Antibodies against Phospholipids

for Diagnosis of the Anti-Phospholipid-Syndrome

Thomas Büttner

Product Manager

MEDIPAN

GA Generic Assays

- Situated near Berlin
- Founded 1992 Medipan, 2002 GA
- About 80 employees
- Manufacturer of test systems for autoimmune diagnostics

Anti-Phospholipid-Syndrome

Definition

The Anti-Phospholipid Syndrome (APS) is one of the most common autoimmune diseases.

The disease is characterized by the appearance of specific antibodies against various phospholipids (e.g. cardiolipins) or phospholipid-binding proteins (e.g. prothrombin or β2-glycoprotein I).

These antibodies cause an increased tendency to coagulate (hypercoagulability) and lead to increased thrombosis.

Anti-Phospholipid-Syndrome

Definition

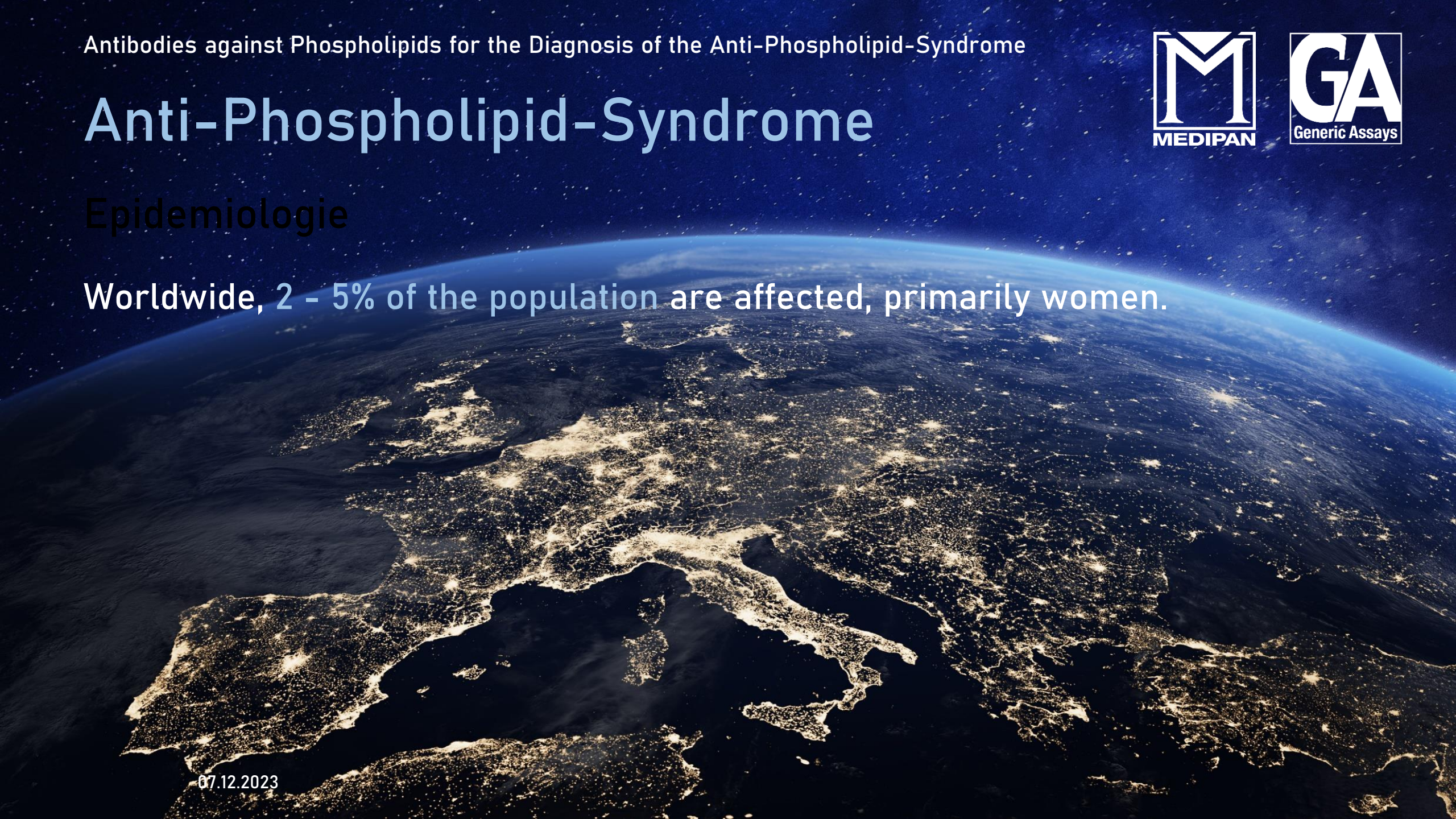
Primary APS (PAPS) Independent from other diseases

Secodary APS (SAPS) occurs in the context of other, mainly autoimmune, diseases (in particular SLE, RA, SjS) or tumours

Anti-Phospholipid-Syndrome

Epidemiologie

Worldwide, 2 - 5% of the population are affected, primarily women.



Anti-Phospholipid-Syndrome

Clinical Symptoms

The clinical picture is characterized by

- an increased occurrence of thromboses and embolisms as well as pulmonary embolisms, heart attacks, strokes, renal infarctions, etc.,
- bleeding and ulcers of the skin (purpura),
- miscarriages and early abortions

- most severe impact: catastrophic APS (CAPS), extensive thromboses in small vessels that supply multiple organs

Anti-Phospholipid-Syndrome

Therapy

The treatment of asymptomatic patients consists of thrombosis prophylaxis, e.g. with acetylsalicylic acid or hydroxychloroquine.

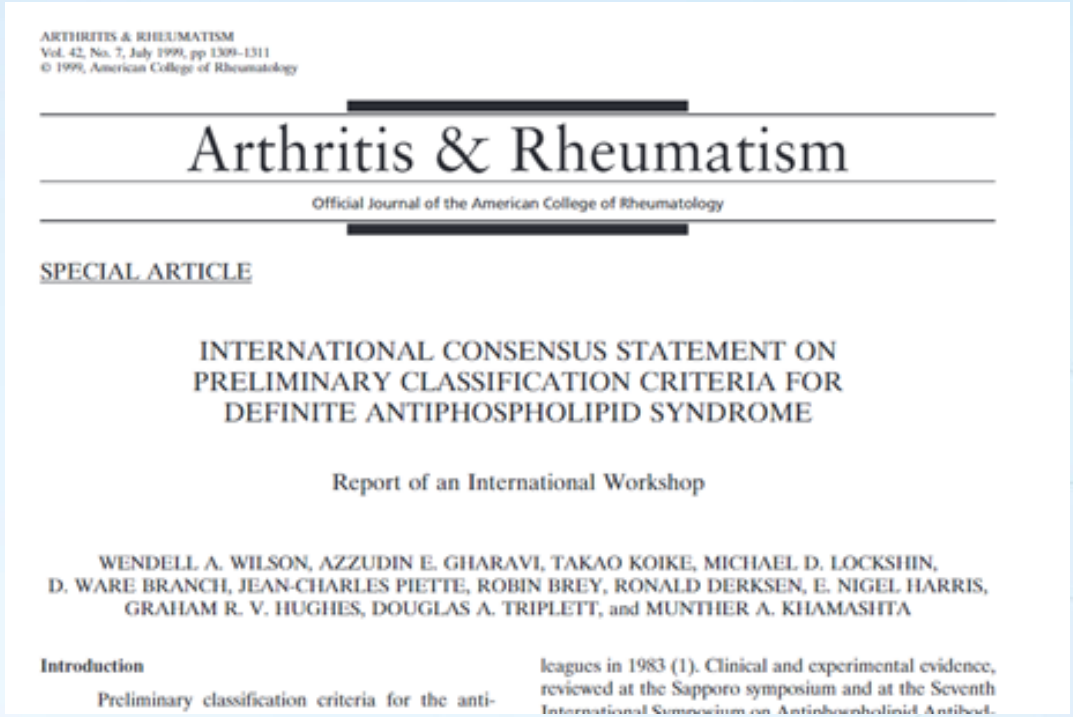
After a thrombosis, the more effective anti-coagulant therapy is the administration of vitamin K antagonists such as phenprocoumon (Marcumar®, Falithrom®).

If necessary, the lifelong therapy is supported by the administration of immunosuppressants.

