

Lupus Academy  
Eastern European Roadshow Meetings: Belgrade

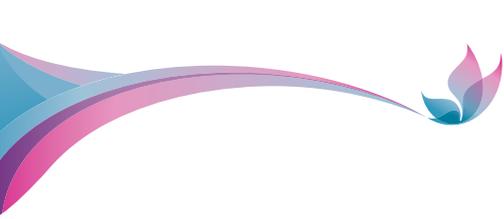
CHC Bežanijska Kosa,  
University Medical  
Center,  
Belgrade, Serbia  
**18th March 2016**

# Abstract Booklet



**LupusAcademy**

Communicate. Educate. Treat.



## Meeting organisation

The content for this activity has been developed under the control of the meeting Chairs: Professor Andrea Doria, Padova, Italy, and Professor Ricard Cervera, Barcelona, Catalonia, Spain, on behalf of the Steering Committee of the Lupus Academy. No supporting companies have had any influence over the presentation of any aspects of this meeting. For information about financial and in-kind support received to assist Lupus Academy in the delivery of its educational programme, please visit the website [www.lupus-academy.org](http://www.lupus-academy.org). CME compliance, accreditation and fulfilment has been facilitated by European CME Forum, on behalf of the Lupus Academy.

## Supporters

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**GlaxoSmithKline, UCB (Gold supporters) and  
Bristol Myers Squibb (Bronze supporter).**

# Welcome

## Dear Friends and Colleagues

On behalf of Lupus Academy, it is with great pleasure to welcome you to the **Lupus Academy's<sup>†</sup> Eastern European Roadshow Meeting at Belgrade University (18th March 2016)**. This meeting is being organised in collaboration with Professor Ljudmila Stojanovich, to whom we are very grateful.

These are exciting times for lupus clinicians and scientists as we embark on new frontiers in the diagnosis, management and novel treatment targets for lupus. This meeting will include a half-day educational programme that reflects the key issues in lupus diagnosis, management and the challenges we face in clinical practice. The educational programme will be delivered through morning plenary sessions and afternoon interactive workshops held at the University.

This meeting will give you the opportunity to meet distinguished clinicians and scientists and, through the sharing of clinical experience, develop your knowledge in this fast moving therapeutic area.

We sincerely hope that this meeting will provide you with new ideas for your clinical work, enhanced enthusiasm for collaborative research, and fruitful discussions with your colleagues who have an interest in improving patient outcomes in lupus.

We look forward to meeting and talking with you in Belgrade.

With kind regards,



**Professor Ljudmila Stojanovich** and the **Lupus Academy Steering Committee**



**Professor Ricard Cervera**  
co-Chairman 2016



**Professor Andrea Doria**  
co-Chairman 2015

Professor Thomas Dörner, Professor Richard Furie, Professor Bevra Hahn, Professor David Isenberg, Professor Munther Khamashta, Professor Roger A. Levy, Professor Ronald van Vollenhoven, Professor Sandra Navarra, Professor Murray Urowitz, Professor Zahir Amoura

<sup>†</sup>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

Friday 18th March 2016			Page
10:00	Opening Address	Ljudmila Stojanovich ( <i>Serbia</i> ), Ricard Cervera ( <i>Spain</i> ) & Andrea Doria ( <i>Italy</i> )	
Plenary I: Diagnosis and Treatment of SLE and APS		<i>Moderators: Ricard Cervera (Spain) &amp; Andrea Doria (Italy)</i>	
10:15	Diagnostic challenges in SLE and APS	Ljudmila Stojanovich ( <i>Serbia</i> )	8
10:45	New trends in the treatment of SLE	Andrea Doria ( <i>Italy</i> )	10
11:15	New trends in the treatment of APS	Ricard Cervera ( <i>Spain</i> )	12
11:45	Discussion		
12:15	Lunch (at leisure)		
Parallel Case Study Workshops			
13:30	<i>Moderator: Andrea Doria (Italy)</i> Neurologic and cardiovascular SLE/APS	 Ljudmila Stojanovich ( <i>Serbia</i> )	16
13:30	<i>Moderator: Ricard Cervera (Spain)</i> Haematologic challenges: Cytopenias	 Dragomir Marisavljevic ( <i>Serbia</i> )	20
15:00	Meeting Close		

## Biographies



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

### Disclosures

Consultant/Advisor:  
GSK

*Professor Cervera is a member of the Lupus Academy Steering Committee, co-Chairman of the Lupus Academy (2016) and has been involved in the planning and development of the Lupus Academy Eastern European 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 Biomèdiques 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.

