



Published in final edited form as:

Arch Pediatr Adolesc Med. 2011 August ; 165(8): 765–766. doi:10.1001/archpediatrics.2011.124.

Autonomic Symptoms at Baseline and Following Infectious Mononucleosis in a Prospective Cohort of Adolescents

Ben Z. Katz, MD, Julian M. Stewart, MD, PhD, Yukiko Shiraishi, PhD, Cynthia J. Mears, DO, and Renee Taylor, PhD

Department of Pediatrics, North-western University, Feinberg School of Medicine and Children's Memorial Hospital (Drs Katz and Mears) and the Department of Occupational Health, College of Applied Sciences, University of Illinois at Chicago (Drs Shiraishi and Taylor); and The Center for Hypotension, New York Medical College, New York (Dr Stewart).

Abstract

Chronic fatigue syndrome (CFS) is a complex condition involving fatigue and musculoskeletal and cognitive symptoms. Six, 12, and 24 months following monospot-positive acute infectious mononucleosis (IM), 13%, 7%, and 4%, respectively, of adolescents met criteria for CFS.¹ As part of their evaluation at baseline and 6, 12, and 24 months following IM, adolescents diagnosed with CFS and recovered controls completed questionnaires regarding autonomic symptoms.

Methods

We enrolled adolescents in the Chicago, Illinois, area with monospot-positive acute IM, as previously described.^{1,2} All case patients with CFS and recovered controls completed the Autonomic Symptoms Checklist–Patient Version (ASC) at baseline and 6, 12, and 24 months following the diagnosis of IM. The ASC was adapted from the Autonomic Symptom Profile,³ has been validated for CFS,⁴ and has been used down to age 12 years.⁵ Scoring was decided a priori; items were graded from 0 to 7 and then weighted from 1 to 4. The *t* test evaluated the differences between autonomic symptoms at baseline and 6, 12, and 24 months following IM in case patients and recovered controls.

Results

Thirty-eight of 39 adolescents diagnosed with CFS at baseline, 34 of 39 diagnosed with CFS 6 months following IM, 20 of 22 diagnosed with CFS at 12 months, and all 13 diagnosed with CFS at 24 months, along with 50 fully recovered controls at baseline, 49 controls 6 months following IM, 59 controls 12 months following IM, and 62 controls 24 months following IM, completed the ASC. Baseline was a median of 2 months following the

©2011 American Medical Association. All rights reserved

Correspondence: Dr Katz, Children's Memorial Hospital, Division of Infectious Diseases, 2300 Children's Plaza, Box 20, Chicago, IL 60614 (bkatz@northwestern.edu).

Author Contributions: Drs Katz, Stewart, and Shiraishi had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Katz, Stewart, and Taylor. *Acquisition of data:* Katz, Shiraishi, Mears, and Taylor. *Analysis and interpretation of data:* Katz, Stewart, and Taylor. *Drafting of the manuscript:* Katz and Shiraishi. *Critical revision of the manuscript for important intellectual content:* Katz, Stewart, Mears, and Taylor. *Statistical analysis:* Taylor. *Obtained funding:* Taylor. *Administrative, technical, and material support:* Katz, Stewart, Shiraishi, Mears, and Taylor. *Study supervision:* Katz, Mears, and Taylor.

Financial Disclosure: None reported.

Additional Contributions: We thank all of the Clinical Research Center study nurses who helped us with the study and the Pediatric Practice Research Group and all of the physicians and school nurses who referred patients into our study.

diagnosis of IM (ranges: <1 month to 5 months for controls; <1 month to 6 months for cases). Four cases were male, as were 12 recovered controls.

There was no difference between cases and controls who did and did not complete the ASC in age, socioeco-nomic status, body mass index, and modifiable activity questionnaire responses. Adolescents diagnosed with CFS and recovered controls did not differ significantly in age, weight, or body mass index. As an example, the range of ASC scores at 24 months for the patients with CFS was 4.76 to 43.73. The ASC scores at baseline and 6, 12, and 24 months following IM in subjects diagnosed with CFS were always statistically significantly higher compared with the ASC scores of the recovered controls (Table).

