Abstracts

Chronic Fatigue Syndrome: A Possible Delayed Hazard of Pesticide Exposure. P. O. BEHAN AND B. A. G. HANIFFAH. *From the University Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland.*

In this study we examined 10 patients who developed the clinical features of chronic fatigue syndrome (CFS) several months to 2 years after exposure to organophosphate insecticides. These patients were compared and contrasted with 10 patients with postviral fatigue syndrome, 10 patients with primary depressive illnesses, and 10 healthy controls. All subjects were extensively investigated by clinical examination, neurophysiological and immunologic studies, biopsy of muscle, a battery of dynamic hypothalamic tests, and the polymerase chain reaction to test for enterovirus in muscle. We found that patients exposed to organophosphates had disturbances of hypothalamic function similar to those in patients with CFS, and some were positive for enterovirus. Two of the patients had developed non-Hodgkin's lymphoma, a finding also reported in other countries' studies on humans exposed to pesticides. These observations may help in understanding the pathogenetic mechanisms involved in CFS.

Reprints or correspondence: Dr. Peter Behan, Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TF, Scotland.

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Estimating Chronic Fatigue Syndrome–Related Symptoms Among Nurses: A Preliminary Report LEONARD A. JASON, STEPHANIE L. TAYLOR, SHARON JOHNSON, STEPHEN GOLDSTON, DOREEN SALINA, PETER BISHOP, AND LYNNE WAGNER. *From the Department of Psychology, DePaul University, and the Department of Psychology and Behavioral Sciences, Northwestern University, Chicago, Illinois.*

This is the first study to assess the prevalence of chronic fatigue syndrome (CFS)-related symptoms in a sample group of nurses. In the fall of 1991 a three-page questionnaire was sent to 3,400 nurses. Questions were based on definitions from the criteria described by Holmes et al. [1]. Stringent definitions were used to classify the nurses as having CFS-related symptoms. Exclusionary illnesses included hypothyroidism, diabetes, heart disease, and psychiatric disorders. Although it is possible that a number of medical and psychiatric conditions were being successfully treated or were a consequence of CFS, our questionnaire was not specific enough to assess these possibilities. Therefore, nurses with exclusionary medical or psychiatric problems were classified as not having CFS-related symptoms.

A total of 1,474 questionnaires were completed and returned, for a response rate of 43.4%. Two hundred two respondents (6%) checked an item indicating that they had experienced debilitating fatigue for ≥6 months. On the basis of self-reported information, 11 nurses met two major criteria of Holmes et al. [1], (>50% reduction in level of daily activities, no exclusionary illnesses) and eight or more criteria for minor symptoms. While all 202 nurses indicated that they had experienced debilitating fatigue for at least 6 months, only 97 had >50% reduction in activity levels. Of those nurses, 39 had eight or more minor symptoms; however, 28 of those nurses had exclusionary medical or psychiatric disorders. In addition, 23 of the nurses reported that CFS had been diagnosed even though only one of these nurses met the criteria of Holmes et al. [1]. These findings must be interpreted with caution because there were no independent medical confirmations.

Nurses might be a high-risk group for CFS-related symptoms. Therefore, future studies might focus on identifying possible etiologic agents. In our ongoing follow-up study, we are reviewing data from standardized psychiatric interviews and the nurses' medical files to diagnose CFS according to American, British, and Australian criteria.

Reprints or correspondence: Dr. Leonard A. Jason, Department of Psychology, 2323 North Seminary Avenue, Chicago, Illinois 60614.

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Closeness of Contacts Between People in Two Clusters of Chronic Fatigue Syndrome: Evidence for an Infectious Etiology? SEYMOUR GRUFFERMAN, ROSLYN A. STONE, NANCY L. EBY, MARY S. HUANG, SUSAN B. MULDOON, AND LILI PENKOWER. *From the Department of Family Medicine and Clinical Epidemiology, University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania.*

This study assessed closeness of interpersonal contacts between individuals in clusters of chronic fatigue syndrome (CFS) as possible evidence of transmissibility or of common exposure to the source of a noninfectious etiologic agent. Two outbreaks of CFS in discrete occupational groups (members of a symphony orchestra and teachers at an elementary school) were studied to assess whether persons with CFS had closer contact with one another than they had with those members of each group who did not have CFS or whether they had more contact with each other than noninfected members had with other noninfected members of each group. Members of the two groups felt that

Reprints or correspondence: Dr. Seymour Grufferman, Department of Family Medicine and Clinical Epidemiology, M-200 Scaife Hall, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261.

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they contracted CFS via workplace exposure to individuals with CFS. Thus, we defined the two occupational groups as the populations at risk.

Since both clusters occurred before the development of a consensus regarding the definition of CFS, a case of CFS was determined by a physician's diagnosis. Using current diagnostic criteria for CFS, five members of the orchestra met the research case definition of CFS. According to the latest Centers for Disease Control and Prevention (CDC) definition, three other members met Group 2 criteria. In the school cluster, three teachers met the current diagnostic criteria for CFS and four did not. Of the four not meeting the criteria, one was later found to have rheumatic fever and the other three met the criteria of Group 2 of the most recent CDC research case definition.

