

**2007 Medical Student Scholarship Winner
John Young**

**Chronic Fatigue Syndrome:
From the Patient to the Public Health Problem**

Mrs. R. is an Italian-American woman in her 40's who, in 1989, began having symptoms of fatigue, sore throats, headaches, and a "general sense of not feeling well." She had always suffered from headaches so, at first, she paid no attention to them and would "shrug off symptoms". However, the symptoms worsened until, after 8 hour workdays she would lie down and "be done for the night." In 1992, after having seen 3 or 4 doctors, she was diagnosed with Chronic Fatigue Syndrome. While researching Chronic Fatigue Syndrome (CFS), I had the opportunity to interview Mrs. R who is the mother of a classmate and dear friend. Through our conversation, I got a personal account of her experience. Mrs. R. added that human component, that is so critical in healthcare, to the academic research I was reading; she helped me to contextualize the disease in a patient-centered manner. Mrs. R's experience is something that afflicts many - the question at hand is whether the illness they suffer from is a public health problem. While the scope of this paper is on the larger scale community problem of CFS, it is critical throughout this discussion to keep in mind the individual patient's battle with CFS, and thus I will quote Mrs. R's own words to guide the discussion.

The public health problem

"Your outlook is different when you know what you're living with is not going to change."

Chronic fatigue syndrome is a disease marked by debilitating fatigue for at least 6 months and may involve numerous rheumatological, infectious, and neuropsychiatric symptoms. In their 2003 review of Chronic Fatigue Syndrome, Afari and Buchwald provide a concise summary of the CDC's revised case definition of chronic fatigue: ...at least 6 months of persistent fatigue that substantially reduces the person's level of activity. In addition, four or more of the following symptoms must occur with fatigue in a 6-month period: impaired memory or concentration, sore throat, tender glands, aching or stiff muscles, multi-joint pain, new headaches, unrefreshing sleep, and postexertional fatigue. Medical conditions that may explain the prolonged fatigue as well as a number of psychiatric diagnoses (i.e., eating disorders, psychotic disorders, bipolar disorder, melancholic depression, and substance abuse within 2 years of the onset of fatigue) exclude a patient from the diagnosis of chronic fatigue syndrome. [1]

With a general idea of what CFS is, we can begin to tackle the issue of whether it is a public health concern. Some definitions are, however, first necessary. The World Health Organization defines health as "A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" [2]. Adding the word "public" to "health," complicates matters. While most health professionals and lay people have an idea about what public health is, there is no single concrete definition. An early, but longstanding definition was presented in 1920 when C.-B.A. Wilson wrote that public health is "...the science and art of preventing disease, prolonging life and promoting health through the organized efforts and informed choices of society, organizations, public and private, communities and individuals" [3]. A more recent definition from the Oxford Textbook of Public Health says that "...public health is the process of mobilizing and engaging local, state, national, and international resources to assure the conditions in which people can be healthy" [4]. Clarifying what constitutes a "public health problem" is no easier. As Harry Stol Mustard wrote, "A health problem becomes a public health responsibility if or when it is of such a character or extent as to be amenable to solution only through systematized social action" [5]. Thomas Parran, the Surgeon General from 1936 to 1948, said that "Whenever a disease is so widespread in its population, so

serious in its effects, so costly in its treatment, that the individual cannot deal with it himself, it becomes a public health problem." [6] As is evident, settling on one definition of "public health problem" is a difficult task and I will not attempt to do so, nor will I present my own definition of a public health problem. That is a battle reserved for public health experts and lexicographers. I do, however, believe that the definitions above have common themes in defining public health problems. Namely, that they are widely prevalent, they cause health damages, and they require organized efforts to treat and/or prevent. It is these three characteristics that are critical in defining whether something is a public health issue.

Prevalence

"There was a group near St. Barnabas that would meet once a month...but I could never quite get to it... I didn't find it helpful, there are so many degrees of debilitation that it's hard to commiserate. It was through the years of becoming a member of the National Society and the Jersey organization and trying to read up that I became aware."

