity in patients with SLE are contradictory, there are many situations that can cause these differences in the results, such as the values accepted as normal, the activity criteria used and the ranges of activity compared in study.^{6, 7} For these reasons, the effects of vitamin D and the molecules related to it, such as its receptor or its active forms, continue to be a field that must be investigated from the different perspectives mentioned.

Learning Objectives

- Review new data in relation to vitamin D and associated molecules
- Discuss the association between vitamin D and the immune system
- Describe the possible associations of the vitamin with the pathogenesis of SLE and the activity indexes of this disease
- Identify the possible areas of research pending in relation to autoimmune diseases and vitamin D

Notes

7. Amital H, Szekanecz Z, Szucs G, et al. Serum concentrations of 25-OH vitamin D in patients with systemic lupus erythematosus (SLE) are inversely related to disease activity: is it time to routinely supplement patients with SLE with vitamin D? *Ann Rheum Dis*. 2010;69(6):1155–7.



Plenary IV: Miscellaneous

Moderator: Guillermo Pons-Estel (Rosario, Argentina)

Dr Claudio Galarza-Maldonado, MD, PhD
Monte Sinai and Hospital del Río, Cuenca, Ecuador

Therapeutic perspectives in SLE

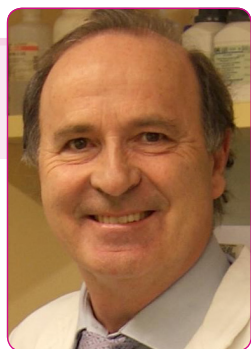
The treatment of systemic lupus erythematosus is based on current evidence and expert opinion. As in other chronic diseases, the objective of the treatment is to induce remission, avoid damage, prevent mortality and at the same time control and relieve symptoms, prevent disability and minimise the side effects of drugs.

The factor to be taken into consideration is to find an appropriate pharmacoeconomic balance and optimal access to medication.

Learning Objectives

- Discuss the optimal goals of therapy
- Describe the therapeutic targets in SLE
- Describe the current and future therapeutic options

[illegible]



Plenary IV: Miscellaneous

Moderator: Guillermo Pons-Estel (Rosario, Argentina)

Dr Jose Ordi-Ros, MD, PhD

Hospital Vall d'Hebron, Barcelona, Catalonia, Spain

APS: What clinicians should know about laboratory tests

References

1. Ortel TL. Antiphospholipid syndrome: laboratory testing and diagnostic strategies. *Am J Hematol.* 2012;87 Suppl 1:S75–81.

2. Moore JE, Mohr CF. Biologically false positive serologic tests for syphilis; type, incidence, and cause. *J Am Med Assoc.* 1952;150(5):467–73.

3. Pengo V, Tripodi A, Reber G, et al. Update of the guidelines for lupus anticoagulant detection. Subcommittee on Lupus Anticoagulant/ Antiphospholipid Antibody of the Scientific and Standardisation Committee of the International Society on Thrombosis and Haemostasis. *J Thromb Haemost.* 2009;7(10):1737–40.

4. Harris EN, Gharavi AE, Patel SP, Hughes GR. Evaluation of the anti-cardiolipin antibody test: report of an international workshop held 4 April 1986. *Clin Exp Immunol.* 1987;68(1):215–22.

5. Loeliger A. Prothrombin as cofactor of circulating anticoagulant in systemic lupus erythematosus. *Thromb Diath Haemorrh.* 1959;2:237–56.

