

## PREVALENCE OF ANTI-CHLAMYDIAL ANTIBODIES IN PATIENTS AFFECTED BY ACUTE MYOCARDIAL INFECTION OR UNSTABLE ANGINA PECTORIS

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### Introduction

Arteriosclerosis is a complex process characterised by inflammatory and proliferative responses to a noxious agent. The basic pathogenetic event is the rise and progressive worsening of endothelial dysfunction, that is particularly due to the presence of increased blood plasma concentration of oxidised low-density lipoprotein (LDL) particles. After phagocytosis of the LDL particles by macrophages and transformation of the latter into foamy cells of arteriosclerotic lesions, the development of the resulting plaques is modulated by a number of factors, such as quantitative composition of the blood serum lipid spectre, coagulation factors, oxidative stress rate, endothelial proliferation, rate of expression of adhesive molecules with continuing migration of monocytes into intima, intensity of the proinflammatory cytokine response, and/or transcription of proatherogenic genes (3, 4, 5, 6, 9, 12).

Particular attention within the theory of the rise and development of arteriosclerosis has been recently paid to the inflammatory and autoimmune pathogenetic aspects. Both can, on an immunopathological basis, contribute to the explanation of possible mechanisms of induction, persistence, and worsening of endothelial inflammation (5, 12) and none of them excludes possible participation of some microorganisms, such as *Helicobacter pylori*, *Chlamydia pneumoniae*, oral bacterial flora such as *Porphyromonas gingivalis*; cytomegalovirus, or herpesvirus (2). Microbial heat shock proteins and lipopolysaccharides of gram-negative bacteria are regarded as particularly hazardous (4, 5, 6, 7). An infection can affect the process of arteriosclerosis by a number of mechanisms, including penetration of the agent into the vessel wall with the subsequent inflammatory response, migration and accumulation of immunocompetent cells, and production of cytokines and cell growth factors; local endotoxin (lipopolysaccharide) release; autoimmune inflammation induced by heat shock proteins; indirect systemic endotoxin effect; induction of a cytokine-mediated

infections (IgA isotype Ab) in the patients affected by AMI or suffering from USAP. The anti-LPS specificity of a part of the Ab is consistent with the presumed increased expression and release of the chlamydial proinflammatory LPS in patients suffering from a chronic infection (1, 3). Unlike CFT, ELISA allows the demonstration of the IgA isotype of Ab that are usually regarded as a marker of an active or a recent infection (10). CFT, demonstrating only the IgM and IgG isotypes, fails to distinguish between an active and an anamnestic infections with a high IgG titre unless the test is repeated. Significant signs of an active chlamydial infection, as demonstrated by the presence of genus- or species-specific Ab (IgA anti-LPS, IgA anti-MOMPs) in the patients suffering from USAP also corroborate the hypothesis of the participation of *C. pneumoniae* in the pathogenesis of coronary arteriosclerosis (2, 3, 4, 6, 7, 9, 10, 11)

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change in the lipid spectre (2). The major candidate agent capable of inducing the events described above is the gram-negative intracellular bacterium *Chlamydia pneumoniae*. The association of infection by *C. pneumoniae* and coronary atheromatosis is apparent from a number of epidemiological and experimental studies documenting the potential of the agent to persist in mononuclear phagocytes and other cells (2), direct detection of *C. pneumoniae* in atheromatous plaques in human patients and animal models studies (detection of live agents, species-specific antigens and species-specific DNA fragments), or from serologically confirmed active infection in patients with coronary artery disease (3, 5, 8, 9, 10,11). The association of serological markers of infection and clinical manifestations of coronary atheromatosis is still topical (10).

This paper presents results of monitoring and assessment of the prevalence of IgA and IgG antibodies (Ab) to the genus-specific chlamydial lipopolysaccharide (LPS) and IgA and IgG Ab to the major species specific membrane proteins of *C. pneumoniae* (MOMPs) in 1. patients suffering from unstable angina pectoris (USAP); 2. patients affected by acute myocardial infarction (AMI); and 3. normal subjects in which USAP and AMI were excluded on the basis of anamnestic data, somatic examination, and ECG.