The first criterion in evaluating whether something is a public health problem is whether or not it is prevalent. Estimating the prevalence of CFS in the population has been difficult because the populations examined, definitions applied of CFS, and sampling collection methods used have varied widely. The estimates of prevalence in the United States are typically in the 0.2 to 0.5% range [7-9]. Gender appears to be a factor that affects CFS: women have a higher prevalence rate with estimates ranging from 0.34 to 0.53%, while men's estimates are usually within 0.081 to 0.291% [7-9]. A person's age appears to be another factor that affects CFS: CFS strikes people in the age range of 40 to 49 most, with estimated prevalences from 0.3 to over 0.8% [7-9]. In contrast, both significantly younger and older age groups had the lowest prevalence rates. In the age range of 18 to 29, prevalence rates ranged from 0.05% to 0.315%, while in the age range of 60 to 69, prevalence rates were from 0.13 to 0.17% [7-9]. The low prevalence of CFS in the older population may be because of a higher prevalence of exclusionary illnesses. The association of race and CFS is a murkier one. Earlier reports, primarily from tertiary clinics, had initially indicated that white women were affected in greater numbers. These findings, however, have been questioned on the basis that white women are probably more likely to have access to and utilize health care [1]. More recent community studies have shown that minorities, in particular, the Latino and Native American populations have the highest prevalence of CFS [7-9]. One study has the Latino prevalence rate at 0.726% while another has the Native American prevalence rate at 2.63% [7, 9]. In contrast, whites' ranges of estimated prevalence are between 0.2% and 0.32% [7-9]. Occupation and household income also appear to be correlated to prevalence of CFS. In one study, breaking down occupation by unskilled/semiskilled, skilled, and professional, it was found that unskilled/semiskilled workers had a prevalence of 0.486% and semiskilled workers had a prevalence of 0.701% compared with professionals who had a prevalence of 0.325% [10]. Similarly, people whose household income was under \$40,000 had a prevalence rate of 0.3% whereas people whose income was more had a prevalence rate of 0.16% [9]. These numbers may seem small so to better gauge these values, it helps to compare them to more commonly known diseases. Utilizing both the US Census Bureau's 2000 summary and US National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database for the year 2002, we can calculate the prevalence rates for a number of cancers [11, 12]: For the four most common cancer types: breast, prostate, colon/rectum, and lung/bronchus cancer, the prevalence rates were calculated to be: 0.815%, 0.652%, 0.374%, and 0.125% respectively. Thus, while CFS is less prevalent than the top three cancer types, it is more prevalent than lung cancer. What is prevalent enough to be considered a public health is a subjective issue. However, it is safe to assume that the lay public and experts alike would agree that lung cancer, at a 0.125% prevalence is

widespread enough that it fulfills that prerequisite of being considered a public health problem. Therefore, CFS also fills the first criterion of being a public health problem - it is quite prevalent.

Damages

"There are physical symptoms and cognitive symptoms. If you try to do too much one day, then you're out for the count. I had to give up my job and not work.... Often I don't sleep through the night.... and there's a diminished capacity to focus... 'brain fog', I think."

The second criterion in determining if something is a public health problem is whether there are health damages. The clinical presentation of chronic fatigue is a good starting point to evaluate the health damages. Fatigue is the hallmark symptom of chronic fatigue syndrome, and is an indicator of the drop in one's physical well-being. What makes the drop more significant is that typically, prior to presenting with CFS, the patient has been fine in terms of physical fitness and energy [13]. Then, there is a sudden onset of fatigue that physical exertion tends to exacerbate. In addition, many CFS patients also have symptoms of anorexia, nausea, night sweats, vertigo, and intolerance to CNS-affecting substances such as alcohol [14]. While the health damages are hard to bear, what makes them even worse are the linked economic and personal co-morbidities. These functional damages can be measured by self reports of how patients felt in terms of energy, wellness, and ability to complete everyday activities. On a scale of 1-100, (100 being the highest functional capacity), those that were not fatigued scored around 80 to 85 while the mean CF score was a 40 [15]. One's energy level is linked to how much activity one can complete in a day, including one's employment duties. The more severely fatigued therefore spend significantly less time working and fewer total hours on meaningful activity than those without fatigue [15]. Thus, it is not surprising that there is a significant difference in employment rates between the non-fatigued (78%) and those suffering from CFS (54%) [15]. The impairment goes beyond the workplace. Patients suffering from CFS report that prior to the onset of their disease, they spent significantly more time on chores [15]. Furthermore, researchers have shown considerable disablement of CFS patients in role functioning, social functioning, and vitality, at levels comparable to other patients suffering from known chronic disabling conditions [15, 16]. The economic damages on both the individual and on a national level are significant as well. The estimated cost for each person with CFS is projected to be over \$9000 [17]. In addition, among the affected individuals that are unemployed and receive disability, there is an average of \$20,000 lost in earnings and wages [18]. The total economic cost of CFS in the US is estimated at \$9.1 billion/year [19]. Given the significant health, social, occupational, and economic damages that CFS causes; it is clear that this is a problem that needs to be addressed.

