Chronic Fatigue Syndrome??

To the Editor.—

Prolonged, persistent, or chronic fatigue may be observed in a wide variety of childhood illnesses. In a previous communication,[1] I warned about the risks of using the label of chronic fatigue syndrome (CFS) in children. The most significant risk was the misdiagnosis and nonidentification of potentially treatable medical conditions. A careful reading of the recent report by Krilov et al[2] only substantiates my concerns.

Of considerable importance is that this report[2] does not define the clinical criteria used for diagnosing CFS in children. Because convalescence from acute viral or bacterial illnesses may take several months, all of the different CFS diagnostic criteria require a minimum of 6 months of symptoms. The current internationally accepted definition[3] of CFS was clearly not used because 50% of the cases had <6 months of symptoms (in 25% it was <3 months). Without a careful definition of clinical symptoms, it is impossible to determine what this report has actually described.

In the title of this article,[2] the term "chronic fatigue" was carefully used, with the suggestion that "chronic fatigue" in children and CFS are not the same entities. In the text itself the expression "chronic fatigue" appears 19 times, the term "CFS" also 19 times, and the term "syndrome" (is this "chronic fatigue" or "CFS"?) 9 times. After carefully reading this report, it appears that all these three terms are being used interchangeably, synonymously, thus simply adding to semantic confusion.

After reviewing the clinical details presented, it appears that a large percentage of the cases were not fully evaluated or were misdiagnosed.

In my own work in evaluating over 400 cases for CFS (the majority being adults), <1% had an inflamed pharynx when seen. The fact that 36% had an inflamed pharynx in this report,[2] and 10% had associated cervical lymphadenopathy, strongly suggest a persistent viral or bacterial infection, not CFS. Once the infectious process cleared, it would be expected that CFS would improve, as was described in the report.

A total of 60% had "significant allergies."[2] Allergic symptomatology, if severe enough, can produce severe and at times debilitating fatigue. Also, there is a compounding problem, that of potential fatigue from anti-allergy medications. It is common clinical experience to see allergic symptoms wax and wane. Withdrawal from an allergen, as may happen with changes in the seasons, would improve the allergic problem, and the fatigue would remit, as was described in this report.

A total of 38% of the cases suffered weight loss.[2] In my own clinical experience weight gain from inactivity is a major problem for the vast majority of adult CFS patients. It is uncommon to see weight loss in CFS. However, weight loss is a common symptom in a large number of medical diseases and in depression.

As I have discussed previously,[1] salt depletion can lead to CFS-like symptoms. This may be the underlying cause of the fatigue seen in many of the teenage cases diagnosed with neurally mediated hypotension.[4] Food faddism and the currently popular notion that salt is "bad for you," particularly in more affluent communities, have made many teenagers victims of unnecessary salt restriction and subsequent salt depletion. In the report,[2] this issue appears not to have been investigated in any of the cases. A change in dietary intake of salt could lead to clinical improvement, as was described in this report.

In my own practice, when evaluating children with chronic fatigue symptoms, the two most common explanations have been psychologic/social difficulties and sleep disorders.

It should be noted that in this report[2] there was no mention of a thorough psychologic or family/social evaluation having been done. Of note is the fact that before the illness 30% of the children had poor school performance and 27% had irregular school attendance. This fact strongly supports the inference that a significant percentage of the cases in this report actually had an underlying psychologic or social problem, which directly produced chronic fatigue symptoms, and which was not identified.

Chronic sleep deprivation in healthy individuals will cause daytime fatigue. A total of 7% of the cases slept only 4 to 6 hours per night.[2] Because sufficient amounts of sleep are crucial to the well-being of a growing child, this result strongly suggests chronic sleep deprivation as a cause of fatigue in these individuals.

The fact that 24% slept 13 to 18 hours per night[2] suggests the possibility of other sleep disorders, including narcolepsy, idiopathic hypersomnia, and obstructive sleep apnea. However, it appears that no one had a sleep study performed. Although sleep polysomnograms should not be done as a routine in the evaluation of fatigue symptomatology, if there is the possibility of a significant sleep disorder, then a sleep study is medically indicated.

There are a number of other inexplicable findings in this report.[2] On initial examination there were individual cases with a macular rash, hepatomegaly, and splenomegaly. The physical finding abnormalities strongly suggest the presence of a definable medical diagnosis in these 3 cases.

On laboratory testing, 4 cases had positive ASO titers, 3 had elevated sedimentation rates, 3 had positive infectious mononucleosis titers, 2 had positive Lyme disease titers, 1 had an abnormal sinus radiograph, 1 had abnormal thyroid tests, and 1 had increased cortisol levels. Respectively, streptococcal illnesses, underlying rheumatic diseases, infectious mononucleosis, Lyme disease, chronic sinusitis, thyroid diseases, and adrenal diseases, all can produce chronic fatigue symptoms. In these cases a medical differential diagnosis had been clearly established. However, it appears that these differential possibilities were ignored.