Professor Cervera is an Associate Editor of the journal *Lupus Science & Medicine* and is on the Editorial Boards of 20 medical journals. He is coordinator of the European Forum on Antiphospholipid Antibodies and of the European Working Party on Systemic Lupus Erythematosus (SLE) (Euro-Lupus Group). 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 and 8th International Congresses on Autoimmunity, the 1st and 2nd 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, 60), 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'.

# Biographies



## Professor Andrea Doria, MD

University of Padova, Italy

Andrea Doria is Professor of Rheumatology and Head of the Unit of Connective Tissue Disease and Rare Rheumatic Diseases, Division of Rheumatology, Department of Medicine, University of Padua, Italy.

### Disclosures

Consultant/Advisor:  
GSK

*Professor Doria is a member of the Lupus Academy Steering Committee, was co-Chairman of the Lupus Academy (2015) and has been involved in the planning and development of the Lupus Academy Eastern European Roadshow Meeting programme and materials.*

Professor Doria received his medical degree and qualification in Rheumatology from the University of Padua. He was Council member of the Italian College of Rheumatology (CRO) between 1999 and 2005 and a Council member of the Italian Society of Rheumatology (SIR) from 2007 to 2010 and from 2013 up to now. He is also a member of American College of Rheumatology (ACR).

Professor Doria has organised over ten international conferences on autoimmunity and was involved as “expert” in the European League Against Rheumatism (EULAR) Standing Committee for the development of clinical and therapeutic recommendations: (1) EULAR recommendations for the management of systemic lupus erythematosus (SLE)—Assessment of the SLE patient (2008–2009); (2) EULAR recommendations for the management of SLE Part II—Neuropsychiatric disease (2008–2009); (3) Joint EULAR and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis (2012). Professor Doria is a member of the Lupus Academy Steering Committee and co-Chaired the 4th Annual Meeting held in Rome 27th February to 1st March 2015. He will also chair the 10th European Lupus Meeting which will be held in Venice (Italy) 5–8th October 2016.

Professor Doria is on the Editorial Boards of several rheumatology and immunology journals, including *Lupus*, *Autoimmunity*, *Clinical and Experimental Rheumatology*, *Autoimmunity Reviews*, *Journal of Autoimmunity*, *Experimental Biology and Medicine*, *Rheumatology Reports*, *Journal Autoimmunity Highlights* and *Reumatismo* (the official journal of Italian Society of Rheumatology).

He has authored over 250 ISI publications on SLE and other connective tissue diseases. These include clinical studies describing new manifestations or subgroups of autoimmune disorders, prognostic risk factors, diagnostic tests and therapeutic interventions, as well as immunochemical studies that evaluate autoantibodies, epitopes and complementary epitopes of autoantigens. In addition, he has authored and co-authored three books, over 90 book chapters and conference proceedings, and over 500 abstracts for national and international conferences.

Professor Doria has a long-standing experience in the clinical management of patients with connective tissue diseases. The Unit in which he works is a tertiary referral rheumatology centre, within Italy, for the diagnosis and management of patients affected with systemic connective diseases. In addition, he has expertise in the management and follow-up of pregnant patients with systemic rheumatic diseases. Professor Doria has also trained over 30 students in Rheumatology.



**Professor Dragomir Marisavljevic, MD, PhD**

Bežanijska Kosa, University Medical Center, Belgrade University, Serbia

Dragomir Marisavljevic is the Chief of the Haematology Department, Professor of Internal Medicine, and a Senior Scientific Advisor at the Bežanijska Kosa, University Medical Center of Belgrade University, Serbia.

Kosa in 2000. Prior to his current positions, Professor Marisavljevic was a Deputy Minister in the Serbian Government from 2002 to 2004.

Professor Marisavljevic has participated in many research projects involving the pathology of haematopoietic stem cells, and from 2006 to 2010 and 2011 to 2016 he was Principal Investigator in scientific projects on the multidisciplinary study of antiphospholipid syndrome, supported by Government of Serbia. He was also Principal Investigator of numerous clinical trials and co-authored more than 400 books, text book chapters and publications in both international and domestic journals.

