Health Information Services Patient Extract

From 11/20/2008 through 3/11/2013

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<tr>
<td>Discharge Reports</td>
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<tr>
<td>Radiology</td>
<td>115</td>
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</table>
KNIGHT CARDIAC CATHETERIZATION LABORATORY FINAL REPORT

PATIENT NAME: WEINER, ROBERT MRN:4645581
AGE: 47
CASE DATE/TIME: 12/13/2011 9:20 AM
DIAGNOSTIC ATTENDING MD: Ik-Kyung Jang, M.D., Ph.D.
DIAGNOSTIC FELLOW MD: Joshua Caplin, P.A.
INDICATION(S): PreBaird Shortness of breath

OVERALL SUMMARY:
RA 1, PCW 6, PA 20/8/12, CO 7.2

DIAGNOSTIC TECHNIQUE: Under ultrasound guidance and lidocaine 2% local anesthesia a 8 F introducer was placed in the right jugular vein and maintained usual fashion. A 7 F balloon tipped catheter was introduced via the venous sheath, the balloon was inflated and catheter was advanced through the right heart chambers into the pulmonary capillary wedge position. Right sided pressures were obtained. Cardiac output was measured using thermodilution. Following the procedure the sheath was sutured in place.
Ik-Kyung Jang, M.D., Ph.D. was present for the critical portions of the procedure and immediately available throughout the entire procedure.

PROCEDURES:
Right Heart Catheterization including oximetry and CO measurement

DIAGNOSES:
Shortness of Breath
Chronic pulmonary heart disease unspecified

EQUIPMENT:
Merit Medical, MAK, Sheath 5F - 10
Cordis, AVANTI+, Sheath 8F - 11
Edwards Lifescience, Swan-Ganz Standard, Swan-Ganz Catheter 7F - 110

HEMODYNAMICS:
STATE: Rest
Thermodilution Cardiac Output (l/min):7.2; CI(l/min/m2):3.14
PVR (dyn*s/cm5):67
Heart rate (bpm):65

PRESSURES:
RA (v/m) 2 / 1
RV (s/edp) 20 / 5
PA (s/d/m) 20 / 8 / 12
PW (v/m) 10 / 6

Vascular Access: Routine
Arterial Access Site: No Arterial Catheter
Fluoro Time: 0.1 min.
ASA Class: 2
Airway Status: Adequate based on assessment

Contrast
None

Volume (ml)
0

Complications
None
None

All medications administered during the patient's stay in the cathlab including pre, during and post procedure were given under direction of Ik-Kyung Jang, M.D., Ph.D.

The surgical/procedural team has confirmed that the Time-Out has occurred.

This report has been electronically signed by Dr. Ik-Kyung Jang
Date: 12/16/2011

This is a Final Cath report. Preliminary Report was submitted initially on 12/13/2011 by Dr. Ik-Kyung Jang

Reference Ranges:
Oxygen saturation
- Arterial: 90-100%
- Mixed venous: 60-80%

ACT (sec)
- 170-230 sec for patients on G2b-3a inhibitors
- 200-240 sec for patients off G2b-3a inhibitors
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<th>CA</th>
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<td>15:30</td>
<td>(135-145)</td>
<td>(3.4-4.8)</td>
<td>(100-108)</td>
<td>(L)</td>
<td>(8-25)</td>
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<td>(135-145)</td>
<td>(3.4-4.8)</td>
<td>(100-108)</td>
<td>(L)</td>
<td>(8-25)</td>
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<td>(3.4-4.8)</td>
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<td>(0.60-1.50)</td>
<td>(1)</td>
<td>(70-110)</td>
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(1) Abnormal if <60 mL/min/1.73m². If patient is African-American, multiply the result by 1.21.

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
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**Date/Time**: 04/06/2010 12:40

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(1)"Desired: > 32 ng/ml".

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**Date/Time**: 06/04/2009 22:39

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(1)Reference range: <7.7

(2)"Desired: > 32 ng/ml".

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

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<td>166 (30-300)</td>
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<td>06/04/2009 22:39</td>
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<td>6.4 (4.5-10.9)</td>
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<td>11/24/2008 17:20</td>
<td>1.62 (0.40-5.00)</td>
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<table>
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(1)MEN: 1.0-12.0
(2)MEN: 2.0-12.0
(1)NORMALS:
8AM-12PM = 5-25 ug/dl
12PM-8PM = 5-15 ug/dl
8PM-8AM = <10 ug/dl
Method change 2/27/08: no effect on reference intervals.

<table>
<thead>
<tr>
<th>Date/Time</th>
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(1)NORMALS:
8AM-12PM = 5-25 ug/dl
12PM-8PM =

Printed: 03/11/2013 12:06 PM
### Laboratory from 11/20/2008 through 3/11/2013 (cont)

<table>
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<th>Time</th>
<th>Result</th>
<th>Method</th>
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<td>(0.0-15.0)</td>
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**Method change 2/27/08: no effect on reference intervals.**

1. The Normal Range reflects non-pregnant females.
2. Several methods exist for estimating the free testosterone levels if a SHBG has also been ordered. One common method is to calculate a free androgen index (FAI). Multiply the total testosterone result [ng/dl] by 3.47 and divide by the SHBG [nmol/L] value. The following reference ranges apply to this FAI:
   - Females: 1.2 to 4.0 (Modified 1/14/2004)
   - Males: 16.6 to 172.9

---

**NOTE:** Several methods exist for estimating the free testosterone levels if a SHBG has also been ordered. One common method is to calculate a free androgen index (FAI). Multiply the total testosterone result [ng/dl] by 3.47 and divide by the SHBG [nmol/L] value. The following reference ranges apply to this FAI:

- Females: 1.2 to 4.0 (Modified 1/14/2004)
- Males: 16.6 to 172.9
Laboratory from 11/20/2008 through 3/11/2013 (cont)

<table>
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<tr>
<td>11/24/2008 17:20</td>
<td>6.3(1)</td>
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</table>

NORMALS:
- 8AM-12PM = 5-25 ug/dl
- 12PM-8PM = 5-15 ug/dl
- 8PM-8AM = <10 ug/dl

Method change 2/27/08: no effect on reference intervals.

Date/Time       | LEAD  | CCOM | UMYOP | MITOENZ |
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<td>SEE DETAIL(3)</td>
<td>SEE DETAIL(2)</td>
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</table>

(1)POS AT 1:20/TITER TO FOLLOW 1.5HR

(1)SPECIMEN SENT DIRECTLY TO ATHENA FROM CARE UNIT
(2)Final Report
Performed at ATHENA DIAGNOSTIC INC., 373 Plantation Sttreet, Worcester, MA 01605

Interpretation
This individual possesses normal mitochondrial respiratory enzyme activities with mitochondrial proliferation. Although the likelihood that this individual is affected with a defect in the respiratory chain has been significantly reduced, this individual may possess an underlying mitochondrial disease.

Technical Results
Respiratory Enzymes Reference Range Result
umol/min/gm tissue

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

cytochrome c oxidase >1.41 6.25
succinate-cytochrome c reductase >0.35 1.99
rotenone-sensitive NADH

cytochrome c reductase >0.52 2.44
NADH dehydrogenase >14.22 24.32
Reference Enzymes

succinate dehydrogenase >0.47 4.20
citrate synthase 7.33 - 12.43 12.92
protein (total) >30.00 82.65

Methods
Biochemical analysis for mitochondrial enzyme activities were performed spectrophotometrically. This analysis, as performed here, are greater than 95% accurate. Mitochondrial respiratory enzyme activities are normalized with respect to citrate synthase activity. Reference values are presented as greater than 50% of the normal median or as the normal range. Citrate synthase activity is utilized as a reference marker to evaluate muscle mitochondrial content.

Comments
This analysis indicates that this individual possesses normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity. This individual's elevated citrate synthase activity reflects mitochondrial proliferation and may be indicative of mitochondrial disease. Mitochondrial proliferation, particularly in the presence of a strong history of maternal inheritance or clinical features is compatible with mitochondrial DNA mutation.

Mitochondrial DNA mutation analysis on patients' muscle tissue and/or blood samples is available through Athena Diagnostics. Please contact Client Services at 1-800-394-4493 for further information.

(3)Final Report
Performed at ATHENA DIAGNOSTIC INC., 373 Plantation Sttreet, Worcester, MA 01605

Enzymes Analyzed Reference Range Result uMol/min/gm/tissue
phosphorylase A+ total >12.00 30.64
phosphorylase b kinase >2.43 21.51
myoadenylate deaminase >15.88 30.92
phosphoglycerate kinase >93.60 298.16
phosphoglycerate kinase >90.36 289.16
phosphoglycerate mutase >181.75 578.78
lactate dehydrogenase >118.15 377.40
carnitine palmitoyltransferase >46.60 101.73
glycogen 0.10-1.50 1.39
Control Enzyme
phosphofructokinase >12.80 54.70

Methods:
Biochemical analysis for myoglobinuria was performed spectrophotometrically and by radionuclide incorporation. This analysis, as performed here, is greater than 95% accurate. Reference values are presented as greater than 50% of the normal median or as the normal range.

Comments:
This analysis did not indicate any deficiencies in the enzymes of the myoglobinuria panel. Therefore, the likelihood that this individual is affected with a disorder related to this panel has been reduced.

07/15/2009 16:10 T = 10
07/15/2009 16:08 T = 6

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

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<th>HGB</th>
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(1) Performed at QUEST CAMBRIDGE, 415 Mass Ave, Cambridge, MA 02139

(NOTE) Reference Range:
- 0.9 mcg/dl For infants to ADULTS
- Detection limit: 2 mcg/dL

HEMATOLOGY

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>WBC</th>
<th>RBC</th>
<th>HGB</th>
<th>HCT</th>
<th>MCV</th>
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<th>PLT</th>
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<tbody>
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Laboratory from 11/20/2008 through 3/11/2013 (cont)

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**IMMUNOLOGY**

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(1) Normal pattern
*** Normal SPEP: Normal pattern ***

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

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<th>ANAH2P</th>
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(1) NEGATIVE AT 1:40 AND 1:160
*** Normal Value: Negative at 1:40 and 1:160 ***

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
To interpret a negative test for antinuclear antibodies (ANA) in a patient suspected of having a rheumatic disease, the following limitations should be noted.

ANA are not detected in all patients with CTD; negative results are obtained with serum from 5% of patients with systemic lupus erythematosus (SLE) and systemic sclerosis, 25% with Sjögren’s syndrome and 50% with rheumatoid arthritis.

If the patient appears to have SLE, for example, but the initial test for ANA is negative, the test should be repeated and the test for anti-Ro antibody should be ordered. Anti-Ro antibody is found in about 65% of patients with ANA-negative SLE.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

Method is fluorescent non-infectious agent antibody test with microscopic evaluation.

<table>
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<td>12/17/2008 21:28</td>
<td>SPECKLED</td>
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</table>

(1) Positive at 1:40. Negative at 1:80 and 1:160 *** Normal Value: Negative at 1:40 and 1:160 ***

(2) Negative at 1:10 *** Normal: Negative at 1:10 ***

To interpret a negative test for antinuclear antibodies (ANA) in a patient suspected of having a rheumatic disease, the following limitations should be noted.

ANA are not detected in all patients with CTD; negative results are obtained with serum from 5% of patients with systemic lupus erythematosus (SLE) and systemic sclerosis, 25% with Sjögren’s syndrome and 50% with rheumatoid arthritis.

If the patient appears to have SLE, for example, but the initial test for ANA is negative, the test should be repeated and the test for anti-Ro antibody should be ordered. Anti-Ro antibody is found in about 65% of patients with ANA-negative SLE.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

Method is fluorescent non-infectious agent antibody test with microscopic evaluation.

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(1) Negative at 1:10

*** Normal: Negative at 1:10 ***

To interpret a negative test for anti-native or double stranded DNA antibodies in a patient suspected of having systemic lupus erythematosus, the following limitations should be noted.

Anti-native or double stranded DNA antibodies are usually detected in SLE patients with active disease, especially in those with active renal disease. Anti-DNA antibodies are usually not detected in SLE patients with spontaneous or drug-induced remissions.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

Method is fluorescent non-infectious agent antibody test with microscopic evaluation.
To interpret a negative test for anti-native or double stranded DNA antibodies in a patient suspected of having systemic lupus erythematosus, the following limitation should be noted. Anti-double stranded DNA antibodies are usually detected in SLE patients with active disease, especially in those with active renal disease. Anti-DNA antibodies are usually not detected in SLE patients with spontaneous or drug-induced remissions.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

*** Normal: Negative at 1:10 ***

### Table: Anti-DNA Antibodies

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<th>SM-CUT</th>
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### Table: Anti-DNA Antibodies

| Flag Key: L (Low or Critical) H (High or Critical) C (Corrected) |

Anti U1 SnRNP Antibodies

Based on ELISA, this patient’s serum is positive for the presence of antibody to the U1 small nuclear ribonucleoprotein (U1 RNP) complex. The U1-RNP antigen consists of the U1 RNA strand in association with nuclear protein 70 kD, A, and C. U1 RNP is a constituent of the spliceosomal complex involved in RNA processing. Anti-U1 RNP antibodies are found in all patients with the mixed connective tissue disease (MCTD), in 30-40% of patients with SLE, and approximately the same proportion of patients with rheumatoid arthritis, Sjogren’s syndrome, and dermatomyositis. Anti-U1 RNP antibodies are found in approximately 50% of patients with polymyositis, 10% of patients with chloroma, and 5% of patients with MCTD.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

*** Normal: Negative at 1:10 ***
syndrome, systemic sclerosis, and some patients with polymyositis. In MCTD, anti-U1 RNP occurs in very high titer and unaccompanied by other antinuclear antibodies. In SLE, anti-U1 RNP antibodies are usually accompanied by anti-Sm antibodies, as well as other ANA. At times, this sensitive assay may be positive in patients who are ANA negative and/or have no discernable connective tissue or other disease.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

EQUIVOCAL

*** Normal: Negative ***

(2)*** Normal: Negative ***

(3)*** Normal: Negative ***

Anti-Sm Antibodies by ELISA
Based on ELISA, this patient's serum is positive for the presence of antibody to the Smith (Sm) antigen. The Sm antigen is a small nuclear RNA protein complex consisting of one of several uridine-rich RNA strands bearing the core proteins B'/B and D. Sm is a constituent of the spliceosomal complex involved in RNA processing. Anti-Sm antibodies detected by precipitation in gel with thymus extract are found in 20-30% of patients with SLE and not in other systemic connective tissue diseases. It is not yet known whether anti-Sm antibodies detected by ELISA have the same specificity for SLE. In SLE, anti-Sm antibodies are usually accompanied by anti-U1 RNP antibodies.

Please see result of gel diffusion assay for precipitating anti-Sm antibodies.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

(4)*** Normal: Negative ***

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(1)*** Normal: Negative ***

Anti U1 SnRNP Antibodies
Based on ELISA, this patient's serum is positive for the presence of antibody to the U1 small nuclear ribonucleoprotein (U1 RNP) complex. The U1-RNP antigen consists of the U1 RNA strand in association with nuclear protein 70 kD, A, and C. U1 RNP is a constituent of the spliceosomal complex involved in RNA processing.

Anti-U1 RNP antibodies are found in all patients with the mixed connective tissue disease (MCTD), in 30-40% of patients with SLE, and approximately the same proportion of patients with rheumatoid arthritis, Sjogren’s syndrome, systemic sclerosis, and some patients with polymyositis. In MCTD, anti-U1 RNP occurs in very high titer and unaccompanied by other antinuclear antibodies. In SLE, anti-U1 RNP antibodies are usually accompanied by anti-Sm antibodies, as well as other ANA. At times, this sensitive assay may be positive in patients who are ANA negative and/or have no discernable connective tissue or other disease.

Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory

(2)*** Normal: Negative ***

Anti-Sm Antibodies by ELISA
Based on ELISA, this patient's serum is positive for the presence of antibody to the Smith (Sm) antigen. The Sm antigen is a small nuclear RNA protein complex consisting of one of several uridine-rich RNA strands bearing the core proteins B'/B and D. Sm is a constituent of the spliceosomal complex involved in RNA processing. Anti-Sm antibodies detected by precipitation in gel with thymus extract are found in 20-30% of patients with SLE and not in other systemic connective tissue diseases. It is not yet known whether anti-Sm antibodies detected by ELISA have the same specificity for SLE. In SLE, anti-Sm antibodies are usually accompanied by anti-U1 RNP antibodies.

Please see result of gel diffusion assay for precipitating anti-Sm antibodies.
### Laboratory from 11/20/2008 through 3/11/2013 (cont)

**Mandakolathur R. Murali, M.D., Director Clinical Immunology Laboratory**

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<td>(&lt;8.0)</td>
<td></td>
</tr>
</tbody>
</table>

(1) This reference range is for the evaluation of inflammation. Order High Sensitivity CRP for cardiac risk status evaluation.

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>RHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/20/2009 18:47</td>
<td>&lt;30</td>
</tr>
<tr>
<td></td>
<td>(&lt;30)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>TTGAB-IGA</th>
<th>GLIADIN-IGG</th>
<th>GLIADIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/24/2008 17:20</td>
<td>0.4</td>
<td>&lt;1.0(1)</td>
<td>1.8(1)</td>
</tr>
</tbody>
</table>

(1) Unit: U
(NOTE) -- REFERENCE VALUE --
<20.0 (Negative)
20.0-30.0 (Weak Positive)
>30.0 (Positive)

(2) Reference range: <4.0
Unit: U/mL
(NOTE) Please note change in reporting effective 10/14/2008.

**INFECTIOUS DISEASE**

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>TREP-AB</th>
<th>WHIP-DNA</th>
<th>GIARD-AB</th>
<th>EBV-LCI</th>
<th>EBV-UCI</th>
<th>EBV-VLOAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/2009 19:39</td>
<td>SEE DETAIL (1)</td>
<td>SEE DETAIL (1)</td>
<td>SEE DETAIL (3)</td>
<td>SEE DETAIL (1)</td>
<td>SEE DETAIL (2)</td>
<td></td>
</tr>
</tbody>
</table>

(1) Test component not applicable or not reported.
Performed by MAYO MEDICAL LABORATORIES NEW ENGLAND, 160 Dascomb Road, Andover, MA 01810

(2) None Detected
Reference range: None Detected
(NOTE) Lower limit of detection is 500 copies/mL.

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>ARSC-WB</th>
<th>HG</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/24/2008</td>
<td>&lt;3(1)</td>
<td>&lt;4(2)</td>
</tr>
</tbody>
</table>

(1)Reference range: <23
Unit: mcg/L
(NOTE)Urine is usually the best specimen for the analysis of Arsenic in body fluids. Blood levels tend to be low even when urine concentrations are high.
(2)Reference range: <=10
Unit: mcg/L

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>AMINO-ACID</th>
<th>INT-AA</th>
<th>AAB</th>
<th>ALA</th>
<th>ALLOIL</th>
<th>ARG</th>
<th>ASA</th>
<th>ASN</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010</td>
<td>SEE DETAIL(2)</td>
<td>SEE DETAIL(1)</td>
<td>12 (7-35)</td>
<td>481 (146-494)</td>
<td>Not det (0)</td>
<td>77 (28-108)</td>
<td>Not det (0)</td>
<td>49 (26-92)</td>
</tr>
</tbody>
</table>

(1)Slightly low serine, otherwise normal.
(2)COMPLETE PANEL, QUANTITATIVE

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>ASPA</th>
<th>CITR</th>
<th>CYTH</th>
<th>CYS-FREE</th>
<th>ETN</th>
<th>GLUA</th>
<th>GLN</th>
<th>GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010</td>
<td>2 (2-9)</td>
<td>32 (10-58)</td>
<td>Not det (&lt;3)</td>
<td>49 (24-54)</td>
<td>7 (&lt;83)</td>
<td>30 (6-62)</td>
<td>527 (340-798)</td>
<td>194 (100-384)</td>
</tr>
<tr>
<td>04/06/2010</td>
<td>6 (2-9)</td>
<td>24 (10-58)</td>
<td>Not det (&lt;3)</td>
<td>39 (24-54)</td>
<td>12 (&lt;83)</td>
<td>44 (6-62)</td>
<td>606 (340-798)</td>
<td>190 (100-384)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>HCS-CYS</th>
<th>HIST</th>
<th>HCS-F</th>
<th>OHPRO</th>
<th>ILE</th>
<th>LEUCI</th>
<th>LYS</th>
<th>METH</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010</td>
<td>Not det (0)</td>
<td>72 (68-108)</td>
<td>Not det (0)</td>
<td>7 (&lt;50)</td>
<td>58 (39-90)</td>
<td>108 (98-205)</td>
<td>157 (119-243)</td>
<td>18 (13-37)</td>
</tr>
</tbody>
</table>

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>ORNI</th>
<th>PHE</th>
<th>PROLI</th>
<th>SERI</th>
<th>TAUR</th>
<th>THREO</th>
<th>TRYP</th>
<th>TYRO</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>67</td>
<td>44</td>
<td>191</td>
<td>63</td>
<td>49</td>
<td>101</td>
<td>46</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>(36-135)</td>
<td>(42-74)</td>
<td>(97-297)</td>
<td>(78-166)</td>
<td>(18-95)</td>
<td>(92-197)</td>
<td>(17-65)</td>
<td>(26-78)</td>
</tr>
<tr>
<td>04/06/2010 12:00</td>
<td>68</td>
<td>40(L)</td>
<td>177</td>
<td>64</td>
<td>118(H)</td>
<td>111</td>
<td>40</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>(36-135)</td>
<td>(42-74)</td>
<td>(97-297)</td>
<td>(78-166)</td>
<td>(18-95)</td>
<td>(92-197)</td>
<td>(17-65)</td>
<td>(26-78)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>VALI</th>
<th>OTHR-AA</th>
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</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>230</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>(172-335)</td>
<td></td>
</tr>
<tr>
<td>04/06/2010 12:00</td>
<td>229</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>(172-335)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>UR-AA</th>
<th>INT-UAA</th>
<th>UR-AAB</th>
<th>UR-ALA</th>
<th>UR-ARG</th>
<th>UR-ASA</th>
<th>UR-ASN</th>
<th>UR-ASP</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>SEE DETAIL(2)</td>
<td>SEE DETAIL(1)</td>
<td>12</td>
<td>193</td>
<td>7</td>
<td>Not det</td>
<td>67</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>(0-35)</td>
<td>(0-35)</td>
<td>(141-601)</td>
<td>(0-44)</td>
<td>(0-35)</td>
<td>(0)</td>
<td>(0-203)</td>
<td>(18-62)</td>
</tr>
</tbody>
</table>