Necessity of organized efforts

"There needs to be some change in the medical field. That in turn will change what's out there in the public."

The third and final criterion of a public health problem is that it requires organized efforts and utilization of resources to deal with. Why does tackling the problem of chronic fatigue syndrome require organized efforts and utilization of resources? It boils down to the complexity of the disease. From the case definition of chronic fatigue syndrome listed earlier, it is evident that the syndrome is not a clear-cut disease with an obvious etiology, pathology, diagnosis, and treatment regimen. The dearth of information and knowledge on CFS is especially striking when put in the context of its age. There have been a variety of historical predecessors to the modern definition of CFS that have been described in medical literature over the past few *centuries*, but CFS only really came to clinical prominence after it was believed to be

linked with severe illness [20, 21]. And so began a concerted effort to unravel the etiology of the disease. The process has been far more difficult than expected. After more than a decade of research, the underlying cause(s) of chronic fatigue syndrome are still unknown.

A Complex Etiology

"Sometimes when you have the fatigue, it sort of masks everything else."

Infectious disease studies were some of the earliest done on chronic fatigue syndrome, with investigations into Epstein-Barr and other possible causative agents [22]. Despite these studies, there has been no consistent evidence that CFS comes from a specific infection [23]. This, however, does not preclude the possibility that they may play some role in CFS. One of the proposed mechanisms by which infectious disease was thought to cause CFS was by disrupting the immune system. Immune system abnormality studies, however, have not been particularly enlightening [1] and so the relationship between infectious disease, disruption of the immune system, and chronic fatigue syndrome remains unclear. Genes have been another major putative cause. Family history studies have shown that people who had relatives with CFS had a higher prevalence of CFS than people who did not have relatives with CFS [24]. Furthermore, in twin studies the concordance rates were higher for CFS between monozygotic twins (38%) than between dizygotic twins (11%) [25]. This data implies that while there is a genetic predisposition of chronic fatigue, genetics do not completely explain the etiology of CFS. One of the more promising avenues of research is in Central Nervous System causes of CFS. Studies have suggested abnormalities in structure and perfusion, poorer performance in information processing tasks, autonomic dysfunction, and abnormalities in the hypothalamic-pituitary-adrenal axis (HPA axis) and serotonin pathways [1]. So far, the HPA axis studies suggesting altered psychological response to stress have been the most consistent and may hold the most promise [1]. Despite the fact that chronic fatigue syndrome involves exhaustion, and many patients report sleep disruptions [26], sleep studies have been inconsistent [1]. In addition, because many patients report exercise intolerance and cope with their illness avoiding physical activity [27], studies have been done evaluating the perception and ability of patients to exercise. Patients perceive the effort required and resulting fatigue as higher than healthy subjects despite the fact that measurable effort is significantly lower, implying that perception of effort and physical inactivity can affect CFS [1]. Furthermore, the ways that patients perceive themselves and their overall condition has also been linked to functional losses as their beliefs and attitudes have a profound impact upon how they respond to the illness. Patients that emphasize the illness to physical attributes while minimizing the psychological or personal contributions of CFS typically fair worse [1]. Like exercise avoidance, more general escape/avoidance strategies have been linked with greater fatigue and impairment [1]. Research has also been carried out to see if CFS is a psychiatric disorder. There is a high prevalence of mood and psychiatric disorders in the CFS population with the amount of psychiatric burden correlated with the CFS severity [28]. Studies have looked at the associations between somatization [*sic*] disorder, anxiety, and major depression with CFS. Evidence pointing towards association of somatization [*sic*] disorder involves a much greater prevalence in the CFS population, while anxiety has been linked to CFS through both prevalence and neurobiological similarities [1]. A good amount of research has been done on the link between CFS and depression, much of it yielding conflicting results. It has been hypothesized that CFS may be the result of overlapping symptoms or that it may be a manifestation of major depression [1]. Other research has indicated that life stress factors may play an important role. There is a high prevalence of emotional neglect and abuse in patients with CFS. Exposure to childhood trauma is associated with a 3 to 8-fold

increased risk of CFS, with exposure to trauma correlating with CFS severity [18]. Some researchers also believe that victimization may lead to "over activity" in the patient prior to the onset of CFS [29]. More recent events such as failure in ambitions or life goals, incapacitating physical injury or illness, as well as other traumatic events are linked to the onset, relapse, and exacerbation of CFS [29,30]. Given the wide breadth of fairly inconclusive research that has been done and is ongoing, it is clear that CFS' etiology and pathology is complex and heterogeneous.

