

EXTENDED *CHLAMYDIA TRACHOMATIS* SEROLOGY: cHSP60 IgG AND ITS ASSOCIATION WITH TUBAL OCCLUSION

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BACKGROUND OF THE STUDY

Chlamydia trachomatis (*C. trachomatis*) is the most common sexually transmitted bacterium worldwide. Bilateral occlusion of the fallopian tubes due to genital chlamydia infection is the most frequent single cause of female infertility and ectopic pregnancy. Some 20-30% of all women who undergo in-vitro fertilisation show evidence of tubal factor infertility. More than 80% of tubal occlusions are attributable to ascending genital chlamydia infection, which in most cases remains asymptomatic. Direct demonstration of *C. trachomatis* in a cervical swab or urine sample certainly confirms an existing genital chlamydial infection, but says nothing about the risk of tubal damage. Antibodies against chlamydial heat shock protein 60 (cHSP60) in women with laparoscopically verified pelvic inflammatory disease (PID) are significantly associated with tubal occlusion (Eckert LO et al., JID 1997). This massive tubal damage is probably caused by an autoimmune cross-reaction with human heat shock protein.

OBJECTIVE

The aim of the study was to ascertain whether the positive predictive value (PPV) for tubal occlusion can be improved by additional testing for *C. trachomatis* cHSP60 antibodies in patients with positive *C. trachomatis* anti-MOMP IgG (extended *C. trachomatis* serology).

MATERIAL AND METHODS

Sera from 126 women who had, for various reasons, to undergo laparoscopy, e.g., for myomata, endometriosis, lower abdominal pain or infertility, were investigated with the *C. trachomatis*-IgG- and IgA-pELISA medac (*C. trachomatis*-specific MOMP antibodies) and the cHSP60-IgG-ELISA medac (medac Hamburg, Germany). 24 out of these 126 women had bilateral tubal occlusion. The remaining 102 patients had macroscopically inconspicuous fallopian tubes, in which there was no evidence of any obstruction by the dye test. The following parameters were determined: frequency of *C. trachomatis* anti-MOMP IgG and IgA and anti-cHSP60 IgG; positive predictive value (PPV) and negative predictive value (NPV) for occluded tubes, odds ratio and serial follow-up of antibodies.

Tab. 1: Risk appraisal for the pathogenesis of occluded tubes taking into account serological *C. trachomatis* findings

	All patients n = 126	24 patients with tubal occlusions n	%	Odds ratio (95% CI)	p-value	
C. trachomatis IgG	neg	87	3	3	32.7	< 0.0001
	pos	39	21	54	(8.8; 121.4)	
C. trachomatis IgA	neg	112	15	13	11.6	0.0001
	pos	14	9	64	(3.4; 39.5)	
cHSP60 IgG	neg	77	5	6	9.1	0.0001
	pos	49	19	39	(3.1; 26.7)	

