



## Editorial

### Understanding chronic fatigue syndrome

### Entendiendo el síndrome de fatiga crónica

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A document was recently published in Spain which reviews the most current aspects of chronic fatigue syndrome (CFS).<sup>1</sup> The work was done by a group of representatives of the associations that are more involved in the treatment and management of these patients, and was promoted by the Research Institute for Rare Diseases at the Carlos III Health Institute.

The main objective pursued by this publication is to draw the attention of health professionals on CFS, because, being a rare disease with a low prevalence in the general population, health care for these patients is often dispersed among a number of specialists and primary care physicians who serve without anyone assuming the clinical monitoring of these patients.

The most characteristic symptom of CFS, and the one for which it is named, is the appearance of intense fatigue that persists over time, which is not accompanied by any known disease that could explain it and which significantly limits patient's functional capacity to perform daily activities. But fatigue is not the only clinical symptom, and other symptoms are combined in frequency and intensity in these patients by CFS into a multi-symptomatic disease that is difficult to manage in clinical practice.

Fatigue has been defined in different ways and it has been classified as general fatigue, physical fatigue or mental fatigue, depending on the disease concerned and the objectives pursued, but so far we still do not understand what fatigue is and how it is produced.<sup>2</sup>

Fatigue is a common symptom among the general population, but much more among patients with different diseases, especially rheumatic diseases. In lupus erythematosus or rheumatoid arthritis, for example, both regarded as chronic inflammatory diseases, fatigue is a common symptom that affects the situation of patients in a major way. In these diseases, an attempt has been made to relate fatigue to certain, more objective variables that are therefore easier to measure, and studies have tried to correlate it with some markers of inflammation such as the DAS activity index in the case of rheumatoid

arthritis, or questionnaires that measure activity in systemic lupus erythematosus, but the best correlation has always been with pain in both diseases.

Like fatigue, pain is also an elusive symptom for the doctor, since it cannot be objectified by other diagnostic tests and often follows an independent course to the underlying disease activity and also does not correlate well with activity variables.

In fibromyalgia, a chronic disease characterized by musculoskeletal pain, there has been a misunderstanding of what the disease is and what it means, both as part of a health system and society in general. The problem, in my view, is that the symptoms of fibromyalgia are not easily discernible, giving rise to interpretations of outside observers, either the physician, the family or society. This approach led in time to deny the existence of fibromyalgia by a part of the health collective, with the negative consequences that this entails for the patient and the health system itself.

The extensive review work, research, development of guidelines for health care, clinical guidelines and other consensus documents that have been developed in recent years has ensured that today few doubt the existence of fibromyalgia and now the main discussion focus is whether to consider it a disease or a syndrome.

The usefulness of consensus documents is that they unify positions and are a good starting point for further action, whether for research, treatment or health care strategies.

In the case of CFS, because of its low prevalence among the population and its poorly objective clinical manifestations, something similar happens, so that the unification of attitudes and approaches makes the publication of this kind consensus documents especially important.

An example will help us understand this better. In a recent publication,<sup>3</sup> a group of researchers has found the presence of a retrovirus called XMRV in peripheral blood mononuclear cells of 67% of CFS patients and 3.7% of the healthy population. This virus had been found earlier in a quarter of patients with prostate cancer,<sup>4</sup> specifically in those patients with an associated alteration in the enzyme RNase L, linked to the activity of interferons and which is related to the response to viral infections. Previously, patients with CFS had been investigated for the possibility of the existence of a hidden infection that explained the clinical picture, and when the

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RNase L enzyme was explored, alterations of this enzyme pathway were established.<sup>5</sup>

To carry out this research it has been essential to have blood samples of patients classified as having CFS and this can only be done if one has previously reached a consensus of what the CFS is and how it is diagnosed, hence the importance of the knowledge of Consensus Documents and the usefulness of the classification or diagnostic criteria.

The similarity between fibromyalgia and CFS,<sup>6</sup> has always been striking because of their similar symptoms, albeit with a predominance of pain in fibromyalgia and fatigue in CFS. Moreover, if we apply the criteria for the diagnosis and classification to both processes, we will see that 50%-70% of patients with a disease meet the criteria for the other. However, there are some other differences between these diseases, as a more equal involvement of both genders, younger age at onset, a more abrupt onset or a poorer response to drug treatment, situations that occur more often in CFS.

This data suggest that, as occurs in most diseases, its expression depends on the genetic predisposition of the patient rather than the causes that trigger it. Returning to XMRV, which appears in almost 4% of the healthy control population, what it tells us is that it is a very ubiquitous virus in the general population, and it falls within reason that infection by this virus in a genetically predisposed subject may trigger the onset of symptoms.

Much remains to be done in this area since there is only one published study and many questions about the relationship between the virus and these diseases. But the fact that we could reach this point has been thanks to the fact that there previously existed a hundred blood samples from patients who had been diagnosed with CFS on the basis of disease consensus and classification documents, which are currently the only tools available to make the diagnosis of CFS.

The virological and genetic studies that will follow may, undoubtedly, provide valuable information.

## References

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