A complex diagnosis and an even more difficult treatment plan

"I've been on many bouts of drugs ...antiviral, antibiotics, antidepressants, human growth hormones, I can't remember all the things I've taken. I would often feel like a guinea pig."

With such an uncertain etiology and pathogenesis, is it any surprise that physicians have a hard time diagnosing CFS? There is no single diagnostic test for CFS. The diagnosis is one of exclusion - the clinician, after determining that the patient matches the CDC's case definition symptoms must then rule out any exclusion criteria and only then make a diagnosis of CFS. I know that I would feel more comfortable making a diagnosis based on a positive laboratory test or physical symptom. Furthermore, the wide range of fairly non-specific symptoms that a patient may display makes this diagnosis all the more difficult. This difficulty translates into the practice of research as well and complicates attempts to compare studies. Once the patient has been diagnosed with chronic fatigue syndrome, what is the appropriate course of action? There are no firmly established treatment recommendations, but the most common allopathic treatments for CFS include prescribed medication, cognitive behavioral therapy, and exercise regimens [1, 10]. There have been a variety of pharmacological agents investigated in the treatment of CFS including immunological, antiviral, anti-inflammatory, and anti-depressant substances. Unfortunately, the controlled studies have been inconclusive and contradictory [1], but physicians continue to prescribe them. Non-pharmacological approaches such as exercise programs and cognitive-behavioral therapy appear to hold more promise. Exercise therapies lead to significant improvements in fatigue, functional status, and fitness that appear to be sustainable with 6-14 months of follow-up and may last even 5 years after treatment [1]. Similarly, cognitive-behavioral therapy can help CFS patients improve their physical and functional well-being, due perhaps to improved coping abilities [1, 29]. In addition, CFS patients who are also suffering from a psychiatric disorder such as depression may see improvement in that disorder from cognitive-behavioral therapy [31]. Exercise programs and cognitive-behavioral therapy, however, are not simple cures. Many patients prematurely drop treatment or do not respond very well, leading to some relapse when they are examined in the long term [29]. Enacting lifestyle change, especially one involving exercise, is not easy as evident by the increasing obesity figures in our nation. With the lack of conclusively effective medical standard regimens, many CFS patients have turned to complementary and alternative medicine (CAM). A recent study showed that CAM usage, in particular chiropractic and massage therapy, was more prevalent in CFS patients (79.6%) than in non-fatigued patients (72.5%) [10]. Given the increase in prevalence, physicians should be aware of the utilization of CAM and their possible positive and negative effects.

Complicated Attitudes

"Physicians across the board are not well versed about it.... Sometimes when I've filled in a form at the doctor's office, they think that it's something I've made up."

The complexity and uncertainty of chronic fatigue syndrome's etiology, diagnosis, and treatment has engendered a significant amount of ignorance, and worse, skepticism, on the part of many in the healthcare system. It was found that in a recent survey of primary care physicians, only 55.8% believed that CFS is a condition that exists [32]! Of these physicians, while 64.7% of them had diagnosed patients with CFS, none of them used the CDC criteria making that diagnosis [32]. Only 14.8% of the practices carried information leaflets on CFS, and none of them had trained nurses or therapists capable of offering support, advice, or treatment [32]. Even among primary care physicians who have a working knowledge of CFS, there is the sense that their lack of specialist knowledge prevents them from providing proper healthcare support [32]. The combination of a complex disease and discrepancies among primary care physicians has effects on the management of the illness and the patient's overall well-being. The same study evaluated patients with CFS who had been referred to a specialized clinic. Out of these patients, two thirds expressed dissatisfaction with the quality of care they received for CFS and reported delays, disputes, or confusion over the diagnosis [32]. Many perceived their doctors as being dismissive, skeptical, and inexperienced with CFS and felt that inadequate and confusing advice was given [32]. In addition, only 51.6% of CFS sufferers indicated that it was their primary care physician that had diagnosed them after an average of almost 7 appointments [32]. These findings are not surprising given the physicians' results. Our overall confusion about CFS, the lack of healthcare education, and the attitudes that come with ignorance all breed distrust in the relationship between CFS patients and their physicians. The complexity of CFS involving its etiology, diagnosis, multi-faceted potential therapeutic approaches, and the lack of education about it make it a problem that must be tackled with organized efforts, fulfilling the third requirement of a public health problem.

