Understanding and Managing Chronic Fatigue Syndrome

慢性疲労症候群(CFS/ME)の理解と症状の管理

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Brain Abnormalities
脳の異常

MRI Scan shows high intensity spots in 80% of cases

SPECT Scan shows decreased blood flow in specific areas

Neuro-psychiatric testing confirms problems with attention, memory, processing speed...
Abnormalities of the sympathetic and parasympathetic nervous system are common, including:

- Tachycardia
- Orthostatic intolerance (syncope) in up to 100% of subjects
- Low plasma volume and red blood cell mass

Tilt Table testing for syncope
Sleep is markedly disturbed in up to 62.5% of patients:

- Sleep apnea
- Parasomnias (sleep walking)
- Narcolepsy
- Upper Airway Resistance
Hypothalamic-Pituitary-Adrenal Axis

視床下部-下垂体-副腎系

The HPA Axis is suppressed leading to lower levels of:

- Thyroid hormone
- Cortisol
- Estrogen
- Testosterone
- Growth hormone
- Prolactin
Immune System

• Elevated levels of CD8+/38+ “cytotoxic” T-cells Poorly functioning natural killer cells
• Upregulation of the 2-5A system and RNaseL
• Increased production of pro-inflammatory cytokines
• Reduced levels of gammaglobulin and IgG subclasses
• Significantly increased prevalence of DR4, DR5, DQ3 and DQ1
• Twin study shows hereditability estimate of 51%
• Significant risk for developing CFS among 1\textsuperscript{st} (OR=2.7), 2\textsuperscript{nd} (OR=2.34), or 3\textsuperscript{rd} degree relatives (OR=2.03)
• Neuroendocrine gene variants (\textit{TPH2}, \textit{COMT}, \textit{NR3C1}) associated with CFS
Oxidative Stress / Energy Metabolism
酸化ストレス/エネルギー代謝

- LDL is increased, HDL decreased
- Isoprostanes increased
- Cellular ATP is decreased
- Mitochondrial oxidative phosphorylation reduced
- Impaired cardiovascular response to exercise
- Abnormal mRNA response to exercise
Post-Infectious CFS/ME
感染後CFS/ME

Dubbo Study
• 11% developed CFS/ME after infection with EBV, Q-Fever, or Ross River Virus
• CFS not more likely in patients with particular premorbid psychiatric and demographic factors

Post-Mononucleosis Study (Miami)
Adolescents with mono met CFS/ME criteria at:
• 6 months (13%)
• 12 months (7%)
• 24 months (4%)
MYTH: CFS/ME is due to depression

作り話: CFS/ME はうつ病に起因する
## Depression versus CFS/ME

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<tr>
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<td>Insidious 知らぬ間に進行</td>
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<td>一部は重複 (頭痛、微熱なし)</td>
<td>頭痛や微熱などの重度の症状</td>
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<td>前途</td>
<td>絶望的、無力感、内向的</td>
<td>率先して行動、療や探求、政治的活動に積極的</td>
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BIOLOGICAL EVIDENCE AGAINST DEPRESSION

うつ病とは反する生物学的な証拠

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<tr>
<td>Cortisol</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>CRH</td>
<td>↑</td>
<td>↓</td>
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Demitrack MA, et al., ”J Clin Endocrinol Metab. 1991 Dec; 73(6): 1224-34
Four Cardinal Symptoms of CFS/ME
CFS/ME の 4 つの中核症状

- Pain (痛み)
- Cognitive difficulties (認知機能障害)
- Fatigue (疲労)
- Sleep disruption (non-restorative sleep) (非回復性睡眠)
Overlap Syndromes (or Comorbidities)

併存疾患
  Irritable bowel or bladder, migraine, sicca (Sjögren’s), orthostatic intolerance...

Epidemiology

疫学
  – No known cause, but triggers have been identified
  – A majority of persons improve over time (months to years)
  – Neither CFS nor FM are degenerative illnesses
CFS/ME Triangle (CFS/ME トライアングル)

Sleep
睡眠

Pain
痛み

Fatigue
疲労
Managing Sleep Problems
睡眠障害の症状管理

• Sleep habits
• OTC Medications:
  – melatonin, diphenhydramine, doxylamine, proprietaries
• Non-hypnotics: Eszopiclone (Lunesta), zaleplon (Sonata), ramelteon (Rozerem)
• Hypnotics: Zolpidem (Ambien) > benzodiazepines
Managing Pain

痛みの管理

- **Non-pharmacological therapies**
  - Rest, cold/heat, balneotherapy, liniments
  - massage, PT, chiropractic, acupuncture
  - TENS, EMS

- **Pharmacologic therapy**
  - Tylenol (acetaminophen), ASA, NSAIDs, coxibs
  - Anti-epileptic drugs: pregabalin, gabapentin, others
  - NSRIs: duloxetine, milnacipran, others
  - Tramadol or Low Dose Naltrexone
  - Narcotics
    - Short acting (hydrocodone, oxycodone)
    - Long acting (oxycodone, morphine, fentanyl)
4 CFS Characteristics

CFSの4つの特徴

• Exertional (労作による)
• Positional (姿勢による)
• Hypersensitivities (過敏性)
• Stress intolerance (ストレスに対する不耐性)
Pacing

ペースの調整

• Rest periods
  10-30 minutes
  Supine or semi-recumbent
  Clear your mind

• Limit setting
  Most push and crash
  Energy conservation
The Fallacy of Push ‘n’ Crash
無理してクラッシュするのは誤り

Pushing hard on two days requires two days of recuperation

Moderation allows you to feel better, do more over the same 4 days!
Activity
活 動

Worst case: couch or bed bound
Evidence: you *can* and *must* be active

Objective limits

– Aerobic interval activity
– Heart rate limited
  • MPHR=230-Age, AT occurs at 0.6 x MPHR
– Pedometer (1000-5000 steps)
Anaerobic Interval Activity
間隔を空けた無酸素運動