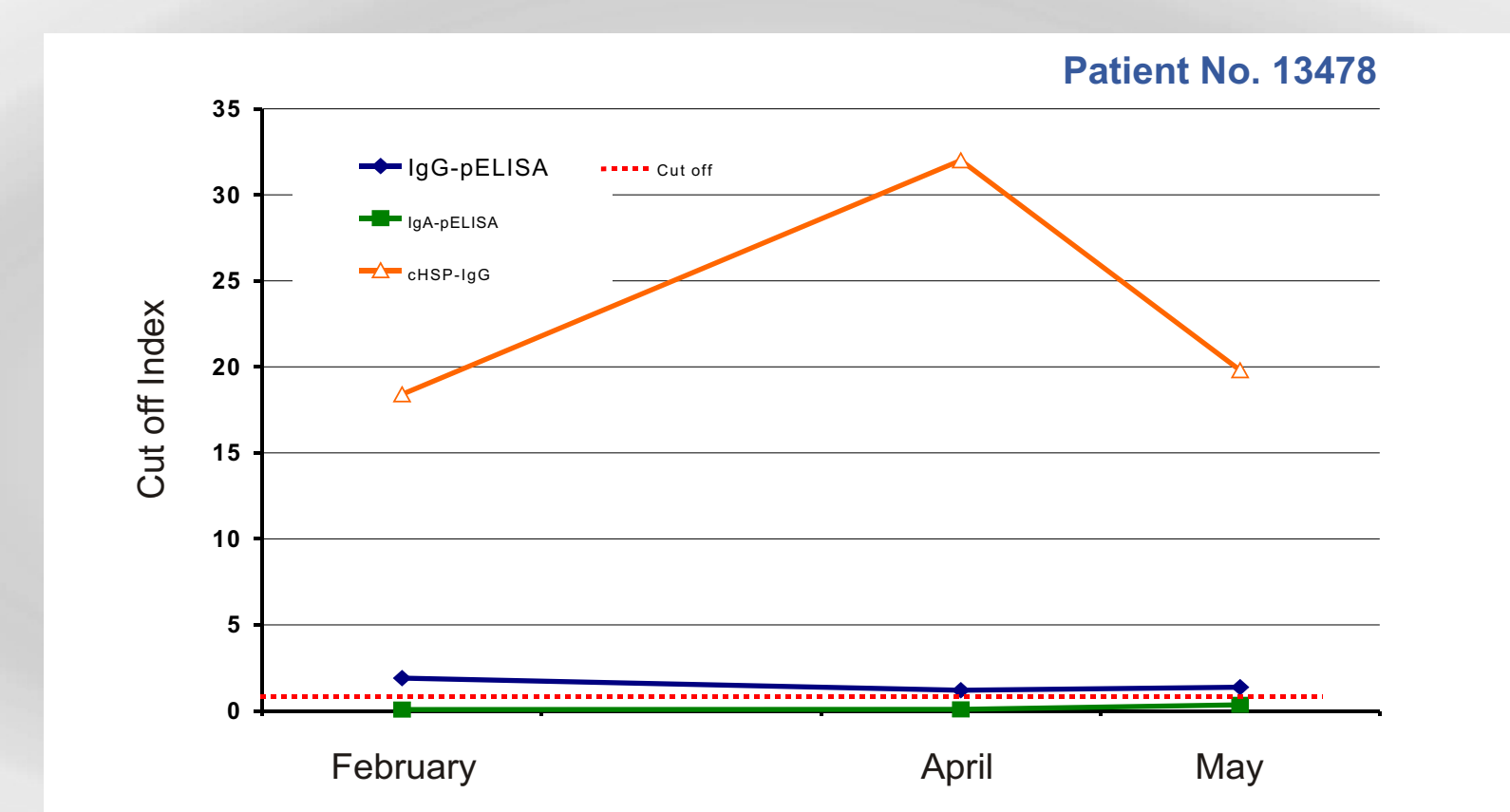
Tab. 2: Predictive values for tubal occlusion taking into account *C. trachomatis* anti-MOMP IgG vs. *C. trachomatis* anti-MOMP IgG and anti-cHSP60 IgG

	Patients n	<i>C. trachomatis</i> anti-MOMP IgG		<i>C. trachomatis</i> anti- MOMP IgG and anti-cHSP60-IgG	
		positive	negative	positive	negative
Occluded tubes	24	21	3	19	5
Patent tubes	102	18	84	11	91
All cases	126	39	87	30	96
		PPV: 53.8% NPV: 96.6%		PPV: 63.3% NPV: 94.8%	

