

Scientifically-based work-up in ME patients

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**CONFERENCE ON MYALGIC ENCEPHALOMYELITIS (ME)
FOR HEALTH PERSONNEL, June 12, 2009**

Stavanger University Hospital, Stavanger, Norway

Medical history

Medical history

- ⇒ infectious events
- ⇒ non-infectious events
 - ⇒ altered immune competence

Questions to ask about onset related events (1)

- Blood transfusion
- Surgery (appendectomy, amygdalectomy, ...)
- Febrile or flu-like illness
- Tick-bite / insect bites
- Chemical / toxic exposure
- Longstanding stress (physical and/or mental)
- Trauma
- URI, sinus infections, pneumonia
- Illness in foreign country

Questions to ask about onset related events (2)

- Female: vaginal infection; cystitis
- Male: prostatitis
- Pets; birds
- Questions about sleep patterns
- Dental infections; fistulas
- Hepatitis B immunization, multiple immunizations
- Pregnancy

Symptoms (1)

Does the patient meet the Holmes and/or Fukuda criteria for CFS?

Which symptoms?

1. Holmes minor criteria
2. +10 symptoms with greatest prevalence difference between Ho and Fu criteria (P. De Becker, 2000)
3. +bleeding gums, TMJ, sinus infections

Symptoms (2)

- Fatigue
- Exercise intolerance
- Mild fever
- Sore throat
- Lymph nodes
- Muscle weakness
- Myalgia
- Headaches
- Arthralgia
- Sleep disturbance
- Neuropsychologic complaints (attention deficit, difficulties with words ...)
- GI disturbance
- Urinary frequency
- Cold extremities
- Photophobia
- Muscle fasciculations
- Lightheadedness
- Exertional dyspnea
- Bleeding gums
- TMJ
- Sinus infections

Somatic work-up (1)

First Round – Laboratory (GP and/or Internal Medicine)

- Complete Blood Count (CBC)
- Comprehensive Metabolic Panel (14)
- Gamma GT
- Intracellular (RBC) magnesium
- IgE
- RF, ANA, fibrinogen, sedimentation rate
- CPK, LDH, cholesterol, triglycerides
- Ferritin, TSH
- Antityroid antibodies
- Serology: Toxoplasmosis, CMV, Mycoplasma, Chlamydia, EBV, herpes, HHV-6, HIV
- Depending on specific symptoms: serology for Rickettsia, Dengue, hepatitis B/C, syphilis, Yersinia, Babesia, ...

Somatic work-up (2)

First Round – Other

- ECG (U + T wave)/ exercise testing/exercise ECG
- Chest X-ray
- Abdominal ultrasound
- Depending on specific symptoms:
 - CT sinuses
 - Echocardiogram
 - Panoramic X-ray of dental roots
 - MRI of the brain
 - Gastroscopy/colonoscopy
 - Pulmonary function test

Somatic work-up (3)

Second Round – Specific laboratory tests (Internal Medicine)

INTESTINAL DYSFUNCTIONS

- **Breath test and blood:** lactose, fructose, food intolerances
- **Urine test:** H₂S metabolites
- **Blood test:** IgA/IgM against intestinal bacteria (Immunobilan)
- **Stool test:**
 - Gut microbial flora, aerobes and anaerobes
 - Parasites
 - Unusual mycoses
 - Amoebiasis
 - Helicobacter
 - Yersinia/Salmonella

AAT (colitis)

pH

Immunobilan

Hafnia alvei / M	Ig3 M	5,75
Pseudomonas aeruginosa/M	Ig5 M	3,62
Morganella morganii / M	Ig12 M	3,58
Proteus mirabilis / M	Ig13 M	1,97
Pseudomonas putida / M	Ig16 M	6,23
Citrobacter diversus / M	Ig17 M	8,16
Klebsiella pneumo / M	Kle Pn M	9,27
Hafnia alvei / A	Ig3 A	2,83
Pseudomonas aeruginosa / A	Ig5 A	4,65
Morganella morganii / A	Ig12 A	-0,30
Proteus mirabilis / A	Ig13 A	-0,12
Pseudomonas putida / A	Ig16 A	3,62
Citrobacter koseri / A	Ig17 A	1,63
Klebsiella pneumo / A	Kle Pn A	1,69

Species / Antibody	Value
Ig3 M	5,75
Ig5 M	3,62
Ig12 M	3,58
Ig13 M	1,97
Ig16 M	6,23
Ig17 M	8,16
Kle Pn M	9,27
Ig3 A	2,83
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Ig12 A	-0,30
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Kle Pn A	1,69

- Intestinal dysbiose
- Leaky gut syndrome

Somatic work-up (3)

Second Round – Specific laboratory tests (Internal Medicine)

INFECTIONS

- Gastro-intestinal biopsies: parvovirus, herpesviruses
- Nose swap: coagulase negative staphylococci
- Vaginal swap, sperm: viruses, mycoplasma, chlamydia
- Lumbar puncture (only if neurological symptoms): HHV-6, chlamydia, mycoplasma
- Blood tests: PCR or serology

Somatic work-up (4)

Second Round – Specific laboratory tests (Internal Medicine)