(1) A number of amino acids were slightly low.
(2) COMPLETE PANEL, QUANTITATIVE

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>BAIB/CRE</th>
<th>UR-CARN</th>
<th>UR-CIT</th>
<th>UR-CYS</th>
<th>UR-GLA</th>
<th>UR-GLN</th>
<th>UR-GLY</th>
<th>UR-HCD</th>
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<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>683</td>
<td>71</td>
<td>Not det</td>
<td>40</td>
<td>19</td>
<td>276</td>
<td>1381</td>
<td>Not det</td>
</tr>
<tr>
<td></td>
<td>(0-804)</td>
<td>(0-35)</td>
<td>(0-35)</td>
<td>(27-150)</td>
<td>(0-106)</td>
<td>(177-672)</td>
<td>(380-1529)</td>
<td>(0)</td>
</tr>
<tr>
<td>07/02/2009 13:56</td>
<td>46</td>
<td>78</td>
<td>Not det</td>
<td>30</td>
<td>11</td>
<td>200</td>
<td>789</td>
<td>Not det</td>
</tr>
<tr>
<td></td>
<td>(0-804)</td>
<td>(0-35)</td>
<td>(0-35)</td>
<td>(27-150)</td>
<td>(0-106)</td>
<td>(177-672)</td>
<td>(380-1529)</td>
<td>(0)</td>
</tr>
<tr>
<td>11/25/2008 11:32</td>
<td>776</td>
<td>90</td>
<td>56(H)</td>
<td>42</td>
<td>15</td>
<td>239</td>
<td>1117</td>
<td>Not det</td>
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<tr>
<td></td>
<td>(0-804)</td>
<td>(0-35)</td>
<td>(0-35)</td>
<td>(27-150)</td>
<td>(0-106)</td>
<td>(177-672)</td>
<td>(380-1529)</td>
<td>(0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>UR-HIS</th>
<th>UR-HCIT</th>
<th>UR-HCS</th>
<th>UR-OHP</th>
<th>UR-ILE</th>
<th>UR-LEU</th>
<th>UR-LYS</th>
<th>UR-MET</th>
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<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>457</td>
<td>Not det</td>
<td>Not det</td>
<td>2</td>
<td>12(L)</td>
<td>157</td>
<td>10(L)</td>
<td>157</td>
</tr>
<tr>
<td></td>
<td>(230-1353)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0-35)</td>
<td>(18-97)</td>
<td>(62-513)</td>
<td>(18-141)</td>
<td>(62-513)</td>
</tr>
<tr>
<td>07/02/2009 13:56</td>
<td>317</td>
<td>Not det</td>
<td>Not det</td>
<td>4</td>
<td>11(L)</td>
<td>78</td>
<td>13(L)</td>
<td>157</td>
</tr>
<tr>
<td></td>
<td>(230-1353)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0-35)</td>
<td>(18-97)</td>
<td>(62-513)</td>
<td>(18-141)</td>
<td>(62-513)</td>
</tr>
<tr>
<td>11/25/2008 11:32</td>
<td>527</td>
<td>Not det</td>
<td>Not det</td>
<td>4</td>
<td>14(L)</td>
<td>127</td>
<td>10(L)</td>
<td>157</td>
</tr>
<tr>
<td></td>
<td>(230-1353)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0-35)</td>
<td>(18-97)</td>
<td>(62-513)</td>
<td>(18-141)</td>
<td>(62-513)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>3MH-CRE</th>
<th>UR-ORN</th>
<th>UR-PHE</th>
<th>UR-PRO</th>
<th>UR-SER</th>
<th>UR-TAUR</th>
<th>UR-THR</th>
<th>TYR-CRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>181</td>
<td>2</td>
<td>31</td>
<td>Not det</td>
<td>174(L)</td>
<td>290</td>
<td>74</td>
<td>71</td>
</tr>
</tbody>
</table>

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
Laboratory from 11/20/2008 through 3/11/2013 (cont)

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>UR-VAL</th>
<th>UR-OAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>19(L) 27-115</td>
<td>SEE DETAIL(1)</td>
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</tbody>
</table>

(1) Ethanolamine 250

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>U-ORGA</th>
<th>CRE-OA</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>&quot;SEE NOTE&quot;(1)</td>
<td></td>
</tr>
</tbody>
</table>

(1)(NOTE) In this sample, there were no unusual organic acids. Performed by MAYO CLINIC DPT OF LAB MED AND PATHOLOGY, 200 First St. SW, Rochester, MN 55905

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>0.42</td>
</tr>
<tr>
<td>07/02/2009 13:56</td>
<td>0.54</td>
</tr>
<tr>
<td>05/20/2009 20:54</td>
<td>&quot;SEE NOTE&quot;(1)</td>
</tr>
</tbody>
</table>

(1)(NOTE) In this sample, metabolites of Ibuprofen were detected. Otherwise, there were no unusual organic acids. Performed by MAYO CLINIC DPT OF LAB MED AND PATHOLOGY, 200 First St. SW, Rochester, MN 55905

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>MDSCRN</th>
<th>NPRUSS</th>
<th>DNPH</th>
<th>ACETST</th>
<th>REDCSUB</th>
<th>INT-UMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>SEE DETAIL(5)</td>
<td>SEE DETAIL(3)</td>
<td></td>
<td>SEE DETAIL(1)</td>
<td>SEE DETAIL(2)</td>
<td>SEE DETAIL(4)</td>
</tr>
</tbody>
</table>

(1) Acetest negative.
(2) Clinitest negative.
(3) DNPH Test negative.
(4) Normal Study.
(5) Nitroprusside test negative.

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)

Printed: 03/11/2013 12:06 PM
This screening test will give a positive result if any disulfide compound is present, including cystine, homocystine, and mercaptolactatecysteine disulfide. False positive interfering substances include acetylcysteine, captopril, penicillamine, and glutathione. A false negative for homocystine can occur if the patient is taking vitamin B6.

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>TCAR</th>
<th>CARN-F</th>
<th>INT-CAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/2009 19:39</td>
<td>61(3)</td>
<td>46(1)</td>
<td>&quot;SEE NOTE&quot;(2)</td>
</tr>
</tbody>
</table>

(1) Acetest negative.
(2) Clinitest negative.
(3) DNPH Test negative.
(4) Normal study. /V.E. Shih, MD
(5) Nitroprusside test negative.

This screening test will give a positive result if any disulfide compound is present, including cystine, homocystine, and mercaptolactatecysteine disulfide. False positive interfering substances include acetylcysteine, captopril, penicillamine, and glutathione. A false negative for homocystine can occur if the patient is taking vitamin B6.

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>TCAR</th>
<th>CARN-F</th>
<th>INT-CAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/25/2008 11:32</td>
<td>SEE DETAIL(5)</td>
<td>SEE DETAIL(3)</td>
<td>SEE DETAIL(1)</td>
</tr>
</tbody>
</table>

(1) Acetest negative.
(2) Clinitest negative.
(3) DNPH Test negative.
(4) Normal study. /V.E. Shih, MD
(5) Nitroprusside test negative.

Date/Time | ACY-CARN | AC/FC RATIO |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>05/13/2010 10:25</td>
<td>SEE DETAIL(1)</td>
<td></td>
</tr>
<tr>
<td>Substance</td>
<td>Value</td>
<td>Reference Range</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>3-OH-hexanoylcarnitine, C6-OH</td>
<td>0.01 nmole/mL</td>
<td>&lt;0.08 (1 da - 7 da)</td>
</tr>
<tr>
<td>Octenoylcarnitine, C8:1</td>
<td>0.39 nmole/mL</td>
<td>&lt;0.48 (1 da - 7 da)</td>
</tr>
<tr>
<td>Octanoylcarnitine, C8</td>
<td>0.49 nmole/mL</td>
<td>&lt;0.91 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>Decenoylcarnitine, C10:1</td>
<td>0.40 nmole/mL</td>
<td>&lt;0.25 (1 da - 7 da)</td>
</tr>
<tr>
<td>Dodecenoylcarnitine, C12:1</td>
<td>0.13 nmole/mL</td>
<td>&lt;0.19 (1 da - 7 da)</td>
</tr>
<tr>
<td>Dodecanoylcarnitine, C12</td>
<td>0.18 nmole/mL</td>
<td>&lt;0.37 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>3-OH-dodecanoylcarnitine, C12-OH</td>
<td>0.02 nmole/mL</td>
<td>&lt;0.09 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>Tetradecenoacylcarnitine, C14:2</td>
<td>0.06 nmole/mL</td>
<td>&lt;0.08 (1 da - 7 da)</td>
</tr>
<tr>
<td>Tetradecenoylcarnitine, C14:1</td>
<td>0.15 nmole/mL</td>
<td>&lt;0.13 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>Tetradecanoylcarnitine, C14</td>
<td>0.06 nmole/mL</td>
<td>&lt;0.24 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>3-OH-tetradecanoylcarnitine, C14:1OH</td>
<td>0.01 nmole/mL</td>
<td>&lt;0.15 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>Hexadecenoacylcarnitine, C16:1</td>
<td>0.04 nmole/mL</td>
<td>&lt;0.12 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>Hexadecenoylcarnitine, C16:1-OH</td>
<td>0.02 nmole/mL</td>
<td>&lt;0.08 (1 da - 7 da)</td>
</tr>
<tr>
<td>Hexadecanoylcarnitine, C16:1</td>
<td>0.19 nmole/mL</td>
<td>&lt;0.05 (8 da - 7 Yrs)</td>
</tr>
<tr>
<td>3-OH-hexadecanoylcarnitine, C16:1-OH</td>
<td>0.01 nmole/mL</td>
<td>&lt;0.10 (8 da - 7 Yrs)</td>
</tr>
</tbody>
</table>

Flag Key: L (Low or Critical) H (High or Critical) C (Corrected)
LINOLEYL-ACETYL-CARNITINE, C18:2 : 0.14 nmole/mL
Ref. Range: <0.12 (1 da - 7 da)
<0.31 (8 da - 7 Yrs)
<0.24 (> or = 8 Yrs)
OLEYL-ACETYL-CARNITINE, C18:1 : 0.27 nmole/mL
Ref. Range: <0.25 (1 da - 7 da)
<0.45 (8 da - 7 Yrs)
<0.39 (> or = 8 Yrs)
STEAROYL-ACETYL-CARNITINE, C18:0 : 0.12 nmole/mL
Ref. Range: <0.10 (1 da - 7 da)
<0.12 (8 da - 7 Yrs)
<0.14 (> or = 8 Yrs)
3-OH-LINOLEYL-ACETYL-CARNITINE, C18:2-OH : 0.00 nmole/mL
Ref. Range: <0.04 (1 da - 7 da)
<0.06 (8 da - 7 Yrs)
<0.06 (> or = 8 Yrs)
3-OH-OLEYL-ACETYL-CARNITINE, C18:1-OH : 0.01 nmole/mL
Ref. Range: <0.03 (1 da - 7 da)
<0.04 (8 da - 7 Yrs)
<0.06 (> or = 8 Yrs)

COMMENTS: ESSENTIALLY NORMAL PLASMA ACYL-CARNITINE PROFILE.

07/01/2009 19:39

[Table with reference ranges and measurements]

07/01/2009 19:39 15(2) 0.3(1)

(1) Reference range: 0.1 to 0.8
Performed by MAYO CLINIC DPT OF LAB MED AND PATHOLOGY, 200 First St. SW, Rochester, MN 55905

(2) Reference range: 5 to 30
Performed by MAYO CLINIC DPT OF LAB MED AND PATHOLOGY, 200 First St. SW, Rochester, MN 55905

MISCELLANEOUS

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>MITO-DNA</th>
</tr>
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<tbody>
<tr>
<td>08/31/2009 22:35</td>
<td>SEE DETAIL(1)</td>
</tr>
</tbody>
</table>

(1) FINAL REPORT
Performed at ATHENA DIAGNOSTIC INC., 373 Plantation Street, Worcester, MA 01605

(NOTE) TECHNICAL RESULTS:
MELAS 3243 tRNA Leu A3243G ABSENT
MELAS 3271 tRNA Leu T3271C ABSENT
MELAS 3252 tRNA Leu A3252G ABSENT
MELAS 3256 tRNA Leu C3256T ABSENT
MELAS 3291 tRNA Leu T3291C ABSENT
MELAS 13,513 NDS G13513A ABSENT
MERRF 8344 tRNA Lys A8344G ABSENT
MERRF 8356 tRNA Lys T8356C ABSENT
MERRF 8363 tRNA Lys G8363A ABSENT
MERRF 8296 tRNA Lys A8296G ABSENT
NARP 8993 ATPase6 T8993G ABSENT
NARP 8993 ATPase6 T8993C ABSENT

INDIVIDUAL IS AFFECTED WITH EITHER MELAS, MERRF, OR NARP SYNDROME, BUT DOES NOT EXCLUDE THE DIAGNOSIS OF THESE SYNDROMES DUE TO MUTATIONS NOT TESTED FOR OR NOT YET RECOGNIZED. THIS ANALYSIS, AS PERFORMED HERE, IS GREATER THAN 99% ACCURATE.

MITOCHONDRIAL DNA MUTATIONS HAVE BEEN ASSOCIATED WITH DIVERSE CLINICAL PHENOTYPES THAT INCLUDE NEUROLOGICAL, GASTROINTESTINAL, CARDIAC, ENDOCRINE AND RENAL ABNORMALITIES. SEVERAL DISTINCT COMBINATIONS OF THESE DIVERSE CLINICAL FEATURES ARE KNOWN TO BE ASSOCIATED WITH SPECIFIC mtDNA MUTATIONS. HOWEVER, A SPECIFIC MUTATION MAY BE ASSOCIATED WITH DIFFERENT PHENOTYPES IN DIFFERENT PATIENTS (CLINICAL HETEROGENEITY), AND A SINGLE CLINICAL PHENOTYPE MAY BE ASSOCIATED WITH DIFFERENT mtDNA MUTATIONS IN DIFFERENT PATIENTS (GENETIC HETEROGENEITY). EIGHTY PERCENT OF ALL KNOWN MELAS SYNDROME CASES ARE REPRESENTED BY THE MELAS 3243 MUTATION, AND THE REMAINING ACCOUNT FOR 10-15% OF MELAS CASES. Similarly, 80% of ALL KNOWN MERRF SYNDROME CASES ARE REPRESENTED BY THE MERRF 8344 MUTATION AND THE REMAINING ACCOUNT FOR APPROXIMATELY 5-10% OF MERRF CASES. THE NARP 8993 MUTATIONS (T>C AND T>G) ACCOUNT FOR APPROXIMATELY 85% OF ALL NARP SYNDROME CASES.

PERCENTAGE LEVELS OF MUTANT mtDNA MAY VARY AMONG INDIVIDUALS WITHIN THE SAME FAMILY, AND ALSO AMONG ORGANS AND TISSUES WITHIN THE SAME INDIVIDUAL DUE TO "HETEROPLASMY". THIS ACCOUNTS FOR THE VARIED CLINICAL PHENOTYPE SEEN IN PATIENTS WITH PATHOGENIC mtDNA DISORDERS. IN A SMALL NUMBER OF INDIVIDUALS, MITOTIC SEGREGATION IN RAPIDLY DIVIDING TISSUE, SUCH AS LEUKOCYTES, MAY RESULT IN THE LOSS OF MITOCHONDRIA CONTAINING ABNORMAL mtDNA. HENCE, PATHOGENIC MUTATIONS MAY BE UNDETECTABLE IN LEUKOCYTES IN INDIVIDUALS HAVING ONE OR ONLY A FEW SYMPTOMS OR IN ASYMPTOMATIC MATERNAL RELATIVES. IF YOUR PATIENT'S TEST RESULT IS NEGATIVE FOR A BLOOD SAMPLE AND CLINICAL PRESENTATION IS CONSISTENT WITH MITOCHONDRIAL DISORDERS, TESTING IN MUSCLE SHOULD BE CONSIDERED FOR COMPREHENSIVE EVALUATION, INCLUDING BIOCHEMICAL ANALYSES.

TEST OF THE mtDNA MUTATIONS AND BIOCHEMICAL ANALYSIS IN MUSCLE IS AVAILABLE THROUGH ATHENA DIAGNOSTICS. PLEASE CONTACT CLIENT SERVICES AT 1-800-394-4493 FOR FURTHER INFORMATION.

Reference Range: NO MUTATION DETECTED
Neurophysiology From 11/20/2008 through 3/11/2013

07/15/2009 Electromyography Laboratory Signed

Lab Electromyography Laboratory
Visit Date 7/15/2009
Ref. Dr. Seton, Margaret

Reason for study:
This is a 44-year-old man who complains of exercise-induced weakness and myalgias of 2 to 3 years duration. This study was requested to evaluate for myopathy.

Nerve conduction studies:
a. Normal right median and ulnar sensory potentials.
b. Normal bilateral sural sensory potentials.
c. Normal right median and ulnar motor nerve conduction studies. Incidental finding of Martin-Gruber anastomosis (ADM).
d. Normal bilateral tibial and peroneal motor nerve conduction studies.

Needle electromyography:
a. Needle EMG of the lower extremities revealed chronic denervation/reinnervation changes in the L2 through S1 myotomes bilaterally.
b. Needle EMG of the right upper extremity did not show any denervation changes.
c. No myopathic changes were seen.

Conclusions:
1. The pattern of neurophysiologic findings in the lower extremities is consistent with bilateral chronic lumbosacral polyradiculopathies.
2. There is no neurophysiologic evidence of myopathy.
3. There is no neurophysiologic evidence of large-fiber sensorimotor polyneuropathy.
4. The non-ischemic forearm exercise test showed a normal increase in the lactate levels but no significant change in the ammonia levels. This finding suggests the possibility of myoadenylatedeaminase deficiency. Clinical correlation is advised.

NON-ISCHEMIC FOREARM EXERCISE TEST PROTOCOL
Time (in minutes) Lactate(0.5-2.2mmol/L) Ammonia (12-48)
Neurophysiology from 11/20/2008 through 3/11/2013 (cont)

mcmol/L
-10 from baseline 1 41
-5 from baseline 1 43
0 baseline, immediate before exercise 1.8 35
1 3.9 30
2 4.8 33
3 2.1 36
4 2.6 39
6 2.3 38
10 1.9 36

Sensory NCS

<table>
<thead>
<tr>
<th>Nerve / Sites</th>
<th>Distance cm</th>
<th>Peak Lat ms</th>
<th>Amplitude µV</th>
<th>Velocity m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>R Median - Dig II Wrist</td>
<td>13</td>
<td>3.15</td>
<td>22.7</td>
<td>52.0</td>
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<tr>
<td>R Ulnar - Dig V Wrist</td>
<td>11</td>
<td>3.15</td>
<td>11.5</td>
<td>47.8</td>
</tr>
<tr>
<td>L Sural - Lat Mall Calf</td>
<td>14</td>
<td>3.70</td>
<td>15.4</td>
<td>47.5</td>
</tr>
<tr>
<td>R Sural - Lat Mall Calf</td>
<td>14</td>
<td>3.75</td>
<td>15.9</td>
<td>49.1</td>
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</table>

Motor NCS

<table>
<thead>
<tr>
<th>Nerve / Sites</th>
<th>Distance cm</th>
<th>Latency ms</th>
<th>Amplitude mV</th>
<th>Velocity m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>R Median - APB Wrist</td>
<td>6</td>
<td>3.45</td>
<td>14.5</td>
<td>-</td>
</tr>
<tr>
<td>Elbow</td>
<td>27.5</td>
<td>8.65</td>
<td>13.9</td>
<td>52.9</td>
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</table>
## Neurophysiology from 11/20/2008 through 3/11/2013 (cont)

### R Ulnar - ADM

<table>
<thead>
<tr>
<th>Location</th>
<th>MUAP</th>
<th>Duration</th>
<th>Amplitude</th>
<th>Polyrhythmic</th>
<th># MUs</th>
<th>Rate</th>
<th>Effort</th>
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<tbody>
<tr>
<td>Wrist</td>
<td>6</td>
<td>2.45</td>
<td>12.1</td>
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<tr>
<td>B. Elbow</td>
<td>23</td>
<td>6.75</td>
<td>10.7</td>
<td>53.5</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>A. Elbow</td>
<td>10</td>
<td>8.70</td>
<td>10.0</td>
<td>51.3</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Stim median at elbow</td>
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<td>8.90</td>
<td>2.0</td>
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### R Peroneal - EDB

<table>
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<tr>
<th>Location</th>
<th>MUAP</th>
<th>Duration</th>
<th>Amplitude</th>
<th>Polyrhythmic</th>
<th># MUs</th>
<th>Rate</th>
<th>Effort</th>
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</thead>
<tbody>
<tr>
<td>Ankle</td>
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<td>3.85</td>
<td>3.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below Fib Head</td>
<td>35</td>
<td>12.45</td>
<td>3.4</td>
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<td></td>
<td></td>
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<tr>
<td>Above Fib Head</td>
<td>10</td>
<td>14.60</td>
<td>3.4</td>
<td>46.5</td>
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### L Peroneal - EDB

<table>
<thead>
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<th>Polyrhythmic</th>
<th># MUs</th>
<th>Rate</th>
<th>Effort</th>
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</thead>
<tbody>
<tr>
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<td>4.65</td>
<td>3.9</td>
<td></td>
<td></td>
<td></td>
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<td>12.80</td>
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<tr>
<td>Above Fib Head</td>
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<td>15.00</td>
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### R Tibial - AH

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<th>Location</th>
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<th>Duration</th>
<th>Amplitude</th>
<th>Polyrhythmic</th>
<th># MUs</th>
<th>Rate</th>
<th>Effort</th>
</tr>
</thead>
<tbody>
<tr>
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<td>4.35</td>
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<td></td>
</tr>
<tr>
<td>Pop Fossa</td>
<td>47</td>
<td>15.45</td>
<td>6.2</td>
<td>42.3</td>
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### L Tibial - AH

<table>
<thead>
<tr>
<th>Location</th>
<th>MUAP</th>
<th>Duration</th>
<th>Amplitude</th>
<th>Polyrhythmic</th>
<th># MUs</th>
<th>Rate</th>
<th>Effort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankle</td>
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<td>3.75</td>
<td>10.0</td>
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<td>Pop Fossa</td>
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<td>14.60</td>
<td>8.4</td>
<td>42.4</td>
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### EMG Summary Table

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<tr>
<th>Muscle</th>
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<th>MUAP</th>
<th>Recruitment</th>
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<tr>
<td></td>
<td>Fib/PSW</td>
<td>Fasc</td>
<td>Misc</td>
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<tr>
<td>L. Gastroc Med</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>L. Tib Anterior</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>L. Vastus Lat</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. First D Int</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Flex Carp Rad</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Triceps</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Biceps</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Deltoid</td>
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<td>None</td>
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<tr>
<td>R. Gastroc Med</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Tib Anterior</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Vastus Med</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Gluteus Max</td>
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<td>None</td>
</tr>
<tr>
<td>R. T Fascia Lat</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>R. Lumbar PSP</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
Fellow Chiawen Liang, MD
Attending Peter Siao, MD*
Sign Date 7/16/2009

* All data has been reviewed by me and I agree with the impression above.
I certify that I WAS present for the key portion of the needle EMG procedure.
Neurophysiology from 11/20/2008 through 3/11/2013 (cont)

IMPRESSION: Normal EEG, recorded in the awake and drowsy states. No epileptiform activity was in evidence. This study was limited by the presence of near-continuous F7 electrode artifact.