RESULTS

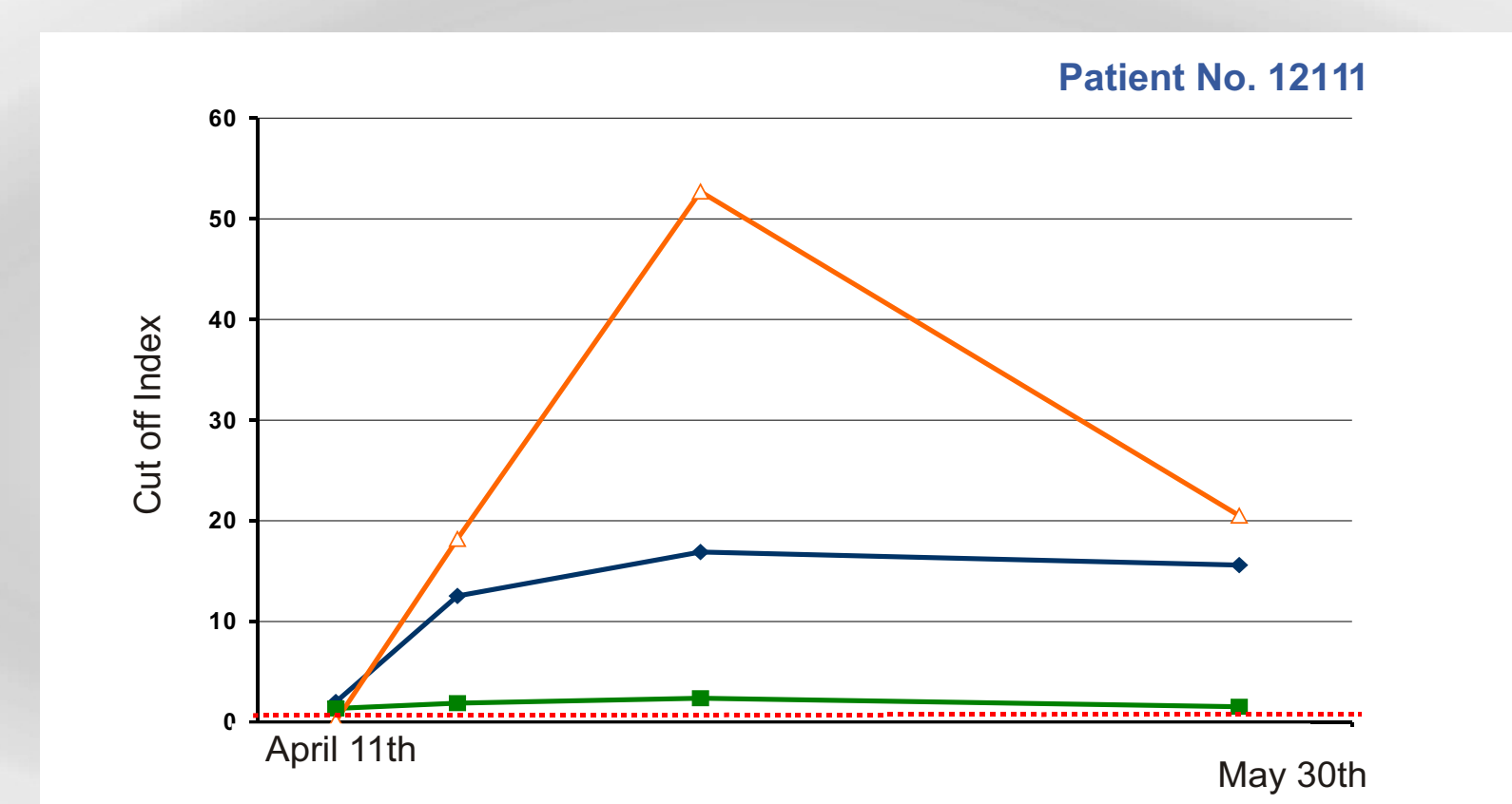
88% (21/24) of women with occluded fallopian tubes gave positive results for *C. trachomatis* anti-MOMP IgG, but only 18% (18/102) of women with open tubes were positive for anti-MOMP IgG antibodies. The values for *C. trachomatis* anti-MOMP IgA and anti-cHSP60 IgG were higher in the patients with bilateral tubal occlusion than in those with open fallopian tubes (IgA 38% vs. 3%, cHSP60-IgG 79% vs. 29%). All differences (Tab. 1) were highly significant (anti-MOMP IgG p < 0.0001, anti-MOMP IgA p = 0.0001, anti-cHSP60 IgG p = 0.0001). The PPV (Tab. 2) for anti-MOMP IgG alone (53.8%) rose by the addition of testing for anti-cHSP60 IgG to 63.3%. The comparable NPV was 96.6% as against 94.8%.

