

Case 1: The tingles

- RS is a 38 year old electrical engineer who complained of tingling in his hands and feet.
- These symptoms were present for 9 months and involved his hands to the forearms and then spread to his feet and upper thighs.
- He also volunteered that when he flexed his neck, he would get an electric-like sensation in his hands and legs.
- He is a homosexual man whose partner recently tested HIV positive. He did practice safe sex.

Neurosurgery?

- He saw his primary care physician who obtained an MRI scan of the cervical spine.
- Based on the MRI results, he was then referred to a neurosurgeon who obtained nerve conduction studies and did not think that he required surgery and referred Mr. RS to a neurologist.
- He was told by multiple physicians that he may have a problem that could antecede becoming HIV positive, despite multiple negative HIV tests.

Additional history and key points on physical examination

- He was noted to be hypothyroid for 2 months. He has a father and 2 siblings with hypothyroidism.
- He was depressed.
- There was no palpably enlarged thyroid gland
- There was no red desaturation or relative afferent pupillary defect.
- The motor examination was normal
- **He had normal reflexes in the upper extremities, brisk reflexes at the knees, absent ankle jerks and downgoing toes.**

Sensory Examination

- He had glove stocking sensory loss to pinprick and light touch. In the upper extremities to the elbow and in the lower extremity to above the knee.
- There was very poor joint position sense in the toes with absent vibration sense to the costal margin.
- The Romberg was negative, but he had difficulty walking on his toes and he was unable to tandem.

How can we localize this lesion and what would you do next?

Think about the Lhermitte's sign and what this means

Lhermitte's sign

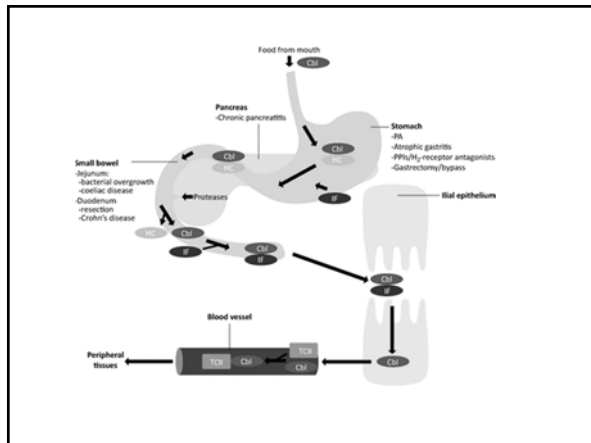
- Sudden electric-like sensation with flexion of the neck
 - It usually implies PATHOLOGY of the posterior columns and we see this with:
 - Demyelinating disease
 - Vacuolar myelopathy (AIDS)
 - B12 deficiency

Test results

- He had a normal hematocrit with a normal MCV
- TSH 2.7 uU/ml
- B12 level **152** pg/ml
- Methylmalonic Acid 1014 nmol/L (N: 90-279)
- Homocysteine 12.8 Umol/L (N: 0-8.9)

Follow-up and take home messages

- The patient was treated with monthly B12 shots and his MMA levels followed. These returned to normal within 6 months.
- It took 12 months for the tingling to slowly disappear and he was left with residual tingling in his toes.
- He also had antiparietal cell and antimicrosomal antibodies present.
- **Final diagnosis: Pernicious Anemia**



The Synthesis of Thymidylate: the rate-limiting factor in the synthesis of DNA



Hesdorffer CS, Longo DL. N Engl J Med 2015;373:1649-1658.

Intracellular metabolism of Vitamin B12

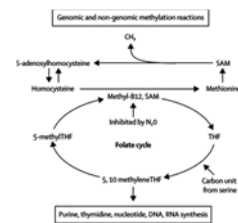
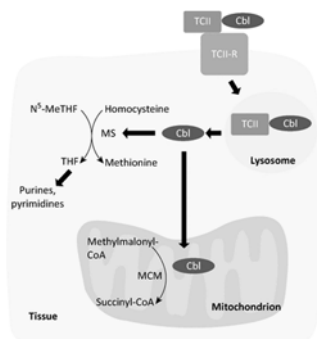


Figure 1. Associations between the folate cycle, vitamin B12, methylation, and nucleotide synthesis. SAM=S-adenosylmethionine. THF=tetrahydrofolate.

Edward Reynolds
Vitamin B12, folic acid, and the nervous system
null, Volume 5, Issue 11, 2006, 949-960
[http://dx.doi.org/10.1016/S1474-4422\(06\)70598-1](http://dx.doi.org/10.1016/S1474-4422(06)70598-1)

Case 2: A bolt of lightning

A 66- year old woman with a past history of migraines with aura, calls you with tingling down the left side of her face and arm.
What do you do over the telephone?

Do you tell her to :

- 1) Take an Aspirin 325mg
- 2) Take her sumatriptan
- 3) Call 911 and go to the nearest emergency room?