For multiple different reasons as discussed above, this report[2] provides extremely strong evidence that CFS should never be used as a diagnosis in children, and should be rarely, if ever, used in adolescents.

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REFERENCES

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In Reply.—

As with any syndrome, the diagnosis of chronic fatigue syndrome (CFS) rests on a combination of patient signs and symptoms and the exclusions of any identifiable cause for the patient's condition.[1] As both of the above letters attest and the history of CFS suggests (with multiple changing names attached to equivalent conditions over the past 100 years), the use of CFS as a diagnosis remains controversial. This diagnosis, given the multiple interacting medical, immunologic, and psychological factors, is unlikely to have a single cause. However, we do believe that the constancy of associated signs and symptoms, (in addition to fatigue), the psychosomatic complaints (apart from depression), and the frequent association of acute onset with an infectious illness (most commonly mononucleosis), justifies the use of CFS as a diagnosis. We believe the major utility of employing such a diagnosis lies in helping patients and families avoid unnecessary multiple medical evaluations and procedures, which many families have pursued (and may continue to pursue) prior and subsequent to referral to our program.

We agree with Dr Plioplys's comment regarding the need to address the potential roles of associated findings. To date, however, neither we nor others who have studied and treated chronic fatigue in children and adolescents have found any one of these findings to be the single cause of the fatigue. Rather, we believe that all of the findings together are what constitutes the syndrome. In our program, we use additional subspecialists (eg, allergists, psychologists, psychiatrists, neurologists) on an individual basis. In reality, many of these evaluations have been performed before our visit without resolution of symptoms. We believe our role in coordinating the use of multiple subspecialties, at times with conflicting opinions or approaches, is beneficial. School issues are a major issue for many of our patients as are work-related disabilities for adults with CFS. These need to be addressed as part of management of most patients, but this alone does not adequately explain the array of findings in these patients. We agree that the psychological issues in these patients need to be considered. Psychological evaluation and support is offered to almost all of our patients during the initial and ongoing physician meetings and through use of the social worker in the Division of Adolescent Medicine. Individual referral to a psychiatrist and/or use of psychotropic medications is based on these assessments. We have on very rare occasions in our population referred patients for a formal sleep disorder evaluation. In support of this not being a primary sleep disorder, the reported sleep irregularities resolve as the patient improves. Most recently, we have established a program with one of our cardiologists to evaluate select patients in whom dizziness and/or lightheadedness is a major complaint by tilt table testing for evidence of autonomic dysfunction or neurally mediated hypotension.[2] In these select individuals salt supplementation and/or pharmacologic therapy has been beneficial. We are presently undertaking a trial to evaluate all patients referred for CFS for this abnormality. We believe this is preferable to the nonspecific use of salt supplementation as suggested by Dr Plioplys.

The Centers for Disease Control and Prevention (CDC) research definition for CFS includes the occurrence of findings for at least 6 months duration.[1] In our program we evaluated all patients referred with the complaint of chronic or prolonged fatigue without requiring 6 months duration of symptoms. However, as discussed in our manuscript, we compared our outcome analyses for patients with >6 months of symptoms with those whose complaints were of shorter duration and found no significant differences.

As for the abnormal clinical and laboratory findings in our patients noted by Dr Plioplys, they were either resolved or felt not be indicative of an active alternative condition before including them in our patient group. For example, in school-aged children the presence of ASO antibody is not necessarily abnormal and does not imply active streptococcal infection or a reactive condition related to recent streptococcal disease. The physical findings of pharyngitis and adenitis were associated with minimal objective changes (ie, mild injection, shotty lymph nodes) and in our opinion were not indicative of acute pathology. The patient's complaints in these areas were typically greater than the objective findings. Although higher than what is seen in Dr Plioplys' patient population, our findings are consistent with other literature report of CFS patients[3] and are part of the CDC research criteria for this condition.[1] The patients with weight loss all had <10% weight loss and after medical evaluation no medical cause for such was elucidated. The difference in this finding from what is described in adults may be related to body image issues unique to adolescents.

We agree with the correspondents that depression, primary or reactive, is likely a part of CFS for a large number of patients. Addressing this in a group with multiple psychosomatic complaints[4] who strongly believe their problems are medical in nature, is a major part of the work with many of these patients.

In conclusion, we still believe the diagnosis of CFS is potentially useful in pediatric patients, and that our differences with Dr Plioplys may be more semantic than substantiative. We use the diagnosis when we believe we have eliminated the medical diagnoses in adolescents with an array of complaints including fatigue and an impressively constant list of multiple physical signs and symptoms that have defied other medical diagnosis. We then use that diagnosis as a mechanism by which to address, hopefully in a coordinated fashion, the medical, immunologic, and/or psychological components in that individual and family. All studies of groups of patients with CFS likely include heterogeneous populations and may not be comparable. As with most such reports our study also suffers from lack of a comparable control group from one to another. Despite these limitations and the retrospective nature of our study, we believe our long-term data offer useful insights into the course of CFS in a group of children and adolescents and supports the use of that diagnosis for these patients.

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