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## Reactive arthritis in relation to internal derangements of the temporomandibular joint: a case control study

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#### **Abstract**

The aim of this study was to find out if reactive arthritis was involved in the aetiology of chronic closed lock of the temporomandibular joint (TMJ) by looking for bacterial antigens in the synovial membrane of the TMJ, and by studying the antibody serology and carriage of human leucocyte antigen (HLA) B27 in patients with chronic closed lock. Patients with reciprocal clicking and healthy subjects acted as controls. We studied a total of 43 consecutive patients, 15 with chronic closed lock, 13 with reciprocal clicking, and 15 healthy controls with no internal derangements of the TMJ. Venous blood samples were collected from all subjects for measurement of concentrations of HLA tissue antigen and serology against *Chlamydia trachomatis, Yersinia enterocolitica, Salmonella* spp., *Campylobacter jejuni*, and *Mycoplasma pneumoniae*. Samples of synovial tissue from patients with closed lock and reciprocal clicking were obtained during discectomy and divided into two pieces, the first of which was tested by strand displacement amplification for the presence of *C trachomatis*, and the second of which was analysed for the presence of species-specific bacterial DNA using 16s rRNA pan-polymerase chain reaction (PCR). There were no significant differences between the groups in the incidence of antibodies against *M pneumoniae, Salmonella* spp. or *Y enterocolitica*. No patient had antibodies towards *C trachomatis* or *C jejuni*. We found no bacterial DNA in the synovial fluid from any patient. The HLA B27 antigen was present in 2/15 subjects in both the closed lock and control groups, and none in the reciprocal clicking group. In conclusion, reactive arthritis does not seem to be the mechanism of internal derangement of the TMJ.

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Keywords: Temporomandibular joint; Internal derangement; Reactive arthritis; Chronic closed lock; Reciprocal clicking; Chlamydia trachomatis

#### Introduction

Internal derangements of the temporomandibular joint (TMJ) are common, with a prevalence of about 20% and a striking, as yet unexplained, female predominance. They usually cause only minor symptoms that need either no treatment or conservative treatment for a limited time. In a few patients

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the symptoms may be so serious that operation is indicated. From a clinical and tissue point of view, two variants of internal derangement have been identified. The first variant is called reciprocal clicking, which is a painful clicking or catching of the TMJ caused by a hypermobile disc with a callus in the posterior part of the disc. This variant shows no sign of degenerative disease, and synovial inflammation (if present) is slight. From a research perspective this group of patients may serve as an excellent control group when patients with degenerative or chronic inflammatory joint disease are being studied. The second variant is chronic closed lock, which presents as impaired painful mobility of the TMJ.

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The characteristics of the tissue in chronic closed lock are a disc with signs of degeneration and a chronically inflamed synovial lining.<sup>3,4</sup>

Reactive arthritis is a known perioinfective sequel to Chlamydia trachomatis and enteric pathogens such as Yersinia enterocolitica, Salmonella spp., Shigella spp., and Campylobacter jejuni. 5-8 Infection with enteric pathogens normally causes gastrointestinal symptoms, which help diagnosis, but C trachomatis infection can pass unnoticed and leave both the patient and the physician unaware of the presence of disease. This is particularly the case in women, where C trachomatis infection is commonly asymptomatic and diagnosed mainly during routine screening. Because the inflammatory reaction of the TMJ seen in patients with chronic closed lock resembles that of reactive arthritis, it has been hypothesised that Chlamydia spp. could be the cause of the inflamed TMJ. The presence of C trachomatis DNA in synovial fluid from patients with internal derangement of the TMJ has been detected by polymerase chain reaction (PCR) in only a single report to our knowledge. <sup>10</sup> However, those authors made no distinction between different diagnoses and included no control group. When Mycoplasma genitalium was also detected in the synovial fluid of the TMJ it was suggested that internal derangements could be a consequence of a sexually transmitted disease. 11 In another uncontrolled study serum antibodies to C trachomatis were present in 14/41 (34%) of a group of patients with internal derangements of the TMJ.<sup>12</sup> In a prospective study, the presence of serum antibodies against C trachomatis was significantly more common in patients with chronic closed lock than in healthy controls, whereas no such association was found for Chlamydia pneumoniae or Chlamydia psittaci. 13