DETAIL: Awake there was rhythmic alpha activity bi-posteriorly at 8-9 Hz and 10-20 uV. Three minutes of hyperventilation produced diffuse, low-amplitude, symmetric slowing. Photic stimulation produced a symmetric driving response. Drowsy sections showed slow-rolling eye movements, alpha decrement and low-to-moderate amplitude, symmetric fronto-central slowing. Sustained sleep was not achieved. No spikes or sharp waves were evident, and there was no electrographic seizure activity present. There was evidence of near-continuous F7 electrode artifact.

ECG: Regular rhythm at 66 to 72 bpm.

I (Dr. Sassower) have performed a complete analysis and interpretation of this EEG and I have written and edited this report as necessary.

Fellow Naymee Velez Ruiz, MD
Attending Kenneth Sassower, MD
Sign Date 6/24/2009
Neurophysiology from 11/20/2008 through 3/11/2013 (cont)

04/18/2009

Sleep Laboratory

Final

Massachusetts General Hospital’s Division of Sleep Medicine
55 Fruit Street, Boston, MA 02114 (USA)

617-724-7426

POLYSOMNOGRAPHY REPORT

Patient: Weiner, Robert
Location: Sleep Laboratory at MGH
ID #: 464-55-81
DOB: 11/12/1964
Age: 44 yrs 5 mos
Gender: M
Requested by: STAKES, JOHN
Medications: NONE

Patient history and indications:
This is a patient with a history of excessive sleepiness and snoring. The patient reported an Epworth sleepiness scale of 2 (where greater than 10 is considered elevated) and has a body mass index (BMI) of 27.

Montage:
This sleep study was performed during the patient’s habitual sleep period, conducted in accordance with standards established by the American Academy of Sleep Medicine.

A technologist was present throughout the entire study.

Montage:
This sleep study was performed during the patient’s habitual sleep period, conducted in accordance with standards established by the American Academy of Sleep Medicine.

A technologist was present throughout the entire study.

Parameters used in this study include:
1. Electro-oculographic tracings (EOG), bilateral
2. Electro-encephalographic tracings (EEG), bilateral leads at the following locations:
   a. Frontal (F3, F4)
   b. Central (C3, C4)
   c. Occipital (O1, O2)
3. Electro-myography (EMG)
   a. Intercostal
   b. Submental
   c. Anterior tibialis
4. Respiratory physiology
   a. Respiratory effort: inductance plethysmography (thoracic and abdominal)
   b. Airflow
      i. Nasal pressure transducer
      ii. Oronasal thermal sensor
   c. Arterial oxygen hemoglobin saturation via pulse oximetry
5. Electrocardiography (EKG)
6. Snoring microphone

SLEEP SCORING DATA AND EEG

Lights Out: 10:44:50 PM
Lights On: 06:08:32 AM
Total Record Time: 443.7

Time (min.)
Total Sleep Time (TST): 340.7
Time in Bed: 443.7

Page 1 of 5
Neurophysiology from 11/20/2008 through 3/11/2013 (cont)

Sleep Latency: 44
Stage R Latency: 161.5
WASO*: 55.5
Sleep Efficiency: 76.8 %

Total Stage N1: 49.2 % of TST
Total Stage N2: 154
Total Stage N3: 87
Total Stage R: 50.5 % of TST
Total Stage W: 99.5

Total Movement Time: 0

*WASO refers to the number of minutes that the patient was awake throughout the night after initially falling asleep. It is often used as a measure of the ability to maintain sleep.

Neither electrographic seizures nor epileptiform discharges were seen.

Arousal Events

<table>
<thead>
<tr>
<th>Number of Arousals</th>
<th>123</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arousal Index</td>
<td>21.7</td>
</tr>
</tbody>
</table>

Respiration Events

<table>
<thead>
<tr>
<th>Total Sleep Time (min.)</th>
<th>340.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Obstructive Apneas</td>
<td>1</td>
</tr>
<tr>
<td>Number of Mixed Apneas</td>
<td>0</td>
</tr>
<tr>
<td>Number of Central Apneas</td>
<td>0</td>
</tr>
<tr>
<td>Number of Hypopneas*</td>
<td>1</td>
</tr>
<tr>
<td>Number of Apneas + Hypopneas*</td>
<td>2</td>
</tr>
<tr>
<td>Apnea Index</td>
<td>0.2</td>
</tr>
<tr>
<td>Hypopnea Index</td>
<td>0.2</td>
</tr>
<tr>
<td>Apnea + Hypopnea Index</td>
<td>0.4</td>
</tr>
<tr>
<td>Number of RERAs</td>
<td>45</td>
</tr>
<tr>
<td>RDI</td>
<td>8.3</td>
</tr>
</tbody>
</table>

Continuous Oxygen Saturation, mean value: 94.2%
Minimum Oxygen Saturation During NREM Sleep: 89
Minimum Oxygen Saturation During REM Sleep: 90
Time ≤ 88% (min.): 0.0
O2 Desaturations: 2
O2 Desaturations Index: 0.3
Cheyne Stokes Breathing: None

Definitions:
1. "Hypopnea" is defined as > 30% decrease in airflow or respiratory effort, by nasal pressure signal excursion, lasting >10 seconds, in association with a 4% or greater oxygen desaturation
2. "apnea" is >90% drop in thermal sensor excursion lasting >10 seconds.

Mild snoring was observed during the study.

Cardiac Events

<table>
<thead>
<tr>
<th>Average Heart Rate during sleep</th>
<th>64</th>
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</thead>
<tbody>
<tr>
<td>Highest Heart Rate During Sleep</td>
<td>90</td>
</tr>
<tr>
<td>Highest Heart Rate During Recording</td>
<td>90</td>
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</tbody>
</table>

No clinically significant ectopy or arrhythmias were seen.
**Movement Events**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>Index</th>
</tr>
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<tbody>
<tr>
<td><strong>Wakefulness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated Limb Movements</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Periodic Limb Movements</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL Limb Movements</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM Arousals</td>
<td>18</td>
<td>3.2</td>
</tr>
<tr>
<td>Isolated Limb Movements</td>
<td>22</td>
<td>3.9</td>
</tr>
<tr>
<td>Periodic Limb Movements</td>
<td>34</td>
<td>6.0</td>
</tr>
<tr>
<td>TOTAL Limb Movements</td>
<td>56</td>
<td>9.9</td>
</tr>
</tbody>
</table>

**INTERPRETATION and RECOMMENDATIONS:**

This patient’s overnight sleep study demonstrated no significant obstructive sleep apnea, with an apnea-hypopnea index (AHI) of 0.3 (events per hour), a minimal respiratory disturbance index (RDI) of 8.3 (events per hour) and an oxygen saturation minimum of 89%. Only 0.1% of the total sleep time was spent with an oxygen saturation of less than 90%.

Some motor restlessness noted during sleep, with some arousal as noted above. If clinically symptomatic and with some significant internight variability, this could be a factor in daytime fatigue.

John Stakes MD
Office Visit

Chief Complaint: FAOD

History of Present Illness: Mr. Weiner is a 47 year old right-handed man with a fatty acid oxidation defect, who presents for neurological care. First visit: 11-16-11; last visit: 11-08-12.

Active Issues:

1. Profound fatigue
2. Mental fog
3. Seeking long-term disability

Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volleyball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner
2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal
3. Heat and cold intolerance
4. Extensive rheumatologic and endocrine work-up have been unrevealing
5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. ?The muscle
mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy.

6. Level III cardiopulmonary testing (Baird III; 12-13-2011) revealed mild impaired oxygen extraction; mild anemia; secondary pulmonary mechanical limit to exercise. These results, to my interpretation, considers a multifactorial etiology for his fatigue, which may include a mitochondrial cytopathy.

7. Fresh muscle biopsy (Fall 2012). The detailed results are scanned on LMR. Essentially, we confirm that Mr. Weiner has a disorder of fatty acid metabolism. However, at this time we are not able to identify the specific component of the fatty acid metabolism is defective. Specifically, CPT I and CPT II activity was normal.

Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal.
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least.
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own.
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated.
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache.
7. Depression - denies any active depression.
8. He has diagnosis of Grove’s disease.

Medication stopped:

2. Creatine in cocktail stopped because of stomach cramps.

Medications:

Mitochondrial cocktail.
Medication Patient's Dose
Thiamine [B1] HOLD | May 2012
Pyridoxine [B6] HOLD | May 2012
Cobalamin [B12] HOLD | May 2012
Vitamin C 1000 mg
Vitamin E 800 IU
Carnitor [L-carnitine] 7,500 mg
alpha-lipoic acid 1,000 mg
Selenium 50 mcg
Coenzyme Q10 [ubiquinone] 1,500 mg
Creatine monohydrate XXXXXX
N-acetyl cysteine [NAC] 1,500 mg
Folinic acid 150 mg
Magnesium orotate 500 mg tid

INTERVAL CHANGES

1. Addition of magnesium and carnitine did not appreciably increase his energy
2. He started a new diet by Timothy Ferris (slow carb diet) in the last couple of weeks. He feels this has improved his alertness but worsened his myalgia.
In essence, he has decreased the amount of carbohydrate and dairy
3. He has stopped doing cabinet making as he is tired

At visit, he is pleasant, interactive, and in no acute distress. He is accompanied by his wife.


Review of Systems: The patient smokes cigarettes (0.571 pack-year history of smoking). He has been drinking alcoholic beverages. He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URTIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aides, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasciculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venous malformation, aneurysm, cavernoma] and psychological [pertinent positives:
loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

General Examination: Temperature was 98.3 degrees Fahrenheit. He appeared well-nourished and well-groomed. The skull and scalp were normal. Ears, nose and throat were normal. His neck was supple and had full range of motion. His trachea position was normal. His thyroid was normal. The chest exam was normal. Abdomen normal.

Neurological Exam:

Mental Status: The patient was alert and oriented to person, place and time. His attention, speech, language, memory, intellect, judgement, mood and flow of thought were normal. Affect was appropriate. There were no hallucinations, delusions, suicidal ideation, homicidal ideation, obsessions or compulsions.

Cranial Nerves: Visual fields were full. Extraocular movements were full. Convergence was normal. There was no nystagmus. Eyelids were normal. Facial sensation was normal. Blink rate was normal. On a 0-4 scale, facial expression was rated normal.

Motor Exam: Muscle bulk was normal. There was normal tone. Strength was normal. Fasciculations were absent. Brdykinesia during tapping movements was absent. Apraxia was absent. There was no ballismus. There was no chorea. There was no dystonia. There were no tics. Myoclonus was absent.

Coordination: There was no resting, postural or intention tremor. Finger-nose-finger was normal. Heel-knee-shin was normal. Hand movements were normal. Posture was rated 0 on a 0-4 rating scale (with 0 being normal), indicating normal erect posture.

Assessment:
1. Mitochondrial disorder: This is a delightful 48 year old gentleman now diagnosed with a fatty acid oxidation defect, who now presents for neurological care and discussion. Mr. Weiner’s exam is essentially normal.

We had an extended discussion with Mr. Weiner and his wife. We reviewed the results and laid the groundwork of our next steps.

Recommendations:
Plan:

1. Mitochondrial cocktail. Continue
2. Future interventions: Trileptal for the AM fogginess; low flow of oxygen therapy at night. He wants to wait on these

He will return to see me in 4 months.

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Shivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations were completed by U. Shivraj Sohur, MD, PhD.
Initial Nutrition Visit

Referring Dx: FAOD - Mitochondrial dx

Referred By: U. Sohur, MD (34009)

Medical Referral Received: Y (in LMR)

Significant PMH:
Fatigue
Myopathy or muscular dystrophy NOS

Pain assessed (0-10):
4 - muscle pain (in tx)

Safe at home?:
defered

Allergies/intolerance:
NKFA

Nutrition related Labs:
no recent

Significant Meds/DNI:

Medications
Acetaminophen W/codeine 30mg 1 TAB (300MG-30MG TABLET ) PO Q6H PRN ,
Levocarnitine 1 GM (330MG TABLET ) PO TID x 30 days;

Supplements/Vitamins:
Metamucil
Mito cocktail:
Thiamine [B1] 200 mg
Riboflavin [B2] 600 mg
Pyridoxine [B6] 200 mg
Cobalamin [B12] 100 microg
Vitamin C 1000 mg
Vitamin E 800 IU
Carnitor [L-carnitine] 7,500 mg
alpha-lipoic acid 1,000 mg
Selenium 50 mcg
Coenzyme Q10 [ubiquinone] 1,500 mg
Creatine monohydrate XXXXXX - harsh on stomach
N-acetyl cysteine [NAC] 1,500 mg
Folinic acid 150 mg

Vital Signs
AGE 47y11.9m
TEMPERATURE 98.3 F
PULSE 68 Regular
BLOOD PRESSURE 114/72 Right Arm
HEIGHT 74 in
WEIGHT 214 lb
BMI 27.5
Pt reports weight stable between 215 and 220 lb.

Wt Hx: lowest 165, highest 220. OK with current wt but would like to be less

Desired wt (per pt):
190 lb

Dietary Assessment:
24hr recall: 1400 Kcals, 12 %protein, 35 % fat (typical 25%), 53% CHO (typical 63, 10 g fiber
B/ Special K with skim milk, strawberries
L/ low fat vanilla Greek yogurt
Sn/ 3-4 pretzel rods
D/Mac and cheese (typical chicken, potato and green vegetable)
Sn/ clementines
Fluid/ 3-4 pints water daily

Exercise Hx:
limited 2/2 pain

Calorie needs/d (Mifflin-St Jeor Equation):
wt maintenance: 2500 kcal/day, 80 g protein, 1000 mg calcium

Patient interview:
Robert c/o fatigue and muscle pain 2/2/ mitochondrial dx.

Prior Nutrition Education/Diet hx:
none

Assessment:

Nutritional Diagnosis/Problems:
Food and nutrition knowledge deficit related to diagnosis of mitochondrial dx as evidenced by inadequate protein intake

Nutrition Recommendations:
- 3 meals and 2-3 snacks daily
- include protein in both meals and snacks during day
- calcium supplement

Intervention:
- Education Materials provided: written goals
- Patient Response: good; pt verbalizes understanding of NCP and states goals are reasonable.

Goals:
- Normalize eating patterns w/ emphasis on regular time intervals between meals (2.5 to 3 hrs) while including PRO, CHO and fats q meal.
- Incorporate protein into snacks as discussed

Recommend visits: 1

Time spent counseling: 40
RTC x prn
Office Visit

Chief Complaint: Fatty acid oxidation defect

History of Present Illness: Mr. Weiner is a 47 year old right-handed man with probable mitochondrial cytopathy, who presents for neurological care. First visit: 11-16-11; last visit: 05-10-12.

ISSUES / NOTES

Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volleyball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner
2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal
3. Heat and cold intolerance
4. Extensive rheumatologic and endocrine work-up have been unrevealing
5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy
6. Level III cardiopulmonary testing (Baird III; 12-13-2011) revealed mild impaired oxygen extraction; mild anemia; secondary pulmonary mechanical limit
to exercise. These results, to my interpretation, considers a multifactorial etiology for his fatigue, which may include a mitochondrial cytopathy.

Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache
7. Depression - denies any active depression
8. He has diagnosis of Grove’s disease

Medication stopped:

1. Provigil - August 2011 - unwell feeling
2. Creatine in cocktail stopped because of stomach cramps

Medications:

Mitochondrial cocktail

Medication Patient's Dose
Thiamine [B1] HOLD | May 2012
Pyridoxine [B6] HOLD | May 2012
Cobalamin [B12] HOLD | May 2012
Vitamin C 1000 mg
Vitamin E 800 IU
Carnitor [L-carnitine] HOLD | May 2012
alpha-lipoic acid 1,000 mg
Selenium 50 mcg
Coenzyme Q10 [ubiquinone] 1,500 mg
Creatine monohydrate XXXXXX
N-acetyl cysteine [NAC] 1,500 mg
Folinic acid 150 mg

INTERVAL CHANGES

1. He is coming back from having had a fresh muscle biopsy in Cleveland, OH (Case Western). I have had several ongoing conversations with Dr. Suzanne Brosse and Dr. Chuck Hoppel. The detailed results are scanned on LMR. Essentially, we confirm that Mr. Weiner has a disorder of fatty acid metabolism. However, at this time we are not able to identify the specific component of the fatty acid metabolism is defective. Specifically, CPT I and CPT II activity was normal.

2. We reviewed an Excel spreadsheet of symptoms he brought with him.

At visit, he is pleasant, interactive, and in no acute distress. He is accompanied by his wife.


Review of Systems: The patient smokes cigarettes (0.571 pack-year history of smoking). He has been drinking alcoholic beverages. Social drinker He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aides, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasiculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venus malformation, aneurysm, cavernoma] and psychological [pertinent positives: loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

General Examination: In his right arm, his blood pressure was 100/78 when lying. Weight was 219 pounds. Temperature was 98.3 degrees Fahrenheit. He
appeared well-nourished and well-groomed. The skull and scalp were normal. Ears, nose and throat were normal. His neck was supple and had full range of motion. His trachea position was normal. His thyroid was normal. The chest exam was normal. Abdomen normal.

Neurological Exam:

Mental Status: The patient was alert and oriented to person, place and time. His attention, speech, language, memory, intellect, judgement, mood and flow of thought were normal. Affect was appropriate. There were no hallucinations, delusions, suicidal ideation, homicidal ideation, obsessions or compulsions.

Cranial Nerves: Visual fields were full. Extraocular movements were full. Convergence was normal. There was no nystagmus. Eyelids were normal. Facial sensation was normal. Blink rate was normal. On a 0-4 scale, facial expression was rated normal.

Motor Exam: Muscle bulk was normal. There was normal tone. Strength was normal. Fasciculations were absent. Bradykinesia during tapping movements was absent. Apraxia was absent. There was no ballismus. There was no chorea. There was no dystonia. There were no tics. Myoclonus was absent.

Coordination: There was no resting, postural or intention tremor. Finger-nose-finger was normal. Heel-knee-shin was normal. Hand movements were normal. Posture was rated 0 on a 0-4 rating scale (with 0 being normal), indicating normal erect posture.

Assessment:
1. Mitochondrial disorder: This is a delightful 47 year old gentleman now diagnosed with a fatty acid oxidation defect, who now presents for neurological care and discussion. Mr. Weiner’s exam is essentially normal.

We had an extended discussion with Mr. Weiner and his wife. We reviewed the results and laid the groundwork of our next steps.

Recommendations:

Plan:

1. Mitochondrial cocktail. We will add Carnitine back in the cocktail
2. Future interventions: Trileptal for the AM fogginess; low flow of oxygen therapy at night. He wants to wait on these

He will return to see me in 4 months.
I spent 60 minutes with this patient, >50% of which was dedicated to counseling/coordination of care.

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Shivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations were completed by U. Shivraj Sohur, MD, PhD.
Chief Complaint: Fatigue

History of Present Illness: Mr. Weiner is a 47 year old right-handed man with probable mitochondrial cytopathy, who presents for neurological care. First visit: 11-16-11; last visit: 02-23-12.

ISSUES / NOTES
Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volley ball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner
2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal
3. Heat and cold intolerance
4. Extensive rheumatologic and endocrine work-up have been unrevealing
5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. ?The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy
6. Level III cardiopulmonary testing (Baird III; 12-13-2011) revealed mild impaired oxygen extraction; mild anemia; secondary pulmonary mechanical limit
to exercise. These results, to my interpretation, considers a multifactorial etiology for his fatigue, which may include a mitochondrial cytopathy.

Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache
7. Depression - denies any active depression
8. He has diagnosis of Grove’s disease

Medication not tolerated / not effective:

1. Provigil - August 2011 - unwell feeling

Medications:

Mitochondrial cocktail

Medication Patient's Dose
Thiamine [B1] 200 mg
Riboflavin [B2] 600 mg
Pyridoxine [B6] 200 mg
Cobalamin [B12] 100 microg
Vitamin C 1000 mg
Vitamin E 800 IU
Carnitine [L-carnitine] 7,500 mg
alpha-lipoic acid 1,000 mg
Selenium 50 mcg
Coenzyme Q10 [ubiquinone] 1,500 mg
Creatine monohydrate XXXXXX
N-acetyl cysteine [NAC] 1,500 mg
Folic acid 150 mg
INTERVAL CHANGES

1. General: he is having nausea, he thinks it is due to the B vitamins
2. Symptoms have been stable
3. We reviewed an Excel spreadsheet of symptoms he brought with him

At visit, he is pleasant, interactive, and in no acute distress.


Review of Systems: The patient smokes cigarettes (0.571 pack-year history of smoking). He has been drinking alcoholic beverages. social drinker He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aides, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasiculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venus malformation, aneurysm, cavernoma] and psychological [pertinent positives: loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

General Examination: In his right arm, his blood pressure was 100/78 when lying. Weight was 219 pounds. Temperature was 98.3 degrees Fahrenheit. He appeared well-nourished and well-groomed. The skull and scalp were normal. Ears, nose and throat were normal. His neck was supple and had full range of motion. His trachea position was normal. His thyroid was normal. The chest exam was normal. Abdomen normal.

Neurological Exam:

Mental Status: The patient was alert and oriented to person, place and time.
His attention, speech, language, memory, intellect, judgement, mood and flow of thought were normal. Affect was appropriate. There were no hallucinations, delusions, suicidal ideation, homicidal ideation, obsessions or compulsions.

Cranial Nerves: Visual fields were full. Extraocular movements were full. Convergence was normal. There was no nystagmus. Eyelids were normal. Facial sensation was normal. Blink rate was normal. On a 0-4 scale, facial expression was rated normal.

Motor Exam: Muscle bulk was normal. There was normal tone. Strength was normal. Fasciculations were absent. Bradykinesia during tapping movements was absent. Apraxia was absent. There was no ballismus. There was no chorea. There was no dystonia. There were no tics. Myoclonus was absent.

Coordination: There was no resting, postural or intention tremor. Finger-nose-finger was normal. Heel-knee-shin was normal. Hand movements were normal. Posture was rated 0 on a 0-4 rating scale (with 0 being normal), indicating normal erect posture.

Assessment:
1. fatigue: This is a delightful 47 year old gentleman with probable mitochondrialopathy, who now presents for neurological care. His symptoms of fatigue and AM mental fog in absence of clear sleep disorder. Mr. Weiner’s exam is essentially normal.

A mitochondrial cytopathy continues to be reasonable, given the story and suggestive muscle biopsy, and Baird III results suggestion mild oxygen extraction issue. We will proceed with fresh muscle biopsy.