The antiphospholipid syndrome (APS) is a disorder characterised clinically by recurrent venous and/or arterial thromboembolic events, or pregnancy morbidity. In addition to these clinical manifestations, the *sine qua non* for the syndrome is the persistent presence of a unique collection of autoantibodies that target specific phospholipid-binding proteins. Diagnostic tests for the detection of antiphospholipid antibodies include laboratory assays that detect anticardiolipin antibodies, lupus anticoagulants, and anti- β 2-glycoprotein I antibodies.¹ These assays originated over 60 years ago, with the identification of the biologic false positive test for syphilis, the observation of 'circulating anticoagulants' in certain patients with systemic lupus erythematosus, the identification of cardiolipin as a key component in the serologic test for syphilis, and the recognition and characterisation of a 'cofactor' for antibody binding to phospholipids.² Although these assays have been used clinically for many years, there are still problems with the accurate diagnosis of patients with this syndrome. For example, lupus anticoagulant (LA) testing can be difficult to interpret in patients receiving anticoagulant therapy,³ but most patients with a thromboembolic event will already be anticoagulated before the decision to perform the tests has been made. Because of the relative non-specificity of the assays used to detect the LA at the time, as well as the insensitivity of the precipitation assays used to detect anticardiolipin antibodies in patients with a biological false positive test for syphilis, Harris and colleagues developed a radioimmunoassay for the detection of anticardiolipin antibodies in patient with systemic lupus erythematosus (SLE) and thrombotic complications.⁴ For ease of use, this assay was subsequently converted to an enzyme-linked immunoassay (ELISA), and quickly became a key analytical approach for the rapid detection of this clinically-important group of autoantibodies. Standardisation of this assay was recognised as a problem from early in its development, however, and this issue remains a concern over 25 years later. The Lupus Anticoagulant/ Antiphospholipid Antibody Scientific and Standardization

Committee (SSC) of the International Society on Thrombosis and Haemostasis (ISTH) reviewed the status of laboratory identification of LA and, in 1991, published several recommendations for clinical laboratory testing and diagnosis. In this communication, the subcommittee recommended four criteria for the diagnosis of a LA.³ The "screening" step uses a phospholipid-dependent assay, such as the dilute Russell's viper venom time (dRVVT), the activated partial thromboplastin time (aPTT), or the dilute prothrombin time (dPT), in which the amount of phospholipid in the assay is diluted to make the test more sensitive to the presence of a LA. The mixing test consists of mixing patient plasma with plasma from a pool of healthy donors (typically on a one-to-one ratio) to confirm the presence of an inhibitory substance in the patient's plasma (as opposed to a factor deficiency). Third, and most importantly, the subcommittee recommended that phospholipid-dependence be demonstrated by the relative correction of the abnormal clotting time following the addition of phospholipid or platelets.³ These three criteria were also recommended by the Lupus Anticoagulant Working Party on behalf of the British Committee for Standards in Haematology, Haemostasis and Thrombosis Task Force that same year. The SSC recommendations were updated in 1995 and 2009,³ but the basic strategy remains the same. The presence of a possible 'cofactor' for the LA effect was first noted in 1959. In the 1970s, it was reported that the LA effect in up to two-thirds of patient plasma samples was 'augmented' by the addition of normal plasma.⁵ In 1989, it was shown that anticardiolipin antibodies do not bind to immobilised cardiolipin if plasma is not used in the assay. All of these observations led investigators to search for a possible cofactor that was critical for autoantibody binding to anionic phospholipids. This search ultimately culminated in separate groups identifying the plasma protein β 2-glycoprotein I as this essential cofactor.⁶ However, patients with a deficiency of β 2-glycoprotein I do not appear to have an increased risk for thrombosis.

Learning Objectives

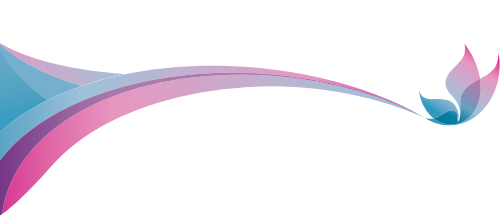
- Discuss the non-specificity of the assays used to detect the lupus anticoagulant (LA). LA can be difficult in patients who are receiving anticoagulant therapy. Falsely positive LA may be due to coagulation factorial deficits, anticoagulant oral treatment or heparin and falsely negative by platelet rich plasma
- Describe fluctuations of anticardiolipin or anti-apolipoprotein H antibodies may be due to the ELISA method rather than the disease itself (SLE)
- Explain that triple-positive antibodies patients (LA, anticardiolipin antibodies, and anti- β 2-glycoprotein I) would be considered to have the highest risk for complications of the syndrome, but many patients have APS with only an antibody type

6. Galli M, Comfurius P, Maassen C, et al. Anticardiolipin antibodies (ACA) directed not to cardiolipin but to a plasma protein cofactor. *Lancet*. 1990;335(8705):1544-7.

Notes

[illegible]

46



LupusAcademy
Communicate. Educate. Treat.