The Problems Diagnosing $B_{12}$ Deficiency
– the Patient Perspective

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About Me

- Age 40
- Female
- Work as a GP
- B$_{12}$ Deficiency
Vitamin B$_{12}$ Deficiency

- 1859 Addison
- “Deadly” Anaemia
- Death within 2-3 years
- Cause not known
Vitamin B$_{12}$ Deficiency

- 1920 George Whipple
- “Bled” dogs
- Fed various Food
- Liver
- Patients treated with Raw Liver
Vitamin B$_{12}$ Deficiency

- 1926 Minot & Murphy
- Looking at Iron
- Co-incidental finding
- Liver extract cured Pernicious Anaemia
- 1934 Whipple, Minot Murphy – Nobel Prize
Vitamin B₁₂ (Cobalamin)

- Water Soluble Vitamin
- Required for
  - Cell metabolism (every cell)
  - DNA Synthesis
  - Fatty Acid Synthesis & Energy Production
  - Red blood cell production
Vitamin B₁₂ (Cobalamin)

• Synthetic / Inactive
  • Cyanocobalamin (from activated charcoal)
  • Hydroxycobalamin (produced by bacteria)

• Naturally Occuring / Active
  • Methylcobalamin (Cytoplasm)
  • Adenosylcobalamin (Mitochondria)
Vitamin $B_{12}$ from diet

- Binds to Haptocorrin (TC1 - Saliva)

$B_{12}$ moves to Stomach

- Parietal Cells Secrete Intrinsic Factor

Absorbed via the ileum (TCII & TCIII)
Vitamin B$_{12}$ from diet

Binds to Haptocorrin (TC1 - Saliva)

B$_{12}$ moves to Stomach

Parietal Cells Secrete Intrinsic Factor

Absorbed via the ileum (TCII & TCIII)
B₁₂ in liver

Transported around body

B₁₂ lost (Bile, Faeces, Urine)

Taken up by cells For use

B₁₂ mopped up By IF in bowel

Enterohepatic Circulation
Vitamin B$_{12}$ Replacement

- Tablets / Fortified Foods
  - Vegans/Vegetarians
  - Have Intrinsic Factor

- Injections (& Sublingual, Nasal, Patch)
  - Pernicious Anaemia
  - Receptors
  - S/C better than IM at high doses
  - No Storage
  - Free B$_{12}$ excreted in Urine
GP - Symptoms

- Age 37 (May 2008)
- Tired all the time
- Flushes
- Intermittent Diarrhoea
- Indigestion
- Poor Sleep
- Shortness Of Breath
- Recurrent UTIs
Investigation - Routine Blood Tests

- FBC (normal MCV)
- U&E
- LFT
- TFT
- Glc
- ESR
Further Symptoms

- Neurological -
- Numbness left foot / Altered Sensation
- Saddle Numbness
- Depression
- ? PMT ? Hormonal
Mar 2009 - $B_{12}$ Deficiency

- $B_{12}$ 130 then 92 (191-663 pg/ml)
- Folate 1 (3-20 nmol/l)
Treatment

- Hydroxocobalamin loading dose
- 6 x injections over 2 weeks.
- Complete resolution of symptoms
- Changed to 3 monthly injections
- Folic Acid 5mg Once Daily for 1 month
Symptomatic Again

- Within 3-4 weeks of injection
- Recurrent Tiredness
- Recurrent Numbness
- Facial Numbness
- Odd Numbness on Breathing
- Tongue
- Throat
Referred To A Neurologist

• Convinced I was dying!
• Or had some deadly disease!

• No Neurological Signs
• Persist with B12 injection
• Increase the dose
Methylcobalamin

- March 2010
- Infusion x 3
- Bi-daily injections
- Increased dose
- The flow of electricity!
- Re-myelination !!!!!!!!!!!!
A Happy Ending

• Really ???????
• Diagnosis took 10 months
• 2 years to symptomatic relief
• Lots of unnecessary anxiety on the way!
• Deadly Anaemia - No Cure
• Lifelong Treatment
• The Only Treatment that works is PRIVATE
Patient Survey

- To members of the Pernicious Anaemia Society
- Online & Paper Survey
- 588 completed
- Non-Patient members eliminated
- 550 analyzed
Patient Sex

Sex

82.3%

17.7%
Age at Diagnosis

- 0-10: 0.8%
- 11-20: 1.6%
- 21-30: 15.3%
- 31-40: 24.7%
- 41-50: 28.2%
- 51-60: 15.7%
- 61-70: 8.3%
- 71-80: 4.7%
- 81-90: 0.8%
Time Taken To Diagnose

- 1 week: 0.6%
- 2 weeks: 0.2%
- 1 month: 1.9%
- 2 months: 1.2%
- 3 months: 2.5%
- 6 months: 11.4%
- 1 year: 18.2%
- 2 years: 21.5%
- 5 years: 22.4%
- 10 years: 4.1%
- 10 years +: 16.1%
Family History
Eye Colour

- Blue: 40.8%
- Brown: 23.6%
- Green: 13.7%
- Hazel: 11.7%
- Blue-green: 6.2%
- Grey: 4.9%
Hair Colour

- Brown: 40.7%
- Grey: 27.7%
- Mousey: 17.3%
- Blonde: 13.1%
- Red: 4.9%
- Black: 4.2%
Grey Colour

Bar chart showing the percentage of people experiencing grey colour at different age groups:
- Teens: 3.0%
- 20's: 19.3%
- 30's: 23.5%
- 40's: 24.6%
- 50's: 19.3%
- 60's: 10.2%
Grey Colour - Men

- Teens
  - 7.4%
- 20's
  - 16.2%
- 30's
  - 30.9%
- 40's
  - 33.8%
- 50's
  - 11.8%
Grey Colour - Women