Recommendations:
Plan:

1. Mitochondrial cocktail. New Rx without B vitamins and carnitines to see if this will abate nausea

<table>
<thead>
<tr>
<th>Medication</th>
<th>Patient's Dose</th>
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<tbody>
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<td></td>
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<tr>
<td>Carnitor [L-carnitine]</td>
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<td></td>
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<tr>
<td>alpha-lipoic acid 1,000 mg</td>
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Notes from 11/20/2008 through 3/11/2013 (cont)

Selenium 50 mcg
Coenzyme Q10 [ubiquinone] 1,500 mg
Creatine monohydrate ON HOLD - May 2012
N-acetyl cysteine [NAC] 1,500 mg
Folinic acid 150 mg

2. Fresh muscle biopsy. Patient wants to proceed. Will request formally with Dr. Kerr/CIDEM/Ohio
3. Future interventions: Trileptal for the AM fogginess; low flow of oxygen therapy at night. He wants to wait on these

We will keep in touch, and determine course of action after results are back from fresh muscle biopsy.

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Shivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations were completed by U. Shivraj Sohur, MD, PhD.
Office Visit

Chief Complaint: Fatigue

History of Present Illness: Mr. Weiner is a 47 year old right-handed man with probable mitochondrial cytopathy, who presents for neurological care. First visit: 11-16-11; last visit: same.

ISSUES / NOTES

Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volley ball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner
2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal
3. Heat and cold intolerance
4. Extensive rheumatologic and endocrine work-up have been unrevealing
5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy
Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache
7. Depression - denies any active depression
8. He has diagnosis of Grove’s disease

Medication not tolerated / not effective:

1. Provigil - August 2011 - unwell feeling

Medications:

Mitochondrial cocktail

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<td>Folinic acid</td>
<td>150 mg</td>
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</tbody>
</table>

INTERVAL CHANGES
1. General: he did not tolerate Provigil. He is taking a part of the mitochondrial cocktail I prescribed - uncertain if he is deriving benefit

2. Symptoms have been stable

3. Level III cardiopulmonary testing (Baird III) revealed mild impaired oxygen extraction; mild anemia; secondary pulmonary mechanical limit to exercise. These results, to my interpretation, considers a multifactorial etiology for his fatigue, which may include a mitochondrial cytopathy

At visit, he is pleasant, interactive, and in no acute distress.


Review of Systems: The patient smokes cigarettes (0.571 pack-year history of smoking). He has been drinking alcoholic beverages. social drinker He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aids, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasiculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venus malformation, aneurism, cavernoma] and psychological [pertinent positives: loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

Assessment:

1. fatigue: This is a delightful 47 year old gentleman with probable mitochondriopathy, who now presents for neurological care. His symptoms of fatigue and AM mental fog in absence of clear sleep disorder. Mr. Weiner’s exam is essentially normal.

A mitochondrial cytopathy continues to be reasonable, given the story and suggestive muscle biopsy, and now Baird III results suggestion mild oxygen extraction issue. He wants to give th mitochondrial cocktail some more time.
Recommendations:

Plan:

1. Mitochondrial cocktail. He can continue to take what he is taking
2. Other interventions: Trileptal for the AM fogginess; low flow of oxygen
   therapy at night. He wants to wait on these

We will keep in touch, and determine course of action after results are back.

I spent 40 minutes with this patient, >50% of which was dedicated to
counseling/coordination of care.

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Sivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations
were completed by U. Shivraj Sohur, MD, PhD.
Notes from 11/20/2008 through 3/11/2013 (cont)

12/12/2011 NARRATIVE NOTE Final Lewis, Gregory D, M.D.

CARDIOLOGY
MASSACHUSETTS GENERAL HOSPITAL

Narrative Note:
Mr. Weiner is a 47 year old right-handed man with probable mitochondrial cytopathy, who with undergo level 3 CPET with invasive hemodynamic monitoring during exercise to further evaluate the functional significance of his mitochondrial dysfunction. Please see Dr. Sohur's comprehensive evaluation from 11/2011 for details of his history and physical exam.

The patient developed fatigue and exercise intolerance starting in 2003. Onset of fatigue was insidious. He used to be an avid volley ball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner. He also was noted to have increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure.

He will have a right heart catheterization with PA line to remain in place and then go to the CPET lab for exercise testing. Routine laboratories will be drawn prior to testing.

Signed electronically by Gregory Lewis, MD

Document Status: Final
Office Visit

Chief Complaint: Fatigue

History of Present Illness: Mr. Weiner is a 47 year old right-handed man with probable mitochondrial cytopathy, who presents for neurological care. First visit: 08-25-11; last visit: same.

ISSUES / NOTES

Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volleyball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner

2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal

3. Heat and cold intolerance

4. Extensive rheumatologic and endocrine work-up have been unrevealing

5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy
Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache
7. Depression - denies any active depression
8. He has diagnosis of Groves disease

INTERVAL CHANGES

1. General: he did not tolerate Provigil. He is taking a part of the mitochondrial cocktail I prescribed - uncertain if he is deriving benefit
2. Symptoms have been stable

At visit, he is pleasant, interactive, and in no acute distress.


Review of Systems: The patient smokes cigarettes (0.571 pack-year history of smoking). He has been drinking alcoholic beverages. social drinker He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aids, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasiculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venus malformation, aneurism, cavernoma] and psychological [pertinent positives:
loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

General Examination: He appeared well-nourished and well-groomed. The skull and scalp were normal. Ears, nose and throat were normal. His neck was supple and had full range of motion. His trachea position was normal. His thyroid was normal. The chest exam was normal. Abdomen normal.

Neurological Exam:

Mental Status: The patient was alert and oriented to person, place and time. His attention, speech, language, memory, intellect, judgement, mood and flow of thought were normal. Affect was appropriate. There were no hallucinations, delusions, suicidal ideation, homicidal ideation, obsessions or compulsions.

Cranial Nerves: Visual fields were full. Discs were normal. Extraocular movements were full. Convergence was normal. There was no nystagmus. Eyelids were normal. Facial sensation was normal. Blink rate was normal. On a 0-4 scale, facial expression was rated normal.

Motor Exam: Muscle bulk was normal. There was normal tone. Strength was normal. Fasciculations were absent. Bradykinesia during tapping movements was absent. Apraxia was absent. There was no ballismus. There was no chorea. There was no dystonia. There were no tics. Myoclonus was absent.

Coordination: There was no resting, postural or intention tremor. Finger-nose-finger was normal. Heel-knee-shin was normal. Hand movements were normal. Posture was rated 0 on a 0-4 rating scale (with 0 being normal), indicating normal erect posture.

Assessment:
1. Fatigue: This is a delightful 47 year old gentleman with probable mitochondrialopathy, who now presents for neurological care. His symptoms of fatigue and AM mental fog in absence of clear sleep disorder. Mr. Weiner’s exam is essentially normal.

A mitochondrial cytopathy is reasonable, given the story and suggestive muscle biopsy. I had a long discussion with the patient, educating him on metabolism disorders and I answered his questions. He wishes to proceed with further diagnostic work-up.
I will continue to proceed in graded stages.

Recommendations:

Plan:

1. Mitochondrial cocktail. He can continue to take what he is taking
2. Work-up. Arrange for level III cardiopulmonary exercise testing (i.e. Baird III)
3. Other interventions: Trileptal for the AM fogginess; low flow of oxygen therapy at night

We will keep in touch, and determine course of action after results are back.

I spent 40 minutes with this patient, >50% of which was dedicated to counseling/coordination of care.

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Shivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations were completed by U. Shivraj Sohur, MD, PhD.
Chief Complaint: Fatigue

History of Present Illness: This is a 46 year old right-handed man with probable mitochondrial cytopathy, who presents for establishment of neurological care.

I will present the narrative in summary for my own records and for direction of care. Source: LMR and patient; he is a good historian.

Mother’s pregnancy; Milestones; childhood into adulthood

1. Mr. Weiner was born at term after a reported uneventful pregnancy, and delivery was uncomplicated. He attained all her other milestones on time.
2. He had a normal childhood into adulthood. He did not have any exposure to chemicals, close head injury or post traumatic stress disorder that he disclosed.
3. He successfully completed a degree in psychology, but eventually became a successful programmer.

Current Illness and Work-up

1. Onset in 2003. Onset of fatigue was insidious. He used to be an avid volley ball player. Over the course of a year, it became increasingly difficult for him to sustain his rhythm in the game and he notes that his work performance began to suffer too. Since, he believes that symptoms have worsened in a stepwise manner.
2. Mental fog. By 2005 he was getting increasingly tired, and he would wake up in a mental fog. He had several sleep studies done. At some point there was question of restless leg. However, Mirapex brought paradoxical insomnia. Eventually the issue became less prominent and at this time he is not taking any medications. Neuropsychological testing ordered by Dr. Felsenstein (MGH ID; main MD investigating his fatigue) was normal.
3. Heat and cold intolerance
4. Extensive rheumatologic and endocrine work-up have been unrevealing.
5. He was evaluated extensively by Dr. Siao (MGH Neuromuscular) for his...
fatigue. The muscle biopsy (11/2009) showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal. Dr. Siao is of opinion that patient has a mitochondrial cytopathy

Other Notes/issues

1. At some point, there was a thought that he had mitral valve prolapse, but an ECHO was normal
2. There is a patch of tingling and numbness under his left nipple. This symptom has been constant for the last 3 years at least
3. Mr. Weiner saw Dr. Sahai (MGH Genetics) in May 2010. Initial testing showed decreased serine, but that apparently normalized on its own
4. For some years, (~2005-2008), he had tinnitus, put since, this symptom has dissipated
5. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy.
6. If Mr. Weiner overexerts, he has a headache
7. Depression - denies any active depression
8. He has diagnosis of Grove’s disease

At exam, he is pleasant, interactive, and in no acute distress.


Developmental History: The gestational age was 40 weeks. The birth weight was 9 pounds 15 ounces. The pregnancy was uncomplicated. The labor was uncomplicated. The delivery was uncomplicated. The neonatal course was uncomplicated.

Family History: Patient's ancestry: Irish, German. There is no family history of similar or pertinent disease.

Social History: Lives with wife He was not accompanied by anyone. Finished degree in psychology The patient is retired. On short term disability from being a computer programmer
Review of Systems: The patient has smoked cigarettes (0.571 pack-year history of smoking), but stopped approximately 13 years ago. He has been drinking alcoholic beverages. He does not drink caffeinated beverages. The following systems reviews were contributory: general [pertinent positives: tinnitus; pertinent negatives: fevers, night sweats, frequent URIs, adenopathy, frequent ear infections, difficulty hearing, uses hearing aids, easy bruising, prolonged or excessive bleeding, anemia, environmental allergies, previous transfusion reactions]; endocrine [pertinent positives: heat intolerance, cold intolerance; pertinent negatives: excessive sweating, hot flashes, orthostatic symptoms, flushing, goiter, thyroid disease, diabetes mellitus, changes in facial features, changes in hands, changes in feet]; neurological [pertinent positives: headaches; pertinent negatives: seizures, previous stroke, vertigo, acute dystonic reaction, chorea, tics, dystonia, muscle cramps, fasciculations, weakness, gait difficulty, syncope, sense of imbalance, falling, memory loss, previous head injury, previous loss of consciousness, previous TIA, arterial venous malformation, aneurysm, cavernoma] and psychological [pertinent positives: loss of energy; pertinent negatives: sadness, depression, anxiety, phobias, irritability, initial insomnia, terminal insomnia, obsessions, hyperactivity, excessive energy, little need for sleep, mania, excessive alcohol intake, binge drinking, alcoholic blackouts, visual hallucinations, auditory hallucinations, previous treatment ECT, previous neuroleptic treatment, previous medical treatment for depression]. The following systems reviews were noncontributory: substance abuse; hematologic/autoimmune and ophthalmological.

General Examination: In his right arm, his blood pressure was 124/78 and his pulse was 80 per minute when sitting. Weight was 225 pounds. He appeared well-nourished and well-groomed. The skull and scalp were normal. Ears, nose and throat were normal. His neck was supple and had full range of motion. His trachea position was normal. His thyroid was normal. The chest exam was normal. His heart was normal. Abdomen normal.

Neurological Exam:

Mental Status: The patient was alert and oriented to person, place and time. His attention, speech, language, memory, intellect, judgement, mood and flow of thought were normal. Affect was appropriate. There were no hallucinations, delusions, suicidal ideation, homicidal ideation, obsessions or compulsions.

Cranial Nerves: Visual fields were full. Discs were normal. The right pupil was 4 mm and the left pupil was 4 mm. After light stimulus, the right pupil was 3 mm and the left pupil was 3 mm. Extraocular movements were full. Convergence was normal. There was no nystagmus. Eyelids were normal. Facial sensation was normal. Blink rate was normal. On a 0-4 scale, facial expression was rated normal.
Motor Exam: Muscle bulk was normal. There was normal tone. Strength was normal. Fasciculations were absent. Brdykinesia during tapping movements was absent. Apraxia was absent. There was no ballismus. There was no chorea. There was no dystonia. There were no tics. Myoclonus was absent.

Sensory Exam: Light touch was normal.

Coordination: There was no resting, postural or intention tremor. Finger-nose-finger was normal. Heel-knee-shin was normal. Hand movements were normal. Posture was rated 0 on a 0-4 rating scale (with 0 being normal), indicating normal erect posture.

Reflexes: Reflexes were evaluated on a 0 to 4 scale, where 0='absent', 1='reduced', 2='normal', 3='increased' and 4='brisk with clonus'. The reflexes were 2 in the right biceps, 2 in the left biceps, 2 in the right knee, 2 in the left knee, 2 in the right ankle, 2 in the left ankle.

Assessment:
1. Fatigue: This is a delightful 46 year old gentleman with probable mitochondrialopathy, who now presents to establish neurological care. His symptoms of fatigue and AM mental fog in absence of clear sleep disorder. Mr. Weiner's exam is essentially normal.

A mitochondrial cytopathy is reasonable, given the story and suggestive muscle biopsy. I had a long discussion with the patient, educating him on metabolism disorders and I answered his questions.

I will proceed in graded stages.

Recommendations:

Plan:

1. Mitochondrial cocktail. I provided him with a new Rx, and stressed that he must take all the components for a synergistic effect
2. We will start Provigil as a stimulant. Side effects discussed in detail
3. Other interventions: Trileptal for the AM fogginess; low flow of oxygen therapy at night

We will keep in touch, and determine course of action after results are back.

I spent 120 minutes with this patient, >50% of which was dedicated to counseling/coordination of care.
Notes from 11/20/2008 through 3/11/2013 (cont)

U. Shivraj Sohur, M.D., Ph.D.
Movement Neurology Staff
Sohur.Shivraj@mgh.harvard.edu

This patient's history, physical examination, assessment and recommendations were completed by U. Shivraj Sohur, MD, PhD.
November 4, 2010

John Stakes, MD
Neurology
Massachusetts General Hospital

RE: WEINER, ROBERT D
MRN: 4645581
DOB: 11/12/1964

Dear John,

Mr. Robert Weiner came to our Neuromuscular Unit. His last visit was on July 12, 2010. Mr. Weiner is a 45-year-old right-handed man who complains of feeling fatigue of 4 years duration. Coenzyme Q10 was started in February 2010. The patient felt better since. L-carnitine was started in July. The patient currently takes coenzyme Q10 of 1000 mg a day and L-carnitine 500 mg twice a day. The patient said that he had a, "decent summer." He was able to commute into Boston twice a week. He was also able to take on some construction project like his father build a shelf in the basement. A few times he swam in the lake. His ability to concentrate at work also improved. Starting around mid-August he started to, "Run out of gas." He is now working from home more than last summer. Overall, the patient is not as good as this past summer but he is still better than in February before coenzyme Q10 was started. The patient's weight is unchanged, 220 pounds.

The patient saw Dr. Sahai in May and was advised to take serine 1000 mg a day since July. The patient denies any numbness of the upper and lower extremities. He is not very active. When he is at home he is quite sedentary. The patient does not do any exercise routine. The patient denies any pain in his body. CURRENT MEDICATIONS: Vitamin D, vitamin C, fish oil, high potency vitamin B, L-carnitine 500 b.i.d., coenzyme Q10 at 1000 mg a day, serine 1000 mg a day.

PERTINENT EXAMINATION: Motor strength testing in the upper and lower extremities 5/5 bilaterally. Deep tendon reflexes, 2 at the biceps, triceps, knees, and ankles bilaterally. Toes downgoing bilaterally. No spasticity in the lower extremities. Sensory examination: intact pinprick and vibratory sensation in the upper and lower extremities. Romberg test: negative. Tandem gait: normal. ASSESSMENT AND PLAN: Fatigue. Muscle biopsy showed findings consistent with mitochondrial disorder. I advised the patient to increase coenzyme Q10 to 2000 mg a day. He will maintain his other medications. I also advised the patient to start on an exercise routine even it is just walking and gradually increase the amount of exercise. He was also advised to follow up with Dr. Sahai at the Genetics and Metabolism Clinic regarding his low serine and other amino acid levels.

The patient will return for a followup visit.

Sincerely,

Peter Siao, M.D.
cc: Dr. HUGH TAYLOR

Printed: 03/11/2013 12:06 PM
Notes from 11/20/2008 through 3/11/2013 (cont)

Visit Note

Patient Name: WEINER, ROBERT D  
MRN: 4645581

Dictated Date: 07/14/2010  
Dictated by: Donna Felsenstein, M.D.

Date of Visit: 07/14/2010

The patient returns for a followup. He has been followed by Dr. Peter Siao Tick Chong. The patient is now on coenzyme Q10. He has been taking 200 mg 3 times a day. He states that he has been doing "a little better." He feels as though for the past few weeks he has more endurance. When he does physical activities, he does not get as "wiped out" as he had previously. He feels that he has been doing better since approximately March. He is able to get through more activities. He feels as though he is definitely more clear headed. He is not searching for words as much as he has in the past.

His review of systems is notable for the fact that he does not have fevers. His appetite has been good. He thinks that he may be having occasional night sweats, maybe 1 time per week. I have asked him to keep track of this. If he continues to have night sweats, further workup would be indicated and the patient understands. He will let me know if this is an ongoing issue.

On physical examination his blood pressure is 122/75, temperature is 97.2, pulse is 60, weight is 227 pounds.

Most of the visit was spent discussing the patient's symptoms and overall plan. The patient has a full physical examination scheduled with his primary care physician in September. A full physical examination was, therefore, not done today. We did discuss the fact that he was doing slightly better. Dr. Chong had recommended to the patient that he increase the coenzyme Q10 to 200 mg 5 times a day which the patient will be doing. He will also be getting carnitine 500 mg by mouth twice a day. He is also taking B complex once a day. He will continue these medications and see how he does. I also discussed the fact with him that if he has a mitochondrial disorder, then it is possible he might benefit from nasal oxygen use at night or while he is at home. He will discuss this with Dr. Chong. The patient will return to see me in 9 to 12 months or as needed.

Donna Felsenstein, M.D.

cc:

DD: 07/14/2010 21:01:21
TD: 07/15/2010 10:59:59
TR: 6750270
BackJob ID: 1259998
VoiceJob ID: 44355577
July 12, 2010

John Stakes, MD
Neurology
Massachusetts General Hospital

RE: WEINER, ROBERT D
MRN: 4645581
DOB: 11/12/1964

Dear John:

I saw Mr. Robert Weiner in our Neuromuscular Unit. His last visit was on 02/19/2010. Mr. Weiner is a 45-year-old right-handed man who complains of feeling fatigued of 4 years' duration. The patient started to take coenzyme Q10 at 200 mg 3 times a day after his last visit. After about a week of CoQ10, the patient noted a moderate improvement in his stamina. If he does more physical activities, he may get wipeouts and recover after a day, rather than a week. The patient is also able to concentrate better. He rates his current level of function as 60%, which is an improvement from a previous 30%.

CURRENT MEDICATIONS: The patient is continuing ribose. His other medications are unchanged, vitamin D, fish oil, vitamin C, multivitamins.

PERTINENT EXAMINATION: Motor strength testing in the upper and lower extremities 5/5 bilaterally. Deep tendon reflexes, 2 at the biceps, triceps, knees, and ankles bilaterally. Toes downgoing bilaterally. No spasticity of the lower extremities.

The patient was also seen at the Genetics and Metabolism Clinic in 05/2010. The patient had normal plasma acetyl carnitine profile. Plasma amino acids showed low levels of serine, (Dictation Anomaly) 4:43 level normal.

Urine showed low levels of leucine, methionine, serine, valine. Plasma level of serine low 63, normal 78 to 166.

The patient had muscle test for myoglobinuria panel that showed normal levels of myoadenylate deaminase and other enzymes. Muscle tests for mitochondrial enzymes showed increased citrate synthase activity that may be indicative of mitochondrial disease. There was not enough muscle tissue for mitochondrial deoxyribonucleic acid mutation.

The patient is currently being treated with coenzyme Q10 at 200 mg t.i.d. His symptoms have improved. I advised the patient to add vitamin B complex and increase coenzyme Q10 to 1000 mg a day and add levocarnitine 330 mg t.i.d. The patient weighs 220 pounds and he is 63 inches tall.

The patient was advised to follow up with the Genetics and Metabolism Clinic with regards to the abnormal amino acids level. The patient will return for followup visit.

Sincerely,

Peter Siao, M.D.

cc: Hugh Taylor, MD, 15 Railroad Avenue, South Hamilton, MA 01982

Notified Dr. Sahai by email the following:

Robert Weiner (4645581) - Serine LOW 174, Valine LOW 19, Methionine LOW 10, Leucine LOW 12

Tomi L. Toler, MS
Licensed Genetic Counselor
CONSULTATION NOTE:

It was a pleasure to meet with Mr. Weiner, when he presented to the Genetics and Metabolism clinic for evaluation of urinary amino acid abnormalities identified during the work-up of his fatigue, myalgias and exercise intolerance.

SOURCE OF HISTORY: Patient and Review of Records

HISTORY OF PRESENT ILLNESS:

Mr. Weiner is a 45-year-old right-handed man, with the chief complaints of fatigue, exercise intolerance, myalgia, mental fogginess and difficulty with concentration of 4-5 years duration.

The patient mentions that he was very active in sports when he was in high school and college. When he got married in 2000, he became less active. In 2002 he started to exercise regularly in the gym. Around 2005, the patient noted that after exercise, he would feel achy and tight. He also had difficulty focusing at work. The patient is a computer programmer and he does complex analytical applications. He found himself gradually reducing his days in the gym. He also developed spasms in his torso that can be triggered by twisting movement of his torso. By the year 2006, he was feeling rundown. After a busy day, he developed tingling of his left anterior chest. He was evaluated in the emergency room and later on had stress test and echocardiogram that were said to be unremarkable. He still has off and on pins-and-needles, paresthesias and tingling of his left chest that is not related to physical activities.

In 08/2006, the patient did 8-10 hours of landscaping work in his friend's yard. The following day he competed in a volleyball game and felt shaky after the game. He also experienced some false sense of bladder urgency at that time. Two days later, the patient felt very sick for a number of days. He noted some mental fogginess. He was also losing track of his thoughts when conversing with someone at work. He was also waking up with strange dreams. In 10/2006 his mental fogginess suddenly cleared up and he was able to do a lot of problem solving at work. However, 2 weeks later the mental fogginess recurred. The patient saw a neurologist at the Lahey Clinic at Peabody and an MRI of the brain was performed which was reported as normal. He also had a sleep study that was normal. The patient continues to feel easily fatigued not just physically but also mentally. Over time he has developed a number of symptoms: Tinnitus, headaches body aches and pain in his thigh muscles.