Comment

Adolescents with CFS 6 months following IM had many more autonomic symptoms than recovered controls, even at baseline (Table). Our data are consistent with those seen in adults⁴ and can be explained in at least 2 ways: (1) Adolescents destined to develop CFS following IM have a preillness disposition to autonomic dys-function. (2) Adolescents who developed CFS had worse IM (as is true for adults⁶), as evidenced by worse autonomic symptoms. The data we collected as part of this study do not allow us to differentiate between these 2 possibilities.

The strength of our study is that a difference in reported autonomic symptoms was seen as early as a median of 2 months following the diagnosis of IM, making it un-likely that prolonged inactivity is the explanation. Perhaps our data will aid in developing a screening test for adolescents at risk for CFS following IM and lead to pre-emptive therapy for preventing CFS in at-risk patients.

Acknowledgments

Funding/Support: Supported by grant R01HD4330101A1 from the National Institute of Child Health and Human Development.

Abbreviations

CFS	chronic fatigue syndrome
IM	infectious mononucleosis

References

1. Katz BZ, Shiraishi Y, Mears CJ, Binns HJ, Taylor R. Chronic fatigue syndrome after infectious mononucleosis in adolescents. *Pediatrics*. 2009; 124(1):189–193. doi:10.1542/peds.2008-1879. [PubMed: 19564299]
2. Katz BZ, Boas S, Shiraishi Y, Mears CJ, Taylor R. Exercise tolerance testing in a prospective cohort of adolescents with chronic fatigue syndrome and recovered controls following infectious mononucleosis. *J Pediatr*. 2010; 157(3):468–472. doi:10.1016/j.peds.2010.03.025. [PubMed: 20447647]
3. Suarez GA, Opfer-Gehrking TL, Offord KP, Atkinson EJ, O'Brien PC, Low PA. The Autonomic Symptom Profile: a new instrument to assess autonomic symptoms. *Neurology*. 1999; 52(3):523–528. [PubMed: 10025781]
4. Newton JL, Okonkwo O, Sutcliffe K, Seth A, Shin J, Jones DEJ. Symptoms of autonomic dysfunction in chronic fatigue syndrome. *QJM*. 2007; 100(8):519–526. doi:10.1093/qjmed/hcm0571. [PubMed: 17617647]
5. Biegstraaten M, van Schaik IN, Wieling W, Wijburg FA, Hollak CEM. Autonomic neuropathy in Fabry disease: a prospective study using the Autonomic Symptom Profile and cardiovascular

autonomic function tests. *BMC Neurol.* 2010; 10:38. doi:10.1186/1471-2377-10-38. [PubMed: 20529242]

6. Hickie I, Davenport T, Wakefield D, et al. Dubbo Infection Outcomes Study Group. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. *BMJ.* 2006; 333(7568):575–580. doi:10.1136/bmj.38933.585764.AE. [PubMed: 16950834]

Table

Autonomic Symptom Score at Baseline and 6, 12, and 24 Months Following IM Among Patients With CFS and Recovered Controls

	CFS Cases		Controls		<i>t</i> Test	<i>P</i> Value
	No. of Subjects	Mean (SD) Score	No. of Subjects	Mean (SD) Score		
Baseline	38	23.63 (9.80)	50	10.47 (8.55)	-6.59	<.001
6 mo	34	19.63 (9.38)	49	4.94 (6.54)	-7.88	<.001
12 mo	20	14.47 (8.75)	59	5.71 (6.67)	-4.09	<.001
24 mo	13	22.72 (10.54)	62	6.05 (7.52)	-5.42	<.001

Abbreviations: CFS, chronic fatigue syndrome; IM, infectious mononucleosis.