**Disclosures**

None

Professor Marisavljevic graduated in 1984 from the School of Medicine, University of Belgrade, as the class valedictorian, before continuing postgraduate studies with support from the Serbian Academy of Arts and Sciences. In 1987 he joined the Institute of Haematology, Clinical Centre of Serbia in Belgrade. He passed his Board Exam in Internal Medicine, becoming a specialist in 1993, before completing his PhD thesis “Evolution of primary myelodysplastic syndromes” and joining Bežanijska



**Professor Ljudmila Stojanovich, MD, PhD**

Bežanijska Kosa, University Medical Center, Belgrade University, Serbia

Ljudmila Stojanovich is the Scientific Director and Research Professor at the Bežanijska Kosa, University Medical Center of Belgrade University, Serbia. Professor Stojanovich received her MD from the Russian Federation in 1978, and continued postgraduate studies in Institute of Rheumatology, Academy of Medical Sciences, Moscow, Russian Federation, under Professor V. Nasonova, from 1984 to 1990. From 1990 to 1994 she finished nostrification of diplomas in Belgrade University Medical School, Serbia/Yugoslavia, where she also completed her PhD in Medicine, with the thesis “Neuropsychiatric manifestations in patients with Systemic Lupus Erythematosus” in 1999.

Antiphospholipid Antibodies/Catastrophic form”, “Multicenter studies on antiphospholipid antibodies, infections and autoimmune diseases”. She is a mentor to and supervises a number of post-doctoral students.

Professor Stojanovich has longstanding experience in the clinical management of patients with autoimmune rheumatic diseases, including SLE, APS and allied diseases.

Professor Stojanovich has been an invited speaker at numerous international meetings; she is a member of the Steering Committee of the “European League Against Rheumatism (EULAR) recommendations for vaccination in patients with Auto-Immune Inflammatory Rheumatic Diseases (AIIRD)”, and EULAR Honorary Member; Chairman of the International Congress “Antiphospholipid syndrome (Hughes syndrome) importance of multidisciplinary approaches 30 years since definition”, 2013; “GRANT 2015” of the EUROPEAN STROKE CONFERENCE for “excellent research in cerebrovascular diseases reviewed by the Scientific and programmer Committees”, and others. She is an Investigator in several clinical trials, including patients with SLE.

**Disclosures**

None

Professor Stojanovich’s research interests include systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), and vaccination in patients with autoimmune rheumatic diseases. She is an Author of three monographs and about 250 articles on various aspects of autoimmune rheumatic disorders, published in both international and domestic journals and in conference proceedings. She is on the editorial boards and reviewer for numerous journals. She is also a member of a number international projects, including “the European Forum on



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## Diagnostic challenges in SLE and APS

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Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), or Hughes syndrome, are probably the most important paradigm of systemic autoimmune disease. Lupus is known as “the great imitator”, because its symptoms mimic many other illnesses. Early diagnosis is critical in avoiding major organ damage; however, the lack of a gold standard test to confirm diagnosis often results in delayed diagnosis or misdiagnosis. According to the classification by the American College of Rheumatology (ACR), four of the 11 criteria have to be positive for a diagnosis of SLE.<sup>1</sup> The Systemic Lupus International Collaborating Clinics (SLICC) group, after 8 years of work, decided to address concerns about the inclusion of many cutaneous, cardiac and neurological manifestations, which were not part of the ACR classification.<sup>2</sup> However, low complement levels are still omitted in the new set of classification criteria for SLE. These criteria were noted to be more sensitive but less specific than the ACR criteria; they also resulted in fewer misclassifications of patients.

Although APS is now a well-described difficult-to-diagnose entity, it took many decades to define the diagnostic criteria. The latest classification criteria for diagnosing APS are the 2006 Sapporo criteria that require the presence of at least one clinical manifestation and one positive laboratory criterion.<sup>3</sup> Following the application of the Sapporo criteria, controversy arose because those criteria identify a more homogeneous group of APS patients at the expense of excluding another, a group collectively referred to as seronegative APS.<sup>4</sup> The need for more guidelines regarding the detection of lupus anticoagulant is now fulfilled by the updated Scientific Standardization Committee guidelines.<sup>5</sup> There are recent studies present on the most promising antibodies of this heterogeneous APS family.<sup>6</sup> Nowadays, APS is increasingly recognised as a multisystem disease, the clinical expression of which may include (many non-criteria APS) cardiac, neurological, haematological, cutaneous and other manifestations.<sup>7</sup> Special attention should be given to secondary APS patients when they are subject to high-risk events: 7–10% of primary APS patients may go on to develop secondary APS with SLE. Despite updates of the diagnostic criteria, the diagnosis of SLE and APS remains difficult.

