

BLOOD CULTURE NEGATIVE ENDOCARDITIS

Akademisk avhandling
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Infektionskliniken, Sahlgrenska Universitetssjukhuset/Östra.

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Avhandlingen baseras på följande arbeten:

- I. M. Werner, R. Andersson, L. Olaison, H. Hogevik. A clinical study of culture negative endocarditis. *Medicine*. 2003;82:263-73
- II. M. Werner, P.-E. Fournier, R. Andersson, H. Hogevik, D. Raoult. *Bartonella* and *Coxiella* antibodies in 334 prospectively studied episodes of infective endocarditis in Sweden. *Scand J Infect Dis*. 2003;35:724-7
- III. M. Werner, J. Gnarpe, A. Odén, R. Andersson, H. Hogevik. *Chlamydia pneumoniae* infection: a risk factor for infective endocarditis? (Submitted)
- IV. M. Werner, R. Andersson, L. Olaison, H. Hogevik. A ten-year survey of blood-culture negative infective endocarditis in Sweden-Aminoglycoside therapy is important for survival. (Submitted)

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ABSTRACT

The lethal disease infective endocarditis (IE) is caused by microorganisms that attack heart valves. Early diagnosis and identification of the causative agents are important for the choice of treatment. Optimal treatment may be difficult to achieve if blood culture negative endocarditis (CNE) is present. This study was designed to estimate the prevalence of CNE, analyze clinical data from CNE patients, and to evaluate different diagnostic criteria. Further purposes were to evaluate the antibiotics used as treatment, to study serological evidence for fastidious bacterial infection and to assess the association of *Chlamydophila pneumoniae* (*C. pneumoniae*) antibodies with an increased risk of development for IE.

We analyzed data from presumptive IE patients in clinics at Borås (n=70) (Paper I) and Göteborg (n=750) (Paper I, II, III) and at the Swedish Endocarditis registry (n=2509) (Paper IV). Serum samples from Göteborg IE patients were tested for the presence of *Bartonella*, *Coxiella burnetii* and *C. pneumoniae* antibodies. Samples from controls selected from the same geographic population were searched for antibodies to *C. pneumoniae*.

Twelve to 27% of all IE episodes were CNE with a mortality of 5-7 %. Antibiotic treatment preceded blood culturing in 45% of the episodes. Women died significantly more often than men with this disease (odds ratio 5.5). For establishing IE diagnosis, the Duke definite criteria were more sensitive but probably less specific than the Beth Israel criteria.

One patient had serologically verified Q-fever IE, but no *Bartonella* was detected. The proportion of *C. pneumoniae* antibodies did not differ significantly in patients with CNE from those with blood culture positive IE. However amounts of *C. pneumoniae* IgA and IgG were significantly higher in women with IE than in the female controls.

The mortality rate was significantly lower in CNE patients treated with aminoglycosides.

CNE occurred in 12-27% of IE patients reviewed here, but antibiotic treatment preceding blood culture diminished the validity of negative test results. Fastidious bacteria were identified mainly by testing with antibodies, yet interpretations of such results are difficult. Clearly, additional methods are needed for diagnosing CNE.

Key words: Infective endocarditis (IE), blood culture negative endocarditis (CNE), blood culture, diagnosis, mortality, *Bartonella*, *Coxiella burnetii*, *Chlamydophila pneumoniae*, prevalence, aminoglycoside.

