Concurrent Sick Building Syndrome and Chronic Fatigue Syndrome: Epidemic Neuromyasthenia Revisited

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Sick building syndrome (SBS) is usually characterized by upper respiratory complaints, headache, and mild fatigue. Chronic fatigue syndrome (CFS) is an illness with defined criteria including extreme fatigue, sore throat, headache, and neurological symptoms. We investigated three apparent outbreaks of SBS and observed another more serious illness (or illnesses), characterized predominantly by severe fatigue, that was noted by 9 (90%) of the 10 teachers who frequently used a single conference room at a high school in Truckee, California; 5 (23%) of the 22 responding teachers in the J wing of a high school in Elk Grove, California; and 9 (10%) of the 93 responding workers from an office building in Washington, D.C. In those individuals with severe fatigue, symptoms of mucous membrane irritation that are characteristic of SBS were noted but also noted were neurological complaints not typical of SBS but quite characteristic of CFS. We conclude that CFS is often associated with SBS.

Recently recognized as an occupational disease, sick building syndrome (SBS) is characterized by symptoms of mucous membrane irritation (e.g., rhinitis, conjunctivitis, and cough), fatigue, and headache [1–5]. Outbreaks of SBS are generally described among employees in multistory office buildings constructed after 1965. Sealed windows, closed fresh-air intake ducts, and an impervious external shell usually describe the structure [6]. In affected individuals symptoms often abate over the weekend when they are away from the job site.

Chemical or microbiological contamination may be found, but more typically the evaluation is unrevealing [1]. Epidemiological studies clearly implicate the workplace, thus discounting earlier suggestions of "mass hysteria" [6–8]. Furthermore, improved ventilation often helps, thereby suggesting that the "tolerable" levels of contaminants may produce the syndrome by acting in concert. As yet unidentified agents, toxin(s) or microbe(s), however, must also be considered.

Chronic fatigue syndrome (CFS), a term recently coined for a long-known condition, is characterized by extreme fatigue with other agreed upon criteria including sore throat, headaches, and neurological complaints [9–13]. The illness often has a sudden onset, demonstrable lymphadenopathy, low-grade fever, and possibly a psychiatric contribution [14, 15]. CFS has followed clearly documented infections with the Epstein-Barr virus, cytomegalovirus, and human herpesvirus type 6 [16, 17]. Psychiatric trauma and exposure to toxins are also apparent precipitating agents [18]. Many patients have elevated titers of antibodies to a number of viruses, abnormal production of interferon, and depressed function of natural killer cells [19–22]. Of these patients 50% to 80% have allergies compared with 17% of the general population [23]. None of the proposed etiologies for CFS have been substantiated. Documented cases of CFS have been reported as part of disease clusters in varying proportions [24–26].

Outbreaks of epidemic neuromyasthenia (ENM), which is known variously as postviral fatigue syndrome, epidemic myalgic encephalomyelitis, and Iceland disease, have been described since 1934 [27–31]. The signs and symptoms are different among varying clusters, thus suggesting that the term *ENM* may actually represent more than one disease process [32–34]. The variability of physical and laboratory findings for ENM is similar to that for CFS, as are the symptoms. Headache, fatigue, and upper respiratory problems are noted in addition to neurological and musculoskeletal complaints that may be quite severe. Many investigators suspect viral causes, although none have been documented.

We describe three outbreaks of SBS associated with the development of CFS. All outbreaks were characterized by perceived poor air quality and the symptomatic triad of SBS of fatigue, headaches, and upper respiratory complaints. The prevalence of severe fatigue varied significantly among the outbreaks, thereby suggesting that the inciting agent(s) differed quantitatively or qualitatively. Nevertheless, the link of CFS with SBS suggests the possibility that the agent(s) responsible for the traditional symptoms of SBS may also trigger CFS.

Methods

Elk Grove, California. In October 1989 the smell of fumes was noted in the J wing of Elk Grove High School, which is located near Sacramento, California. Two teachers soon became ill, thereby prompting complaints about the building to the school district. Within months 19 of the 23

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Clinical Infectious Diseases 1994;18(Suppl 1):S43–8

1058–4838/94/1801–0007$02.00

teachers in the J wing (~20% of the entire faculty) complained of an illness characterized by recurrent sinusitis, headache, and fatigue. Additional complaints included cough, sore throat, tender cervical lymph nodes, myalgias, and depression.