Fig. 1: Patient with ascending *C. trachomatis* infection (bilateral tubal occlusion)



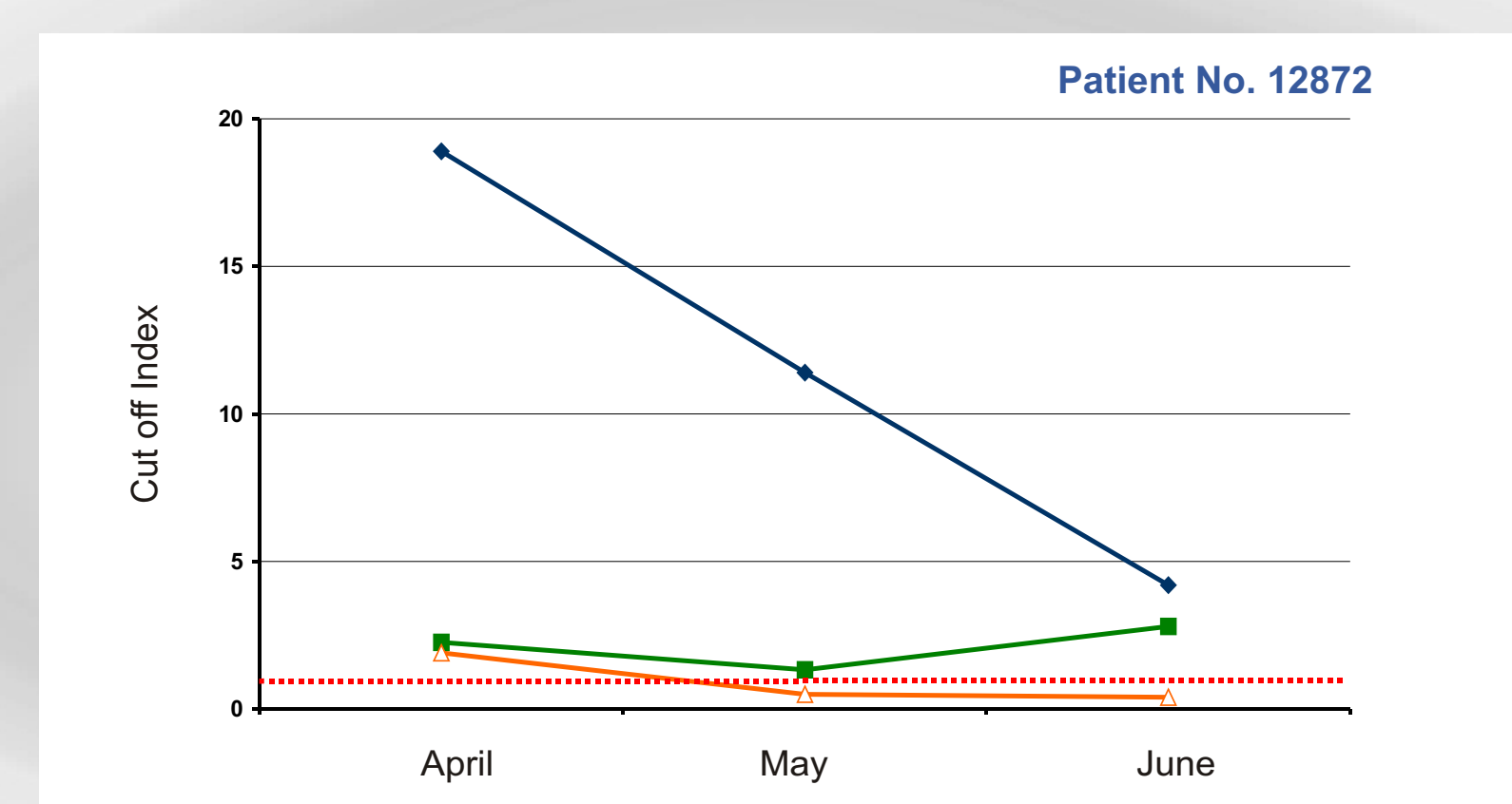
C. trachomatis antigen positive at first examination → treatment → 6 weeks later *C. trachomatis* antigen negative

Fig. 2: Patient with ascending *C. trachomatis* infection (perihepatitis)



C. trachomatis antigen positive at first examination → treatment → 3 weeks later *C. trachomatis* antigen negative

Fig. 3: Patient with acute *C. trachomatis* infection (lower abdominal pain)