In 03/2007 his new PCP started him on low dose Celexa and gradually increased the dose but the patient was experiencing side effect of feeling "wired" and jittery. Celexa was changed to Effexor, but he did not experience any improvement. In the summer of 2007 he saw a psychiatrist. The psychiatrist started him on another antidepressant, which made him "wired and miserable." In the fall of 2007, the patient was feeling better after weaning off antidepressant. He then saw a second psychiatrist who told him that he was not depressed. He was then referred to an Infectious Disease specialist who diagnosed him as having chronic fatigue. In the fall of 2008 the patient was noted to have positive anti- SM and RNP antibodies. The patient was then referred to a rheumatologist who felt that he did not have a rheumatologic problem. Subsequently he was referred to the neurology service, and an EMG and forearm exercise test were performed in 07/2009. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity did not show any abnormalities. There was no evidence of large fiber sensorimotor polynineuropathy and no evidence of myopathy. Nonischemic forearm exercise test showed a normal increase in lactate levels but no significant change in ammonia levels suggesting the possibility of myoadenylate deaminase deficiency.
As part of his work-up he was noted to have low testosterone levels and cortisol. Is under the care of the Endocrinology service. A follow-up ACTH stimulation test was normal. In addition urinary amino acid abnormalities were identified during the work-up and is here today for further evaluation and management for the same.

REVIEW OF SYSTEMS:

Currently the patient complains of pain in his thighs and hips, shoulders and calves at rest. Soreness in his muscles fluctuates from day to day. There is no clear relationship to physical activities. Denies hearing loss or change in visual acuity. Denies dysuria or hematuria or discoloration of urine. Denies seizures or loss of consciousness. No diplopia, ptosis, or dysarthria. Denies chest pains, palpitations but has occasional dyspnea on exertion. No diarrhea, vomiting or constipation. Occasional sensation of food getting stuck, but no definite dysphagia. No unusual odors.

The patient has not been exercising in the gym for the past 3 years. He has gained 25 pounds. He sleeps from 11:00 until 09:30 in the morning. He does not feel refreshed when he wakes up. It takes awhile for him, about 10 minutes, to get out of bed.

CURRENT MEDICATIONS: CoQ 10, Vitamin D 2000 per day, fish oil, vitamin C, multivitamins, Advil 2 tablets about 3 times a week, ribose 15 gm a day.

PAST SURGICAL HISTORY: Status post appendectomy, status post right knee arthroscopic surgery when he was in his 30s. The patient has a history of right shoulder pain in 2005 and 2006.

FAMILY HISTORY:

Ancestry is Irish and Austrian Jewish. No known consanguinity. Father is 80 years old with history of hypertension and CAD s/p coronary bypass surgery. Mother passed away last summer at the age of 82 from accidental drowning. Mother had problems with reflux disease and chronic bronchitis in the last 10 years of her life.

The patient has 2 brothers and 2 sisters. His older brother has a history of depression and is taking Zoloft. One sister has atrial septal defect that was repaired. Another brother has gout. He has 11 nephews and nieces. A nephew (brother’s son) had an ASD that was repaired when he was 3-years old.

Maternal uncle has Parkinson disease. One maternal aunt died in infancy from what is believed to be SIDS and another aunt has MR related secondary to untreated PKU. One maternal cousin has Tourette’s disease and another suffered from recurrent pneumothoraces.

No family history of neuromuscular disorders or inborn errors of metabolism.

SOCIAL HISTORY:

Computer programmer, works from home 4-5 hours/day. Married, no biologic children. He does not smoke. He drinks socially.

PHYSICAL EXAMINATION (LIMITED):

Well-groomed, well-nourished and articulate gentleman. Appears concerned but not ill appearing man and in no acute distress. Height 6’2”, Weight 220 Lbs, Pulse is about 74.

His skin is a bit dry, but there are no obvious lesions, no angiookeratomas. The head, eyes, ears, nose, and throat are unremarkable. The neck is supple without thyromegaly. The abdomen is soft, flat, and nontender. No organomegaly or masses.
Extremities are without clubbing, cyanosis, or edema. The patient was alert and oriented to person, place and time. His attention, speech, language, intellect, and flow of thought were normal. There was no resting, postural or intention tremor. Muscle bulk was normal. There was normal tone. Strength was normal. Gait normal. There was no dystonia. There were no tics. Sensory Exam: Light touch was normal.

RELEVANT INVESTIGATIONS:

- CK level was normal at 65.
- EMG revealed no evidence of a myopathy or neuropathy, but did show bilateral lumbosacral polyradiculopathies.
- Forearm exercise test showed a normal rise in lactate levels, but no significant rise in ammonia, raising the possibility of myoadenylate deaminase (MAD) deficiency.
- Mitochondrial DNA testing (MELAS, MERRF, NARP) was negative.
- Left quadriceps femoris muscle biopsy (11/23/2009). Showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity that may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal.
- Sleep study (2009): Reported as normal
- MRI of the lumbar spine (08/2009): Mild degenerative changes of the lumbar spine without any spinal canal stenosis or neural foraminal narrowing
- Urinary Amino Acids showed low levels of a number of amino acids including alanine, leucine, methionine, 3-methylhistidine, serine, taurine, threonine, and valine
- CBC, CMP, TFT’s, ESR, Iron, TIBC, Ferritin: Normal

SUMMARY:

Mr. Wiener is a 45-year-old right-handed man, with the chief complaints of fatigue, exercise intolerance, myalgia, mental fogginess and difficulty with concentration of 4-5 years duration. The investigations performed thus far have failed to identify an underlying etiology. Several specialty services including Neurology, Rheumatology and Endocrinology are involved in his care. During part of his work-up was noted to have an abnormal urinary amino acid profile and is here today for further evaluation and management of the same. His physical examination today was essentially normal.

I explained that variations in the urinary amino acids are quite common and do not always suggest an underlying metabolic disorder. In some cases they simply represent a dietary artifact. In other cases they may point towards an inborn error of metabolism. In Mr Wiener’s case, several amino acids are low, but are not in a pattern suggestive of an inborn error of metabolism. However it would be prudent to repeat the study. In addition urinary organic acid and plasma amino acid analysis is required to conclusively exclude some associated inborn errors of metabolism. In some cases of chronic fatigue syndrome low urinary and plasma amino acids, especially serine (one of the amino acids that is low in his case) have been noted, but currently a diagnosis of this condition cannot be established using the amino acid profile. If serine levels are low in the repeat urinary amino acid analysis and in the plasma it may be worthwhile to consider serine supplementation.

The possibility of a mitochondrial disorder was raised but has not been conclusively established. The absence of multisystemic involvement, elevated lactate and normal mitochondrial DNA testing point away from a mitochondrial disorder but an isolated mitochondrial myopathy still remains on the differential. The treatment for the mitochondrial disorders is non-specific and involves treatment with a cocktail of vitamins and he already on CoQ10 and multivitamins. I suggest he continue with these. We may consider starting Carnitine empirically too.

PLAN:

- Specimen to be collected and sent for plasma amino acids, acylcarnitines, urinary amino acids and organic acids.
- Continue follow-up with other specialists.
-A follow-up with our service has been suggested in 2-3 months. Will discuss results and consider additional investigations at the time. In the meanwhile if there are any other questions/concerns please do not hesitate to contact me at 617-726-1561.

Inderneel Sahai, MD
Attending Genetics and Metabolism

CC:

Mr Robert Weiner
31 Orchard Road
South Hamilton, MA 01982

Dr Hugh Taylor
15 Railroad Avenue
South Hamilton, MA 01982

I spent 60 minutes with this patient, >50% of which was dedicated to history gathering, and counseling/coordination of care.
Notes from 11/20/2008 through 3/11/2013 (cont)

04/13/2010 NURSING VISIT Final Midgley, Nan S.

INFECTIOUS DISEASE ASSOCIATES
MASSACHUSETTS GENERAL HOSPITAL

Reason for visit Cort-stim test

History of present illness Pt RTC for Cort. Stim Test. Pre cortisol and ACTH level drawn. Cortrosyn 0.25mg IM L deltoid. Lot# C0064H9, exp. date 7/11 and mfr-Amphastar. Pt tolerated injection with no problems. Pt to RTC in 1 hr for post cortisol level.

Follow up F/U lab results.

Nan S. Midgley, RN

Signed electronically by Nan S. Midgley, RN
Document Status: Final
Notes from 11/20/2008 through 3/11/2013 (cont)

Visit Note

Patient Name: WEINER, ROBERT D  
MRN: 4645581  
Dictated Date: 04/08/2010  
Dictated by: Donna Felsenstein, M.D.

Date of Visit: 04/06/2010

The patient returns for followup. He reports that his symptoms have been up and down. Some weeks are better and some weeks are worse. He reports that this has been the case over the past 4 years, although he feels his overall trend has been downward. He does deny a sore throat or recurrent swollen glands. He did have a muscle biopsy performed as previously noted. He is waiting for the final tests regarding the genetic markers. He does complain of both physical and mental fatigue. He did start coenzyme Q10, 100 mg 2 times a day and increased it to 200 mg 3 times a day. He is tolerating it well. He does not feel that there is a significant difference, although he may be a bit "perkier." He does state that he does have some increase in mental clarity. He has been able to take on a few small projects around the house. He does continue to experience pain in his thighs and hips after exertion. He is able to work roughly 5 hours per day.

His medications include coenzyme Q10, vitamin D and ribose.

On physical examination, he is well appearing. Blood pressure 115/60. Pulse 76, temperature 98.7. Weight was 226 pounds. On examination, the patient had 5 out of 5 strength in his upper and lower extremities bilaterally.

I had a long discussion with the patient regarding his symptoms. It is possible that he has chronic fatigue syndrome although the issue of mitochondrial abnormality remains under evaluation. The patient does have an appointment scheduled with Dr. Shih in 05/2010. Of note was the fact that he did have a few urine amino acids that were low. The exact meaning of this is unclear. I await Dr. Shih's evaluation regarding this issue. I will send off plasma amino acids at the present time so that these will be available for his visit with her. The patient has also had an elevated lactate level on several occasions. I will e-mail Dr. Peter Siao Tick Chong regarding this abnormality. The patient will return for followup.

Donna Felsenstein, M.D.

cc:
February 19, 2010

John Stakes, MD  
Neurology Department  
Massachusetts General Hospital

RE: WEINER, ROBERT D  
MRN: 4645581  
DOB: 11/12/1964

Dear John:

Mr. Robert Weiner came to our Neuromuscular Unit for a followup visit. I saw him initially on 08/31/2009. Mr. Weiner is a 45-year-old right-handed man who complains of feeling fatigue of 4 years' duration. His symptoms started some time in 2005 with post exercise aching and tightness with some problem with concentration associated with his work as a computer programmer. Since his last visit, the patient has not observed any changes. He continues to have muscle soreness associated with physical activities. Most of his muscle aching is in his thighs and hips but he also has some myalgia of his arms. Walking would aggravate his myalgia. The patient also complains of feeling "foggy mentally." He is not able to work as much as he used to, but his supervisor is quite understanding about his problem. The patient works from home. He sleeps from 11:00 until 09:30 in the morning. He does not feel refreshed when he wakes up. It takes awhile for him, about 10 minutes, to get out of bed. The patient works at home from 10:30 until 03:30. His weight has not changed recently, but it has increased from a year ago. The patient now weighs 220, a year ago he weighed 212, 4 years ago he weighed 185 pounds. The patient denies any restless legs syndrome. His neck size is 17 inches. He had a previous sleep study in 04/2009 that did not show any significant obstructive sleep apnea.

CURRENT MEDICATIONS: Vitamin D 2000 per day, fish oil, vitamin C, multivitamins, Advil 2 tablets about 3 times a week, ribose 15 gm a day.


The patient had a left quadriceps femoris muscle biopsy on 11/23/2009. This study showed mildly increased variation in fiber size and rare small fibers. Electron microscopy showed several foci of subsarcolemmal accumulation of mitochondria with occasional mitochondria showing mildly increased complexity of internal structure. The muscle mitochondrial enzyme study showed normal mitochondrial respiratory enzyme activities with abnormally elevated citrate synthase activity which may be indicative of mitochondrial disease. It reflects mitochondrial proliferation. The muscle biochemical analysis for myoglobinuria panel including myoadenylate deaminase enzyme was normal.

MRI of the lumbar spine 08/31/2009 showed mild degenerative changes of the lumbar spine without any spinal canal stenosis or neural foraminal narrowing.

ASSESSMENT AND PLAN:
Exercise intolerance with myalgia and complaints of mental fogginess with difficulty with concentration. I advised the patient to start taking coenzyme Q10 at 200 t.i.d.
I also referred the patient to Dr. Vivian Shih with regards to the low levels of urinary amino acids that were found in the past including alanine, leucine, methionine, 3-methylhistidine, serine, taurine, threonine and valine. The patient has seen a nutritionist. The patient is not a vegetarian. The patient will return for a followup visit.

Sincerely,

Peter Siao, M.D.

cc: DR. HUGH TAYLOR

RE: WEINER, ROBERT
MRN: 4645581
DOB: 11/12/1964

Reason for consultation: Muscle biopsy

Dear Dr. Siao:

Thank you for referring Mr. Weiner for a muscle biopsy for evaluation of his fatigue, myalgias and exercise intolerance. Briefly, Mr. Weiner is a 45-year-old right-handed man who has noted a sensation of fatigue for the past 3-4 years. He was previously active in sports and in the gym, but for the past 3 years, he has not been able to exercise in the gym due to his fatigue and pain. He noticed soreness in his muscles after working out and that his recovery time became longer. He has pain in his thighs, but also in hips, calves and shoulders. He denies muscle cramps, no myoglobinuria. He also notes that he sleeps 10-11 hours daily, but still feels mentally and physically fatigued. His only form of exercise now is walking.

His EMG revealed no evidence of a myopathy or neuropathy, but did show bilateral lumbosacral polyradiculopathies. His CK level was normal at 65. His forearm exercise test showed a normal rise in lactate levels, but no significant rise in ammonia, raising the possibility of myoadenylate deaminase (MAD) deficiency. His urine amino acids showed low levels of a number of amino acids. Mitochondrial DNA testing (MELAS, MERRF, NARP) was negative. A muscle biopsy is requested to evaluate further for myopathy, and a piece of the muscle has been requested to be sent to Athena for testing for MAD and mitochondrial enzyme levels.

Past medical/surgical history: Right knee arthroscopic surgery (in his 30's), appendectomy, right shoulder pain
ROS: Positive for: 20 pound weight gain, occasional dyspnea on exertion, sensation of food getting stuck, but no definite dysphagia, joint pains in hands and feet. Negative for: no diplopia, no ptosis, no dysarthria, no hearing loss, no bowel or bladder incontinence, no numbness, no chest pain, no rashes, no seizures
Medications: None (he is not on aspirin, Plavix or other anticoagulants)
Allergies: No known drug allergies
Family history: His father has a history of CAD, HTN, prediabetes. Mother passed from drowning at age 82. He has 2 brothers and 2 sisters. No family history of neuromuscular disorders
Social history: Computer programmer, works from home 4-5 hours/day. Married, no biologic children. He does not smoke. He drinks wine.
Exam: He has a moderate built. Height 6’2, weight 220. Blood pressure: 134/88, HR 71
His examination shows: Good muscle bulk throughout. No atrophy, no fasciculations. On manual muscle testing, strength was full power throughout the upper and lower extremities. Gait is normal.

Labs: 11/19/09 Platelets 310 and PT/INR (12.4/1.0) within normal limits.

Impression and Plan: Mr. Weiner has been affected by fatigue, myalgias and exercise intolerance raising the question of a myopathy. His EMG showed no myopathic units, but his forearm exercise test raised the possibility of MAD deficiency. A number of amino acids in his urine were also noted as low. Question of myopathy, specifically testing for MAD enzyme levels and mitochondrial myopathy has been requested. We will plan for Left quadriceps muscle biopsy, as requested. Risks and benefits of the procedure were discussed (including, but not limited to, bleeding, bruising, infection) with the patient and consent was obtained. All questions were answered. We will do the biopsy under local anesthesia in our procedure room. He is aware that he will follow-up with Dr. Siao for the biopsy results.

Thank you for your referral.

Sincerely,

Namita Goyal, MD
Visit Note

Patient Name: WEINER, ROBERT D MRN: 4645581
Dictated Date: 10/08/2009 Dictated by: Donna Felsenstein, M.D.

Date of Visit: 10/05/2009

The patient returns accompanied by his wife. He states that he was seen by Rheumatology. He informs me that he was told that the test was likely to be a false positive. Repeat testing was negative. He was seen by Dr. Stakes and he is sent for an EMG, which was done on 07/15/2009. The conclusion was that there was no evidence of myopathy, no evidence of large fiber sensory motor polyneuropathy. There was a normal increase in lactate level but no significant change in the ammonia levels. This finding was suggestive of the possibility of myoadenylate deaminase deficiency. The patient was referred to Dr. Peter SiaoTickChong of the Neuromuscular Unit. Dr. Chong ordered blood tests for mitochondrial myopathy evaluation. In addition, the urine amino acids showed low levels of a number of amino acids and it was suggested that the patient have a nutrition consult. A muscle biopsy was being considered.

The patient reports that he took amitriptyline 20 mg at bedtime for a while. Initially he thought he was improved. However, this was not sustained and he eventually stopped the amitriptyline, after which he felt poorly and took a while for him to recover. He, therefore, has not continued on the medication. Instead he has begun ribose supplements.

His weight was 220 pounds. Blood pressure was 108/70. Pulse was 72. Temperature was 97.2.

The majority of the visit was spent discussing the workup by the neurologist as well as his ongoing symptoms. As indicated to the patient, he will follow up with Dr. Chong. He will see nutrition, given the abnormal amino acids. He is also informed that his vitamin D level is low and he is taking vitamin D supplements. I have advised him also to follow up with the Endocrine Unit as well as his PCP to help improve his sleep. The patient will pursue this with Dr. Stakes and his primary care physician, Dr. Taylor. All questions were answered for both the patient and the patient's wife, who accompanies him on the visit.

Of note, the patient has low testosterone level. It was suggested that he repeat this and follow this up with Endocrine, as this might be contributing to some of his symptomatology as well. The patient understands. The patient will return to see me in 6 months. A flu shot was recommended today.

__________________________
Donna Felsenstein, M.D.

cc:
August 31, 2009

John Stakes, M.D.
Neurology
Massachusetts General Hospital

RE: WEINER, ROBERT D
MRN: 4645581
DOB: 11/12/1964

Dear John,

Thank you for referring Mr. Robert Wiener to our Neuromuscular unit. Please allow me to review his history and physical findings with you. Mr. Wiener is a 44-year-old right-handed man, who came in with a chief complaint of fatigue of 3-4 years duration. The patient was very active in sports when he was in high school and college. When he got married in 2000, he became less active. In 2002 he started to exercise regularly in the gym. Around 2005, the patient noted that after exercise, he would feel achy and tight. He also had difficulty focusing at work. The patient is a computer programmer and he does complex analytical applications. He found himself gradually reducing his days in the gym. He also developed spasms in his torso that can be triggered by twisting movement of his torso. By the year 2006, he was feeling rundown. After a busy day, he developed tingling of his left anterior chest. He was evaluated in the emergency room and later on had stress test and echocardiogram that were said to be unremarkable. He still has off and on pins-and-needles, paresthesias and tingling of his left chest that is not related to physical activities. He may have 1 to 2 weeks without the tingling.

In 08/2006, the patient did 8-10 hours of landscaping work in his friend's yard. The following day he competed in a volleyball game and won the tournament, but he felt shaky after the game. He also experienced some false sense of bladder urgency at that time. Two days later, the patient felt very sick for a number of days. He noted some mental fogginess. He was also losing track of his thoughts when conversing with someone at work. He was also waking up with strange dreams.

At the end of 09/2006, the patient was still feeling foggy. In 10/2006 his mental fogginess suddenly cleared up and he was able to do a lot of problem solving at work. However, 2 weeks later he developed mental fogginess again. The patient saw a neurologist at the Lahey Clinic at Peabody. MRI of the brain was normal. He also had a sleep study that was normal.

The patient continues to feel easily fatigued not just physically but also mentally. He developed a number of symptoms: Tinnitus, headaches body aches and pain in his thigh muscles.

In 03/2007 his new PCP started him on low dose Celexa and gradually increased the dose but the patient was experiencing side effect of feeling "wired" and jittery. Celexa was changed to Effexor, but he did not experience any improvement. In the summer of 2007 he saw a psychiatrist. The psychiatrist started him on another antidepressant, which made him "wired and miserable." In the fall of 2007, the patient was feeling better after weaning off antidepressant. He then saw a second psychiatrist who told him that he was not depressed. He was then referred to an Infectious Disease specialist who diagnosed him as having chronic fatigue. In the fall of 2008 the patient saw Dr. Felsenstein who noted positive anti-SM and RNP antibodies. The patient was then referred to Dr. Margaret Seton, who told him that he does not have any rheumatologic problem. The patient was then referred to you because his sleep study showed early onset REM sleep but the multiple sleep latency test was unremarkable. You ordered an EMG and forearm exercise test that was done on 07/15/2009. The EMG of the lower extremities showed findings consistent with bilateral chronic lumbosacral polyradiculopathy. EMG of the right upper extremity showed no abnormalities. There was no evidence of large fiber sensorimotor polyneuropathy and no evidence of myopathy. Nonischemic forearm exercise test showed a normal increase in lactate levels but no significant change in ammonia levels suggesting the possibility of myoadenylate deaminase deficiency.

Currently the patient complains of pain in his thighs and hips, shoulders and calves at rest. Soreness in his muscles fluctuates from day to day. There is no clear relationship to physical activities. The patient has not been exercising in the gym for the past 3 years. He has gained 25 pounds. This summer, the patient felt relatively good in July. However after helping his father fix and paint his house, the patient felt a recurrence of his symptoms. He denies any muscle cramps in the arms and legs. He has occasional stiffness of his lower back and low back pain even prior to 2000. The patient denies sciatica. He denies any significant neck pain, although he has some
neck stiffness, but no radicular pain in his arms. The patient denies passing dark-colored urine after strenuous physical activities.

PAST MEDICAL HISTORY: Status post appendectomy, status post right knee arthroscopic surgery when he was in his 30s. The patient has a history of right shoulder pain in 2005 and 2006.

SOCIAL HISTORY: Married, 2 stepsons, 24 and 27 years of age. The patient has no biological children. He does not smoke and he denies alcohol abuse. He smoked some joints when he was in college. The patient drinks wine 0-8 glasses a week.

FAMILY HISTORY: Father is 79 years old with history of coronary bypass surgery, hypertension and prediabetes. Mother passed away last summer at the age of 82 from accidental drowning. Mother was having problem with reflux disease and chronic bronchitis in the last 10 years of her life. The patient has 2 brothers and 2 sisters. His older brother has a history of depression and is taking Zoloft. Another brother has gout. One sister has atrial septal defect that was repaired. Maternal side of the family has a history of colon cancer. Maternal uncle has Parkinson disease. Paternal side of the family has a history of diabetes.