A detailed questionnaire was sent to all 23 teachers in the J wing of Elk Grove High School ~1 year after the beginning of the outbreak and 6 months after the ventilation was improved. The teachers provided informed consent on the questionnaire. Questions regarding individual characteristics (including age, sex, race, marital status, and time spent in the J wing) were first on the questionnaire followed by a detailed list of questions relating to both CFS and SBS (including otorhinologic, neurological, mucocutaneous, musculoskeletal, and allergic symptoms). Those individuals with unexplained fatigue were further asked about the characteristics of that fatigue (including duration, degree, onset, variability, etc.).

Twenty-three age- and sex-matched control subjects were selected from a list of the remaining 94 faculty members not teaching in the J wing. The answers of the 22 teachers in the J wing who responded contrast with those of the 21 responders from the control group (data provided under Results). All responders suspected of meeting previously published criteria for CFS [9] were interviewed by a physician who also reviewed their medical history.

Washington, D.C. Twenty-two workers of the Federal Department of Justice presented to union officials in October 1986 with headaches, upper respiratory complaints, and symptoms of eye irritation. Five employees had recently had viral or atypical pneumonia. Complaints of stuffy air and diesel fume odors prompted an air quality evaluation of the office building. Employees noted headaches, fatigue, and myalgias. Additional problems included memory difficulties, low-grade fevers, and eye tearing. Many individuals ultimately received treatment for allergic rhinitis, sinusitis, and related complaints. Some employees had cyclic symptoms, and some noted significant improvement in their conditions after an absence from the building.

Five years after the initial complaints and ≥1 year after several modifications to improve the intake and flow of fresh air, the federal workers were evaluated by a questionnaire similar to the one used in Elk Grove, but this questionnaire was anonymous and less detailed. By random selection (every third worker), 115 of the ~350 workers of the Federal Department of Justice were questioned, and 93 (81%) responded.

Separately, 20 of the 350 workers presented as self-selected individuals with a severe illness. After informed consent was obtained, all workers suspected of having CFS were interviewed by a physician, either in person or by telephone.

Truckee, California. During the outbreak of an illness in the Lake Tahoe area marked by persistent fatigue and a variety of symptoms often seen in CFS [13, 17, 24, 26], teachers at a high school in Truckee, California, noted that the illness in their school appeared to concentrate in those using a single conference room. Approximately 1 year after the initial report of an outbreak [35], an in-person interview questionnaire, similar to the one used in Elk Grove, was administered to six of the 10 teachers who frequently used this room. All six teachers were carefully questioned by a physician, and their health records were examined. Health information about the remaining four teachers was obtained by telephone after informed consent was obtained.

Statistical methods. In all cases differences between groups in proportions were compared with use of standard χ^2 analysis (2×2 contingency table) with $P < .05$ as the significance level.

Results

Elk Grove, California. The J wing was built of brick and cinder block in 1960 and has no windows, thus limiting ventilation to that available from a malfunctioning variable air volume duct system of heating and air conditioning (HVAC). The system was triggered only by thermostat demand, thereby permitting hours to go by without air circulation. The fresh-air dampers were 50% closed, and the fresh-air intake was within feet of the stale-air exhaust. The air filters were fouled by dirt and bird droppings and not changed for an indeterminate period.

An idling gasoline-powered cart that contaminated the circulating air would be parked in the HVAC utility room for varying periods. The building had twice been flooded (1986 and 1988), and water stains were noted on the acoustic ceiling tile as well. An art room with volatile organic chemicals was not separately ventilated.

An attic with torn fiberglass batting insulation served as a common return air plenum. The outflow ducts were covered with a fine dust. Air flow was erratic, with temperatures exceeding 90°F in some rooms. Ventilation generally stopped at 3:30 P.M., not to resume until the following morning.

An industrial hygiene survey documented CO_2 levels acceptable to the Occupational Health and Safety Regulation Authority but in excess of the standards of the American Society of Heating Refrigeration and Air-Conditioning Engineers because of insufficient air flow. Excessive levels of volatile organic chemicals (toluene, xylene, and formaldehyde) were not detected. Tests for fungi and bacteria were unremarkable.

Upon receiving the results of the study, the school instituted recommendations that included constant air circulation with fresh-air dampers fully opened, elimination of exhaust contamination, and appropriate cleaning. Symptoms continued despite these measures.

Five teachers (four women and one man) fulfilled the previously published criteria [9] for CFS. Four teachers required a leave of absence and seven ultimately filed for workmen's

Table 1. The prevalence of symptoms of SBS.