### Methods

Set : **patients:** AMI (n = 156, incl. 126 males and 30 females, mean age 60.8 years); USAP (n = 38, incl. 28 males and 10 females, mean age 68.9 years);

**controls:** (n = 62, incl. 32 males and 30 females, mean age 58.5 years).

Tests:

1. complement fixation test (CFT) detecting genus-specific Ab to chlamydiae without isotype discrimination (antigen supplied by Bioveta);
2. indirect immunoassay (ELISA) demonstrating species-specific Ab to *C. pneumoniae* (IgA and IgG anti-MOMPs, ELISA, Vircell);
3. indirect immunoassay (ELISA) demonstrating genus-specific Ab to chlamydial LPS (IgA and IgG anti-LPS, rELISA medac) using a *Chlamydia*-specific recombinant antigen in the set;
4. indirect microimmunofluorescence (MIF) demonstrating species-specific Ab to *C. pneumoniae*, *C. trachomatis*, and *C. psittaci* (IgA and IgG anti-MOMPs, MRL Diagnostics)

The set AMI and the control subjects were examined by the tests 1 through 4, and the set USAP by the tests 3 and 4 only.

Tested clinical material: blood serum ; statistical processing:  $\chi^2$

## Results

The difference in the prevalence of anti-chlamydia Ab demonstrated by CFT between the AMI patients and the control subjects was highly significant ( $X^2 = 7.795$ );). As the isotype IgA fails to bind complement, it can be assumed that the antigen used in the test detected genus specific Ab of the IgG and IgM classes. Compared with the control subjects, the AMI patients showed also a higher prevalence of anti-LPS IgA Ab ( $X^2 = 8.528$ ). The USAP patients showed higher levels of both IgA and IgG anti-LPS ( $X^2 = 9.176$  and  $5.815$ , respectively) and IgA antiMOMPs ( $X^2 = 31.717$ ) than the control subjects. All the differences were highly significant at  $p = 0.01$ .

Table 1: Prevalence of IgA and IgG Ab to the genus-specific chlamydial lipopolysaccharide (CFT, anti-LPS ELISA) and the major species-specific membrane proteins of *C. pneumoniae* (ELISA anti-MOMPs, MIF anti-MOMPs) in patients suffering from USAP, or affected by AMI and in healthy control subjects.

Test	Ig	USAP n=48	Controls n=62	$X^2$	AMI n=156	Controls n=62	$X^2$
CFT	Ig +				28 (18%)	3 ( 5%)	7.795 <sup>++</sup>
	Ig -				128(82%)	59 (95%)	
ELISA (MOMPs)	IgA +				87 (56%)	31 (50%)	
	IgA -				69 (44%)	31 (50%)	
	IgG +				146(94%)	53 (85%)	
	IgG -				10 ( 6%)	9 (15%)	
ELISA (LPS)	IgA +	31(65%)	22 (35%)	9.176 <sup>++</sup>	89 (57%)	22 (35%)	8.528 <sup>++</sup>
	IgA -	17 (35%)	40 (65%)		66 (42%)	40 (65%)	
	IgG +	32 (67%)	27 (43%)	5.815 <sup>++</sup>	89 (57%)	27 (43%)	
	IgG -	16 (33%)	35 (57%)		66 (42%)	35 (57%)	
MIF (MOMPs)	IgA +	35 (73%)	12 (19%)	31.717 <sup>++</sup>	44 (28%)	12 (19%)	
	IgA -	13 (27%)	50 (81%)		112(72%)	50 (81%)	
	IgG +	42 (88%)	54 (87%)		125(80%)	54 (87%)	
	IgG -	6 (12%)	8 (13%)		31 (20%)	8 (13%)	

<sup>++</sup> highly significant difference ( $p = 0,01$ )

## Discussion

Statistical analyses of results obtained in the patients and the control subjects have corroborated the assumption of an increased prevalence of acute *Chlamydia*