Anti-Phospholipid-Syndrome

Classification of Disease

Sapporo criteria, 1999



ARTHRITIS & RHEUMATISM
Vol. 42, No. 7, July 1999, pp 1309–1311

Arthritis & Rheumatism

Official Journal of the American College of Rheumatology

SPECIAL ARTICLE

INTERNATIONAL CONSENSUS STATEMENT ON PRELIMINARY CLASSIFICATION CRITERIA FOR DEFINITE ANTIPHOSPHOLIPID SYNDROME

Report of an International Workshop

WENDELL A. WILSON, AZZUDIN E. GHARAVI, TAKAO KOIKE, MICHAEL D. LOCKSHIN, D. WARE BRANCH, JEAN-CHARLES PIETTE, ROBIN BREY, RONALD DERKSEN, E. NIGEL HARRIS, GRAHAM R. V. HUGHES, DOUGLAS A. TRIPLETT, and MUNTHER A. KHAMASHTA

Introduction

Preliminary classification criteria for the anti- leagues in 1983 (1). Clinical and experimental evidence, reviewed at the Sapporo symposium and at the Seventh International Symposium on Antiphospholipid Antibod-

Anti-Phospholipid-Syndrome

Classification of Disease

Sapporo criteria, 1999

- Presence of clinical symptoms

- One or more episodes of arterial, venous or small-vessel thrombosis in any tissue or organ; confirmation by imaging or histopathological procedures
- Pregnancy diseases (stillbirths, premature births, spontaneous abortions)

- Laboratory parameter

- Cardiolipin antibodies of IgG and/or IgM type, medium or high titre measured by a standardised, β2-glycoprotein-dependent ELISA
- Positive Lupus anticoagulant in plasma,

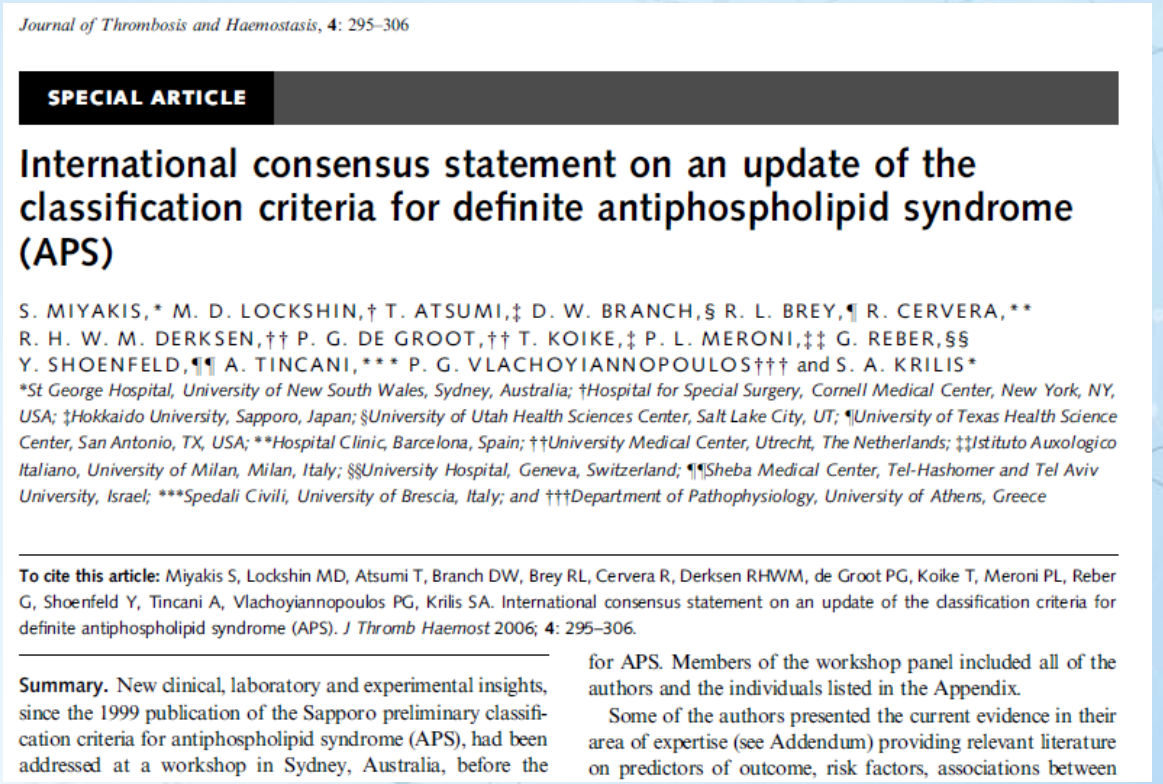
- detection at two or more points in time at least 6 weeks apart;

Anti-Phospholipid-Syndrome

Classification of Disease

Sapporo criteria, 1999

Revised criteria Sydney, 2004



Journal of Thrombosis and Haemostasis, **4**: 295–306

SPECIAL ARTICLE

International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)

S. MIYAKIS,* M. D. LOCKSHIN,† T. ATSUMI,‡ D. W. BRANCH,§ R. L. BREY,¶ R. CERVERA,** R. H. W. M. DERKSEN,†† P. G. DE GROOT,†† T. KOIKE,‡ P. L. MERONI,‡‡ G. REBER,§§ Y. SHOENFELD,¶¶ A. TINCANI,*** P. G. VLACHOYIANNOPOULOS††† and S. A. KRILIS*

**St George Hospital, University of New South Wales, Sydney, Australia; †Hospital for Special Surgery, Cornell Medical Center, New York, NY, USA; ‡Hokkaido University, Sapporo, Japan; §University of Utah Health Sciences Center, Salt Lake City, UT; ¶University of Texas Health Science Center, San Antonio, TX, USA; **Hospital Clinic, Barcelona, Spain; ††University Medical Center, Utrecht, The Netherlands; ‡‡Istituto Auxologico Italiano, University of Milan, Milan, Italy; §§University Hospital, Geneva, Switzerland; ¶¶Sheba Medical Center, Tel-Hashomer and Tel Aviv University, Israel; ***Spedali Civili, University of Brescia, Italy; and †††Department of Pathophysiology, University of Athens, Greece*

To cite this article: Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RHWM, de Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006; **4**: 295–306.

Summary. New clinical, laboratory and experimental insights, since the 1999 publication of the Sapporo preliminary classification criteria for antiphospholipid syndrome (APS), had been addressed at a workshop in Sydney, Australia, before the for APS. Members of the workshop panel included all of the authors and the individuals listed in the Appendix.

Some of the authors presented the current evidence in their area of expertise (see Addendum) providing relevant literature on predictors of outcome, risk factors, associations between

Anti-Phospholipid-Syndrome

Classification of Disease

Sapporo criteria, 1999

Revised criteria Sydney, 2004

- Additional Laboratory parameter

- Positive detection of antibodies to β2GPI of the IgG and/or IgM type at least twice in serum or plasma with a titre level above the 99th percentile is to be classified as a laboratory analytical criterion for APS using standardised ELISA.

- Check-up after initial antibody detection should be carried out at least every 12 weeks (instead of the previous 6 weeks)

Anti-Phospholipid-Syndrome

Classification of Disease

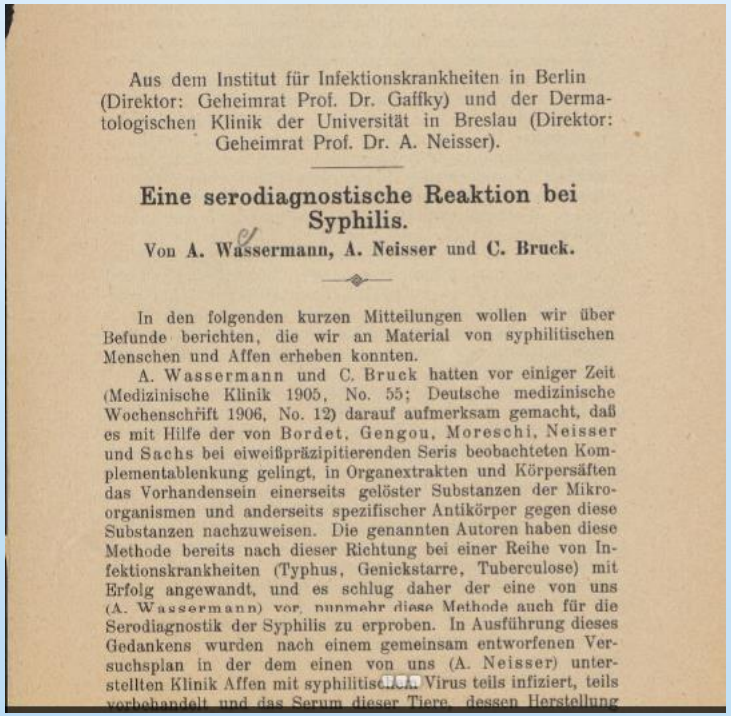
Detection of antibodies necessary for classification of Anti-Phospholipid syndrome beside clinical symptoms

Differentiation from other thrombophilic events !

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1906: reaction of sera from Syphilis patients with preparation from bovine heart (Cardiolipin) – complement fixation



Aus dem Institut für Infektionskrankheiten in Berlin (Direktor: Geheimrat Prof. Dr. Gaffky) und der Dermatologischen Klinik der Universität in Breslau (Direktor: Geheimrat Prof. Dr. A. Neisser).