Symptom	No. (%) of individuals in indicated outbreak with symptom: Elk Grove, J wing teachers (n = 22)	Elk Grove, Control teachers (n = 21)	P value*	Washington, D.C. (n = 93)
Headache	13 (59)	4 (19)	<.009	39 (42)
Sore throat	15 (68)	4 (19)	<.003	21 (23)
Cough	9 (41)	4 (19)	NS	20 (22)
Fatigue	15 (68)	3 (14)	<.001	34 (37)
Frequent colds	13 (59)	2 (10)	<.002	22 (24)
Sinusitis	17 (77)	9 (43)	<.03	42 (45)

NOTE. NS = not significant.
* Compares the J wing and control populations of Elk Grove.

Table 3. The prevalence of neurological symptoms.

Symptom	No. (%) of individuals in indicated outbreak with symptom: Elk Grove, J wing teachers (n = 22)	Elk Grove, Control teachers (n = 21)	P value*	Washington, D.C. (n = 93)
Headache	13 (59)	4 (19)	<.009	39 (42)
Dizziness	4 (18)	2 (10)	NS	27 (29)
Decreased concentration	10 (45)	2 (10)	<.03	23 (25)
Decreased memory	11 (50)	4 (19)	NS	18 (19)
Weakness	6 (27)	2 (10)	NS	7 (8)

NOTE. NS = not significant.
* Compares the J wing and control populations of Elk Grove.

compensation. The course of the illness has varied, but most individuals remained ill 2½ years after the onset.

The results of the study are noted in tables 1–4 and figure 1. Fatigue was noted by 15 (7 men and 8 women) of the 22 responders from the J wing (study group) and 3 (2 men and 1 woman) of the 21 age- and sex-matched control subjects who responded ($P < .001$). The prevalence of severe fatigue and CFS is noted in figure 1. In addition, symptoms more common in the study group than in the control group, respectively, included the perception of fever, 36% vs. 0 ($P < .005$); frequent headaches, 59% vs. 19% ($P < .009$); tender cervical lymph nodes, 41% vs. 0 ($P < .003$); nasal pressure or pain, 45% vs. 10% ($P < .02$); and unexpected generalized fatigue after reasonable levels of exercise, 55% vs. 14% ($P < .005$). In the study group, 10 of the 15 individuals with fatigue noted the onset of fatigue after a head cold; 7 of the 14 who were treated with antibiotics mentioned a temporary improvement in their conditions.

The five teachers in the J wing who had severe fatigue had significantly more neurological symptoms than did the control subjects; these included headache, 5 (100%) vs. 4 (19%) ($P < .004$); dizziness, 4 (80%) vs. 2 (10%) ($P < .006$); decreased concentration, 5 (100%) vs. 2 (10%) ($P < .001$); decreased memory, 5 (100%) vs. 4 (19%) ($P < .001$); and weakness 5 (100%) vs. 2 (10%) ($P < .001$).

Washington, D.C. The 30-year-old 13-story office building was sealed with no functioning windows. Two sources provided the air flow: a high-pressure HVAC unit on the roof that supplied variable air flow to only the outer offices and a low-pressure constant-volume HVAC system on each floor that was directed at only the inner offices. Air from both systems mix in the halls and vestibules and return to the different HVAC systems through separate ducts. Both sys-

Table 2. The sex prevalence of fatigue.

Characteristic, sex	No. (%) of individuals in indicated outbreak with characteristic: Elk Grove, J wing teachers	Elk Grove, Control teachers	Washington, D.C.*
Total population	22 (100)	21 (100)	93 (100)
Men	10 (45)	10 (48)	28 (35)
Women	12 (55)	11 (52)	52 (65)
Fatigued population	15 (68)	3 (14)	34 (37)
Men	7 (47)	2 (67)	6 (19)
Women	8 (53)	1 (33)	25 (81)
Severely fatigued population†	5 (23)	0	9 (9)
Men	1 (20)	0	2 (22)
Women	4 (80)	0	7 (78)

* Not all individuals who returned questionnaires from Washington, D.C., included sex.
† The severely fatigued population is included in the fatigued population noted above.

Table 4. The prevalence of neurological symptoms in those teachers with severe fatigue who were in the J wing of the Elk Grove High School compared with the entire control population.

Symptom	No. (%) of individuals with symptom: Severely fatigued J wing teachers (n = 5)	Control teachers (n = 21)	P value
Headache	5 (100)	4 (19)	<.004
Dizziness	4 (80)	2 (10)	<.006
Decreased concentration	5 (100)	2 (10)	<.001
Decreased memory	5 (100)	4 (19)	<.001
Weakness	5 (100)	2 (10)	<.001