### Learning Objectives

**At the end of the presentation, participants will be able to:**

- Recognise the heterogeneous clinical aspects of the different subtypes of SLE and APS.
- Understand the difference in immunology and pathology of the onset of SLE and APS.
- Discuss the importance of a multidisciplinary approach in correct diagnosis SLE and APS patients.
- Understand how to approach non-criteria and seronegative SLE and APS.
- Recall the SLE and APS classification criteria, risk stratification and unmet treatment needs.





**Professor Andrea Doria, MD**  
University of Padova, Italy

## New trends in the treatment of SLE

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1. Doria A, Iaccarino L, Ghirardello A, et al. Long-term prognosis and causes of death in systemic lupus erythematosus. *Am J Med* 2006; 119(8): 700-6.
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Survival of patients with systemic lupus erythematosus (SLE) has improved dramatically over the last few decades; however, patients with SLE still display a four-to-five fold higher standardised mortality rate compared with the general population.<sup>1</sup> Persistent disease activity and drug side effects, especially with corticosteroids, are responsible for increased organ damage, which in turn is predictive of more damage and death.<sup>2</sup> Accordingly, reducing disease activity and sparing corticosteroid use are unmet needs in the management of SLE patients.<sup>3</sup>

In meeting these needs, new biologic agents are proving to be very promising, since when added to the standard of care they appear to reduce disease activity and spare the need for corticosteroids. Belimumab is currently the only biologic agent approved for SLE, following successful completion of two randomised controlled trials (RCTs) in which it met the primary end points and was well tolerated.<sup>4,5</sup> Post-hoc analyses revealed that patients with higher disease activity and musculoskeletal and skin manifestations are the best responders to belimumab.<sup>6</sup> However, these indications are not sufficient for optimal use of the drug. Thus, further data coming from clinical practice settings are welcome. Conversely, the biologic rituximab was not approved for SLE due to the failure of two RCTs. However, due to its effectiveness in open-label studies and registries,

rituximab continues to be used in daily clinical practice in SLE patients with severe and refractory manifestations.

In order to optimise disease outcomes, we can also use new therapeutic strategies. Treat-to-target seems to be very promising, with major targets including disease remission and low disease activity. We know that remission and low disease activity are associated with better outcomes and prolonged survival.<sup>2,7</sup> However, no widely accepted definitions of remission and low disease activity are available to date.

From a clinical perspective, we can define clinical remission as the absence of signs and symptoms or urinary and haematological abnormalities due to the immune pathways involved in the disease in patients who are corticosteroid free and in clinical-serological remission. In other words, complete remission can be defined as a clinical-serological healing in patients who are free of any treatment. However, complete remission is often hard to accomplish for the majority of patients with SLE, whereas clinical remission without corticosteroids or with a minimal dose of corticosteroids could be acceptable alternative targets. Low disease activity, even with low dose steroids, may also be a reasonable target in order to minimise development of organ damage.<sup>8</sup>





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

## New trends in the treatment of APS

Currently, there is consensus on treating patients with antiphospholipid syndrome (APS) and thrombosis with long-term oral anticoagulation, and to prevent obstetric manifestations with the use of aspirin and heparin. These recommendations are based on randomised controlled trials and observational studies. Despite of this body of evidence, there are grey areas where knowledge is scarce or does not exist. In other words, there is a subset of patients whose APS is difficult to manage. Some examples include patients with “seronegative” APS, those who do not display formal (clinical or laboratory) classification criteria for APS, and

those with recurrent thrombotic events despite optimal anticoagulation. In addition, there are those patients with clinical manifestations that are not included in the current classification criteria, such as haematologic manifestations (thrombocytopenia and haemolytic anaemia), neurologic manifestations (chorea, myelitis or multiple sclerosis-like lesions), nephropathy and heart valve disease associated with antiphospholipid antibodies, and those selected cases of thrombotic APS where anticoagulant treatment is withdrawn when antiphospholipid antibodies have become persistently negative.