CURRENT MEDICATIONS: None

ALLERGIES: No known drug allergies.


MOTOR EXAMINATION: Motor strength testing 5/5 strength in all 4 extremities. Deep tendon reflexes 2 at the biceps, triceps, knees and ankles bilaterally. Toes downgoing bilaterally. No spasticity of the lower extremities.

SENSORY EXAMINATION: Intact pinprick sensation in the upper and lower extremities, and face and trunk. Vibratory sensation intact in the upper and lower extremities. Romberg test negative. Tandem gait fair.

ASSESSMENT AND PLAN: In summary, we have a 44-year-old man who over the past 3-4 years has developed body aching and feeling fatigued both physically and mentally. He also complains of mental fogginess and inability to concentrate. His laboratory workup initially showed positive anti-SM and RNP antibody. But, the latest blood tests in 07/2009 showed that they were negative. Anti-J01 antibody was also negative. CK was normal. Latest ANA was also negative. Rheumatoid factor less than 30. Serum protein electrophoresis normal. The patient had Lyme antibody and RPR that were negative. Urine showed low levels of a number of amino acids in 07/2009. TSH normal. Anti-gliadin and endomysial antibody negative. The patient also had an MRI of the brain and EEG that were unremarkable.

His forearm exercise test showed normal increase in lactate but no significant rise in ammonia.

I ordered the blood tests for mitochondrial myopathy evaluation. I will send a copy of this letter to Dr. Taylor and suggest nutrition consult. The patient's urine amino acids showed low levels of a number of amino acids including alanine, leucine, methionine, 3-methylhistidine, serine, taurine, threonine, and valine. The patient will return for a followup visit. Eventually he might need a muscle biopsy.

Sincerely,

Peter Siao, M.D.

c: Dr. HUGH TAYLOR

DD: 09/01/2009
TD: 09/01/2009 18:19:40
TR: 6750112
BackJob ID: 1037826
VoiceJob ID: 39216884
Interval History:
Five years ago, patient active, successful computer programmer. However, he began to notice difficulty recovering from exercise. He noticed trouble focusing at work. Had some tingling in his chest which led to a cardiac workup which was negative. Three years ago, had a weekend of exhausting activity which he had difficulty recovering from. Sought more workup from PCP. Was sent to neurologist, who did not identify any problems on sleep study or MRI. Went to second PCP who recommended Celexa. Patient felt wired but no improvement in cognitive function. Switched him to Effexor which also made him wired. Sent to a psychiatrist who discovered a family history of depression and began patient on Zoloft (brother on same drug). Again, patient experienced side effects on Zoloft and stopped the medication. Sent to a second psychiatrist who felt patient was not depressed. Returned to second PCP who referred him to an Infectious Disease M.D., who suggested the possibility of chronic fatigue syndrome. Referred patient to Dr. Felsenstein here at MGH who found an autoimmune abnormality and was referred to a rheumatologist, who felt it was a false positive. Dr. Felsenstein obtained a testosterone which came back at 187. Patient referred to Neurology who rechecked the Testosterone and found it to be 308 at 4:47 in the afternoon. Testosterone was checked again on 7/1 and found to be 304 at 12:50 in the afternoon. During these last set of consultations, the patient switched to a third PCP, whom he has not yet met.

Patient is married. No problems with getting an erection, maintaining it, or having an ejaculation. Relations are extremely rare however, which the patient attributes to depression in his wife. Masturbatory activity intact. Patient did not try to have children during his first marriage. In his second (current marriage), he and his wife did try to conceive, but she suffered two pregnancy losses. During that evaluation, the patient did have a semen analysis which was reportedly "normal."

At work, patient still feels that at his best, his is performing at 80% of his previous max. At his worst, he is performing at 30% of his max. Working about 25 hours a week. Almost no physical activity now. Last year, he began coaching a girls volleyball team, but did not return to that activity this year because of his exhaustion.

Dr. Felsenstein suggested Amytryiptylline to help with sleep and he has been moderating the dose. Now he is on 20 mg each night to sleep.

Past medical history:
Knee surgery in 1991

Review of systems:
Describes "tingling" in his chest wall.

Changes to Allergies
NKA: No Known Allergies - reaction: [added]

Habits
Smoking status: former smoker - one pack per week but quite about 10 years ago.
Alcohol use status: none/minimal.
Drug use status: none.

Family history:
Father has had triple bypass surgery and is taking an oral medication "to control his blood sugars."
Social history:
Irish

Physical Measurements:
- BP: 118/72

Exam:
- General: Well developed, well nourished, appearing stated age, in NAD
- Skin: Negative
- Facial hair: modest
- Striae: Negative
- Vitiligo: Negative
- Axillary hair: full
- HEENT: Nerves grossly normal, PERRLA, EOMI, visual fields full to testing.
- Neck: Negative
- Thyroid: No nodules
- Lymph: No significant lymphadenopathy
- Chest: No chest wall tenderness, normal PA diameter
- Breasts: Symmetric, without masses. No galactorrhea.
- Gynecomastia: Negative
- Cardiac: Regular rate and rhythm, Normal S1, S2, No murmur, gallop, rub
- Pulmonary: Lungs clear to auscultation and percussion.
- Abdomen: Soft, NT, ND, without HSM
- Extremities: No clubbing, cyanosis, or edema.
- Vascular: Peripheral pulses intact.
- Neurologic: Nonfocal.
- Pubic hair (Tanner 1-6): 6
- Hypospadias: none
- L Testis (mL): 20
- L Testis: Not cryptorchid, not retractile, no masses, no varicocele.
- R Testis (mL): 20
- R Testis: Not cryptorchid, not retractile, no masses, no varicocele.

Problems:

Fatigue.

Impression:
44 year old man with a four year history of decreased exercise capacity and decreased ability to perform at work. In seeking an etiology, the patient had a testosterone measured, which was originally 187 but then was greater than 300 on two subsequent measurements. These values are reassuring that the patient does not have testosterone deficiency; he also has intact erectile and ejaculatory function. What is puzzling however is a reported decrease in nocturnal/early AM erections, which would suggest a vascular or neurologic issue.

Plan:
Obtain an early AM testosterone measurement as well as prolactin and SHBG.
Will continue to monitor patient's symptoms and progress.
Have patient return to clinic in 6 months if not sooner.
Notes from 11/20/2008 through 3/11/2013 (cont)

DX Tests Ordered:
T, SHBG, PRI.

Minutes spent in counseling/coordination of care:
>50%

Stephanie B. Seminara, MD

cc: taylor, hugh

Signed electronically by Stephanie B. Seminara, MD
Document Status: Final
Visit Note

Patient Name: WEINER, ROBERT D MRN: 4645581
Dictated Date: 07/05/2009 Dictated by: Donna Felsenstein, M.D.

Date of Visit: 07/01/2009

The patient returns for followup accompanied by his wife. He reports that he took the amitriptyline and tried it in different amounts. He increased it up to 15, then 20, but was feeling groggy so decreased it to 10 at bedtime again. On that amount he feels that he is doing a little bit better. He feels that his concentration is somewhat improved. He can accomplish more work and is substantially more productive than he had been before. He reports that he is able to take on more complicated projects than he was. He saw Dr. Seton and the patient reports that he felt that she was informed that the lab work was more likely to be false-positive and that he did not have a connective tissue abnormality. He reports that his testosterone level was low and this was being pursued. The patient reports that he did have a chest x-ray at the Lahey Clinic in 03/2006 and was told that this was okay.

On physical examination he is well-appearing. Blood pressure 115/80. Temperature 96.2. Weight was 219 pounds. Pulse was 78. Evaluation of his testicles shows normal testicular size. No obvious masses on his testicles. The patient notes a small, firm nodule further up in his groin area. I can palpate a small what feels like firm nodule about 2-3 mm, which feels like a calcified structure high up on his vas deferens.

The patient is to show this to his primary care physician. He has a followup endocrine appointment in 08/2009. I have advised the patient to obtain a chest x-ray today as this has not been done recently. He will continue the amitriptyline for now. In addition, I will also send some repeat urine amino acids as there were some minor abnormalities previously. I will check a testosterone level as well as total and free carnitine. I will check an EBV, DNA, PCR. I will repeat the ANA, anti-Rho, anti-Law, anti-SM and anti-RNP to again see if these are positive or are a lab fluctuation. The patient will return to see me in 3 months.

____________
Donna Felsenstein, M.D.

cc:

DD: 07/05/2009 13:40:29
TD: 07/05/2009 14:00:58
TR: 6750218
BackJob ID: 38286431
VoiceJob ID: 38286431
Mr. Weiner has recently been seen also by Dr. Margaret Seton, and Dr. Seton has suggested that the patient may need workup for myopathy. He does describe since 2006 that there was a gradual and progressive decline in his ability to exercise and approximately 2 years ago stopped all athletic exercise. He feels that after a simple commute to Boston or doing some simple chores with his wife on the weekends he will feel exhausted. He also has said that he is said to be in a "mental fog" which was problematic in his work in computer software. He states that he had a paradoxical insomnia associated with the Mirapex, sleeping deeply for several hours and then having severe insomnia thereafter. This was discontinued. He has increased his Elavil from 10-15 and then to 20 mg but it was no better than at the 10 mg and also had some daytime carryover affect from the sedating quality to the Elavil. He has returned to 10 mg a day. Recently however he has noted some significant uptake in his energy and his mental performance was at a level that it was 4 years ago. He states that during this time his brain is "so much clearer." He feels he can focus again but wonders how long this will be the case. He also has had some tinnitus and left peripectoral paresthesias. An MR of the brain was performed in the past at Lahey which was unrevealing. He does have this post exertional proximal aching. His reflexes are symmetric with plantars flexor. There is no fasciculations seen. His sensation is intact. His plantar responses were flexor. He has good power in the office and is able to rise easily from a chair without pushing off. I would recommend that further study be performed including an EMG (despite normal sedimentation rate, CPK and aldolase). His testosterone was notably below the lower limits of normal and this should be reassessed. An EEG may also be useful. I plan to see him in followup after these studies have been performed to further analyze the basis for his chronic fatigue and his muscle symptoms. His myalgias after exercise are clearly more in the proximal shoulder girdle and in the hip girdle region.

John W. Stakes, M.D.

cc:
HUGH TAYLOR
Donna Felsenstein, M.D.
Margaret Seton, M.D.

DD: 06/22/2009 18:04:26
TD: 06/23/2009 09:02:51
TR: 6750212
BackJob ID: 990132
VoiceJob ID: 37640108
Mr. Weiner is a 44-year-old man who is referred to this clinic in consultation because of a low titer ANA 1:40 to 1:160, in the setting of positive Sm and RNP by ELISA (12/2008). His history is that 4 years ago, following aggressive competitive volleyball, he began to have muscle weakness, pain and woke up with flu-like symptoms. Over the last years this has evolved such that he feels that his "tank is empty" and that this is the source of his fatigue. He has evolved no significant muscle weakness, but suffers from myalgias after exertion. The fatigue has been as disabling as he has given up many activities. He has seen a psychiatrist in consultation for depression, but despite trying multiple medications directed at this, he has had no response and never received a diagnosis of depression. He continues to work. He modifies his work life. He has had no autonomic symptoms. No evolution of sensory deficit or motor dysfunction over the long term. His only note, was that sometimes he will get constipated following these episodes of myalgias. He also feels that his cognitive function is not optimal. He has been diagnosed with restless sleep, and put on Elavil, which has helped his sleep patterns at night. Otherwise it is difficult to elicit any signs or symptoms that would point towards a specific myopathic process.

His history is negative for systemic inflammatory rheumatic disease, and his physical exam is fairly benign. Except for pressure urticaria that was elicited, there is no evidence of loss of muscle bulk, tone or strength. Neurologic exam is intact. Nail beds are clear and there is no rash. Perhaps there are some mild sicca symptoms.

IMPRESSION: Exercise-induced myalgias
PLAN: Evaluation with EMG, exercise muscle testing and consider muscle biopsy. At this time the working diagnosis is some kind of metabolic or inherited myopathy. This patient was seen with Dr. Jenica Upshaw

Margaret Seton, M.D.
Dictated Date: 06/04/2009
Dictated by: Margaret Seton, M.D.

The patient was seen with Dr. Jenica Upshaw. I have interviewed and examined the patient, reviewed the pertinent laboratory and radiographic studies, and discussed my findings with the patient and Dr. Upshaw. I have confirmed her history, examination and plan, and agree with her recommendations as outlined.
Notes from 11/20/2008 through 3/11/2013 (cont)

Reason for Consult: referred by Dr. Feldenstein for fatigue, positive ANA, Sm,RNP by ELISA

History of Present Illness:

44M who was previously very healthy, very active volleyball player until four years ago when he noticed increasing fatigue, especially after activity as well as cognitive slowing. He reports feeling very sore "all over" but with myalgias especially prominent in shoulders, hips and overall very tired after work outs, his fatigue has progressed to where he started missing work at first once or twice a week and now is having to work from home most days. He used to play volleyball 3 times a week as well as going to the gym and now is very fatigued after much shorter work outs.

He is a computer programmer and at the same time he noticed that found it harder to concentrate and understand complex problems also noticed problem with short term memory, while long term memory is intact.

He also reports recent problems with sleep, specifically with vivid dreams and problems with sleep wake cycle, especially from 2 to 6 am. He had a sleep study that showed no significant OSA but did show some motor restlessness, tried mirapex for a few days for possible restless legs but this made the insomnia worse. He is now taking low dose amiptriptyline which has helped his sleep.

In the past few years he has also developed scaling and pruritis of scalp aggravated by hair hitting scalp such that he now shaves his head entirely with no residual scaling or pruritis. In addition to scaling of scalp he has a linear erythematous rash of upper abdomen along pressure line of skin fold.

He complains of proximal myalgias but no weakness, has arthralgias especially involving distal joint pain hands and toes.

His hands and feet more sensitive to cold in last four years, turning red with exposure to cold, but not white.

Does report dry mouth in past several years, wakes up with dry mouth drinking more water, no increase in cavities, only one in last several years, no dry eyes, no sore throat or odynophagia.

Had some tingling left chest (prompted ETT-MIBI nl and TTE), no SOB, no muscle weakness

No weight loss, fevers or night sweats

Denies feeling of depressed, did get treated empirically with antidepressants for short term without any improvement in his fatigue, has been evaluated by psychiatrist who did not think his s/s c/w depression either

Denies testicular atrophy, impotence or changes in body or pubic hair

Past Medical History

Right knee medial meniscal tear age 25 s/p surgical

Appendectomy

Medications:

Amitriptyline 15mg qd

ASA, Advil PRN for myalgias

Allergies:

NKDA

Family History:

Mother drowned at age 81 (last years), "arthritis" not sure if RA "chronic bronchitis", non smoker

Father alive, CABG at age 75, diagnosed with CAD in early 70s

Brother: depression and anxiety since 20s

Brother: obesity, gout

Sister: healthy

Sister: healthy, ASD repaired in 20s

Social History:

Works as computer engineer, married with 2 stepsons, worked in college with hazardous chemicals (waste disposal company)
tob: 1ppd x 5 years, quit 20 years ago
EtOH: 1-2 glasses wine, 2-4 nights a week
drugs: none

Physical Exam:
BP 128/86, P 81, Temp 98.3 F, Wt 218.4 lb H 6'2" O2 SAT 95
Gen: well appearing male, somewhat flat affect but NAD
Skin: linear erythematous rash along skin fold upper abdomen/lower chest c/w contact urticaria
HEENT: PERRL, no conjunctival injection,
COR: RRR no M/R/G
Chest: CTA
Abd: NABS, soft ND, NT
Neuro: CN III-XII intact, nl tone of all muscles, no rigidity, no fasciculations, 5/5 strength, 2+ reflexes, nl sensation

Pertinent Recent Labs:
ANA positive 1:40, negative 1:80, 1:160; speckled pattern
positive anti-SM antibody and anti-RNP antibody.
dsDNA neg
Anti-Sm 0.64
Anti- RNP 3.16

Assessment and Plan:
44M with progressive pattern of myalgias and fatigue worse after activity a/w cognitive slowing with essentially normal exam and labs notable for mildly positive ANA. His clinical picture is not consistent with SLE or other rheumatologic disease. Suspect that there is a metabolic condition such as a metabolic myopathy to explain his symptoms
- repeat ANA
- send chem 10, Vit D, testosterone
- referral for EMG/NCS, possible muscle biopsy and further evaluation for possible metabolic myopathy
Visit Note

Patient Name: WEINER, ROBERT D
Dictated Date: 05/21/2009
Date of Visit: 05/20/2009

HISTORY OF PRESENT ILLNESS: The patient returns for followup accompanied by his wife. He has seen Dr. Stakes on 2 occasions. During the first appointment the patient was set up for a sleep study. During his second appointment the results of the sleep study was reviewed with him by Dr. Stakes and the question of restless leg syndrome was raised. As the patient felt that the amitriptyline 10 mg at bedtime was no longer being effective, the patient was tried on Mirapex initially one a night and then increase to 2. On Mirapex the patient says that he awoken during the night and remained up throughout the night and was unable to sleep raising the question of paradoxical insomnia.

The patient reports that when he gets fatigued he notes joint discomfort in his hands and his feet. He does report feeling stiff and feels as though his joints are puffy although there may be a question of some redness, this is a soft finding. The patient has an appointment to see Dr. Seton in June.

REVIEW OF SYSTEMS: Otherwise negative.

PHYSICAL EXAMINATION: He is well-appearing. Blood pressure 100/70. Temperature 96.7, weight was 219 pounds, pulse is 68. The patient had 5/5 strength in his upper and lower extremities bilaterally. He had no obvious joint swelling or erythema.

The issues were again reviewed with the patient and his wife. Mirapex, the patient has a question of restless leg syndrome, which might be contributing to his fatigue and difficulty getting a good night sleep. Mirapex seemed to give him paradoxical insomnia. The patient seemed to have some improvement on amitriptyline although it appeared to wear off after a while, thus he raises a question of going back on amitriptyline at a higher dose. As discussed, the patient is reasonable to try amitriptyline 20 mg at bedtime. The patient is cautioned regarding the side effects including drowsiness and is aware not to operate machinery or to drive if he is experiencing any drowsiness or side effects of the medication. The patient understands. The patient informs me that he has a new primary care physician, Dr. Hugh Taylor, Family Medical Associates, 15 Railroad Avenue, South Hamilton, Massachusetts, 01982; the phone number is 978-468-7381.

The patient will try the amitriptyline and let me know how he is doing. He will have a follow up appointment with Dr. Stakes. He will see Dr. Seton for evaluation of the positive anti-SM antibody and anti-RNP antibody.

Donna Felsenstein, M.D.

cc:

TD: 05/22/2009 20:37:01
TR: 6750250
BackJob ID: 968482
VoiceJob ID: 36915817
Mr. Weiner states that the Elavil appeared to work for approximately 10 days-2 weeks and then effectiveness subsided. Overnight sleep study performed 04/18/2009 was reviewed with him in detail. He had no significant obstructive apnea or other significant sleep disordered breathing, but he did have some significant motor restlessness seen with 34 periodic limb movements during sleep, an index of 6 per hour. When evaluated with (Dictation Anomaly)histogram, it is possible that this may be the stimulus for arousal from sleep and for him having recollections of dream-related activity as well as difficulties with arousals from those states. This is most notable in the first half of the night. It is suggested that perhaps a trial of medication for the periodic limb movements may be useful such as Mirapex 0.125-0.25 mg 1 hour before the hour of sleep. He is willing to undergo a brief trial of this medication with escalation from 0.125 to 0.25 mg after 5 nights if there is no benefit. Hopefully, this would have a significant prolonged benefit if reducing the frequency of the limb movements as they may be associated with arousal, the REM related problematic states. I have asked him to be in touch with me after the first 10-day trial.

Thank you for allowing me to continue to see this nice gentleman and participate in his care.

John W. Stakes, M.D.

CC:
Donna Felsenstein, M.D.

TD: 05/07/2009 14:45:53
TR: 6750219
BackJob ID: 957530
VoiceJob ID: 36672931
Visit Note

Patient Name: WEINER, ROBERT D
Dictated Date: 04/08/2009
Date of Visit: 04/06/2009

The patient returns accompanied by his wife. He states that he was taking the amitriptyline. He reports that he had several nights of good sleep right after the amitriptyline was initiated and seemed to feel better overall. He was seen by Dr. Pollack for neuropsych testing on a "good day." He was taking 10 mg of amitriptyline at that time. He feels that the amitriptyline helped for a couple of weeks then he stopped it. He reports that he tapered it down and then discontinued it as he ran out of his prescription but is also scheduled to have a sleep study and he thought he should not be on it for the sleep evaluation. He therefore has been and is off the amitriptyline at the present time. He will was seen by Dr. Stakes who did set up a sleep study which is scheduled for 04/18/2009. He has a subsequent appointment with him at in 05/2009. The patient was scheduled to see Dr. Seton but this had to be rescheduled and he will be calling the office to reset up the appointment.

The patient reports that he took a vacation with his family on a boat. He describes it as a "physical ordeal." He felt awful after that with severe arthralgias. He now feels as though he is finally recovering from that episode.

On physical examination he is well appearing. Blood pressure 100/60. Pulse 72. Temperature 97. Weight was 215 pounds.

I reviewed the results of the neuropsych testing with the patient. Overall he did quite well with relatively mild and isolated difficulties with test vigilance and speed information processing. He apparently failed to display frank difficulties with memory, word finding or executive functioning skills as planning and organization on formalized measures. It is felt possible that his daily cognitive complaints might be secondary to his fatigue and reduced concentration and a question of adding cognitive enhancing medication to his regimen was raised by Dr. Pollack. I discussed this with the patient and he will follow up with his physicians and with Dr. Stakes when he sees him next. The patient will return to see me after he sees Dr. Stakes and Dr. Seton to discuss any interventions made at that time and his overall progress. The patient and his wife feel comfortable with this plan.

Donna Felsenstein, M.D.

cc:

TD: 04/08/2009 16:04:16
TR: 6750158
BackJob ID: 936477
VoiceJob ID: 36174284
Notes from 11/20/2008 through 3/11/2013 (cont)

Visit Note

Patient Name: WEINER, ROBERT D
MRN: 4645581
Dictated Date: 03/19/2009
Dictated By: Arthur L. Boland, M.D.

Date of Visit: 03/19/2009

HISTORY OF PRESENT ILLNESS: Mr. Weiner has continued to have some problems with his shoulder. It bothers him particularly in the evening. The injection did help, but he did not have complete relief of pain. He is very anxious to get back to coaching volleyball. He coaches the Brookline High School team. Each time he has gone back to lifting some weights with some gentle rotational exercises or serving a ball, he begins to have pain again. He did get significant relief from the last injection, but it plateaued and now it is recurring.