Eine serodiagnostische Reaktion bei Syphilis.

Von **A. Wassermann, A. Neisser** und **C. Bruck.**

In den folgenden kurzen Mitteilungen wollen wir über Befunde berichten, die wir an Material von syphilitischen Menschen und Affen erheben konnten.

A. Wassermann und C. Bruck hatten vor einiger Zeit (Medizinische Klinik 1905, No. 55; Deutsche medizinische Wochenschrift 1906, No. 12) darauf aufmerksam gemacht, daß es mit Hilfe der von Bordet, Gengou, Moreschi, Neisser und Sachs bei eiweißpräzipitierenden Seris beobachteten Komplementablenkung gelingt, in Organextrakten und Körpersäften das Vorhandensein einerseits gelöster Substanzen der Mikroorganismen und anderseits spezifischer Antikörper gegen diese Substanzen nachzuweisen. Die genannten Autoren haben diese Methode bereits nach dieser Richtung bei einer Reihe von Infektionskrankheiten (Typhus, Genickstarre, Tuberculose) mit Erfolg angewandt, und es schlug daher der eine von uns (A. Wassermann) vor, nunmehr diese Methode auch für die Serodiagnostik der Syphilis zu erproben. In Ausführung dieses Gedankens wurden nach einem gemeinsam entworfenen Versuchsplan in der dem einen von uns (A. Neisser) unterstellten Klinik Affen mit syphilitischem Virus teils infiziert, teils vorbehandelt und das Serum dieser Tiere, dessen Herstellung

Professor August von Wassermann

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1946: Further development of the Wassermann test by Harris, Rosenberg and Riedel

Veneral disease Research Laboratory (VDRL Test)

⟶ formation of anti-Cardiolipin Antibodies following the Treponema infection

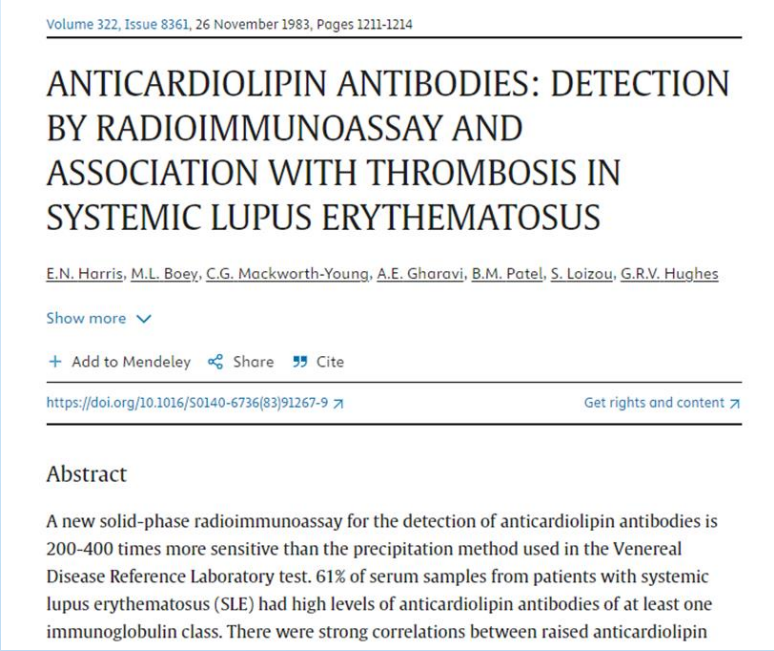
Later: false positive VDRL tests in patients with

- Collagenoses (especially Systemic Lupus erythemtosus)
- other infections: Lepra, Mononucleosis infectiosa, Virus hepatitis

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1980s: solid-phase assays for the detection of anti-phospholipid antibodies



Volume 322, Issue 8361, 26 November 1983, Pages 1211-1214

ANTICARDIOLIPIN ANTIBODIES: DETECTION BY RADIOIMMUNOASSAY AND ASSOCIATION WITH THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

E.N. Harris, M.L. Boey, C.G. Mackworth-Young, A.E. Gharavi, B.M. Patel, S. Loizou, G.R.V. Hughes

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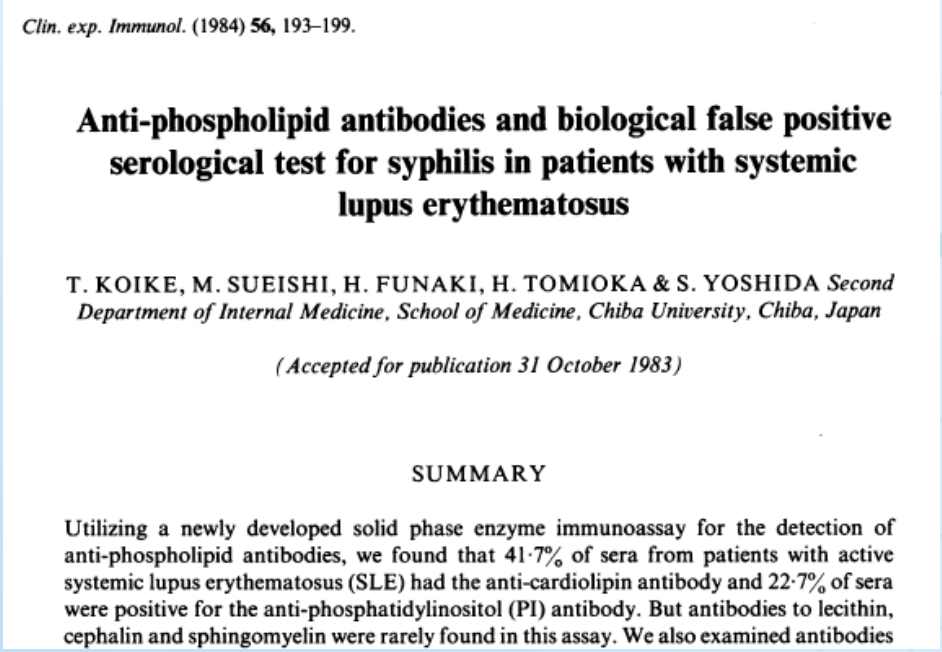
https://doi.org/10.1016/S0140-6736(83)91267-9 Get rights and content

Abstract

A new solid-phase radioimmunoassay for the detection of anticardiolipin antibodies is 200-400 times more sensitive than the precipitation method used in the Venereal Disease Reference Laboratory test. 61% of serum samples from patients with systemic lupus erythematosus (SLE) had high levels of anticardiolipin antibodies of at least one immunoglobulin class. There were strong correlations between raised anticardiolipin



Clin. exp. Immunol. (1984) **56**, 193–199.

Anti-phospholipid antibodies and biological false positive serological test for syphilis in patients with systemic lupus erythematosus

T. KOIKE, M. SUEISHI, H. FUNAKI, H. TOMIOKA & S. YOSHIDA *Second Department of Internal Medicine, School of Medicine, Chiba University, Chiba, Japan*

(Accepted for publication 31 October 1983)

SUMMARY

Utilizing a newly developed solid phase enzyme immunoassay for the detection of anti-phospholipid antibodies, we found that 41·7% of sera from patients with active systemic lupus erythematosus (SLE) had the anti-cardiolipin antibody and 22·7% of sera were positive for the anti-phosphatidylinositol (PI) antibody. But antibodies to lecithin, cephalin and sphingomyelin were rarely found in this assay. We also examined antibodies

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1990s: cofactor for anti-phospholipid antibodies in autoimmune diseases

Proc. Natl. Acad. Sci. USA
Vol. 87, pp. 4120–4124, June 1990
Medical Sciences

Anti-phospholipid antibodies are directed against a complex antigen that includes a lipid-binding inhibitor of coagulation: β_2-Glycoprotein I (apolipoprotein H)

(anti-cardiolipin antibodies/lipid–protein complex/thrombosis)

H. Patrick McNeil*, Richard J. Simpson†, Colin N. Chesterman*, and Steven A. Krilis*‡

*University of New South Wales, School of Medicine, Saint George Hospital, Kogarah, 2217 Australia; and †Joint Protein Structure Laboratories, The Ludwig Institute for Cancer Research and The Walter and Eliza Hall Institute for Medical Research, Parkville, 3050 Australia

Communicated by K. Frank Austen, March 15, 1990

ABSTRACT **Anti-phospholipid (aPL) antibodies that exhibit binding in cardiolipin (CL) ELISA can be purified to >95% purity by sequential phospholipid affinity and ion-exchange chromatography. However, these highly purified aPL antibodies do not bind to the CL antigen when assayed by a modified CL ELISA in which the blocking agent does not contain bovine serum, nor do they bind to phospholipid affinity**

We have previously noted that when aCL antibody-containing fractions derived from ion-exchange chromatography of plasma were applied to phosphatidylserine or CL affinity columns, there was no binding of the antibody despite the fact that when plasma containing these antibodies was applied to these columns, aCL antibodies could be purified. This suggested that there was a cofactor also present in

J Immunol. 1992 Jun 15;148(12):3885-91.