### Learning Objectives

**At the end of the presentation, participants will be able to:**

- Recognise the main unmet needs in the management of the APS.
- Describe the current recommendations for the treatment of thrombotic and obstetric manifestations of APS.
- Discuss the alternative options for the management of difficult APS cases.
- Discuss new trends in research on new therapies for APS.





## Case Study Workshops

**Friday 18th March 2016**

### Parallel Case Study Workshops

*Moderator: Andrea Doria (Italy)*  
Neurologic and cardiovascular SLE/APS



Ljudmila Stojanovich (*Serbia*)

*Moderator: Ricard Cervera (Spain)*  
Haematologic challenges: Cytopenias



Dragomir Marisavljevic (*Serbia*)

### Please Note

These workshops will be held in breakout rooms. Please follow the appropriate signs/symbols corresponding to the workshops you are registered to attend.



**Moderator:** Professor Andrea Doria (Italy)

**Presenter:** Professor Ljudmila Stojanovich (Serbia)

## Neurological and cardiovascular SLE/APS



### **Case study 1: Status post-multifocal cerebral infarction with chorea and cognitive dysfunction.**

A 30-year-old Caucasian male has had a previous diagnosis of autoimmune haemolytic anaemia, and was maintained on prednisone 60 mg/d. Three years ago he developed neurological symptoms, including hemiparesis, chorea, cranial neuropathies (optic neuritis) and cognitive impairments (but no motor deficits).

The patient was admitted to hospital, and his diagnostic work-up showed thrombocytopenia, leukopenia, positive ANA, anti-dsDNA hypocomplementemia and aPL (LA, aCL at high titres). His MRI showed grey matter lesions (an axial T-w image shows left and right infarctions). A diagnosis of systemic lupus erythematosus (SLE) and secondary antiphospholipid syndrome (APS) was made.

The patient received high-dose steroids with monthly pulses of cyclophosphamide, followed by steroids and hydroxychloroquine with adequate anticoagulation therapy. This resulted in the normalization of haematological indicators, and in the disappearance of neurological symptoms.

The patient's lupus was controlled well with low-dose aspirin, prednisone and hydroxychloroquine for a few years. Unfortunately, he stopped taking his medication. During a follow-up visit after two years, the patient mentioned the reappearance of his haematological symptoms with fever, fatigue, neutropenia with nephrotic-range proteinuria, and haematuria with normal creatinine. A kidney biopsy showed mixed World Health Organization (WHO) class II and class III glomerulonephritis. He was treated with 6-monthly IV cyclophosphamide infusions, followed with mycophenolate mofetil. A few months later the patient was in a stable condition.

**Discussion points:** *A difficult diagnosis of a man with a complex of CNS neuropsychiatric SLE and secondary APS, but without classical SLE manifestations: skin, serositis or arthritis.*

### **Case study 2: Neuropsychiatric multisystem manifestations, including severe autonomic nervous system dysfunction in SLE with Catastrophic APS (CAPS).**

A 47-year-old Caucasian female patient had been a long time smoker. She was previously diagnosed with different subtypes of cutaneous lupus erythematosus, and for 18 years received antimalarials with permanently low doses of steroids, prescribed by a dermatologist. The patient had five miscarriages, and inferior superficial thrombophlebitis in the extremities, as well as an abdominal aortic bypass due to occlusion.

In 2013, the patient was seen by a rheumatologist for the first time, and was admitted to hospital. Symptoms at the time included malar rash, polyarthritis, lymphadenopathy, headache (thrombocytopenia, neutropenia, ANA, anti-dsDNA, and hypocomplementemia, LA, aCL at high titres). Diagnosis of SLE and secondary APS was made, and the patient was prescribed corticosteroids, hydroxychloroquine and low-dose aspirin. She remained stable over the following months, but then discontinued therapy voluntarily.

The patient's condition worsened 6 months after discontinuing treatment: bilateral ischaemia and gangrene of both feet occurred suddenly, necessitating amputations of a few toes of both feet. Cerebral micro thrombi were diagnosed on MRI scans. Pulmonary micro thrombosis and acute respiratory distress syndrome then supervened with bilateral infiltrates, accompanied by pleural effusions (MSCT). Five days later her clinical progression was marked by the development of neuropsychiatric multisystem manifestations, including CNS lupus (seizures and stroke: EEG, MRI), and signs of severe autonomic nervous system dysfunction (parasympathetic and sympathetic), which was diagnosed by applying cardiovascular reflex tests according to Ewing. The patient presented acutely to the Emergency

Department and was diagnosed with CAPS (Asherson's syndrome) with pulmonary micro thrombosis (MSCT), chronic venous insufficiency, and peripheral arterial thrombosis. Intravenous pulses of steroids were again administered together with IV pulses of cyclophosphamide, IV heparin, infusions of frozen plasma and IV immunoglobulin. Following 16 hours of this therapy, the patient suddenly died.