PHYSICAL EXAMINATION: He has full forward flexion, full abduction, equal external rotation and equal and symmetrical internal rotation. I could not detect any weakness. He has a positive impingement sign. Some mild tenderness in the subacromial area. No AC joint or sternoclavicular tenderness.

DIAGNOSIS: Right shoulder impingement syndrome.

RECOMMENDATION: I prepped his shoulder with Betadine and alcohol in the sterile technique. Injected the shoulder again with some dexamethasone, also 8 cc of 1% lidocaine. I told him to see how this progresses. If it is not getting better after these injections, a trial of physical therapy, which has not really worked, then he may need to think about scoping it. I have told him I would refer him to one of my colleagues.

___________________________
Arthur L. Boland, M.D.

cc:

TD: 03/20/2009 07:00:58
TR: 6750218
BackJob ID: 922329
VoiceJob ID: 35839915
HISTORY OF PRESENT ILLNESS: Mr. Weiner is a 44-year-old gentleman who had been in generally excellent health, but referred by Dr. Donna Felsenstein for significant fatigue. He has also seen physicians at the Lahey clinic and underwent a sleep study, which although it revealed an early onset REM sleep, the multiple sleep latency test was unremarkable and did not meet criteria for narcolepsy. He has a history that dates to approximately 4 years ago when he started having difficulty with focus and concentration at work associated with fatigue and generalized achiness. He thought that perhaps he was "burned out" in his software work and decided to take a month off. He visited family and friends, but returned to work a month later but felt no better. He states that he exercises regularly, but feels achy after workouts and he felt he was having more difficulties being effective at his job. In fact of late, he must work out less intensely, skipping more of the workouts. Particularly beginning in 03/2006, he felt "run down, tired and achy." He also began to note a tingling discomfort approximately in the left anterior pectoral region of a pins-and-needles and numbness. Cardiac evaluation with stress test with an echo was unremarkable. He states that he has been a volleyball enthusiast and took a 1-week volleyball vacation in 05/2006. However, at the end of a beach volleyball of tournament in 08/2008, he felt extremely shaky and "wiped out" for several days and also felt unsteady on his feet. He states that since that time he has "never been the same." He feels he is not focusing, he feels shaky with exercise, and he feels like one would sense a day or 2 after they have "had the flu." He states that he feels perpetually "wiped out."

He has been seeing Dr. Felsenstein who has also suggested more recently a trial of amitriptyline which seemed to help for a few days, but then he seemed to be "back where he started." I have certainly suggested that he speak with her further concerning a slight elevation in the dose of medication. He states in the fall of 2006 he felt that he was 30% off his efficiency at work and he was having some tinnitus. This seems to wax and wane and he also began to have unusual sleep patterns. He would go to bed at 10:00 p.m. and have a latency of 30 minutes, but then awaken at 12:30 or 1:30 a.m. with a vivid dream. He would take a sip of water and fall back asleep and then fall into vivid dreams where he would reawaken throughout the night. In the morning he would feel "exhausted." He states that he has active dreams about every other month but has had no history of motor restlessness or periodic limb movements by his self report. He states in the early morning, his sleep is better. He states the first 1-1/2 hour of sleep, he is fine and the last 1-1/2 hour of sleep he is fine, but in between he seems to be on a "roller coaster." He claims to be up 4 to 10 times at night, but not up to void. He states he continues to be tremulous and exertion seems to be a significant trigger. He states in 03/2007, he started using Celexa and it was "like speed and felt extremely wired in the morning." But his muscle still was achy and he also tried Effexor and felt great for a week but then "crashed." He never tried trazodone. His brother is on Zoloft due to depression. He found no benefit from these medications. Also, he notes "I'm not depressed" and off SSRIs he has felt overall much better. He has seen a 2nd primary care physician as well as an infectious disease doctor, Dr. Wolfe, in Beverly and Dr. Felsenstein who is testing him to understand if there is some underlying infectious or inflammatory situation. His anti-RNP antibody and anti-Smith antibody were positive. His routine chemistries have otherwise been unrevealing as well as an SPEP and an ANA which was negative as well as an anti-double-stranded DNA, which was negative. His blood cortisol was 8.5 and cosyntropin stimulated cortisol series was unremarkable by report. A brain MRI by report with contrast was normal. According to Dr. Felsenstein's note, he was being referred to Dr. Margaret Seton for further rheumatologic assessment due to the generalized aching and discomfort.

On examination today, he is an alert and cooperative man with fluent speech. His affect seems appropriate for the given
circumstance. He has had no fevers or chills of late. He has had no other specific joint swelling per se. He has had no other paresthesias or numbness or tingling or weakness or problems with balance or coordination. He has noted no change in eyesight. There was a history of some disequilibrium along with the tinnitus. His power is symmetrical with normal bulk and tone throughout. His vibration sense and cold sensation as well as joint position sense was symmetric and there was no definite dermatomal hypalgesia or hypesthesia. Plantar responses were symmetrical. There was no appendicular or axial ataxia.

I find no signs on neurologic examination to suggest episodic demyelination as a cause for his fatigue. I would suggest that we reassess his overnight sleep study as he does describe frequent REM-related awakenings. The basis of these remain uncertain based upon the summary of the Lahey study. I plan to see him in followup after the sleep study has been performed.

Thank you for asking me see this nice gentleman and participate in his care signed.

___________________________
John W. Stakes, M.D.

cc:
Donna Felsenstein, M.D.

TD: 03/06/2009 19:08:06
TR: 6750224
BackJob ID: 912574
VoiceJob ID: 35607510
Robert Weiner is a 44-year-old, right-handed, married male with a college education. He was referred for a neuropsychological evaluation by Dr. Donna Felsenstein in the context of a constellation of symptoms including mental and physical fatigue, concentration difficulties, word-finding trouble, achiness, dizziness, and sleep disturbance. Mr. Weiner has undergone numerous evaluative studies in an effort to elucidate an etiology for his symptom complex. The records indicate that a brain MRI conducted on 11/28/06 was normal. An all night sleep study apparently raised the question of narcolepsy, but a follow up daytime sleep study was read as normal. Recent blood work was felt to raise the possibility of lupus or connective tissue disease, and a further evaluation through MGH Rheumatology has consequently been ordered. A referral to neurology has also been made. The current, formal neuropsychological evaluation was requested by Dr. Felsenstein as a means to obtain objective data regarding Mr. Weiner’s cognitive functioning.

Presenting concerns:

Mr. Weiner came unaccompanied to today’s appointment and provided the additional history that follows. He dated the onset of his symptoms to four or five years ago, when he began to experience difficulty at his job as a computer system architect. He recalls having trouble concentrating at work as well as reading codes that he had written a couple of years prior. He reports that he had initially ascribed his difficulties to working too hard and elected to take a month off. He did not, however, notice much improvement in function upon his eventual return. He subsequently began to experience physical symptoms, such as feeling “run down” and “achy.” Then, in August of 2006, after returning to work from a very physically active weekend, he “crashed.” He recalls feeling exhausted and experiencing dizziness upon standing. He took another brief leave from work, but continued to experience great difficulty concentrating when he came back. At some point later, he took a long weekend to attend his nephew’s wedding. When he returned, he initially felt “like his old self” but started “sinking” again just a few days later. He points out that, over the past few years, this has been his pattern. He may have a few days of feeling good followed by a few weeks of fatigue and cognitive difficulties. Over time, however, the periods of higher functioning have become less frequent.

When asked to summarize his current cognitive issues, he cited the following: concentration difficulties, mental fatigue, a tendency to lose his train of thought, and word finding difficulties. Whereas he was always good at tackling complex tasks at work (e.g., taking on large jobs and breaking them down), he now finds himself feeling overwhelmed and wondering where to start. Upon further querying, he indicated that his memory has also been impacted. For example, just this morning, he began to read an article in the Boston Metro and failed to initially recognize that he had read the same article a couple of hours earlier. He has also put movies in his Netflix queue without realizing that he has already rented and watched them. He also has difficulty learning new driving routes. His reading is affected such that he may lose track of what he has already read.

With respect to ADL functioning, he reported that his wife has always managed the household finances and has also always taken on the “lion’s share” of the shopping and meal preparation. Mr. Weiner reports that he continues to drive without difficulty.

Upon further review of systems, Mr. Weiner pointed out that his current cognitive difficulties constitute a significant change from his baseline, as he had previously viewed himself as “clever, clear thinking, and high energy.” While he has consequently found his difficulties to be both discouraging and frustrating, he maintains hope that his treaters with uncover a cause and potential treatment. With respect to sleep, he reported that his sleep patterns had been disrupted for the past couple of years, as he would have trouble falling asleep followed by several episodes of waking up from vivid dreams. He was prescribed amitriptyline three weeks before the current evaluation, which seems to have decreased the frequency of his awakenings.
Developmental and social histories:

Mr. Weiner’s early developmental history is unremarkable. He described himself as a fairly hard working student, who always did particularly well in the maths and sciences. He holds a bachelor’s degree from SUNY Binghamton. He is employed as a computer system architect. He resides with his wife.

Medical history:

Medical history is notable only for knee surgery (1989). Current medications include amitriptyline.

Family history:

Mr. Weiner’s mother did this past August at age 81. The records indicate that she had poor pulmonary function and bronchitis as well as GERD. Mr. Weiner’s father is alive at age 79 with a history of CAD status post CABG.

Behavioral Observations

Mr. Weiner came unaccompanied to today’s appointment. He presented as a pleasant man who easily engaged in casual conversation and who willingly participated in the evaluation procedures. His affect was somewhat restricted in range. His speech was somewhat slowed in rate, but was otherwise of normal volume and prosody. His language was fluent, grammatically-correct, and devoid of notable word finding difficulties, and his thoughts were logical and goal-directed. Mr. Weiner sustained his attention adequately across the test session and appeared to understand questions and test instructions without difficulty. He also appeared to put forth his best effort. The following results are thus believed to provide a valid indication of his current level of cognitive functioning.

Examination Results

General Intellectual Functioning

Based upon his educational and occupational histories, together with his performance on both the WTAR (a single word reading test) and select subtests from the WAIS-IV, Mr. Weiner’s baseline intellectual skills are estimated to lie in the superior to very superior range (WTAR Standard Score = 122, 93rd %ile; WAIS-IV Similarities, Vocabulary, and Block Design: 91st to 98th %ile).

Orientation/Attention/Executive Functioning

Mr. Weiner was oriented in all three spheres. He was also able to retrieve the names of both the current President of the U.S. and his immediate predecessor.

Working memory was assessed by having him repeat, reverse, and re-sequence strings of digits (WAIS-IV Digit Span). Here, his performance was high average for age (75th %ile). His performances on WAIS-IV tests of processing speed were relatively weaker, as his scores on these two subtests fell in the low average and average range, respectively (Symbol Search: 16th %ile; Coding: 50th %ile). Together, his scores yielded a Processing Speed Index that falls at the low end of the average range (PSI: 30th %ile).

Mr. Weiner completed select subtests from the D-KEFS, a test battery that targets various executive functioning skills. First, the D-KEFS Trail Making Test, a measure that assesses visual scanning, motor speed, sequencing, and the speeded shifting of mental set, was given. His completion speeds across the five separate test conditions ranged from average to high average (37th to 75th %ile). His strongest performance was seen on the Motor Speed condition, one that removes visual search demands. No significant performance was decrement noted on the most challenging, Number-Letter Switching condition. Next, the D-KEFS Verbal Fluency Test was given, a measure that is sensitive to lexical access, the ability to initiate and sustain behavior, and the use of guided search strategies. Here, his performances again ranged from average to high average (Letter Fluency: 37th %ile; Category Fluency: 75th %ile; Category Switching: 25th %ile). This time, the introduction of cognitive set shifting demands did result in a slight performance decline (Contrast measure: Category Switching vs. Category Fluency = 9th %ile). Finally, Mr. Weiner performed extremely well on the D-KEFS Tower Test, a measure of planning and problem solving, with his attained score falling in the superior range (97th %ile).

Sustained attention and task vigilance were assessed via administration of the Continuous Performance Test. On the CPT, letters of the alphabet appear on a computer screen at varying time intervals. The task is to press the space bar as quickly as possible for all letters other than the letter “X.” While he maintained a low error rate, his average reaction time was slow and became considerably less consistent as the administration progressed. His reaction times also slowed down abnormally in response to longer inter-stimulus intervals. While both findings can suggest problems maintaining attention, his Neurological Confidence Index was borderline (No Decision, Confidence Index = 50%).

Language

Printed: 03/11/2013 12:06 PM
Confrontation naming ability, as assessed via the Boston Naming Test, was high average (59/60 correct, 81st %ile).

Visuoconstructual/visuospatial ability

Mr. Weiner’s performances on tests of visuoconstructual ability were consistently intact, as he achieved a superior score on the WAIS-IV Block Design subtest (91st %ile) and rendered an accurate copy of the Rey Osterrieth Complex Figure (raw score = 34/36, >16th %ile).

Memory

Mr. Weiner was given a few measures to assess his ability to learn and retain newly-encountered information. Here, his performances were consistently intact.

First, on a verbal list-learning test (CVLT-2), Mr. Weiner displayed very superior ability to learn a list of 16 words across five successive learning trials (98th %ile), and his use of semantic clustering (i.e., organizational) strategies to learn the word list also fell in the very superior range (99th %ile). Retention of the list items following the passage of both brief and 20-minute delay periods was strong as well, with 15 of the 16 items recalled at each interval (both scores: 84th %ile). Recognition discriminability was 100% (16/16 correct hits, 0 false positive errors).

Next, on the WMS-3 Logical Memory subtest, his immediate and delayed recall of a pair of orally-presented stories fell in the average and high average range for age, respectively (LM Recall I and II: 63rd and 75th %ile). Recognition memory performance was intact as well (27/30 yes-no items correct, 65th %ile).

Finally, Mr. Weiner was to recall the Rey Osterrieth Complex Figure (described earlier) both three and 30 minutes following the initial copy phase. Note that he had not been forewarned that his memory for the figure was to later be tested. At each delay interval, he was able to recall the figure’s overall gestalt and several of its inner details (immediate recall: 22/36, 58th %ile; delayed recall: 24/36, 73rd %ile). Again, he also performed well on subsequent recognition memory testing (20/24 yes-no items correct, 31st %ile).

Emotional functioning

Mr. Weiner endorsed mild current depressive symptomatology on the BDI-II (raw score = 16) and mild current anxious symptomatology on the BAI (raw score = 13). Note that, on the former scale, some of his endorsements pertained to his presenting complaints of reduced energy, fatigue, and concentration difficulties, whereas, on the latter, some pertained to the dizziness and neurologic symptoms he has described. That said, various ‘cognitive’ symptoms of both depression and anxiety were also endorsed (e.g., sadness, nervousness).

Summary

In summary, Robert Weiner is a 44-year-old, right-handed male referred for a neuropsychological evaluation by Dr. Donna Felsenstein in the context of a constellation of symptoms including mental and physical fatigue, concentration difficulties, word-finding trouble, achiness, dizziness, and sleep disturbance. Mr. Weiner is currently undergoing a comprehensive work-up in an effort to elucidate an etiology for his complaints. The current evaluation was ordered such that objective data regarding his cognitive strengths and liabilities could be obtained.

Based upon his educational and occupational histories, together with his performance on an intelligence screen, Mr. Weiner’s premorbid intellectual abilities are broadly estimated to lie in the superior range. While none of his attained cognitive test scores fell outside of normal limits for age, it is suspected that some of his average and low average scores represent a decline in a previously very high functioning individual. In general, it appears that Mr. Weiner had relatively greater difficulty on tests requiring rapid response generation — for example, his performances on tests requiring rapid visual search, rapid generation of words to a letter cue, and the rapid responding to visual cues on a computer monitor were among his weakest. Consistent with some of his presenting concerns, mild difficulties with task vigilance/sustained attention were seen on a challenging computer administered test. While these mild (relative) difficulties were observed, it should be emphasized that the majority of Mr. Weiner’s formal cognitive test performances were very strong, with many of his attained scores falling well above age-based expectations. Included among his strengths are his abstract reasoning, problem solving, visual analysis/integration, confrontation naming, and memory retention skills.

In sum, overall, today’s test findings provide evidence for relatively mild and isolated difficulties with task vigilance and speeded information processing/response generation. While these observations are consistent with some of his presenting complaints, he failed to display frank difficulties with memory, word finding or such executive functioning skills as planning and organization on formalized measures. The etiology of his symptom complex apparently remains unclear to his treaters, and various possible causes are being explored. It is hoped that Mr. Weiner will perceive his generally strong neuropsychological test performances as reassuring. It seems likely that some of his daily cognitive complaints (e.g., memory, word finding difficulties) are secondary symptoms of his fatigue and reduced concentration. At this juncture, I am wondering whether the possibility of adding a cognitive enhancing medication to his treatment regimen (e.g., a stimulant) might be considered. I also plan to discuss various behavioral strategies he might employ within his daily life in an effort to improve his attentional functioning in an upcoming telephone feedback.
The current data should be considered a baseline against which to measure future neuropsychological test performances. I would be more than happy to see him again should he observe any further changes in his cognitive functioning.

It was a pleasure meeting and working with Mr. Weiner. He and his treaters should feel free to contact me at (617) 726-2623 if I can answer any questions concerning this report.

Lauren E. Pollak, Ph.D., ABPP-CN
Clinical Neuropsychologist

<table>
<thead>
<tr>
<th>Name</th>
<th>R Weiner</th>
</tr>
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<tr>
<td>MRN</td>
<td>4645581</td>
</tr>
<tr>
<td>DOB</td>
<td>11/12/64</td>
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<td>DOE</td>
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<td>Ed</td>
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**NEUROPSYCHOLOGICAL EXAMINATION**

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<tr>
<th>Test</th>
<th>Raw</th>
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<th>T</th>
<th>SS</th>
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<tr>
<td>Wechsler Adult Intelligence Scale (WAIS-IV)</td>
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Printed: 03/11/2013 12:06 PM
**Number Sequencing**
- 27
- 11
- 63
- Average

**Letter Sequencing**
- 27
- 11
- 63
- Average

**Number-Letter Switching**
- 65
- 11
- 63
- Average

**Motor Speed**
- 22
- 12
- 75
- High Average

**Verbal Fluency**
- Total Letter: 37
  - 9
  - 37
  - Average
- Total Category: 44
  - 12
  - 75
  - High Average
- Category Switching Total: 12
  - 8
  - 25
  - Average
- Category Switching Accuracy: 10
  - 8
  - 25
  - Average
- Total Set-Loss Errors: 1
  - 11
  - 63
  - Average
- Total Repetition Errors: 0
  - 12
  - 75
  - High Average

**Motor Speed**
- Total Score: 25
  - 16
  - 97
  - Superior

**Wechsler Memory Scale 3rd ed (WMS-III)**

**Subtests**
- Information/Orientation: 14

**CPT**
- Clinical Profile, Confidence Index: 50.00
  - No Decision
  - Hit RT: 79.65
    - A Little Slow
  - Hit SE Block Change: 93.02
    - Mildly Atypical
  - Hit RT ISI Change: 83.23
    - Mildly Atypical

**Language**
- Boston Naming Test: 59
  - 0.90
  - 59
  - 113
  - 81
  - High Average

**Visuospatial Functions**
- Rey-Osterrieth Complex Figure Test
  - Copy: 34
    - >16

**Memory**
- Wechsler Memory Scale 3rd ed (WMS-III)

**Auditory Memory**
- Logical Memory
  - Recall I: 43
    - 11
    - 63
    - Average
  - Recall II: 29
    - 12
    - 75
    - High Average
  - Recognition: 27
    - 65
    - Average
  - % Retention: 85
    - 11
    - 63
    - Average

- California Verbal Learning Test-II
  - Trials 1-5 Total: 68
    - 2.00
    - 70
    - 130
    - 98
    - Very Superior
  - Learning Slope Trials 1-5 Total: 1.6
    - 0.50
    - 55
    - 108
    - 68
    - Average
Documentation of Time:

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<td>_<em>x</em></td>
<td>96120</td>
<td>Neuropsychological Test administered by computer</td>
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Mr. Weiner has been resting although doing some of his exercises. He does find that his Thera-Band external rotation exercises aggravate it. He has continued to have some discomfort in that shoulder with those kind of activities. He has played volleyball for several months.

On examination today, he does have some pain on resisted external rotation, but he seems to have excellent strength. He has a mildly positive impingement sign. Most of his tenderness is in the posterior area of the shoulder over the external rotator and the posterior capsule.

His right shoulder was prepped with Betadine and alcohol and sterile technique. Two mL of Kenalog and 8 mL of 1% lidocaine was injected into the joint. He is going to rest this and then resume activities as tolerated. He is going to call and let me know the results of this over the long run.

Arthur L. Boland, M.D.
### Notes from 11/20/2008 through 3/11/2013 (cont)

<table>
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<tr>
<th>Date of Visit</th>
<th>Visit Note</th>
<th>Final</th>
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<td>01/28/2009</td>
<td>Visit Note</td>
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**Patient Name:** WEINER, ROBERT D  
**Dictated Date:** 01/29/2009  
**Date of Visit:** 01/28/2009

**HISTORY OF PRESENT ILLNESS:** The patient returns for followup accompanied by his wife. He reports that he feels "about the same." He reports that his sleep continues to be of poor quality waking up many times during the night with "crazy dreams." He also reports that he is very thirsty throughout the night and will finish a bottle of water that he keeps by his bedside, as he sips on it throughout the night. This would indicate that he is actually not sleeping adequately.

In the last few years, he reports that his symptoms wax and wane, however he has felt worse over the past 3-6 months. He does not wake up with any energy. He continues to have difficulty focusing on problems at work. He feels as though the ringing in his ears has worsened, particularly at night. His headache comes and goes a couple of times per day. It is a "global headache." He finds that when he keeps a hat on his head during the day time and keeps his head warm, he feels a little bit better.

**REVIEW OF SYSTEMS:** Otherwise unremarkable.

**PHYSICAL EXAMINATION:** Blood pressure is 110/64. Temperature 98.2. Pulse 72. Weight was 215.5 pounds.

The visit was spent reviewing the patient's history from his prior visit as well as the blood work that was sent. Of note is the fact that the vitamin D level was normal at 41 with normal being between 33 and 100. The patient is on vitamin D supplements. The patient's blood work is noted for positive anti-SM and anti-RNP. His ANA and double-stranded DNA, however are negative. Thus the meaning of these 2 positive tests is unclear. Generally, they would raise the possibility of lupus or connective tissue disease. I have called Dr. Margaret Seton of the Rheumatology Department who will see the patient and evaluate him for lupus, etc.