Heterogeneity of anticardiolipin antibodies defined by the anticardiolipin cofactor

E Matsuura [1], Y Igarashi, M Fujimoto, K Ichikawa, T Suzuki, T Sumida, T Yasuda, T Koike

Affiliations + expand

PMID: 1602135

Abstract

Anticardiolipin antibodies (aCL) found in sera from patients with SLE react with cardiolipin (CL) in the presence of a 50-kDa serum cofactor. The cofactor, which was identified to be beta 2-glycoprotein I by sequencing the N-terminal amino acids, not only enhances CL binding by antibodies in SLE but also depresses it by antibodies associated with syphilis. Cofactor-dependent binding of aCL in SLE to solid phase CL was competitively inhibited by the simultaneous addition of fluid phase CL but was unaffected by either prior or simultaneous addition of a high excess of the cofactor. Binding of aCL in

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1990s: cofactor for anti-phospholipid antibodies in autoimmune diseases

Ann Ital Med Int. 1993 Jul-Sep;8(3):171-4.

Anti-cardiolipin antibodies in HIV infection are true antiphospholipids not associated with antiphospholipid syndrome

M Falco [1], A Sorrenti, R Priori, F L Luan, V Pittoni, M G Agresti, G Valesini

Affiliations + expand

PMID: 8217481

Abstract

The aim of the present study was to evaluate the fine specificity of anticardiolipin (aCL) antibodies detectable in the sera of patients with HIV infection. aCL are generally associated with thrombotic events in autoimmune diseases. A solid phase ELISA which discriminates between aCL binding to phospholipids and aCL binding to phospholipid/beta 2-glycoprotein I (cofactor) complex was employed. Thirty-nine HIV and 20 aCL positive systemic lupus erythematosus (SLE) sera were examined. In HIV sera, reduced binding to phospholipid was seen if cofactor was added. On the contrary, in SLE-sera the cofactor improved aCL binding. No thrombotic events were recorded in HIV

Differences between antibodies between autoimmunity and infection !

Anti-Phospholipid-Syndrome

History of APS Diagnostics

1990s: cofactor for anti-phospholipid antibodies in autoimmune diseases

J Exp Med. 1994 Feb 1;179(2):457-62. doi: 10.1084/jem.179.2.457.

Anticardiolipin antibodies recognize beta 2-glycoprotein I structure altered by interacting with an oxygen modified solid phase surface

E Matsuura [1], Y Igarashi, T Yasuda, D A Triplett, T Koike

Affiliations + expand

PMID: 7507506 PMCID: PMC2191370 DOI: 10.1084/jem.179.2.457

Free PMC article

Abstract

Anticardiolipin antibodies (aCL) derived from the sera of individuals exhibiting the antiphospholipid syndrome (APS) directly bind to beta 2-glycoprotein I (beta 2-GPI), which is adsorbed to an oxidized polystyrene surface. Oxygen atoms were introduced on a polystyrene surface by irradiation with electron or gamma-ray radiation. X-ray photoelectron spectroscopy revealed the irradiated surfaces

No phospholipids necessary for antibody determination !

Anti-Phospholipid-Antibodies

3 Types of antibodies under the same name!

- Antibodies to phospholipids
- Antibodies to phospholipid.cofactor complexes
- Antibodies to cofactor proteins

Standardisation ?

Anti-Phospholipid-Syndrome

Standardisation ?

E.J. Favaloro (Dept. of Haematology, Institute of Clinical Pathology and Medical Research, Western Sydney Area Health Service, Westmead, NSW, Australia)

RCPA Immunology Newsletters, 5, 2, 2003, pp. 3-6

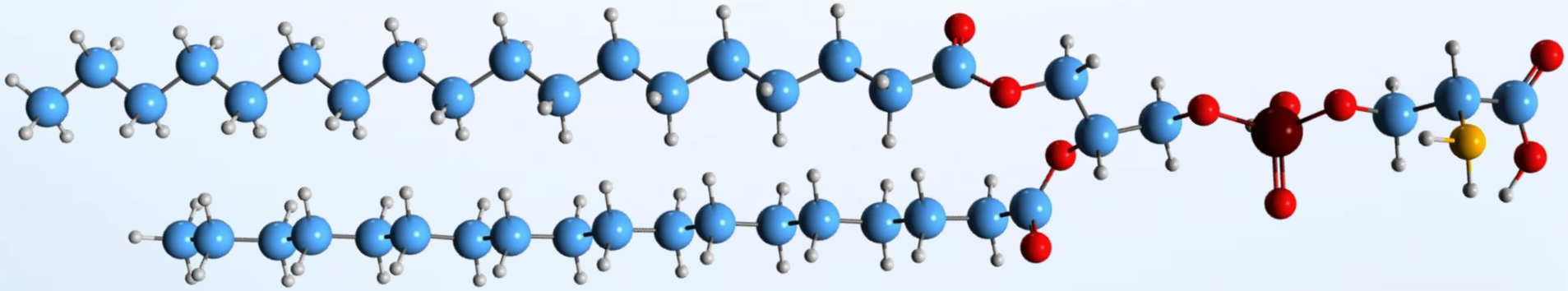
Testing of 7 commercial Anti-Cardiolipin Assays in 56 laboratories (RCPA Quality Assurance Program)

What antibody are we talking about ?

Phospholipids

Structure

Phospholipids, e.g. phosphatidylcholine (lecithin), phosphatidylethanolamine, phosphatidylserine or phosphatidylinositol, are polar, phosphorylated lipids in the cell membrane.



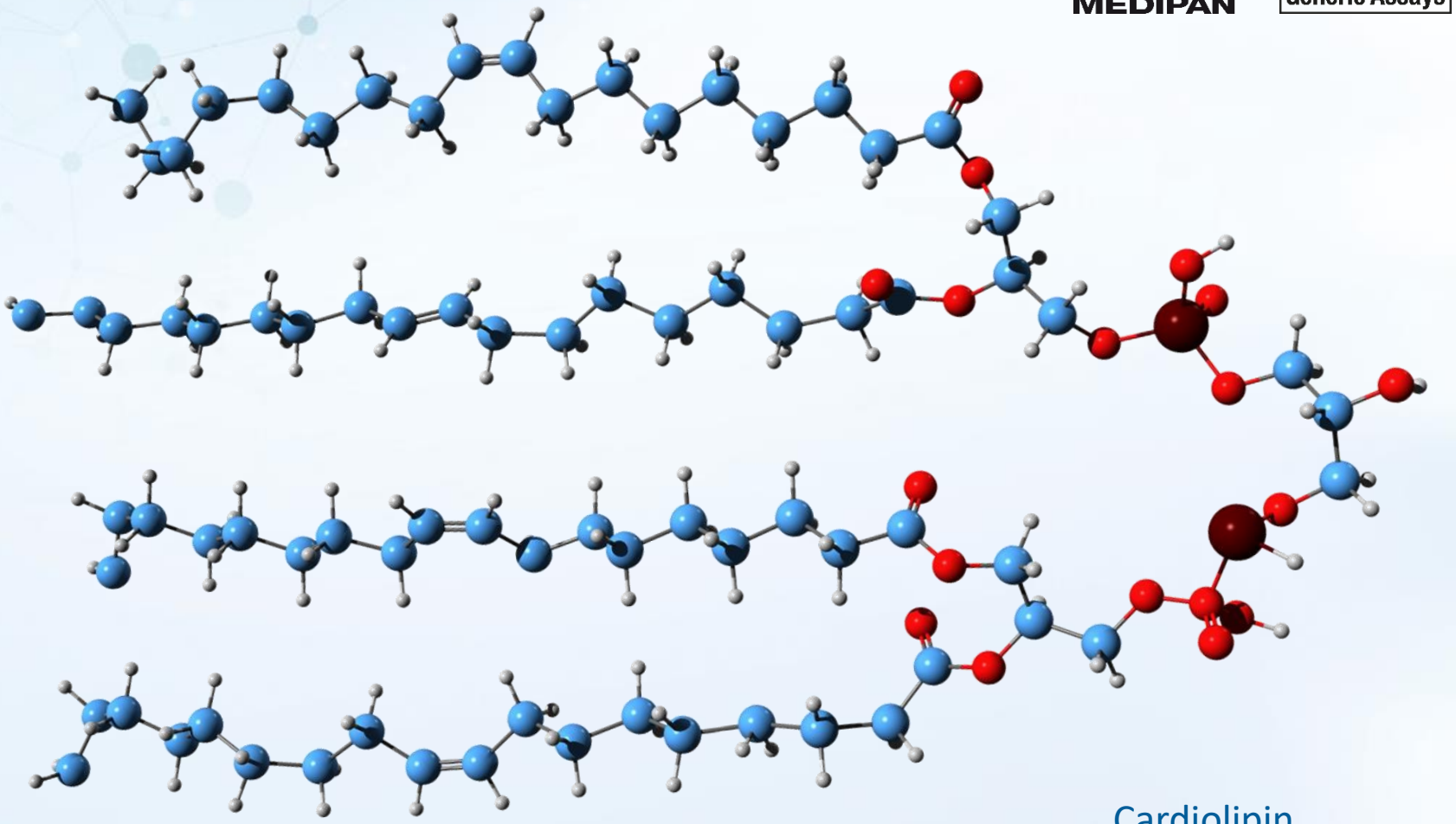
Phosphatidylserin

Cardiolipins

Structure

Cardiolipins are phospholipids with four fatty acid residues.

