

Letters to the Editor

Fatigue as the Chief Complaint

Epidemiology, Causes, Diagnosis, and Treatment

by Prof. Dr. med. Peter Maisel, Prof. Dr. med. Erika Baum, and Prof. Dr. med. Norbert Donner-Banzhof in issue 33–34/2021

Chronic Fatigue Syndrome Deserves Its Own Guideline

According to the authors, chronic fatigue syndrome (CFS) should have its own guideline and “will not be dealt with any further in this article” (1). Indeed, this common complex disorder, which in Germany remains underdiagnosed and misdiagnosed (ca 250 000 in Germany) should have been given its own guideline long ago. This, however, does not exist—and for this reason the disorder could have been explicitly explained in the article “Fatigue as the Chief Complaint,” since paralyzing fatigue is one of the main symptoms in CFS. The article also refers to “a syndrome that has been defined in various ways, without any uniform etiology, and with varying diagnostic criteria.” But reliable criteria for the diagnosis of this complex neuroimmunological disorder exist (the Canadian consensus criteria). According to the current state of research, what it is definitely not is psychological, psychosomatic, or socially caused fatigue (more than 1800 studies in the past decade). This is, however, the implicit message of the article, in which a woolly comment on CFS is linked to declarations regarding primarily psychologically/psychosocially caused fatigue.

Vitamin B12 Deficiency as the Cause

In general practice, fatigue is a major topic in the consultation, especially with patients with non-acute conditions. The article mentions many causes. But I missed clearer indications of nutrition related and behavioral causes. On the one hand, in these times when a healthy and ethically justifiable diet is gaining in importance, dietary/nutritional habits should be an integral part of medical history taking. In all experience, especially younger patients have adopted a vegetarian or even vegan diet.

In the absence of adequate substitution of vitamins and iron supplements, this often results in a striking deficiencies in B vitamins, especially vitamin B12. Vitamin B12 deficiency can cause pronounced symptoms of exhaustion and fatigue, even in the low normal range. This cause should therefore always be considered

In Reply:

We thank Pfnür and Lösch for their readers’ letters and wish to comment on the aspects raised as follows.

The data on myalgic encephalomyelitis (or encephalomyelopathy)/chronic fatigue syndrome (CFS) are voluminous and sometimes controversial. A brief summary in our review article would not have done justice to this situation (1). Since 1986, more than 20 definitions of the syndrome have been published. Euromene, the European expert consensus group for ME/CFS, in 2020 recommended the criteria from the US Institute of Medi-

In the conclusion, the authors say that in patients “with an unremarkable history, physical examination, and basic laboratory test battery” organic disorders are highly unlikely. But is it logical, medically correct, and medically justifiable to conclude from one tiny unremarkable detail (basic laboratory tests) among thousands of laboratory variables: it can’t be anything bad? In CFS, these basic variables are normal—in difference to numerous other laboratory variables. This is also the case for long COVID and, for example, migraine—but in contrast to CFS, these are accepted as disorders and are naturally diagnosed on the basis of clinical criteria.

It is of the greatest importance to differentiate CFS from less severe disorders that are accompanied by fatigue with great clarity and objectivity as a severe physical disorder.

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in the context of the symptom fatigue and also tested for in the laboratory.

Furthermore, it is worth mentioning that vitamin D deficiency in patients who work long hours in indoor spaces (office, factory, warehouse, etc) or those who spend all their time indoors because of illness should be excluded, as vitamin D deficiency can be a contributing factor to other causes of fatigue. DOI: 10.3238/arztebl.m2022.0053

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cine (IOM) as ideal for use in primary care and the criteria from the US Centers for Disease Prevention and Control (CDC) as a screening alternative but as obligatory in the context of the so far optional symptom “post-exertional malaise” (PEM) (2). The criteria from the Canadian consensus conference are recommended for secondary care and research. In the opinion of the Euromene group, the diagnosis of ME/CFS is a purely clinical decision in view of the lack of biomarkers, the causes of the syndrome remain unknown causes, and treatment is symptomatic as causal treatment does not exist. The recently updated ME/CFS

guideline from the UK Institute for Health and Care Excellence (NICE) basically underlines the importance of the named definitions but considers that a diagnosis can be made after three months, rather than the six months recommended by the IOM criteria (3). In Germany, IQWiG (the Institute for Quality and Efficiency in Health Care) is currently working on a report on ME/CFS, which will probably be published in 2023. Because of the inconclusive state of research, we avoided in our article to commit to unknown etiology (1). In our view, laboratory tests, in combination with a medical history, clinical examination, and if needed further technical investigations should be used to exclude other disorders that may be of noteworthy in terms of a differential diagnosis and for which specific treatments exist, in the sense of an avertible dangerous disease course. Non-targeted laboratory tests would not be helpful in view of the lack of ME/CFS biomarkers and would only increase the risk of false positive findings, with well known negative consequences.

A long-term vegan or vegetarian diet, illness-related resorption disorders, or resorption inhibiting medications can without question result in substitution dependent deficiencies in vitamin B12, iron, and—depending on the extent of exercise taken and exposure to sunlight—vitamin D. Questions regarding previous illnesses and medications taken are components of our recommendation for taking medical histories, as well as the question what the patients themselves think might be the cause, in the context of which special dietary regimens are often mentioned. In the additional DEGAM patient questionnaire on fatigue that we recommended in our article, questions about nutritional changes, special diets, and medicines taken require mandatory answers. We do, however, regard critically the premature explanation of fatigue in the absence of the named risk factors with moderately

lowered vitamin or ferritin concentrations without existing anemia or neurological disorders. This poses the risk of overlooking important other causes. In the absence of concomitant anemia fatigue improved as a result of iron supplementation only in premenopausal women with low ferritin concentrations. In low normal concentrations of vitamin B12, cognitive performance and depression did not improve after vitamin substitution, for the symptom fatigue, no robust data exist (4). Vitamin D deficiency does not correlate with increased fatigue (5).

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Conflict of interest statement
 The authors of all contributions declare that no conflict of interest exists.

CLINICAL SNAPSHOT



Kaposi's Sarcoma Under Tyrosine Kinase Inhibition

A 91-year-old female presented with multiple purple-reddish plaques and firm nodules on both legs. The painful lesions had been spreading proximally from the lower legs to the thighs for 5 months. Mucous membranes were unaffected. The patient's medical history included rheumatoid arthritis that had been treated with immunosuppressants for many years, firstly with methotrexate and, in the preceding 3 years, with a janus kinase 1/2 inhibitor. Histopathological analysis revealed dense capillary vessel-like and partially thrombosed vascular proliferation, demonstrating a positive immune response for human herpesvirus 8 (HHV8). The latter confirmed the diagnosis of Kaposi's sarcoma (KS). Apart from classic, endemic, and HIV-related forms, KS

very rarely occurs in serologically negative HIV except, as in this case, in connection with medication such as immunosuppressive therapies, which promote a reactivation of herpesviruses. Remission may occur with discontinuation of immunosuppressive therapy. Due to the patient's significantly reduced general condition, she expressed the wish for an overall palliative plan, as part of which no further local or systemic therapeutic strategies were used.

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