Members of the groups were asked about their personal contacts with the other members of their group before and during the early phase of each cluster. Contacts were assessed through a hierarchical series of 11 questions that ranged from whether they knew the other person to whether they had had intimate contact with that person. Using these data, we developed methods to test the null hypothesis that there were no differences in the frequency or types of contacts between pairs of CFS patients and pairs chosen at random from the cohorts. Since the data consist of $n(n-1)/2$ pairs of yes/no responses that are not independent, standard statistical methods used to compare two proportions do not apply here. Thus, for each exposure variable, we compared the observed proportions of case-to-case (C-C), case-to-noncase (C-NC), and noncase-to-noncase (NC-NC) pairs who had interpersonal contact, then computed a Knox-type test statistic and compared it with a corresponding test statistic from a simulated permutation distribution of subject pairs.

The first cluster affected eight individuals from the 67-member orchestra. Data were obtained for all eight members with CFS and 50 members without CFS. The second cluster affected seven teachers in an elementary school with a total of 38 teachers. Data were obtained for all seven teachers with CFS (one was found to have rheumatic fever) and 21 teachers without CFS. In the orchestra, members with and without CFS were very similar in mean age, race, and marital status. There were more women than men with CFS. In the school, teachers with CFS were slightly older than those without CFS, but the two groups were similar in sex, race, and marital status.

In the orchestra, there were significantly more C-C pairs than C-NC or NC-NC pairs who reported having shared an eating utensil ($P = .037$) or having shared a bedroom ($P = <.0001$). There were more C-C pairs for the variables "playing together in a chamber group" ($P = .085$) and "riding in a car together" ($P = .056$), but neither result was significant. The data on sharing a bed with a person and on intimate sexual contact were inevaluable because of the small numbers of such pairs (only one such pair in the C-C group). In the school investigation, there were also more contacts between C-C pairs than NC-NC pairs for the variables "riding in a car together" ($P = .08$), "riding on a bus together" ($P = .10$), and "eating a meal together" ($P = .10$). Although the differences observed in terms of proportions of C-C vs. NC-NC pairs with the specific shared exposure were similar in magnitude to those found for members of the orchestra, none of the differences were statistically significant, probably because of the smaller size of the school group.

These data suggest that in clusters of CFS, affected individuals appear to have had more frequent, and probably more intimate, contact with one another than with unaffected individuals, or than unaffected individuals had with each other. This result suggests interpersonal transmission or a common source of exposure to an etiologic agent.

Results of an Investigation of Three Clusters of Chronic Fatigue Syndrome. SEYMOUR GRUFFERMAN, PAUL H. LEVINE, NANCY L. EBY, SUSAN B. MULDOON, MARY S. HUANG, THERESA L. WHITESIDE, LILI PENKOWER, AND RONALD B. HERBERMAN. *From the Department of Family Medicine and Clinical Epidemiology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.*

Results of the investigation of three apparent clusters of chronic fatigue syndrome (CFS) occurring in three well-defined populations are reported to illustrate pitfalls to be avoided in the investigation of future clusters. We conducted multidisciplinary investigations of three clusters of CFS in very different, well-defined populations: members of a symphony orchestra, teachers at an elementary school, and members of a convent.

The first cluster was brought to our attention because of the diagnosis of non-Hodgkin's lymphoma in one of the members of the orchestra. The second cluster was brought to our attention by a patient who knew of our interest in CFS clusters. Since both clusters occurred before the development of a consensus regarding the definition of CFS, a case of CFS was defined by a physician's diagnosis.

Through a review of their medical records, we found that five members of the orchestra met the current Centers for Disease Control and Prevention (CDC) research case definition of CFS. The residual three cases met Group 2 criteria according to the latest CDC definition. In the school, where review of teachers' medical records was not possible, we used questionnaire data to determine that three teachers met the diagnostic criteria for CFS, and four did not. Of the four cases who did not meet the criteria, one was later diagnosed as having rheumatic fever; the other three met Group 2 criteria of the recent CDC research case definition of CFS. The third cluster was in a convent where we made a more intensive effort to define each case by making detailed clinical evaluations of severely affected individuals. However, we report the findings for this group to illustrate how individuals in an apparent CFS cluster tend to mistakenly label other diseases as CFS. This cluster was brought to our attention by a colleague who treated two of the nuns and knew of our interest in CFS clusters.

In the third study, only assays of viral immunity were done, whereas in the first two clusters laboratory studies included assays of cellular immunity (natural killer [NK] cell activity, T cell assays, mitogen stimulation, etc.) and viral immunity (antibodies to Epstein-Barr virus [EBV], human herpesvirus type 6 [HHV-6], cytomegalovirus, and human T cell leukemia virus I/II). For reasons of similarity in age, race, and socioeconomic

Reprints or correspondence: Dr. Seymour Grufferman, Department of Family Medicine and Clinical Epidemiology, M-200 Scaife Hall, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261.

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