# Comparison of Viral Antibodies in 2 Groups of Patients with Fibromyalgia

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***ABSTRACT***. ***Objective.*** The etiologies of fibromyalgia (FM) are unknown. In some cases an acute onset following a flu-like episode is described; in other cases patients report slowly developing disease. We previously found increased prevalence of enterovirus IgM antibodies in patients with acute onset of FM compared to healthy controls. We looked for differences in antimicrobial IgM antibodies in acute versus nonacute onset FM.

***Methods.*** Two well defined, comparable groups of patients with FM (acute 19, nonacute 20) were studied for antibodies in serum to an array of viruses including IgM antibodies.

***Results***. In most viruses no IgM antibodies were found. However, about 50% of the patients with acute FM onset had IgM antibodies against enterovirus compared to only 15% of the slow onset patients.

***Conclusion.*** The higher prevalence of IgM antibodies against enterovirus in patients with acute onset of FM may indicate a difference in the etiology or the immune response in these patients. (J Rheumatol 2001:28:601–3)

*Key Indexing Terms:*
FIBROMYALGIA ENTEROVIRUS ANTIBODIES ETIOLOGY

The fibromyalgia syndrome (FM) is a common musculoskeletal disorder that has recently been accepted as a nosographic entity. The syndrome is clinically, but not etiologically well described[1,2]. The condition has been known variously as fibrositis, nonarticular rheumatism, and myalgic encephalitis[3]. A related but differently named condition, chronic fatigue syndrome (CFS), may have several overlapping clinical features and possibly the same underlying etiopathology. Up to 70% of patients with FM also meet criteria for CFS[4].

Different infectious agents have been suspected as triggers of both FM and CFS[5], but results have been difficult to reproduce, and treatment with antibacterial or antiviral drugs has failed[5,6]. However, since infectious agents may trigger the immune system by activating cytokines[7] and central neurohormonal circuits, their release may lead to symptoms described by patients and nurture hypotheses pointing to an immunoinflammatory etiology[2,8].

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Our recent findings of circulating IgM antibodies to enterovirus[9] encouraged us to enlarge our study group and split it into 2 categories to investigate differences in acute versus nonacute onset of FM.

## MATERIALS AND METHODS

*Patients*. A total of 307 files from patients with FM were examined. Of 51 randomly selected patients who were asked to join the study 39 were entered. All met the 1990 American College of Rheumatology criteria for FM, but differed in that 19 of them described acute onset of FM closely connected to a viral-like disease, and 20 developed FM slowly over years. All were women, mean age 48 versus 46 years (range 24–63), and their duration of symptoms was 11 versus 7 years (range 3–20) for the acute versus the nonacute group. No patient described signs of ongoing infection at the time of investigation. Medication had been withdrawn for a period of time needed for complete elimination before clinical and laboratory testing to avoid interfering drug effects.

Patients were given detailed information and had given their written consent.

*Methods*. Patients were studied according to protocol for immune abnormalities, and involvement of the central and the autonomic nervous system, inflammatory rheumatic disease, and markers of previous or ongoing infections. Previous diseases, presence of pain, fatigue, morning stiffness, and constitutional signs were recorded and evaluated according to the Fibromyalgia Impact Questionnaire (FIQ) and visual analog scale (VAS) for pain. A physical examination and tender point count was performed. Patients followed a flowchart (Figure 1), and data were collected. This investigation included antibody profiles, a muscle biopsy, and a lumbar puncture.

Laboratory tests were performed in the laboratory of the hospital and at the Statens Seruminstitut by trained bioanalysts. Conventional blood tests included erythrocyte sedimentation rate, C-reactive protein, red and white blood cell count, liver biochemistry, antibodies to striated muscle, antibodies to smooth muscle, antinuclear antibodies, anticardiolipin antibodies, and rheumatoid factor.