C. trachomatis antigen positive at first examination → treatment → 7 weeks later *C. trachomatis* antigen negative

DISCUSSION AND CONCLUSION

- Extended *C. trachomatis* serology (anti-MOMP serology, cHSP60-IgG) has decisive advantages for determining the course of genital chlamydial infection:
 - a positive cHSP60 IgG in women with existing genital chlamydial infection may point to an ascending infection,
 - ascending *C. trachomatis* infections require prolonged antibiotic treatment, e.g., 20 days instead of 10 days for acute *C. trachomatis* infection,
 - a positive cHSP60 IgG in combination with a positive *C. trachomatis* anti-MOMP IgG suggests an increased risk of tubal damage.
- Extended *C. trachomatis* serology in asymptomatic women with existing *C. trachomatis* infections appears to be an efficient marker for an increased risk of tubal damage.
- Further studies are planned to estimate the risk of tubal damage by using the anti-cHSP60-IgG titre.

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EXPANDED *CHLAMYDIA TRACHOMATIS* SEROLOGY: CHSP60 IGG AND ITS ASSOCIATION WITH TUBAL OCCLUSION

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Chlamydia trachomatis infection is the most prevalent sexually transmitted bacterial disease worldwide and the primary single cause of female infertility and ectopic pregnancy. About 20-30% of all women who undergo in vitro fertilisation have tubal factor infertility and more than 80% of tubal occlusion is due to ascending genital chlamydial infection, which remains asymptomatic in most cases. Direct detections, e.g. by DNA amplification, of *C. trachomatis* in cervical swabs or first-void urine prove current genital chlamydial infection, but provide no information about the risk of tubal damage. Antibodies against chlamydial heat shock protein 60 (cHSP60) have been found to be significantly associated with tubal occlusion (Eckert LO et al., JID 1997) in women with laparoscopically verified PID possibly by autoimmune crossreactions with the human heat shock protein. The aim of this study was to investigate whether the positive predictive value for tubal occlusion can be improved by combined detection of anti-*C. trachomatis* MOMP and anti-cHSP60 antibodies (expanded *C. trachomatis* serology). Antibodies against cHSP60 were measured by using the first commercially available cHSP60-IgG test.

126 women who underwent laparoscopy for different reasons, e.g. myoma, endometriosis, lower abdominal pain, infertility, were investigated by *C. trachomatis*-IgG-pELISA medac (*C. trachomatis* specific MOMP antibodies) and cHSP60-IgG-ELISA medac (medac, Hamburg, Germany). 24 of these 126 women had bilateral tubal occlusion, 102 had macroscopically normal fallopian tubes and showed no obstruction in the chromopertubation tests.

18% (18/102) of the women with normal fallopian tubes were positive for anti-MOMP IgG in pELISA, while 88% (21/24) of the women with occluded tubes were positive. The positive predictive value of anti-MOMP IgG for tubal occlusion was 53.8%, the negative predictive value was 96.6%. Reactivity for both anti-MOMP IgG and anti-cHSP60 IgG was found in 11% (11/102) of the women with open tubes and in 79% (19/24) of the women with bilaterally occluded tubes. The positive predictive value for tubal occlusion of the expanded *C. trachomatis* serology was 63.3% compared with 53.8% for anti-MOMP IgG alone. The negative predictive value for tubal occlusion was 94.8% (expanded serology) compared with 96.6% (anti-MOMP IgG).

Positive cHSP60-IgG in women with positive *C. trachomatis* MOMP-IgG (expanded *C. trachomatis* serology) indicates a higher risk of tubal damage compared with patients with negative cHSP60-IgG. In women with current genital chlamydial infection (positive direct detection test) a positive cHSP60-IgG may indicate ascending infection and warrant a longer antibiotic treatment, e.g. 20 days instead of 10 days. Chlamydial tubal infection often remains clinically asymptomatic unless superinfection by vaginal bacteria occurs, e.g. in women with bacterial vaginosis. Expanded *C. trachomatis* serology including cHSP60-IgG in asymptomatic women with current chlamydial infection and positive MOMP-IgG appears to be the only marker associated with a higher risk of tubal damage. Studies are needed to determine the relative risk of tubal damage in cHSP60-IgG positive compared with cHSP60-IgG negative women with current genital chlamydial infection.