

Uncertain Syndromes

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GULF WAR SYNDROME

- group of **poorly understood symptoms** experienced by > 100,000 American, British, and Canadian veterans of Persian Gulf War (1992).

- **onset** - within few months of returning from Persian Gulf.
- **symptoms** **predominantly involve nervous system**: problems with memory, reasoning, concentration, and attention, headache, fatigue, dizziness, depression, difficulty sleeping, muscle / joint pain, cough, chest pain, skin rashes, diarrhea, impotence.
- **possible etiology**:
 - 1) exposure to number of toxic substances (chemical weapons, biological warfare, depleted uranium weapons, insecticides, smoke from burning oil wells).
 - 2) variety of airborne substances
 - 3) vaccination with anthrax vaccine
 - 4) use of pyridostigmine tablets.
- **diagnosis and treatment** have not been established.
- veterans who have Gulf War syndrome do not have higher hospitalization or death rate.

MULTIPLE CHEMICAL SENSITIVITY SYNDROME (IDIOPATHIC ENVIRONMENTAL INTOLERANCE)

- **recurrent, multiple nonspecific symptoms** attributed to **low-level exposure*** to **chemically unrelated substances commonly occurring in environment**.

*inhaled, touched, or ingested

Etiologic theories:

- 1) **immunologic** - some patients have biologic abnormalities (e.g. B cells↓, IgE↑).
- 2) **psychologic** - **form of somatization disorder**, panic attack, agoraphobia, neurasthenia (no-longer-used psychologic diagnosis).
- 3) may represent emergence of **new culture-bound disorder** in United States and Europe.

Symptoms are numerous and usually involve more than one organ system:

No clinically detectable organ dysfunction or related physical signs!

- lack of consistent dose response! (e.g. symptoms may not be replicated after exposure to high levels of substance).
- patients often go to great lengths to avoid these agents by changing residence and employment, avoiding all foods containing "chemicals," sometimes wearing masks in public, or avoiding public settings altogether.
- very high levels of depression and anxiety in this population.

Diagnosis - by exclusion; *consultation with allergy specialist* may be necessary.

Treatment - **psychologic support*** and **avoidance** of perceived triggers (but social isolation and costly and highly disruptive avoidance behaviors should be discouraged!).

*not to demonstrate that cause is psychologic (patients do not believe that) but rather to help patients cope with their suffering.

CHRONIC FATIGUE SYNDROME

- **long-standing, severe, disabling fatigue** (usually for ≥ 6 mo that interferes with daily activities*) without demonstrable muscle weakness or other underlying disorders.

*have to lie down to rest after briefest exertion; if patients plan activity in evening, they may spend entire day resting in advance.

- psychologic diagnoses (depression, anxiety, etc) are also typically absent.
- precise cause remains unknown; etiologic theories:
 - 1) psychologic factors
 - 2) chronic viral infection (old names of syndrome - *chronic Epstein-Barr virus infection, postviral fatigue syndrome*).
 - 3) allergic reactions or immunologic abnormalities (e.g. excessive cytokine release)
 - 4) neuroendocrine abnormalities (e.g. ↓production of corticotropin-releasing hormone)
 - 5) abnormal levels of neurotransmitters
 - 6) inadequate cerebral circulation
 - 7) elevated levels of ACE
 - 8) familial or genetic component (relatives of patients have increased risk of developing syndrome).

PREVALENCE 2-38/100,000 people.

- females ≥ males.
- most often 25-45 yrs old.
- in office-based studies prevalence is highest among whites; community surveys indicate higher prevalence among blacks, Hispanics, and American Indians.
- most famous "outbreaks" occurred in Los Angeles County Hospital in 1934; in Akureyri, Iceland, in 1948; in Royal Free Hospital, London, in 1955; in Punta Gorda, Florida, in 1956; and in Incline Village, Nevada, and surrounding communities in 1985.

Clinical Features

- **onset** is usually **abrupt** in previously active individual; many patients report **initial viral-like illness** (with swollen lymph nodes, extreme fatigue, fever, and upper respiratory symptoms).
- commonly accompanied by symptoms of **depression** (much of this depression may be reactive, but prevalence exceeds that seen in other chronic medical illnesses).
- once pattern of illness is established, symptoms may fluctuate somewhat.
- fortunately, syndrome does not appear to progress (many patients experience gradual improvement, and minority recover fully).

Diagnostic criteria:

1. Unexplained, persistent, or relapsing chronic **FATIGUE** that is new or has definite onset; that is **not due to ongoing exertion**; that is **not substantially alleviated by rest**; and that **substantially reduces** occupational, educational, social, or personal **activities**
2. At least 4 of following for ≥ 6 mo*:
 - 1) impaired short-term memory (self-reported) severe enough to substantially reduce occupational, educational, social, or personal activities
 - 2) sore throat (nonexudative **pharyngitis**)
 - 3) low-grade **fever**
 - 4) tender, enlarged, painful cervical or axillary **lymph nodes**
 - 5) muscle pain
 - 6) abdominal pain
 - 7) multijoint arthralgia (without joint swelling or tenderness)
 - 8) headaches that are new in type, pattern, or severity

- 9) unrefreshing sleep
- 10) postexertional malaise lasting > 24 h
- 11) cognitive difficulties (esp. concentrating and sleeping)
*must not predate fatigue.

Treatment:

- 1) **psychologic support** (individual or group therapy) - patient should be informed what is known about illness.
- 2) non-sedating **antidepressants**
- 3) **physical rehabilitation** programs; persistent / prolonged rest should be firmly discouraged!
- 4) **NSAIDs** alleviate headache, diffuse pain, and feverishness.
- 5) guide patients away from unproven therapeutic modalities which are most toxic, expensive, and unreasonable.

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