They are the only phospholipids synthesized in the mitochondria.



Cardiolipin

Antibodies against Phospholipids

Cofactor ß2-glycoprotein I

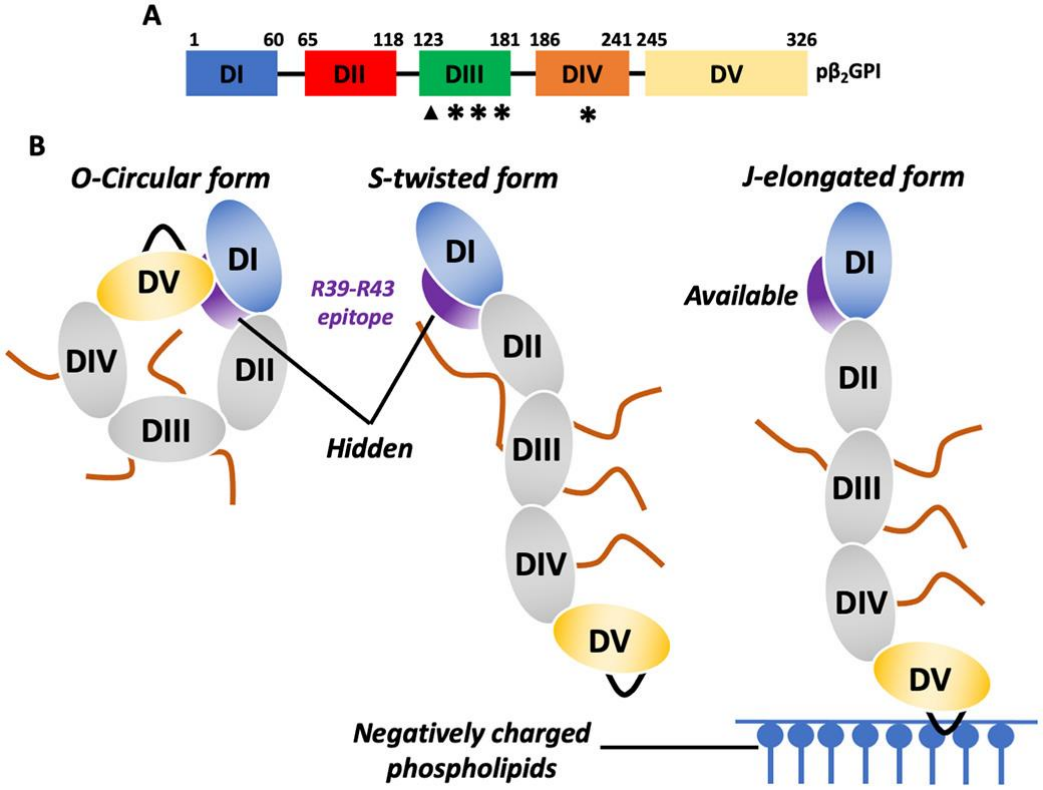
Plasma protein: 200 mg/L

Molecular weight: about 50 kDa

may play a role in coagulation, bind to platelets, mitochondria and negatively charged substances such as heparin, DNA, dextran sulphate and negatively charged phospholipids

ß2-Glycoprotein I

326 amino acids organized in 5 domains (DI – DV)



opening of circular structure by binding to negatively charged phopsholipid

hidden epitope on domain I available for antibodies

Ruben E, Planer W: J. Biol. Chem. (2020) 295(31) 10794–10806

Antibodies against Phospholipids

Standardisation?

UK NEQAS
Immunology, Immunochemistry & Allergy

Sample 234-1 was a single donor serum from a patient with an elevated concentration of IgM anti-phospholipid antibodies diluted with pooled normal human serum.

Sample	Analyte	Target Response
234-1	ACA IgG	Negative
	ACA IgM	Positive
	Anti-B2-Glycoprotein IgG	Equivocal
	Anti-B2-Glycoprotein IgM	Positive
	Anti-Phosphatidyl Serine IgG	Negative
	ACA (Screen Only)	Positive

Antibodies against Phospholipids

Standardisation?

Sample	Analyte	Target Response
234-1	ACA IgG	Negative
	ACA IgM	Positive
	Anti-B2-Glycoprotein IgG	Equivocal
	Anti-B2-Glycoprotein IgM	Positive
	Anti-Phosphatidyl Serine IgG	Negative
	ACA (Screen Only)	Positive

UK NEQAS
Immunology, Immunochemistry & Allergy

Anti Phospholipid Antibodies - Sample 234-1

Distribution : 234 **July 2023** **Participant** 90323

ACA IgG

Your Results

ACA IgG: Negative
Quantitation: 2.1
Unit: Units/ml
Method: Enzyme Immunoassay/ELISA
Manufacturer: Generic Assays

	Returns	Positive	Negative	Mean	Range
Other ...					
Other ...	**4**	**1**	**3**	**2**	**0 - 4**
Other ...	4	1	3	2	0 - 4
Units/ml					
Chemiluminescence	**117**	**0**	**117**	**8**	**0 - 18**
A. Menarini - Zenit RA	22	0	22	1	0 - 6
HOB-BioCLIA	2	0	2	6	5 - 7
IDS-iSYS	11	0	11	1	0 - 4
Inova QUANTA Flash	77	0	77	11	0 - 18
Other ...	5	0	5	10	6 - 15
Enzyme Immunoassay/ELISA	**283**	**0**	**283**	**4**	**0 - 27**
A. Menarini - Zenit EIA	2	0	2	5	0 - 10
AESKU	16	0	16	5	1 - 10
Biosystems	1	0	1	2	2 - 2
CLS AUTOZYME	3	0	3	8	6 - 10
Diesse	1	0	1	4	4 - 4
Euroimmun	9	0	9	3	2 - 5
Generic Assays	2	0	2	2	2 - 2
Human-Imtec	2	0	2	17	6 - 27
Immunoconcepts	1	0	1	6	6 - 6
In House	1	0	1	4	4 - 4
Inova	21	0	21	4	1 - 9
ORGenTec	24	0	24	3	1 - 4
ORGenTec Alegria	8	0	8	4	4 - 5
Other ...	4	0	4	6	6 - 7
Phadia 100 EliA	2	0	2	3	3 - 3
Phadia 1000/2500 EliA	10	0	10	3	3 - 4
Phadia 250 EliA	176	0	176	3	2 - 12
Multiple Particle Based Assays	**36**	**35**	**1**	**30**	**9 - 36**
Bio-Rad Bioplex 2200	35	35	0	30	23 - 36
THERADIAG (BMD)	1	0	1	9	9 - 9

07.12.2023

Antibodies against Phospholipids

Standardisation?

Sample	Analyte	Target Response
234-1	ACA IgG	Negative
	ACA IgM	Positive
	Anti-B2-Glycoprotein IgG	Equivocal
	Anti-B2-Glycoprotein IgM	Positive
	Anti-Phosphatidyl Serine IgG	Negative
	ACA (Screen Only)	Positive

UK NEQAS
Immunology, Immunochemistry & Allergy

Anti Phospholipid Antibodies - Sample 234-1

Distribution : 234 **July 2023** **Participant** 90323

Anti-B2 Glycoprotein IgG

Your Results

Anti-B2 Glycoprotein IgG: Negative
Quantitation: 4.4
Unit: Units/ml
Method: Enzyme Immunoassay/ELISA
Manufacturer: Generic Assays

	Returns	Positive	Negative	Mean	Range
Units/ml					
Chemiluminescence	**112**	**74**	**38**	**25**	**0 - 60**
A. Menarini - Zenit RA	22	0	22	1	0 - 3
HOB-BioCLIA	1	0	1	8	8 - 8
IDS-iSYS	10	0	10	1	0 - 1
Inova QUANTA Flash	74	70	4	34	0 - 60
Other ...	5	4	1	27	5 - 45
Enzyme Immunoassay/ELISA	**246**	**1**	**245**	**4**	**0 - 26**
A. Menarini - Zenit EIA	1	0	1	1	1 - 1
AESKU	15	0	15	4	0 - 8
Corgenix	1	0	1	4	4 - 4
Diesse	1	0	1	5	5 - 5
Euro Diagnostica	1	0	1	4	4 - 4
Euroimmun	6	0	6	3	2 - 3
Generic Assays	2	0	2	2	0 - 4
Human-Imtec	2	0	2	4	3 - 5
In House	1	0	1	1	1 - 1
Inova	16	0	16	3	0 - 5
ORGenTec	19	0	19	2	1 - 4
ORGenTec Alegria	6	0	6	5	4 - 6
Other ...	3	0	3	3	0 - 6
Phadia 100 EliA	2	0	2	3	3 - 4
Phadia 1000/2500 EliA	13	0	13	5	1 - 6
Phadia 250 EliA	157	1	156	4	1 - 26
Multiple Particle Based Assays	**35**	**35**	**0**	**26**	**14 - 30**
Bio-Rad Bioplex 2200	34	34	0	26	22 - 30
THERADIAG (BMD)	1	1	0	14	14 - 14

07.12.2023

Antibodies against Phospholipids

Standardisation?