Genetic and immunological factors may also be important in the development of arthritis of the TMJ. In patients with general reactive arthritis induced by a distant bacterial infection, the genotype HLA B27 has often been found. <sup>14</sup> The presence of a HLA B27 genotype also seems to predispose the patient to a more severe form of reactive arthritis. <sup>15</sup> No particular HLA has been found to be dominant in patients with chronic closed lock of the TMJ.

The aim of this study was to find out if reactive arthritis is involved in the aetiology of chronic closed lock of the TMJ by looking for bacterial antigens in the synovial fluid of the TMJ, for the presence of antibodies on serology, and for the carriage of HLA B27 in patients with chronic closed lock, and using patients with reciprocal clicking and healthy subjects as controls.

#### **Patients and Methods**

#### Patients and controls studied

We assumed a frequency of 50% antibodies towards *Chlamy-dia* spp. based on previously published data, which gave us 80% power at p=0.05, when the number of subjects/group

was 13.<sup>3,12</sup> We excluded patients less than 18 years of age, and those with generalised joint disease or other local disease of the TMJ. Consecutive patients referred to the Department of Oral and Maxillofacial Surgery, Institute of Dental Medicine, were included: 15 diagnosed with chronic closed lock, 13 with reciprocal clicking, and 15 healthy subjects with no internal derangements of the TMJ. Inclusion criteria for patients were adult patients who required discectomy for closed lock or reciprocal clicking of the TMJ. Reciprocal clicking was defined as painful reciprocal clicking or catching of the TMJ. Chronic closed lock was defined as painful impaired mobility of the TMJ. The inclusion criteria for controls were healthy adult patients who were having one or more third molars removed. The study was approved by the ethics review board in Stockholm. All patients gave signed consent before the study.

#### Clinical and surgical procedures

All subjects were asked to complete a mandibular function impairment questionnaire, which gave a score of functional severity ranging from 0 (minimum) to 21 (maximum). <sup>16</sup> They were also asked to grade their pain and functional disabilities associated with the TMJ according to a 10-grade visual analogue scale (VAS), where 0 denotes no pain and 10 the worst pain imaginable. Maximum mandibular movements were recorded as well as pain during the movements. Tenderness, or clicking, or both, on lateral and posterior palpation of the TMJ was recorded. All patients had a computed tomographic (CT) scan of the TMJ, and discectomy was done according to previous descriptions. <sup>2</sup> The healthy controls had their third molars removed.

#### Collection of samples and laboratory procedures

Samples of venous blood were collected preoperatively from patients and control subjects and stored in -20 °C until analysis. Samples of patients' synovial tissue was collected during operation from the posterior disc attachment (the synovial membrane) and divided into two parts. One was immediately stored in -20 °C and transported to the Clinical Microbiology Unit, Karolinska University Hospital, Huddinge, and the other was stored in 4% neutral buffered formaldehyde solution for further analyses with 16s rRNA pan-PCR. <sup>17</sup> The presence of *C. trachomatis* in tissue samples was screened by strand displacement amplification of C trachomatis cryptic plasmid (BD ProbeTec<sup>TM</sup>ET Chlamydia trachomatis Amplified DNA Assay Collection Kit, Becton Dickinson, NJ, USA). We used quantitative detection of IgM and IgG antibodies against C trachomatis, Y enterocolitica, Salmonella spp., C jejuni and Mycoplasma pneumoniae by indirect enzymatic immunoassay where antibodies were allowed to bind antigen-coated microtitre strips followed by enzymatic detection by enzyme conjugated monoclonal antihuman antibodies (AniLabsystems Ltd OY, Finland). 18-22 HLA tissue

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