What now?

"It's about changing your attitude and outlook. ..It 's about being more flexible."

I have shown that CFS is indeed a public health problem, fulfilling the three characteristics of being prevalent, causing health damages, and requiring organized efforts. The more relevant question now is: what can be done about it? I believe that there are three aspects involving CFS that can be improved upon: research, education, and the application of treatment regimens. Clearly, these aspects are interconnected, each one informing and potentiating the other two, with improvements on one yielding positive effects on the others. Looking at the research on CFS, in particular the research on its etiology, it is clear that it is broad, covering everything from genetics to immunology to psychiatry to lifestyle. To help focus the research, Mark Demitrack suggests viewing CFS as the "final common pathway expression of an illness that has developed by an accumulation of intrinsic and extrinsic factors shaped in an individual over the course of time," rather than as a single disease state [33]. He then states that more research should be done on improving the way in which symptoms and functional ability are assessed [33]. I could not agree more. I think, however, that more importantly we should delineate a consistent method of determining whether a patient or research participant fits the CDC case description. In the literature, there is wide variety in the evaluation of whether the participant is suffering from CFS with some researchers relying purely upon self-assessments, others involving clinical assessment by a trained interviewer, and others relying upon physician diagnosis. This makes it difficult when comparing different studies and might be improved upon by including more explicit guidelines in the CDC case description to be adhered to when determining whether a participant has CFS. The research aspect of CFS is not the only field marked by confusion. The surveys on primary care physicians' and patients' beliefs on CFS highlight the need for more education and awareness. Healthcare providers (including physicians, nurses, assistants, etc.) need to be better versed in diagnosing and treating CFS if they are to be effective. At the very least,

physicians should be aware of CFS and have it in the differential diagnosis when they are evaluating a patient. This can start at the medical school level. As far as I know, our curriculum at Robert Wood Johnson and those of many other medical schools do not cover CFS. A greater awareness of CFS will go a long way in building trust between the doctor and CFS afflicted. I think also that frank acknowledgement of the complexity of CFS and just how little we know about it is appropriate. Rather than dismissing it because we don't understand it, healthcare providers should reassure patients that while we know very little about it, it is a very real condition with medical and psychiatric factors and that research is under way to find treatments. Furthermore, physicians should be able to direct patients towards reliable resources and support centers so that they are not relying on potentially unreliable resources as might be found on the Internet. A recent survey reviewed 225 websites on chronic fatigue syndrome and found that only one-third of websites advised readers to clarify information with an appropriate health physician and avoided the inclusion of inaccurate statements [32]. By distributing pamphlet literature to primary care centers, we can work towards properly educating physicians and patients while properly directing the latter to more resources. Also, because 62.1% of CFS patients gained information on CFS from newspaper or magazine articles [32], a public awareness ad campaign might be beneficial to raise the overall public's awareness of CFS. The third aspect that I think can be improved upon is the administration and management of long-term treatment. CFS' multi-faceted nature, damages, and treatment requires the coordination between patients, agencies, and health care providers to improve the health and quality of life for CFS patients. Therefore in addition to being better-educated, primary care physicians should be coordinating the care of CFS patients with other specialists - including exercise, cognitive-behavioral, occupational, and CAM therapists, psychiatrists, and social workers. A more ambitious improvement upon care would be the establishment of multidisciplinary teams at health centers. These teams could function by providing treatment, resources, support, and advocacy to patients. Despite CFS' complex nature, unknown etiology and pathology, and the current lack of education of large segments of our population and most strikingly our healthcare providers, I believe that through coordinated, well-organized efforts in research, education, and administration of care, strides can be made towards tackling the public health problem of chronic fatigue syndrome.

"I'm always open to new things. Someday there will be something that makes a significant change and then I can move on."

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