- Teens: 4.1%
- 20's: 23.6%
- 30's: 26.2%
- 40's: 22.1%
- 50's: 14.4%
- 60's: 9.7%
General Symptoms

- Waking Up Tired: 97.6%
- Brittle Nails with Ridges: 86.8%
- Dry Skin: 61.3%
- Flushes/Fever: 48.4%
- Brittle Nails: 40.0%
- Hair Loss often with premature greying: 36.3%
- Swollen, 'Beefy' & Sore Tongue (Glossitis): 30.5%
- Weight Loss: 22.4%
- Jaundice: 7.7%
Neurological
RS / CVS / GU

- “The Sighs” 75%
- Palpitations 55%
- UTIs 23%
GI Symptoms

- Unexplained Diarrhoea 60%
- Indigestion 40%
- Constipation 40%
- Stomach Cramps 39%
- Loss Of Appetite 30%
- Loss or Change in Taste 26%
Emotional Symptoms

- Irritability 77%
- Isolation 65%
- Mood Swings 57%
- Suicidal Thoughts 20%
SMH

- Depression 44% (8.7%)
- Tinnitus 37% (10%)
- Psoriasis/Eczema 28% (17%)
- Folic Acid Deficiency 25% (0.5-16%)
- Arrhythmia 22%
- Hypothyroidism 21% (3.5%)
- Acne Rosacea 15% (5%)
- Vitiligo 14%

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Coeliac Disease</td>
<td>8%</td>
<td>(1.0%)&lt;sup&gt;6&lt;/sup&gt; Coeliac.org.uk</td>
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<tr>
<td>Rheumatoid Arthritis</td>
<td>7%</td>
<td>(2%)&lt;sup&gt;7&lt;/sup&gt; Matsumoto, 2007</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.5%</td>
<td>(4.8%)&lt;sup&gt;1&lt;/sup&gt; What Health</td>
</tr>
<tr>
<td>Previous H Pylori</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td>Stomach Ulcers</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>3.6%</td>
<td>(1%)&lt;sup&gt;8&lt;/sup&gt; Al Hammadi, 2010</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>2.2%</td>
<td>(1.3%)&lt;sup&gt;9&lt;/sup&gt; Ross 2010</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>1.1%</td>
<td>(0.2%)&lt;sup&gt;10&lt;/sup&gt; Cureserch.com</td>
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</tbody>
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Investigations

- B12 /Folate Level 94.3%
- Intrinsic Factor ABs 45.5%
- Parietal Cell ABs 24.4%
- Endoscopy 21.8%
# Abnormal Investigations

- **Low Folate Level**: 25.5%
- **Positive IFA**: 17.5% (38%)
- **Positive PCA**: 13.3% (55%)
- **Abnormal OGD**: 6.2% (28%)
B12 Replacement

- Hydroxocobolamin 70.7%
- Cyanocobalamin 21.0%
- Methylcobalamin 15.1%

- Some cross over
Route

- Injection (IM/SC)  93.6%
- Sublingual Tablets  6.8%
- Sublingual Drops  1.7%
- Sublingual Spray  1.2%
- Tablets  4.1%
- Nasal Spray  0.4%
- Patches  0.0%
Administration

- GP Surgery  81.4%
- Self  14.7%
- Family / Friend  4.2%
- Private Clinic  3.2%
Frequency Of Injection

- More than once a day: 1.2%
- Daily: 2.0%
- 2-3 times per week: 2.2%
- Weekly: 6.3%
- Every 2-3 weeks: 2.9%
- Every 4-6 weeks: 20.5%
- Every 8-10 weeks: 20.7%
- Every 12 weeks: 48.1%
- None: 1.6%
Misdiagnosis

- Total misdiagnosis: 44.7%
- Depression: 14.3%
- ME / CFS: 4.7%
- GI Diagnosis: 4.5%
- Other Anaemia: 4.2%
- Thyroid Disease: 3.2%
- Musculoskeletal: 2.9%
- Nothing wrong: 2.9%
Other Misdiagnoses

- Hormonal: 2.5%
- MS: 2.2%
- Asthma / COPD: 1.3%
- Allergy: 1.1%
- Overweight: 1.1%
- Poor Diet: 0.7%
- Diabetes: 0.7%
- Other: 2.6%
“You are female and over 40. You are bound to feel tired!”
Comments

“I think its probably just your shoes rubbing. Try some new ones!”
Comments

“Pull yourself together, there’s nothing wrong!”
Comments

“Are you trying to take advantage of being off work and getting sick pay?”
Patient:

“My doctor didn’t have a clue. I was diagnosed by my dentist!”
Current Regime - Satisfied?

- 66.3% Yes
- 33.7% No
Investigation & Diagnosis?

- Very Poor: 22.2%
- Poor: 11.0%
- Unreasonable: 2.8%
- Inadequate: 16.4%
- Undecided: 9.3%
- Adequate: 9.0%
- Reasonable: 9.5%
- Good: 8.8%
- Very Good: 7.8%
- Excellent: 3.2%
Summary from a Patient Perspective

• Think of checking $B_{12}$ levels
• Listen to your patients when they tell you they need more B12
By intramuscular injection:

Pernicious anaemia and other macrocytic anaemias without neurological involvement, initially 1 mg 3 times a week for 2 weeks then 1 mg every 3 months

Pernicious anaemia and other macrocytic anaemias with neurological involvement, initially 1 mg on alternate days until no further improvement, then 1 mg every 2 months
Neurological
Summary from a Patient Perspective

• Treat the patient’s symptoms, not their blood test results
Thank You for your time.

Any Questions?