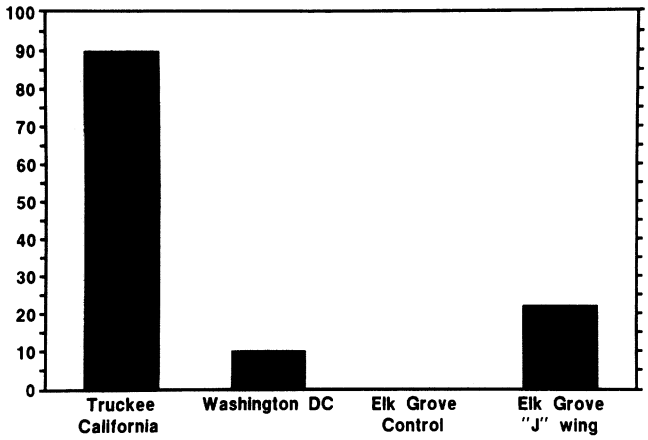

Figure 1. The prevalence (%) of severe fatigue.

tems are capable of admitting fresh air. The dampers are set for ≥25% fresh-air intake, although it had been the practice to shut them during the cooling season.

Since 1986 the building has been evaluated 15 times, including air samples for volatile organic compounds, fungi, and bacteria; humidity levels; and lead levels in drinking water. No significant abnormalities were documented, although inadequate air flow and marked differences in temperature and humidity levels were occasionally noted. The fresh-air intake for two floor HVAC units was sealed temporarily because of concerns related to exhaust from nearby construction work machinery with no apparent beneficial effects.

Results from the 93 workers who responded are noted in tables 1, 2, 3, and 5 and figure 1. The fatigue started suddenly in 44% of these individuals (53% of whom noted the onset after a head cold or sinusitis). Frequent pressure in the forehead was described by 33% of the responders and nasal pressure or pain, by 27%. Unexplained muscle weakness was noted by 8% of these workers. Used as a distractor, the listing of frequent pain on urination was noted by only 3% of these individuals. Of the responders, 82% felt better when they were out of the building; 97% complained of too little air flow, and 83% described the air as stuffy.

Because of the anonymous nature of the questionnaire, those individuals with severe fatigue could not be interviewed. Separately, however, 20 self-selected individuals presented to the investigators with significant symptoms. Five of these workers (four women and one man) met previously published criteria for CFS [9].

Truckee, California. Coincident with, and reported as part of an outbreak of CFS in northern Nevada and California [13, 17, 24], nine of 10 high school teachers who used a single, small, poorly ventilated conference room became ill sequentially. All nine teachers required a leave of absence, and two retired. Eight teachers remain ill 5 years after the onset of the outbreak. The one unaffected teacher spent less time than the others in the conference room, often doing his work outdoors.

The conference room was one of four rooms serviced by an all-water heating system installed in 1985. It functioned by using variable air flow over a coil filled with hot water. The fresh-air vents were sealed with no other source of fresh air available. There were no functioning windows or air conditioning. A spirit duplicator and two coffee machines were in the room.

The onset of illness was generally sudden, evolving over ~1 month, and fatigue was the predominant symptom. Headaches, myalgias, and dyspnea were other common complaints. Photophobia was often noted, with difficulty keeping the eyes open even in darkness. Many individuals experienced recurrent sinusitis. The prevalence of severe fatigue is noted in figure 1.

Discussion

The three outbreaks of SBS noted above were characterized by the traditional complaints of SBS of headache, fatigue, and upper respiratory symptoms. Mucous membrane irritation and complaints of fatigue and headache are typical of SBS. This report, however, also describes a severe fatigue associated with neurological complaints consistent with CFS. In each case no clear association with a particular pollutant, toxin, or microbe is documented, but in all three outbreaks, there was inadequate ventilation and the clear perception by those individuals questioned of "stale air." Most apparent in Elk Grove and Truckee, the disease was concentrated in areas isolated by HVAC systems. In Elk Grove the prevalence of CFS was greater among teachers in the J wing, as were the more typical symptoms of SBS.

Inadequate ventilation was the probable cause of SBS in 53% of the buildings investigated by the National Institute for Occupational Safety and Health and at least part of the problem in the two outbreaks noted here [1]. As noted in the similar experiences of other investigators, however, im-

Table 5. The prevalence of neurological symptoms in those workers with severe fatigue in Washington, D.C., compared with the remaining population of workers.

