Public Comment
Rosemary Underhill

A Neglected Subgroup of Patients with ME/CFS

My name is Rosemary Underhill and I trained as a physician, a surgeon and an obstetrician in London, England. I wish to present to this committee a request for some research in a neglected subgroup of patients with ME/CFS.

The name Benign Myalgic Encephalomyelitis (ME) was coined to describe a cluster outbreak of a disease in London, England in 1955 (Leading article 1956). As a medical student at the time, I myself witnessed this cluster outbreak. The name Chronic Fatigue Syndrome (CFS) was coined by the CDC to describe another cluster outbreak of a similar disease in Nevada, USA in 1984 (Holmes 1988). Many cluster outbreaks of a similar disease have been described around the world at different times, but other names have been used. E.g., Non-paralytic polio in Los Angeles, Iceland disease in Iceland, Neuro-myasthenia in Florida, Tapanui flu in New Zealand. (Ramsey 1988, Hyde 1992) Hyde found that 63 cluster outbreaks of a disease resembling ME and CFS, were reported between 1934 and 1990 and 27 of them were in the USA. (Hyde 1992) Outbreaks occurred in the USA on average about one every two years.
Levine followed up patients from cluster outbreaks in the USA and New Zealand and found that many patients did not recover their health, and their continuing symptoms fulfilled diagnostic criteria for CFS and/or ME (Levine 1992, Levine 1997), so patients whose illness started in cluster outbreaks make up a sub-group of patients with ME/CFS.

Diseases occurring as cluster outbreaks separated in space and time are usually caused by one or more closely related infectious agents. Much research has been done in recent years, looking for a possible causal agent for ME/CFS, but no known pathogen has been shown to be the cause. Research into causal pathogens for ME/CFS has been hampered by several problems:

Firstly, most research has been carried out on sporadic cases of the disease and case definitions used for diagnosis demand that the symptoms be present for six months. Six months after illness onset, it may not be readily apparent whether any infectious agent could be primarily causal, a triggering agent which activates the causal agent, reactivation of a latent infection, or an opportunistic infection developing subsequent to the original illness. The importance of investigating patients in cluster outbreaks is that they can be diagnosed early on in the illness and this provides a unique opportunity to find a causal pathogen which may not be actively replicating later on in the disease and also an opportunity to distinguish primary pathology from secondary pathology.

Secondly, it has often been stated that ME/CFS is not contagious. There is much evidence that this statement is not true. For example:

1. Ramsey reported on 16 cluster outbreaks of ME/CFS and showed that affected patients have often been closely associated in families, communities, hospitals, or schools. In these outbreaks, the incubation period was measured variously as 4-10 days (Hyde 1992) and the disease tended to spread from person to person

2. I and my colleague did some research into family members of sporadic cases of CFS. (Underhill, O'Gorman) We found that patients' genetically unrelated spouses and partners had an increased prevalence of an illness diagnosed as CFS compared with the community prevalence, with a relative risk of 7.6 - 13.5, (3.2% of spouses had the illness compared with community prevalence of 0.42% and 0.235% (Jason et al 1999, Reyes et al. 2003). Additionally, 6.5% of spouses had idiopathic chronic fatigue
3. De Becker and his colleagues found that in 6.5% of his 1,500 patients, CFS followed a few days after a blood transfusion.

I request the CFSAC to recommend that the CDC's Epidemic Intelligence Service (EIS) investigate this subgroup of patients with ME/CFS.
I recommend that the EIS and also the ME/CFS research community actively seek out cluster outbreaks of every illness resembling ME/CFS and investigate both the patients involved and also their close contacts in the hope of finding the causal pathogen of this devastating disease.

I have written a list of some actions to be taken and investigations which should be done in future cluster outbreaks, but since I am out of my allotted time, I ask the committee to read them.

Suggested protocol for investigating cluster outbreaks of ME/CFS.

- Physicians and States public health authorities need to be educated as to the characteristics of cluster outbreaks of ME/CFS and be encouraged to report suspected outbreaks of the illness early on to the CDC
- The case definition for patients in cluster outbreaks needs to be refined. Some cluster outbreaks, while superficially resembling various descriptions of ME or CFS may have dissimilar features, and may be found to be caused by a known pathogen
- Patients from cluster outbreaks need to be tested for both known pathogens and also unknown pathogens by all currently available means. Especially is the need to look for a neurotropic and a B lymphotropic virus, which can affect Killer T cell activity and which may be difficult to cultivate
- Contact controls, as well as non-contact controls need to be recruited. Contacts of patients have been shown to have immune system changes similar to those of the patients. (Grufferman 1994, Abbott 1994, Stewart 2003). They may be asymptomatic carriers of a possible pathogen for ME/CFS, they may be incubating the illness and subsequently develop the illness, or they may have developed an immunity to the disease
- Patients need to be tested to see whether the immune changes and other pathological changes found in sporadic cases of ME/CFS are also found early in the illness
- Investigation of the mode of transmission of the pathogen, the attack rate, and the incubation period for cluster outbreak cases should be undertaken
- Follow up of cases for at least two years is important to determine the rate of recovery.

References

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