HEAVY METALS

- Blood test: heavy metal hypersensitivity (MELISA®)
- Saliva: PrPc
- Urine after chelation challenge: heavy metals exposure

Metal exposure Metal hypersensitivity: Melisa®


Mineral analysis in urine,
following chelation challenge

MICRO TRACE MINERALS Gmbh environmental & clinical laboratory

Röhrenstrasse 20 D-91217 Hersbruck
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Telefax: +49 (0) 9151/2308

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MINERAL ANALYSIS

Urine

Lab Number
IUR92853

Doctor	Prof. Dr. K. De Meijler		
Patient Name	[REDACTED]		
Clinical Information	post 250mg, 5ml DMPS+150ml NaCl 0.3%; 2hr		
Test Date	20. Mai. 09	D.O.B.	31.12.1987
	Sex	f	Creatinine (g/l)
			0,3

Essential Macro- & TraceElements (mg/g creatinine)	Low	Acceptable Range	High
Acceptable Range Test Value			
Calcium	55,00 -- 245,00	137,05	*****
Magnesium	12,00 -- 150,00	89,75	*****
Zinc	0,07 -- 7,00	3,64	*****

Essential Trace Elements (mcg/g Creatinine)	Low	Acceptable Range	High
Acceptable Range Test Value			
Chromium	0,10 -- 3,50	0,00 Low	<
Cobalt	< 5,00	0,97	*****
Copper	1,45 -- 60,00	651,86 High	*****
Iron	2,00 -- 95,00	12,34	*****
Manganese	< 4,50	2,95	*****
Molybdenum	9,70 -- 100,00	13,03	*****
Selenium	12,00 -- 90,00	10,24 Low	*****
Vanadium	< 70,00	0,24	*****

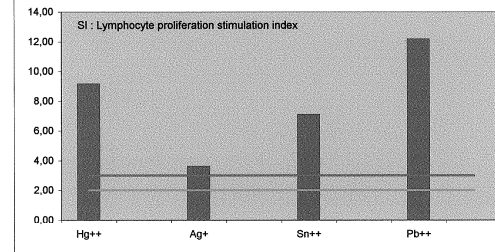
Potentially Toxic Elements in mcg/g Creatinine	Low	Acceptable Range	High
Acceptable Range Test Value			
Aluminium	< 125,00	19,75	*****
Arsenic	< 15,00	7,67	*****
Barium	< 8,22	1,04	*****
Beryllium	< 1,20	0,94	*****
Cadmium	< 1,50	0,13	<
Lead	< 5,00	4,88	*****
Mercury	< 1,00	16,56 High	*****
Nickel	< 3,00	27,69 High	*****
Silver	< 1,40	1,47 High	*****
Tin	< 5,00	3,23	*****

* The 95percentile Ranges represent baseline urine values and are calculated on the creatinine value. The utilized range is 0.3 to 3.0 g/L creatinine (WHO 2005). For chelator-specific information see attachments.

Accreditation: DIN EN ISO 17025; Quality control: Dr. Rauland PhD; Validation: Dr E.Blaurock-Busch PhD

Melisa test sample result

Ag ou Me	microgr/ml	Cpm	D Cpm	SI	Nbr Blastes	Commentaires
C1		1224				
C2						
C3						
PPD1						
PPD2						
PHA		6695				
PHA1						
Hg++		11209	9985	9,16		POS
Ag+		4418	3194	3,61		POS
Sn++		8696	7472	7,10		POS
Pb++		14909	13685	12,18		POS



Somatic work-up (3)

Second Round – Specific laboratory tests (Internal Medicine)

IMMUNE FUNCTION ASSAYS

- Immunophenotyping:
 - Total lymphocytes (CD25⁺CD14⁻CD3⁺)
 - Activated T-cells (CD25⁺HLADR⁺CD8⁺CD38⁺)
 - CD4/CD8⁺ cells and ratio
 - Ratio memory/virgin CD4⁺ cells
 - NK-subsets; NK cytotoxicity
 - B lymphocytes (CD19⁺CD5⁺)
 - CD57 cells
- Cytokine profile: Th1/Th2, inflammatory cytokines
- C4A
- Elastase
- IgG subclasses

Neuropsychological evaluation

Duration: 3 hours with sufficient rest

⇒ Psychiatric evaluation

- Semi-structured interview (DSM-IV) for depression, anxiety disorders and PTSD
- MMPI-II
- Coping checklist
- SF-36
- SCL-90-R
- GHQ-30

⇒ Neurocognitive evaluation

- Intelligence
- Memory (verbal and visual)
- Reaction time
- Attention
- Mental flexibility
- Interference
- Index of general body strength
- Simple motor speed
- Word fluency

Possible specific triggers for ME in Norway

- Undiagnosed food intolerances: cow milk/gluten
- Molds-houses: *Aspergillus niger* antibodies, C4A marker
- Tick-borne disease:
 - CD57 + lymphocytes low
 - *Borrelia*
 - *Bartonella*
 - *Coxiella*
 - *Rickettsia*
 - *Anaplasma*
 - *Babesia*
- Mercury in food – fat fish, artificial sweeteners
- Copper in old pipes
- Genetic predisposition
- Lack of vitamin D