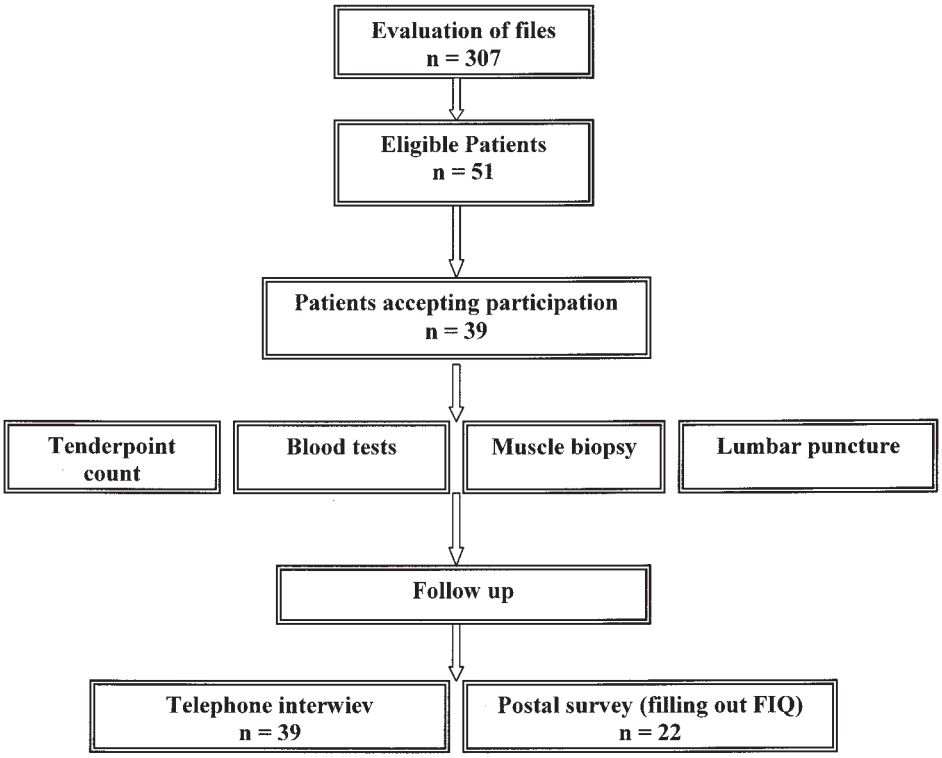


*Figure 1*. Flowchart for patients in the research program.

*Statistics*. Fisher's exact test was performed for comparing different variables. Cutoff values were set at 2.5 × standard deviation of healthy controls.

## RESULTS

No significant difference was found by conventional blood tests in the acute (n = 19) versus nonacute patients (n = 20). We found no IgM antibodies to most viruses tested. Patients with acute onset of FM did not differ from the nonacute patients with respect to the self-reporting systems, clinical, functional, or laboratory data. However, we found a higher prevalence of circulating IgM antibodies against enteroviruses in the patients with acute onset of FM after viral disease (Table 1) compared to the nonacute group, half the patients with acute onset and only 15% of the nonacute group harboring such antibodies ($p < 0.04$).

*Table 1*. Circulating IgM antibodies against viral agents in 2 groups of patients with FM and healthy controls.

| | Acute Patients, n = 19 | Nonacute Patients, n = 20 | Healthy Controls, n = 19 |
|---|---|---|---|
| Hepatitis virus C/B | 0 | 0 | — |
| CMV IgM | 0 | 0 | 1 |
| HHV6 IgM | 3 | 0 | 2 |
| Rubella IgM | 0 | 0 | 0 |
| ParvoB19 IgM | 0 | 0 | 0 |
| Enterovirus IgM | 9*** (n = 17) | 3* (n = 19) | 2** |

*Fisher's exact test, **p < 0.04, ***p = 0.06. CMV: cytomegalovirus.

## DISCUSSION

In healthy persons virally induced pain usually disappears after a short while. In FM and related syndromes patients report ongoing and persistent pain from muscles accompanied by a large number of constitutional, nervous, and immune system related symptoms[10]. Triggers such as infections, physical or psychological trauma, hypermobility, and low back pain have been assumed to be important[1,3,11]. An abnormal reactivity of the nervous and the immune system in hypersensitive individuals may be instrumental in the pathogenesis[12-14]. Neurotropic viruses such as enteroviruses could be eliciting factors in some patients[8,12]. Enterovirus antigen and RNA have been found in the muscle and tissues of patients with CFS[12], and evidence of circulating IgM/antigen complexes has been found, the virus being isolated from 22% of the patients[15]. Increased antibody titers may reflect an immunologic dysfunction[3] or an infection.

The findings in our investigation (Table 1) compare well with our earlier findings[9]. Although a certain patient recall bias cannot be completely excluded, we tried to eliminate this factor by neutral questioning of the patients.

Our data may suggest an ongoing abnormal immune response or a possible relationship between a previous

infection with enterovirus and FM in some patients. In continuing investigations we will look for enterovirus genome sequences in spinal fluids and muscle biopsies from the 2 groups of patients.

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