Cardiolipin Antibodies

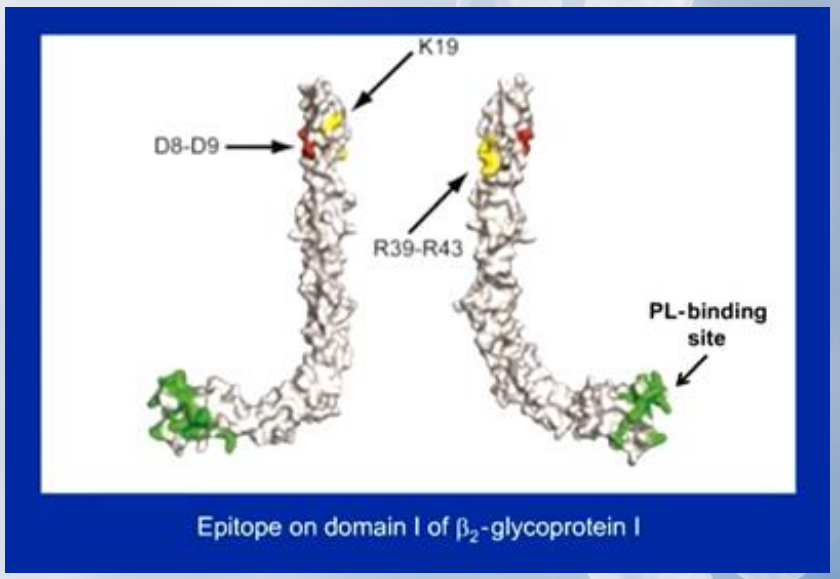
accepted protocol: cofactor dependent antigen

ß2-glycoprotein I

domain I specific assays?

QUANTA Flash® $ß_2$GP1 IgG

QUANTA Flash® $ß_2$GP1 Domain 1



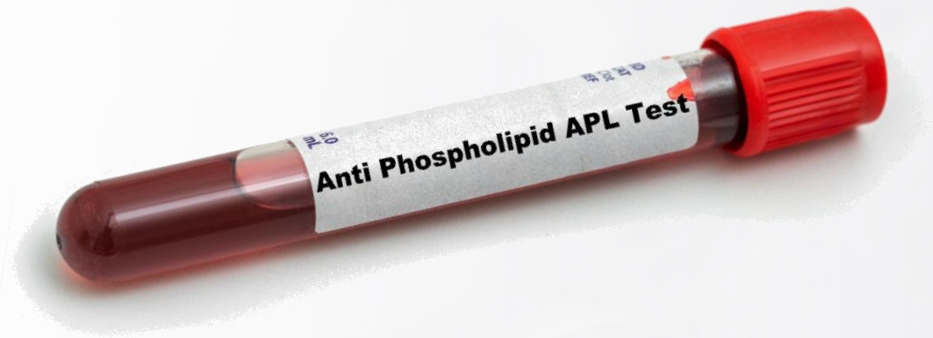
P. de Groot, Utrecht

Anti-Phospholipid-Syndrome

Diagnosis

Diagnosis is based on clinical symptoms and laboratory findings.

In laboratory diagnostics, detection is primarily carried out by the determination of antibodies against phospholipids (e.g. against cardiolipin) and associated proteins (e.g. β2-glycoprotein I).



Anti-Cardiolipin

Assays from Generic Assays (Elisa)

The Anti-Cardiolipin is a ELISA immunoassay for the quantitative determination of IgG and/or IgM antibodies against cardiolipin-ß2GPI in human serum.

Anti-Cardiolipin screen

Assays from Generic Assays (Elisa)

The Anti-Cardiolipin screen is a ELISA immunoassay for the semi-quantitative determination of IgG/IgM/IgA antibodies against cardiolipin-ß2GPI in human serum.

07.12.2023

Product Portfolio

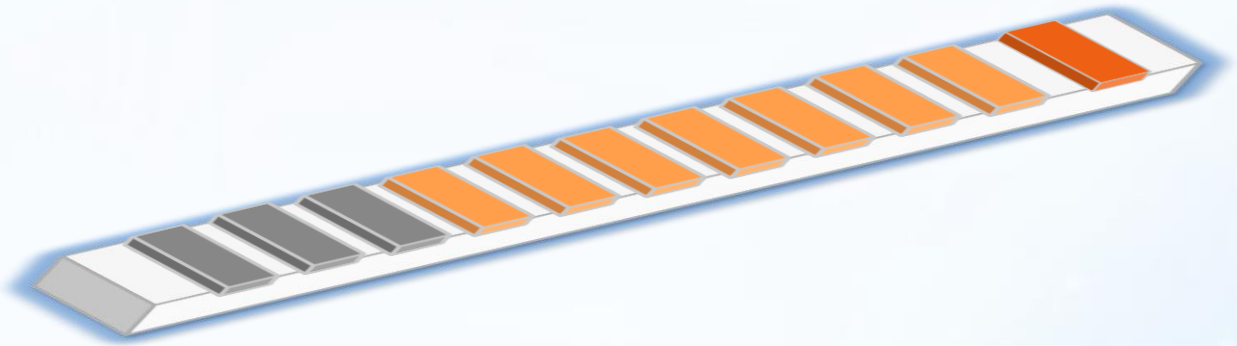
ELISA for the Diagnosis of Anti-Phospholipid-Syndrome

IgA + IgG + IgM Detection	IgG or IgM Detection
Anti-Cardiolipin Screen	Anti-Cardiolipin
Anti-ß2-GP-I Screen	Anti-ß2-GP-I
	Anti-Phosphatidyl-Serin
	Anti-Phospholipid Screen

Anti-Phospholipid Dot (IgG, IgM)

Multi-parameter Assay from GA Generic Assays

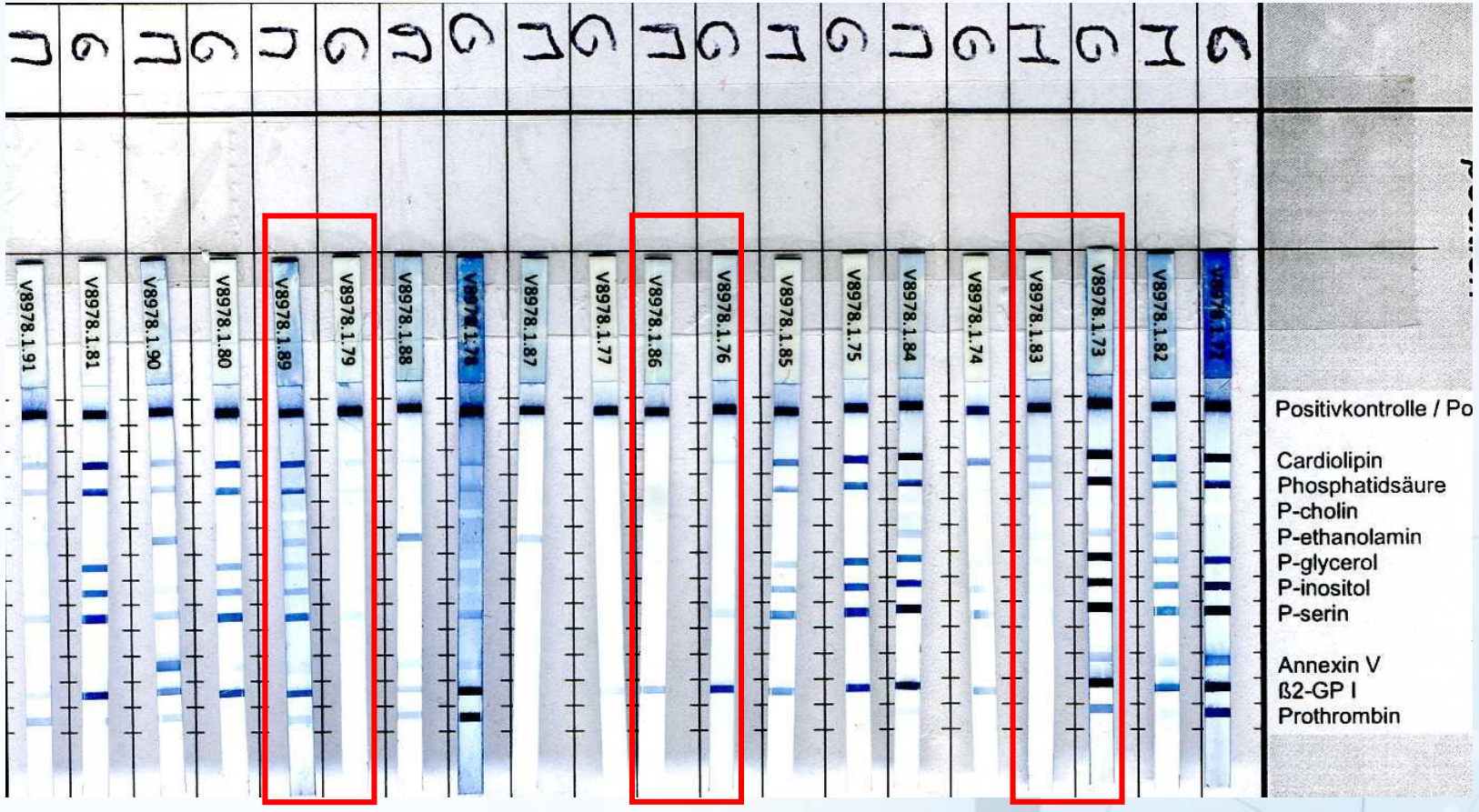
The Anti-Phospholipid Dot is a line immunoassay (Elisa principle) for the qualitative determination of IgG / IgM antibodies against 7 phospholipids and 3 serum proteins in human serum.