**Discussion points:** *History of several years of moderate SLE, treated with antimalarials with permanently low doses of steroids, which the patient discontinued on several occasions, with the final diagnosis being CAPS.*

*What were the precipitating factors for CAPS in this patient: infection, discontinuation of prescribed therapy, cigarette smoking, or surgical procedure?*

### **Case study 3: Unrecognised SLE leading to severe neurological and cardiovascular manifestations.**

A 52-year-old Caucasian female was admitted to the critical care unit with symptoms and signs of non-ST elevation acute myocardial infarction as a first manifestation of coronary artery disease. Previously, at the age of 34 she had her first transient ischaemic attack (TIA) and 4 years later another neurological attack. Her MRI after her second TIA showed cerebral grey matter lesions (an axial T-w image shows left and right infarctions). She has been a smoker for several years. By the time of coronary artery disease development the possibility of systemic autoimmune disease had not been taken into account. Coronary angiography was performed and revealed no significant lesions on the epicardial coronary arteries but myocardial necrosis as the consequence of coronary artery thrombosis with spontaneous thrombolysis. A transthoracic echocardiography exam showed normal dimensions of cardiac chambers, with hypokinetic basal segments of lateral, anterior and inferior wall of the left ventricle the ejection fraction of which was estimated at 45%. Also, mitral valve regurgitation 2+ was revealed with no pericardial effusion.

Presence of previous neurological stigmata with this specific occurrence of coronary artery disease led to suspicion of APS. Therefore, during this hospitalisation the patient was seen by the rheumatologist for the first time. Livedo reticularis presence was noted as well as exanthema, bilateral ankle oedema and SLE with secondary APS was suspected.

Outpatient diagnostic work-up showed normal blood count with positive ANA and high titres of aPL (aCL IgG and  $\beta$ 2 GPI IgG). A diagnosis of SLE and secondary APS was made. She is also carrier of the MTHFR mutation (homozygote) and PAI 1 (heterozygote). A kidney biopsy was not performed due to preserved functionality.

The patient's lupus was controlled well with low-dose aspirin, prednisone and hydroxychloroquine with oral anticoagulation therapy. During a follow-up visit after 4 years, the patient is without any cardiac or neurological symptoms with complete stabilization of haematologic parameters.

**Discussion points:** *Unrecognized SLE and secondary APS in female of young age and low prevalence of standard atherosclerotic risk factors led to repeated neurological and cardiovascular manifestations.*

### **Case study 4: Acute myocardial infarction development in male SLE patient: multidisciplinary approach saving lives.**

A male Caucasian patient, and long time smoker, had been diagnosed with SLE at the age of 39; he was previously treated with antimalarials for cutaneous lupus erythematosus. Four years after, at the age of 43, he developed acute myocardial inferior infarction with ST elevation, and was successfully treated at that point with thrombolytic therapy. Transthoracic echocardiography revealed normal dimensions of the cardiac chambers with akinesis of the inferior wall of the left ventricle and preserved ejection fraction of 60%. Valves were functional, without vegetations and pericardial effusion has not been revealed. Corticosteroid therapy has been continued during this hospitalisation along with antimalarials, dual antiplatelet therapy (aspirin and clopidogrel), statins and beta blockers. Under the care of the rheumatologist, the patient was discharged in stable state with no residual ischaemia of the myocardium.

Twenty days later the patient was admitted to hospital again, but this time with signs and symptoms of the septic state, hypotension, malar rash and pleural effusion, toxic granulations in neutrophils with thrombocytopenia and leukopenia. He was successfully treated with pulses of steroids and antibiotics, along with the rest of the prescribed cardiac therapy, and discharged in stable condition.

*Continued over*



## Case Study Workshop

During the following 7 years he remained under the care of the rheumatologist, cardiologist, and neurologist – due to symptomatic episode with no ischaemic or the thrombotic lesions of the CNS on repeated MRI scans. He is now treated with low dose corticosteroids and antimalarials along with the vigorous control of the standard atherosclerotic risk factors. Suspicion of secondary APS has not been confirmed.