The patient has very poor sleep by history. As discussed with him, it would be important to try to improve his sleep. It may not make his symptoms 100% better, although it is likely to help him to some degree. To this end, I have also given him a prescription for a low dose amitriptyline 10 mg at nighttime which I have advised him to take. I warned him that it might cause some drowsiness, particularly when he first starts using the medication and therefore he should not take it the night before a he needs to drive on the following morning. In addition, the patient has an appointment with Dr. Stakes on 03/03/2009. There are several things that would need to be addressed during that visit. In particular, a radiculopathy should be ruled out, the patient has ongoing headaches, which need to be evaluated, he has been having cognitive problems, which should also be evaluated, as well as sleep disruption. Of note is the fact that the patient did have some laboratory results forwarded to me. This includes a neurology evaluation that was done at the Lahey Clinic on 04/26/2007. Their impression at that time was that he likely has chronic fatigue syndrome. The patient had an all night sleep study, which was noted for an apnea/hypoxemia index of 2 per hour with a average SAO2 desaturation of 93%. He had a few spontaneous arousals noted and early REM onset was noted. The sleep efficiency was 83%. Snoring was heard. There was no periodic limb movement. The EKG at that time showed bradycardia. The early onset of REM sleep was felt to correlate with narcolepsy, therefore, the patient had a multiple sleep latency test,
which was felt to be normal. There is a note in the chart that the patient had a brain MRI on 11/28/2006 with contrast, which was said to be normal.

In addition, it may be helpful for the patient to be evaluated with neuropsych testing to determine to what degree he truly has cognitive difficulties and to see whether or not he can be helped with retraining.

In addition, a cortisol stimulation test was to be done. The patient reports that he did have a flu test. The patient will return to see me in April after he has been evaluated by Dr. Stakes and the Neuropsych Department.

Donna Felsenstein, M.D.

cc:

TD: 01/30/2009 09:27:40
TR: 3579320
BackJob ID: 889141
VoiceJob ID: 34993413
Notes from 11/20/2008 through 3/11/2013 (cont)

01/28/2009          CHART UPDATE          Final          Worrall, Daniel P., N.P.

INFECTION DISEASE ASSOCIATES
MASSACHUSETTS GENERAL HOSPITAL

Reason for visit Cort-stim test

Assessment and plan Per order of Dr. Felsenstein administered 0.25mg Cortrosyn reconstituted in 1.0ml NS IM to pt's L deltoid. (L) C0039G8, (E) 6/10. Pt tolerated well. Pre-stim value drawn prior to administration, post due in 1 hour.

Daniel P. Worrall, NP

Signed electronically by Daniel P. Worrall, NP

Document Status: Final
The patient comes for evaluation for fatigue. He is referred by Dr. Lucas Wolfe. The patient is accompanied by his wife throughout the visit with his permission. His wife was not present in the room during his physical examination.

The patient is a 44-year-old man. He says he was an active computer programmer in the financial industry. He is thus a "program architect." He spends most of the day sitting at his computer.

The patient reports that 2-3 days per week he would lift weights and do the treadmill as well as circuit training. He played volleyball 1-2 nights per week. He did woodworking at home. He builds cabinets and placed sheet rock. His wife reports that about 4 years ago she noted that he was withdrawn and introspective as well as somewhat detached. He became more frustrated with inability to do his work effectively. He had some word-finding difficulties as well as losing track of conversation. He had difficulty orchestrating projects at work. He started to decrease the number of workouts that he did per week because he was "weary, tired." These symptoms of fatigue progressed such that he decreased his gym activities. Three years ago he took a month off from work to see if he would recover. He was having difficulty thinking. He did not feel better after that month. He was able to donate blood up until about 3 years ago but then stopped. In February 2006 he felt achy, tired, started getting tingling in his chest under his left arm. He went to bed, called his primary care physician who noted some abnormalities on his EKG and referred him to the Emergency Room where he had an evaluation including a stress test and was told all was okay. He does report having an echocardiogram in 04/2006. He reports that he was able to play in a volleyball tournament. Work was okay although "not great." He was clearly able to do his work better than he can now. In 08/2006 he helped a friend fix up his house, played in a volleyball tournament on a 2-man team. He was very tired after that tournament, had fitful sleep, and began to have vivid dreams, which have continued. Later that week he was ill, felt shaky and dizzy and went back to bed. He took several days off from work. He reports that the tingling in his chest was coming and going for a period of 6 months.

He reports that over the past 2-1/2 years he has had numerous tests. He has seen a neurologist. He reports that he had an MRI of his head and was told this was okay. He had a sleep study which raised the question of narcolepsy. He reports having therefore had a daytime sleep study and was told this was also okay. He started having ringing in his right ear which has persisted and is there all the time. He was treated briefly with amoxicillin for 2 weeks for the possibility of a urinary infection, although this did not improve his symptoms. In November 2006 he also began to have pain in his throat. He was told he had carotidynia. He took Advil which helped the pain in his neck. He began to have pain in his joints including his fingers as well as aching muscles. He saw a 2nd primary care physician who told him he had depression and placed him on Celexa. This helped his sleep and he felt more alert for a brief period of time. His joint pains continued. His primary care physician increased the dose and ultimately changed him to Effexor. He was okay for a couple of weeks but then his symptoms did not continue to improve. He was seen by psychiatry 2007 who then changed his medication to Zoloft without any effect. Ultimately he discontinued all the SSRIs and felt much better off of the psych medications. He went back to his primary care physician who then referred him to Dr. Lucas Wolf, who made the diagnosis of chronic fatigue syndrome.

The patient presently complains of difficulty concentrating. He sleeps 9-12 hours per day. He does wake up to 2-3 times per night. He has vivid dreams and is very tense. His wife states that when he is dreaming he is running in the bed. He may be in and
out of his dreams for awhile. He goes to bed at 10:00 p.m., wakes up at 1:00 a.m. Dreams on and off until 3:00 a.m. and then sleeps more steadily until 9:00 or 9:30 a.m. He takes a long time to wake up. It takes several hours for him to feel fully awake and alert. He is tired a lot but is not able to nap. If he does a lot of activity he will feel ill a couple of days later and will be "wiped out" for 1-2 weeks. He would feel both physically and mentally tired.

REVIEW OF SYSTEMS: Noted for ringing in right ear only. This is continuous. He does continue to have the tingling in his left chest under his left arm described as a pins-and-needles sensation, as well as a numbness sensation though he does not really lack sensation. He has similar sensations in his fingers and toes and balls of his feet, which come and go. At present he is working from home 3-4 days per week. He goes into the office 1-2 days per week. He works 5-6 hours per day. Some days he is exhausted and cannot think straight and is unable to do any tasks for his job. This happens 1 day every 2 weeks approximately. He denies any fasciculations.

PAST MEDICAL HISTORY: Also noted for the surgery on his knee in 1989. He took ampicillin in 10/2006 and is not on any other medications at the present time.

ALLERGIES: He does not have any drug allergies.

His last tetanus shot was 5-10 years ago. He is unsure and will follow up with his primary care physician. It was recommended that he have a TDAP as well as a flu shot. He is not allergic to medications.

FAMILY HISTORY: Father is alive at 79 with with history of CAD status post CABG. Mother died at age 81. She had poor pulmonary function and bronchitis as well as GERD. She apparently died as a consequence of "drowning."

He lives with his wife for the past 8 years. He had a previous marriage. He denies any other sexual contact other than his present wife. He does not have any pets. He has 2 stepsons and grandchildren. He feels that he is too tired to play with his grandchildren very frequently. He has lived in Syracuse, Limerick Island, Cosanovia, NY and now the Boston area since 1986. He frequently traveled to upstate New York as well as the Adirondacks and liked to do backpacking and hiking with his wife. He does not do woodworking projects. He also hikes in Vermont. He last did tracking in the Adirondacks 5-6 years ago. He traveled to Belize in 2002 or 2003. He did snorkeling and scuba diving. He did develop diarrhea while there. He denies sexual contact with his wife for the past year.

Of note, his wife states that they are having some issues given the frustration of his illness, guilt that he experiences and her own frustration dealing with his chronic illness.

PHYSICAL EXAMINATION: He was non-ill appearing. Weight was 208. He was afebrile although the temperature was recorded as 95.8 by the MA. Blood pressure was 128/88. Pulse was 83 and regular. He had no skin rash. TMs were clear. Fundi were benign. Pupils are equal, reactive to light and accommodation. Pharynx is clear. He had no palpable thyroid. His chest was clear. There was no cardiac murmur. No palpable liver or spleen or abdominal tenderness. He had no testicular masses. He had 5/5 strength in his upper and lower extremities bilaterally. He had normal sensation to light touch. Vibration was normal except possibly in the big toes bilaterally. Position was normal. Reflexes were symmetric throughout with downgoing toes. Cranial nerves 2-12 were intact.

Review of the of his laboratory data reveals normal electrolytes on 05/07/2007. Cholesterol was slightly elevated. I defer this to his primary care physician to follow up. PSA, T4-T3 and FT1 were normal. B12, ferritin, TSH were normal. CRP was 2.6. The patient had a white count on 12/14/2007 that was 7.3 with hematocrit of 40.9. Of note, he had 39 polys, 45 lymphs and 5 eos. There were 2 bands. He did have a Lyme serology test done on 12/14/2007, which showed negative IgM, IgG and IgA antibodies. This was done at the Imugen laboratory. IgG Western blot showed a burgdorferi G39/40 positive band 58 and on 49736 strain, positive 62 bands. Parvovirus IgM and IgG were negative in 11/19/2007. Methylmalonic acid was normal. CMV
IgM was negative. Hepatitis A antibody was nonreactive. Hepatitis B core antibody was nonreactive. Hepatitis C antibody was nonreactive. Hepatitis B surface antibody and antigen were negative. Rheumatoid latex screen was negative.

In summary, this is a patient who has symptoms of both physical and mental fatigue for several years, which has clearly worsened. He has had significant word-finding difficulties as well as concentration difficulties. I do not have the results of all of his laboratory tests. It would be helpful for the patient to have a full sleep evaluation given the vivid dreams and "running" in his sleep, which raises the question of restless leg syndrome. If he is not sleeping adequately and effectively this could certainly contribute to his concentration difficulties as well as worsening any symptoms of chronic fatigue. I therefore recommend that further sleep evaluation be pursued by his PCP, Dr. Timothy Oman, Lahey Hamilton Family Practice. Alternatively, this can certainly be done here so that he is evaluated for other sleep abnormalities in addition to sleep apnea.

In addition, I would recommend that the patient have neuropsychiatric testing to help determine the extent of the difficulties that the patient is having. He continues to have ringing in his ears and a full neurological evaluation including evaluation of the tinnitus would be helpful. He has had a history of tingling of his chest on the left side, which raises the question of a radiculopathy. Again, neurological evaluation would be of benefit. I am happy to refer the patient to someone at Mass General for both neuropsychiatric testing and neurologic evaluation.

In addition, the patient and his wife are having some difficulties with their marriage given his chronic illness. I have made some suggestions to them regarding their lifestyle, which might help both the patient and her deal with his illness more effectively. In addition, I suggested to the patient that he pace his activities so that he has more energy throughout his week. This would include a consistent, but very low level of exercise rather than an intermittent more stressful level of exercise. A low level exercise would help maintain his muscle tone without overextending himself. The patient understands that he should exercise to the point that he continues to feel well and should not get to the point of stressing himself. In addition, I suggested that they may pace their personal activities such as playing with the grandchildren for shorter periods of time, which would allow them, both to visit with the grandchildren but might not stress them. His wife might have individual times when she might enjoy the grandchildren on her own. I also suggested they have counseling as well as support services from the Chronic Fatigue Support Group. They will think about my recommendations and return for followup after neuropsychiatric testing and neurology evaluation. In addition, a battery of blood tests were sent today to see if other etiologies can be ruled out. These would include urine amino acids as well as vitamin D, TSH, cortisol levels, TTG, IgA and IgG, Giardia, Whipple's testing, etc. The patient will return to see me in 6-8 weeks.

Donna Felsenstein, M.D.

cc: Dr. Timothy Oman
Lahey Hamilton Family Practice

TD: 11/29/2008 09:04:01
TR: 3579258
BackJob ID: 851442
VoiceJob ID: 34023001
OPERATIVE REPORT

NAME: WEINER, ROBERT D
UNIT NUMBER: 464-55-81

FLOOR: 

SURGEON: Namita Goyal, MD

PREOPERATIVE DIAGNOSIS: Myalgias, evaluate for myopathy.

POSTOPERATIVE DIAGNOSIS: Myalgias, evaluate for myopathy.

NAME OF OPERATIVE: Left quadriceps muscle biopsy.

ANESTHESIA: Local.

DESCRIPTION OF PROCEDURE: The patient was brought to the procedure room, placed supine on the table and the left thigh was extended. A time-out was performed. The left thigh was prepped and draped in the usual sterile fashion. Lidocaine 1% with epinephrine mixed with 0.25% Marcaine was used to infiltrate the left thigh over the region of the quadriceps. Subsequently, a longitudinal incision was made with a #15 blade and carried down through the subcutaneous tissue to the muscle fascia, which was incised. The quadriceps muscle was identified and 4 blocks of tissue, approximately 1 x 0.5 x 0.5 cm was excised. This was transported immediately to the Neuropathology Lab.

After the specimen was removed, Bovie electrocautery was used. Hemostasis was achieved and subsequently the wound was closed in layers; 3-0 Vicryl deep dermal interrupted sutures were placed, followed by 4-0 Monocryl running subcuticular suture. Steri-Strips, dry sterile dressing and Tegaderms were applied.

The patient tolerated the procedure well. There were no apparent complications. Sponge counts were correct x2 and instrument counts were correct x1. As the attending surgeon, I was present for the entire procedure.

NAMITA GOYAL, M.D.

Electronically Signed
NAMITA GOYAL, M.D. 11/24/2009 11:54

cc:
CLINICAL DATA:
45-year-old man with fatigue for the past 3-4 years. He was previously active in sports and in the gym, but for the past 3 years, he has not been able to exercise in the gym due to his fatigue and pain. He denies muscle cramps, no myoglobinuria. He also notes that he sleeps 10-11 hours daily, but still feels mentally and physically fatigued. His EMG revealed no evidence of a myopathy or neuropathy, but did show bilateral lumbosacral polyradiculopathies. His CK level was normal at 65. His forearm exercise test showed a normal rise in lactate levels, but no significant rise in ammonia, raising the possibility of myoadenylate deaminase (MAD) deficiency. His urine amino acids showed low levels of a number of amino acids. Mitochondrial DNA testing (MELAS, MERRF, NARP) was negative.

FINAL DIAGNOSIS:
SKELETAL MUSCLE (LEFT QUADRICEPS):

MILDLY INCREASED VARIATION IN FIBER SIZE AND RARE SMALL FIBERS (SEE NOTE).

NOTE: The diagnosis is based on the examination of hematoxylin and eosin stained slides, modified Gomori's trichrome, oil red O, PAS, NADH reductase, SDH, COX, and ATPase (at pH 4.3, 4.6, and 9.4) stains. Cross sections show mildly increased variation in fiber size with rare small fibers that measure 20-25 microns. Rare fibers show focal reduction of staining (seen on both H/E and Gomori trichrome) and lack of normal staining pattern, suspicious for focal mild degeneration or myonecrosis. There is no inflammation, regeneration, or increased number of internalized nuclei. Gomori trichome shows normal pattern of staining with no evidence of ragged red fibers, nemaline rods, inclusions or increased interstitial fibrosis. PAS and Oil red O show normal patterns of staining of all fibers with no evidence of abnormal glycogen or lipid accumulation. NADH staining is unremarkable. ATPase at pH 4.3, 4.6, and 9.4 reveal type a 2 fiber predominance and rare small fibers of both types; definite fiber type grouping is not noted, although a small group of type 1 fibers (about 8 fibers) is noted. SDH positive, COX negative fibers are not seen. Results of one micron epon and electron microscopic examination will be reported in an addendum.

GROSS DESCRIPTION:
Received fresh are four pieces of soft red muscle measuring 2.0 cm x 1.0 cm x 0.5 cm in aggregate. The tissue is divided for enzyme histochemistry, EM studies and remaining tissue is frozen in LN2 for prospective studies.
Final Diagnosis by Di Tian M.D., Ph.D., Electronically signed on Monday November 30, 2009 at 02:12:31AM
By his/her signature above, the pathologist listed as making the Final Diagnosis certifies that he/she has personally reviewed this case and confirmed or corrected the diagnoses.

ADDENDUM NOTE:
REASON: Result of ultrastructural examination.
NOTE: EM shows a normal contractile apparatus in all the myocytes. Occasional fibers show mild disarray in contractile apparatus. Several small foci of subsarcolemmal accumulation of mitochondria are noted, and occasional mitochondria show mildly increased complexity of internal structure; however, no paracrystalline inclusions or other diagnostic abnormalities are seen. An unremarkable blood vessel is present. A lipofuscin droplet is noted. No abnormal accumulation of storage material is seen.

Addendum #1 by Di Tian M.D., Ph.D., Electronically signed on Monday December 14, 2009 at 07:46:14PM
By his/her signature above, the pathologist listed as making the Final Diagnosis certifies that he/she has personally reviewed this case and confirmed or corrected the diagnoses.

PART : Muscle (Left thigh), Biopsy
**Massachusetts General Hospital Pulmonary & Critical Care Unit**

**Name:** Robert D. Weiner  
**DOB:** 11/12/1964  
**Age:** 47  
**Sex:** M  
**Height:** 75 in  
**Weight:** 218 lb  
**BMI:** 27.4  
**Smoker:** X  
**Pack years:** 8  
**Diagnosis:** 1: Dyspnea  
**Visit:** Outpatient

---

### Spirometry at BTPS

<table>
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<tr>
<th>Test</th>
<th>Actual</th>
<th>Predicted</th>
<th>% Pred</th>
<th>CI Range</th>
<th>ATS</th>
<th>Pre Bronchodilator</th>
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<tr>
<td>FEV1</td>
<td>L 3.36</td>
<td>4.53</td>
<td>74</td>
<td>3.69</td>
<td>5.37</td>
<td>A m</td>
</tr>
<tr>
<td>FVC</td>
<td>L 4.41</td>
<td>5.74</td>
<td>77</td>
<td>4.62</td>
<td>6.86</td>
<td>A m</td>
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<tr>
<td>FEV1 / FVC</td>
<td>% 76</td>
<td>79</td>
<td>96</td>
<td>71</td>
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<tr>
<td>FEF@67%</td>
<td>L/s 2.68</td>
<td>4.22</td>
<td>64</td>
<td>2.55</td>
<td>5.89</td>
<td>N</td>
</tr>
<tr>
<td>PEFR</td>
<td>L/s 13.55</td>
<td>10.22</td>
<td>133</td>
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<tr>
<td>FVC</td>
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<td>5.74</td>
<td>75</td>
<td>4.62</td>
<td>6.86</td>
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**Date of Test:** 12/13/2011  
**Date/Time of Hb:** 12/13/2011 01:17  
**Date/Time of Manual Entry:** 12/13/2011 01:30  
**Date/Time of Approval:** 12/22/2011 02:41  
**Temp:** 23°C  
**Pressure:** 761mmHg  
**BTPS:** 1.049

---

**Legend**  
N = Normal  
A = Abnormal  
m = Mild  
M = Moderate  
S = Severe  
ATS = Accepted Test Standards
Pulmonary from 11/20/2008 through 3/11/2013 (cont)

**ABG**

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<tr>
<th>Condition</th>
<th>pH</th>
<th>PaO2</th>
<th>PaCO2</th>
<th>HCO3-</th>
<th>O2 Sat</th>
<th>Alv O2</th>
<th>AaDO2</th>
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<td>Normal room air</td>
<td>7.37 to 7.43</td>
<td>87 to 99</td>
<td>36 to 44</td>
<td>23 to 32</td>
<td>99 to 107</td>
<td>5 to 15</td>
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<tr>
<td>Rest (Room Air)</td>
<td>None</td>
<td>7.52</td>
<td>109.0</td>
<td>30.0</td>
<td>24.7</td>
<td>99.6</td>
<td>-----</td>
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<tr>
<td>Rest (Ergometer)</td>
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<td>7.36</td>
<td>106.0</td>
<td>33.0</td>
<td>18.8</td>
<td>99.1</td>
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**Respiratory Muscle Forces**

| MEP (cmH2O) | 91 | 94 |
| MIP (cmH2O) | 104 | 137 |

**MGH Physician Interpretation**

FEV1 and FVC are reduced. FEV1/FVC is normal. Maximal respiratory muscle pressures are normal. The reduced FEV1 and FVC and normal FEV1/FVC suggest a restrictive ventilatory deficit. The possibility can be tested by measurement of TLC. ABG at rest revealed a respiratory alkalosis and with exercise the ABG revealed a respiratory alkalosis in addition to a metabolic acidosis. No hypoxemia was observed at rest or with exercise.

The above represents my personal interpretation of this test:

Pulmonary Fellow: Puja Kohli, M.D.

Signed: Leo C. Ginns, M.D.

---

**Patient:** Weiner, Robert D.  
**Test Date:** 12/13/2011  
**Page:** 2 of 2
**Radiology From 11/20/2008 through 3/11/2013**

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<td>Ordering Provider: SIAOTICKCHONG, PETER MD</td>
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**HISTORY:**
Back Pain persisting for more than 1 month despite conservative treatment - Radiculopathy (such as pain, numbness, abnormal reflexes) persisting for more than 1 month despite conservative treatment. RoeID8092681

**REPORT:**
Reviewed by Dr. Mara Kunst

**TECHNIQUE:** Magnetic resonance imaging of the lumbar spine was performed WITHOUT injected contrast using standard department protocols.

**COMPARISON:** None.

**FINDINGS:** The alignment is normal. The vertebral body heights are preserved. Multilevel loss of intervertebral disk space height and T2 signal hyperintensity is seen at all levels imaged levels, with sparing at L4-5 and L5-S1. The conus terminates at L1. The distal spinal cord, conus medullaris, and cauda equina are normal in signal intensity and morphology. The background bone marrow signal is normal, without evidence of fracture, or suspicious marrow replacing lesion. There is a small Schmorl’s node in the superior L5 vertebral body endplate.

T12-L1: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing.

L1-2: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing.

L2-3: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing.

L3-4: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing.

L4-5: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing. There is mild bilateral facet hypertrophy.

L5-S1: A diffuse disk bulge in the ventral subarachnoid space but causes no significant canal stenosis or neural foraminal narrowing. There is mild bilateral facet hypertrophy.

The surrounding soft tissues appear unremarkable.
IMPRESSION:

Mild degenerative changes of the lumbar spine as detailed above, but without significant spinal canal stenosis or neural foramina narrowing.

PROVIDERS:  SIGNATURES:
KUNST, MARA M M.D.  KUNST, MARA M M.D.
HISTORY:
Malaise and fatigue - 44 year old man with fatigue. RoeID7571551

REPORT:
Frontal and lateral views of the chest.

COMPARISON: None

FINDINGS:
Lines/tubes: None.
Lungs: The lungs are well inflated and clear. There is no evidence of pneumonia or pulmonary edema.
Pleura: There is no pleural effusion or pneumothorax.
Heart and mediastinum: The heart and the mediastinum are normal.
Bones: The thoracic skeleton is unremarkable.

IMPRESSION:
Normal Chest.
Clear lungs without evidence of pneumonia or edema.

PROVIDERS:  
GREENE, REGINALD E MD

SIGNATURES:  
GREENE, REGINALD E MD