Hydrophobic membrane

- Reaction control
- phospholipids: cardiolipin, phosphatic acid, ph-cholin, ph-ethanolamine, ph-glycerol, ph-serine, ph-inositol,
- cofactors: ß2-GPI, annexin V, prothrombin

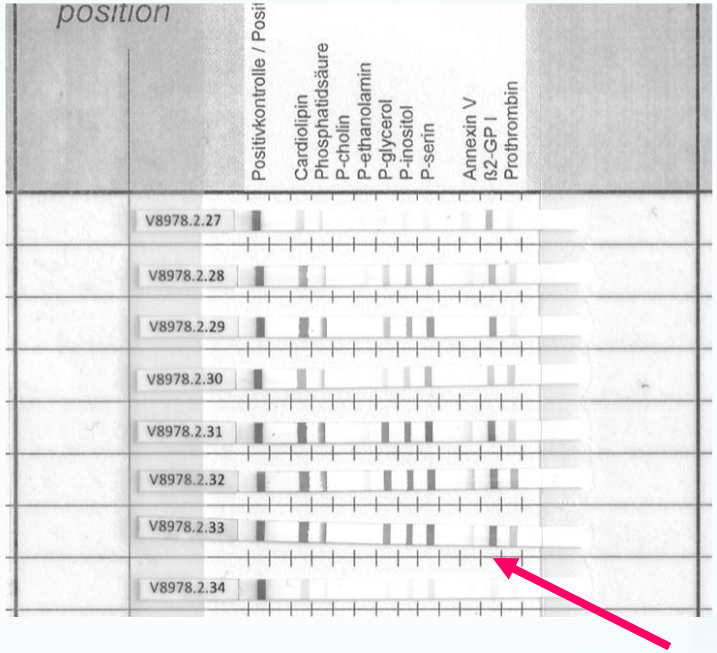
Anti-Phospholipid Dot (IgG / IgM)



Prof. René Louis Humbel, Luxemburg

Anti-Phospholipid Dot (IgG / IgM)

Anti-Phospholipid 10 Dot (REF 5012)
Patients with manifest APS:
IgG results:



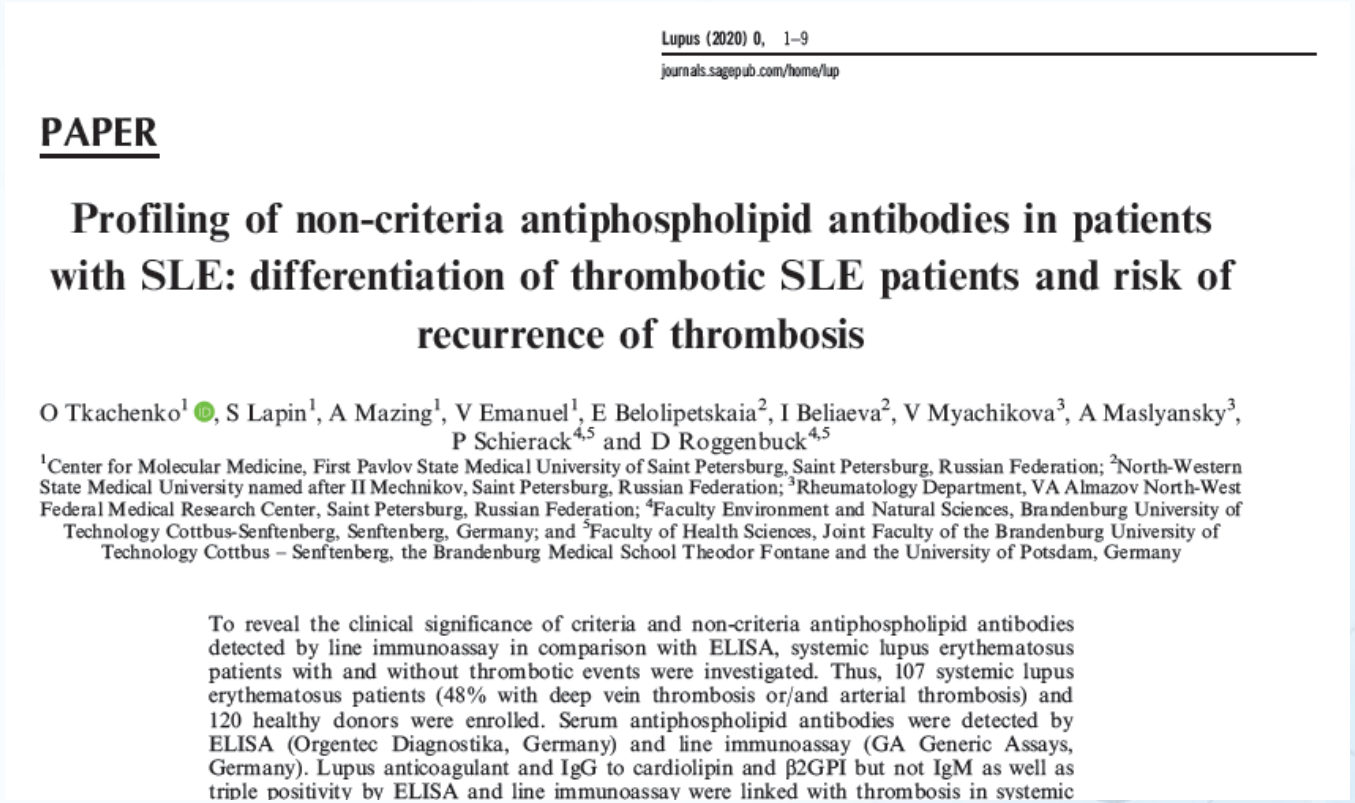
- often reaction of all anionic phospholipids and ß2-GP I

DotDiver Anti-Phospholipid:

VDRL pos. sera (Treponema infection):

no reaction with ß2-GPI

Anti-Phospholipid Dot (IgG / IgM)



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PAPER

Profiling of non-criteria antiphospholipid antibodies in patients with SLE: differentiation of thrombotic SLE patients and risk of recurrence of thrombosis

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To reveal the clinical significance of criteria and non-criteria antiphospholipid antibodies detected by line immunoassay in comparison with ELISA, systemic lupus erythematosus patients with and without thrombotic events were investigated. Thus, 107 systemic lupus erythematosus patients (48% with deep vein thrombosis or/and arterial thrombosis) and 120 healthy donors were enrolled. Serum antiphospholipid antibodies were detected by ELISA (Orgentec Diagnostika, Germany) and line immunoassay (GA Generic Assays, Germany). Lupus anticoagulant and IgG to cardiolipin and β2GPI but not IgM as well as triple positivity by ELISA and line immunoassay were linked with thrombosis in systemic

Why checking for 10 parameters ?

Diagnostic advantages of detection of multiple parameters

Anti-Phospholipid Dot (IgG / IgM)

Why checking for 10 parameters ?