Symptom	No. (%) of individuals with symptom		*P* value
	Severely fatigued workers (n = 9)	Remaining workers (n = 84)	
Headache	8 (89)	31 (37)	<.001
Dizziness	3 (33)	24 (29)	NS
Decreased concentration	5 (56)	18 (21)	<.05
Decreased memory	5 (56)	18 (21)	<.05
Weakness	1 (11)	6 (7)	NS

NOTE. NS = not significant.

proved ventilation did not eliminate the symptoms [36]. Despite more than adequate fresh air by conventional standards, symptoms persisted in most of the affected individuals. Paradoxically, those individuals with milder symptoms were more likely to report symptomatic abatement when removed from the buildings, while those who were severely affected found little respite. Most particularly, the upper respiratory symptoms and fatigue continued in those individuals who were both severely and mildly affected, thereby suggesting a continued unrecognized toxic exposure, an elusive infection, or a self-perpetuating process triggered by the unknown original insult. None of those individuals classified as having CFS were cured by increased outdoor air flow.

The quality of that outdoor air was not examined, however. Outdoor pollution has a significant effect on indoor populations and may be the continuing toxic exposure in these cases. In a study of nurses working indoors, headache and cough correlated with outdoor concentrations of photochemical oxidants rather than indoor levels of CO or NO_2 [37].

As with previously described ENM, an illness also often linked to a building, a wide spectrum of severity is noted [33]. ENM, however, appears to be a heterogeneous group of illnesses, and while many investigators have considered ENM, myalgic encephalitis, epidemic CFS, atypical poliomyelitis, Iceland disease, etc., as a nosological entity [33, 34], more recent reports have stressed the differences between a number of outbreaks and recommend more detailed attention to cluster descriptions [13, 24, 32].

ENM often includes symptoms indistinguishable from those of SBS: the triad of headache, fatigue, and upper respiratory complaints associated with various neurological and musculoskeletal afflictions. Unlike ENM, air-borne pollutants rather than undiscovered microbes are believed to cause SBS. Indeed, the National Institute for Occupational Safety and Health has documented many symptomatic cures of SBS after increased fresh-air intake [1].

Although outbreaks of CFS have been described, the association we have noted with SBS has not been specifically mentioned as such. CFS has attracted considerable attention in the lay and scientific communities and has also been the subject of several symposia and workshops [15, 38, 39] in an attempt to characterize this illness and clarify the etiologic and pathogenetic mechanisms involved. A working case definition was developed for research purposes in 1988 [9] in an effort to aid investigative communication and has subsequently been modified [40].

An abundance of outdoor pollutants in epidemics of CFS and SBS has not been described but should be considered. Pollutants, allergens, atmospheric inversions, and additional weather changes may act in concert to cause directly or indirectly the troublesome symptoms known by so many terms, including SBS, CFS, and ENM.

Because of the considerable overlap in clinical presentation between SBS and ENM, similar pathogenic processes may be involved. It is important to note that CFS, defined for research purposes to be an illness of unexplained etiology with at least 6 months of severe debilitating fatigue, is documented only sporadically in ENM and has not been specifically noted in SBS. "Sporadic CFS," a case not associated with a cluster, has been noted to be triggered by a primary infection with Epstein-Barr virus, cytomegalovirus, and human herpesvirus type 6, viruses endemic in the community that often produce asymptomatic infection [41]. Since exposure to chemicals, such as tung oil [42], has also been observed to precede the onset of CFS, it is quite likely that CFS is an occasional outcome of an exposure to an infectious agent, a chemical toxin, or both and that the attack rate depends on the virulence or strength of the precipitating agent as well as host susceptibility. A variety of immunologic and hormonal abnormalities have been described in patients with CFS [19–22], as has evidence of psychological stress.

Nasal irritation, often caused by pollutants as well as sustained by pollutants after an initial viral infection, can produce many of the symptoms noted in the three outbreaks described [43]. Indeed rhinologic symptoms were noted disproportionately in the affected individuals. Sinusitis, frequent upper respiratory infections, sore throats, nasal pressure or pain, and tender anterior cervical lymph nodes characterized the outbreak in the J wing of the Elk Grove High School. Ten of the 15 fatigued individuals noted the onset after a head cold. Seven of the 14 individuals who were treated with antibiotics described a temporary improvement in their conditions.

Nasal irritation is considered responsible by many investigators for only local symptoms, although it is clearly capable of causing fatigue [44]. Significant changes in cardiovascular and respiratory functions are caused by nasal reflexes [45]. Alternatively, nasal injury may trigger a disease process in predisposed individuals. CFS, often associated with sinusitis, may be initiated but not caused by that illness.

Our data do suggest, however, that CFS can occur in the setting of SBS. Like ENM described in the older literature, SBS is characterized by a spectrum of signs and symptoms that, when severe, constitute an illness indistinguishable from CFS. Our data also suggest that CFS, which is often triggered by infectious agents, can likewise occur in a predisposed individual after exposure to a noninfectious agent or agents. A working case definition for SBS should be established, as it has been for CFS, to better define the syndrome and facilitate better communication among investigators.

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