• Persons with CFS cannot tolerate anaerobic activity
• Anaerobic means not enough oxygen gets to muscles.
• Most PWCs can only exert 3-5 minutes before reaching the Anaerobic Threshold.
• Then rest for 5 minutes.
Heart Rate Limits

心拍数の限界

- The AT (Anaerobic Threshold) always occurs at the same heart rate
- Keep the heart rate below that limit
- Predicted max HR = 230 - age in years
  - 230 - 50 years = 180 MPHR
- Maximum HR = MPHR x 0.6
  - 180 x 0.6 = 108 beats/minute
We know from experience that:

- 1000 steps per day is too little
- 5000 steps per day is too much for most
Severely Affected Patients
重症患者

- Home visits from the doctor or specialist
- Occupational therapy to improve the home environment
- Home physical therapy (range of motion or resistance against gravity, supine)
- Home Health Aid or caregiver
- Balanced nutrition and healthy organic or whole foods
- Pleasant activities
- Socialization
Severely Ill Patients
重症患者

• Minimize medications and supplements
• Prescribe medications in very low doses and titrate slowly
• Stress management and grief/loss counseling
• Encouragement
• Lowered expectations for themselves and from others

Above all the severely ill need “peace of mind and a feeling that they and their family were taken care of, so that they could use all their energy on getting better.”

(Irma Pinxterhuis, PhD, Oslo University Hospital, Norway)
Pediatric CFS/ME
Epidemiology
小児のCFS/ME
疫学
• Prevalence
  – USA: 100-300 per 100,000
    • 5-12 years old: none
    • 13-17 years old: 181 per 100,000
  – Japan: about the same
• Gender
  – M:F :: 1:2 to 1:5
Comparison of Symptoms in Adolescents and Adults
青年と成人における症状の比較

<table>
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<tr>
<th>SYMPTOM</th>
<th>CHILD</th>
<th>ADULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Neurologic</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>Abdominal Pain*</td>
<td>97</td>
<td>84</td>
</tr>
<tr>
<td>Headache</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>Sore Throat*</td>
<td>97</td>
<td>90</td>
</tr>
<tr>
<td>Eye Pain / Photophobia*</td>
<td>97</td>
<td>88</td>
</tr>
<tr>
<td>Lymphodynia*</td>
<td>91</td>
<td>78</td>
</tr>
<tr>
<td>Myalgia</td>
<td>91</td>
<td>96</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>Rash*</td>
<td>88</td>
<td>56</td>
</tr>
<tr>
<td>Fever / Chills</td>
<td>72</td>
<td>84</td>
</tr>
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Differences Between Adolescent and Adult Definitions

• De-emphasizes fatigue and highlights symptoms (dizziness, decreased endurance, pain, & flu-like)
• Symptoms endured for only three months
• Abdominal symptoms have been added to list
• Autonomic symptoms added (orthostatic intolerance, palpitations, dizziness, shortness of breath)
• Symptoms rated according to severity
  1 = not present
  4 = moderate
  7 = severe
• Symptoms must be either moderate to severe to meet criteria
Pediatric CFS/ME Management

小児のCFS/MEの病状の管理

• Similar to adult management
  
  Sleep, pain > orthostatic intolerance, GI

• Must address
  
    – Education
    – Social development
    – Psychological issues such as school phobia
### Prognosis in Adolescents

(15 Year Follow-Up)

<table>
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<th>Condition</th>
<th>Number (Percentage)</th>
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<td>Completely resolved</td>
<td>13 (37%)</td>
</tr>
<tr>
<td>Well, but not resolved</td>
<td>15 (42.9%)</td>
</tr>
<tr>
<td>Remaining ill</td>
<td>4 (11.4%)</td>
</tr>
<tr>
<td>Very Ill</td>
<td>3 (8.6%)</td>
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Bell DS, April 1998 CFSCC Report
Summary of Pediatric CFS/ME

小児のCFS/MEのまとめ

• CFS has a high prevalence in adults, but a lower prevalence in adolescents (100-300/100,000)
• Symptoms are similar to adults, but more abdominal pain, orthostatic intolerance, sore throat, photophobia and rash
• Diagnosis is made by “case definition”
• Management is supportive and symptomatic, must address education and social development
• Prognosis is favorable in adolescents
Supplements
サプリメント

- Multivitamin
- B12
- Vitamin D3
- Magnesium
- Calcium
- DHEA

- Acetyl carnitine
- NADH / CoQ10
- Lysine
- d-Ribose

- Methyl-folate
- Folinic Acid
- Phosphatidyl Serine
Advanced Therapies
高度な治療法

- Orthostatic Intolerance
  - Water, salt, fludrocortisone, beta-blockade
- Modified Elimination Diet
  - Avoid gluten, dairy
- Viral or Immunological Symptoms
  - Valtrex, Isoprinosine, Nexavir, Valcyte
- Low dose cortisol
  - 10-15 mg hydrocortisone
- Human Growth Hormone
  - Recombinant hGH > secretagogue
- Ampligen
- Rituxan / rituximab
Summary

• Biological evidence for CFS is abundant
• CFS is not due to depression
• Begin management by addressing pain and sleep disorders first
• It is important to stay physically active, but not too active to trigger a flare
Summary (continued)

まとめ

• Use interval activity, heart rate monitoring, or steps-per-day to prevent over-exertion

• The severely ill require additional care and resources, but can be rehabilitated

• Advanced therapy may benefit specific subsets of patients

Don’t ever give up!

決してあきらめないで！
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