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. nonsedating 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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