**Discussion points:** *Patients with SLE in the settings of known accelerated atherosclerosis are in special need for multidisciplinary approach. Special attention towards standard atherosclerotic risk factors reduction is of high importance.*

### Learning Objectives

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

- Understand the importance of the first symptoms of SLE and APS in young patients.
- Discuss the importance of a multidisciplinary approach for the correct diagnosis SLE and APS patients.
- Understand the importance of taking a more aggressive approach towards prevention and control of standard atherosclerotic risk factors in this subgroup of patients.
- Identify the best candidates for early intervention, especially patients with presence of cardiac manifestations that may be a risk factor for several types of CNS involvement in SLE/APS.



**Moderator:** Professor Ricard Cervera (Spain)

**Presenter:** Professor Dragomir Marisavljevic (Serbia)

## Haematologic challenges: Cytopaenias



### Case study 1

A 45-year-old Caucasian female patient presented in September 1991 with a 2-week history of fatigue, headache and subtle cognitive impairments, but without motor deficits. Her background history included Raynaud's Syndrome, diagnosed 4 years earlier, and during the last year she noticed polyarthralgia, face erythema, hair loss and photosensitivity. She had an early miscarriage 5 years ago, then one pregnancy with healthy child birth followed by eight more miscarriages (in the first and second trimesters).

Investigations revealed severe anaemia, mild thrombocytopenia, indirect hyperbilirubinaemia, elevated LDH, low haptoglobin, positive Coombs test, ESR 40, ANA 1:40, positive anti-dsDNA, positive LA, beta-2 GP1 Ab positive in medium titer, normal urinary sediment and urine negative for protein. She was diagnosed with haemolytic anaemia, systemic lupus erythematosus (SLE), secondary antiphospholipid syndrome (APS) and treated with prednisolone, azathioprine and antiplatelet drugs for 6 months. After that low dose prednisolone, antiplatelet drugs and hydroxychloroquine were prescribed.

Twenty years later more intensive cognitive impairments without motor deficits reoccurred. In that time an MRI showed lacunar ischaemic changes. MSCT panarteriography was revealed an abdominal aortic aneurysm of 2.2 cm in length with organised thrombus with level of ANA 1:80. Treatment included hydroxychloroquine, dual antiplatelet therapy, prednisolone, cyclophosphamide pulses, and a tricyclic antidepressant.

**Objective:** *Dominant clinical manifestations of antiphospholipid syndrome, long SLE history and low ANA.*

### Case study 2

A 26-year-old Caucasian female, and mother of a 4-year-old daughter, was diagnosed with SLE in 1997 based on the presence of photosensitivity, asymmetric non-erosive arthritis of small hand joints, occasional mouth ulcers and positive ANA (1/32).

She was treated with oral corticosteroids (20 mg) and hydroxychloroquine. Despite symptoms like fatigue, non-erosive polyarthritis, and mild leukopenia and anaemia, prednisolone dose was reduced to 5 mg/day after few months with prescription of NSAIDs as required and hydroxychloroquine.

Five years after diagnosis she was admitted to hospital due to fever and acute symptoms of tenderness, swelling and redness of the left knee joint. Laboratory results showed low neutrophil count (WBC  $1.7 \times 10^9/l$ ), ANA + (1/640) homogenous, positive anti-dsDNA, ESR 95, low C3/4, high CRP. She was treated with parenteral antibiotics and *Staphylococcus aureus* was isolated in the pus obtained by incision of the knee. After that she was treated with an adequate dose of steroids (methylprednisolone pulses) and her septic condition was resolved.

**Objective:** *If SLE is not adequately treated, complications like sepsis and severe disease manifestations could be expected.*

### Case study 3

A 41-year-old female presented in November 2008 with spontaneous bruising and complaining that she had been forgetful for some time. Her history included episode of pericarditis and pleurisy 3 months prior, malar rash, intermittent arthralgia and occasionally a low platelet count was noted. She also had two previous miscarriages. Investigations revealed low platelet count of  $11 \times 10^9/l$  (normal above  $140 \times 10^9/l$ ), ANA 1/20, ESR 25, positive LA, positive aCI IgM in medium titer, normal urine sediment and no proteinuria. MRI revealed one small lacunar ischaemic change. Platelet sequestration test revealed premature splenic platelet sequestration.