Diagnostic advantages of detection of multiple parameters

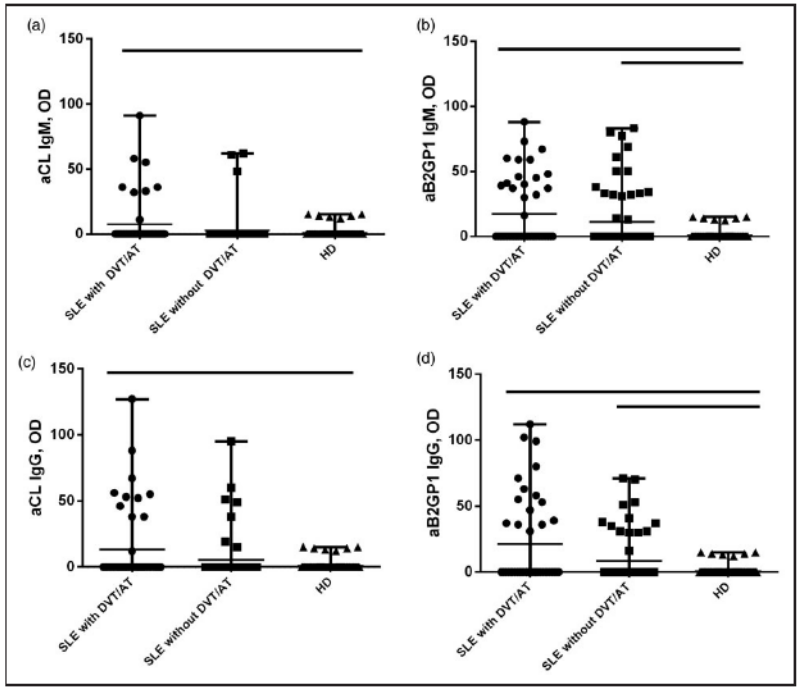


Figure 2 Comparison of quantitative anti cardiolipin (aCL) IgM (a) and anti-beta 2 glycoprotein I (aß2GPI) IgM (b), aCL IgG (c), aß2GPI IgG (d) analysis by line immunoassay (LIA) in systemic lupus erythematosus (SLE) patients with deep vein thrombosis (DVT)/ arterial thrombosis (AT) ($n=47$), SLE without DVT/AT ($n=60$) and healthy donors (HD) (n = 120). OD: optical density.

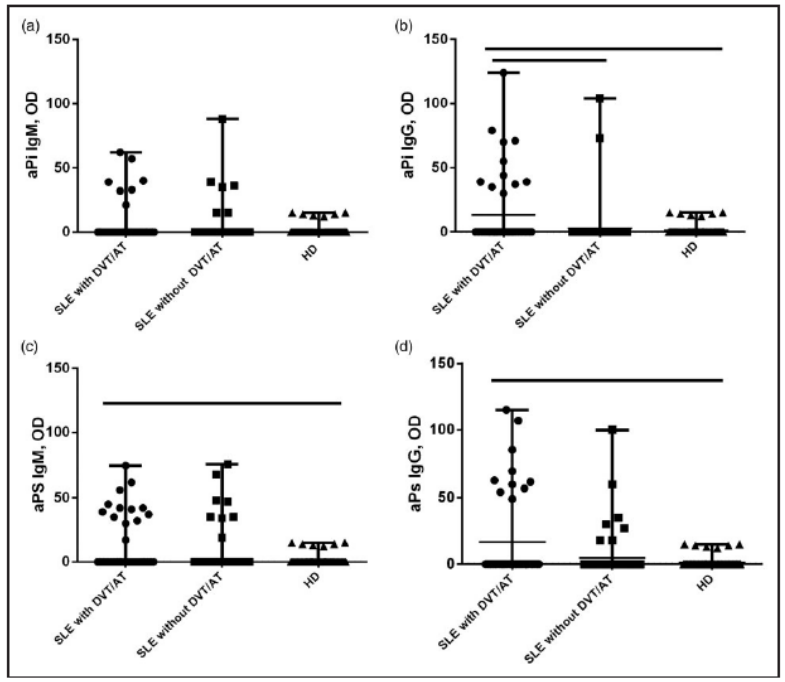
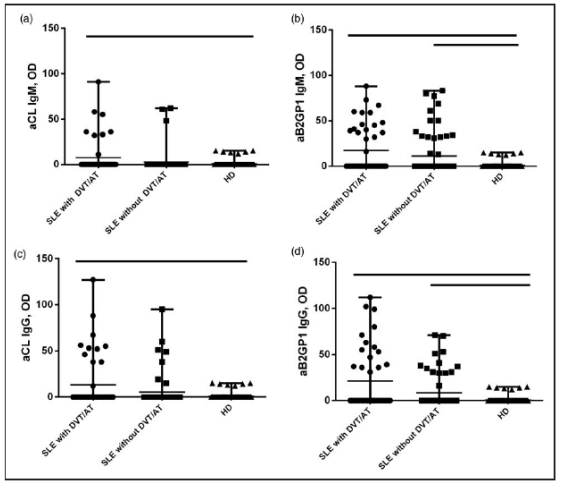


Figure 3 Comparison of quantitative antibodies to phosphatidylinositol (aPi) IgM (a) and antibodies to aPi IgG (b), antibodies to phosphatidylserine (aPs) IgM (c), aPs IgG (d) analysis detected by line immunoassay (LIA) in systemic lupus erythematosus (SLE) patients with deep vein thrombosis (DVT)/ arterial thrombosis (AT) ($n=47$), SLE without DVT/AT ($n=60$) and healthy donors (HD) ($n=120$). OD: optical density.

Anti-Phospholipid Dot (IgG / IgM)

Why checking for 10 parameters ?

Diagnostic advantages of detection of multiple parameters



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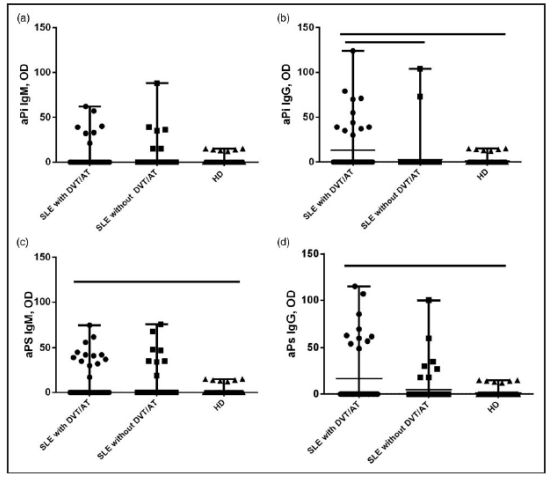

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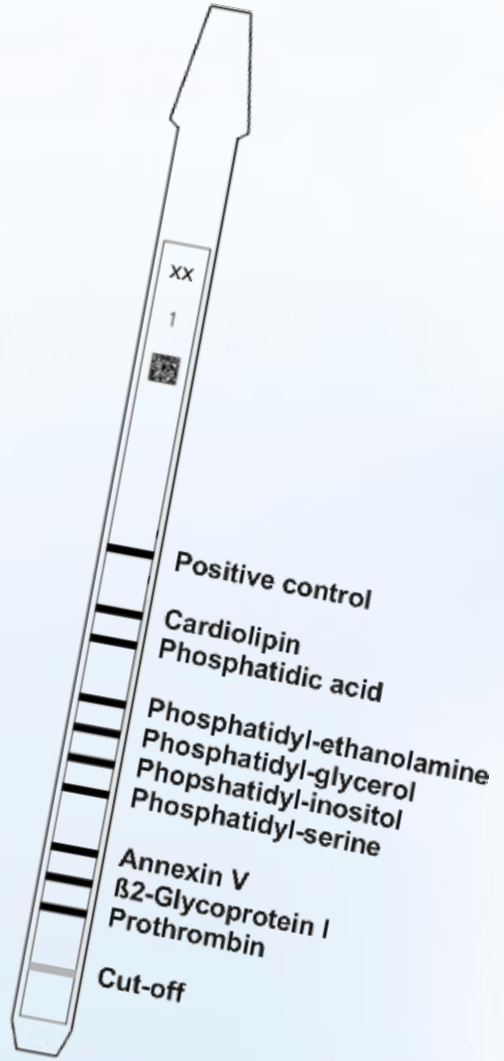
- Association of non-criteria APL with thrombotic risk in SLE patients
- IgG to PI and PS show significantly higher levels in SLE with deep vein thrombosis/arterial thrombosis than without
- Occurrence of >4 IgG antiphospholipid antibodies is independent risk factor for thrombotic effects

DotDiver Anti-Phospholipid IgG / IgM

DotDiver2.0, Test Strips and Reagents



Antibodies against Phospholipids for the
Diagnosis of the Anti-Phospholipid-Syndrome

Thomas Büttner

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Anti-Phospholipid-Syndrome

Thank you for your attention

CERTIFIED DIN EN ISO 13485 CERTIFIED

On Track to achieve
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Thank you for your attention !