How to distinguish hemisensory symptoms:

- Migraine: The sensory symptoms of migraine usually have a march. It is **SLOW** over 3-5 minutes and usually represents a spreading depolarization.
- **So in this patient you would ask the question: How quickly did the symptoms spread?**
- Seizure and TIA: The march is quick over a few seconds to a minute.

What is the definition of TIA?

- a) Transient deficit lasting less than 24 hrs.
- b) Deficit which improves (but not resolves) within 24 hours.
- c) Transient deficit lasting less than 30 min.
- d) Transient deficit lasting up to an hour.
- e) All of the above

NEW DEFINITION

TRANSIENT ISCHEMIC ATTACK

TIA is a brief episode of neurological dysfunction caused by focal brain or retinal or spinal cord ischemia, with complete resolution of symptoms in **less than an hour and without evidence of infarction.**

NEJM. 2002; 347:1013-1016.

TIA old vs. new definition

- | | |
|-----------------------------------|---|
| • <u>Time Based</u> | • <u>Tissue Based</u> |
| • Deficit \leq 24 hours. | • <1 hr event without evidence of infarction. |
| • Suggests Benign | • Indicates potential ischemic danger. |
| • Delays Intervention | • Encourage IMAGING and intervention |
| • Inaccurately predicts ischemia. | • Good ischemic predictor |
| • Diverges from CAD | • Consistent with CAD |
| • tPA- Could be a TIA | • tPA- Almost all are stroke |

You were concerned and sent the patient to the ED: R sided DWI abnormalities

- Despite complete symptom resolution, 20% to 50% of patients with TIA have evidence of acute tissue infarction on MRI

Common Risk Factors for TIA

- Age >50 y
- Hypertension
- Diabetes mellitus
- Elevated cholesterol levels
- Smoking
- Carotid stenosis
- Hx TIA or stroke
- History of paroxysmal or persistent Atrial Fibrillation
- History of Coronary Artery Disease (CAD) or Peripheral Arterial Disease (PAD)
- Family Hx CAD, CVD, or PAD before age 60 y

What other disorders should clinicians consider in patients with suspected TIA?

- Seizure
Abrupt onset and termination; often includes ☐ responsiveness, involuntary movements, and/or incontinence during; usually lethargy or confusion after
Focal findings occur + resolve over hrs to days
May accompany stroke (~2%-3%)
- Other diseases that can cause a seizure: Tumor, hypoglycemia
- Demyelinating disease
- Cervical spine disease

How do you use the history and physical to consider a diagnosis of TIA

- EXAMINE THE PATIENT
- Look for signs of vascular disease: bruits, absence of peripheral pulses
- FEEL THE PULSE FOR A WHILE
- EXAMINE THE FUNDI: look for signs of hypertensive retinopathy

TIA guidelines : AHA and ASA Stroke 2014 updated since 2011: 77 pages of text

- No new recommendations for treatment and screening of **hypertension and dyslipidemia**
- After a TIA or ischemic stroke, all patients should probably be **screened for DM** with testing of fasting plasma glucose, HbA1c, or an oral glucose tolerance test.
- All patients with TIA or stroke should be screened for **obesity** with measurement of BMI.
- For patients who are able and willing to **initiate increased physical activity**, referral to a comprehensive, behaviorally oriented program is probably recommended (Class IIa; Level of Evidence C).
- It is reasonable to conduct a **nutritional assessment** for patients with a history of ischemic stroke or TIA, looking for signs of overnutrition or undernutrition (Class IIa; Level of Evidence C).
- Patients with a history of ischemic stroke or TIA and signs of undernutrition should be referred for individualized nutritional counseling (Class I; Level of Evidence B).

Case 3 : Headache

A 23-year-old woman has a 3-year history of headache. The headaches occur 3 times monthly and are associated with nausea and severe pain that causes her to take to bed. The pain is squeezing quality, sometimes throbbing and is preceded by yawning and irritability. The headaches are triggered by stress and travel and last up to 24 hours.

Which of the following is the most likely diagnosis?

- A. Cluster headache
- B. Migraine headache
- C. Sinus headache
- D. Tension headache

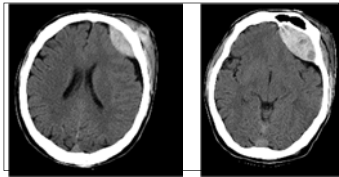
Migraine Diagnosis

- Pulsatile quality, slow in onset, yet pain intensifies
- Unilateral in location
- Nausea or vomiting
- Photo- or phonophobia
- Always ask about family history
- Ask about car sickness as a child

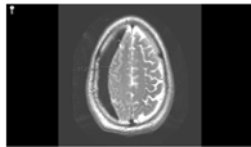
Red Flags for Headache: Low Threshold to image

- **Acute sudden onset**
- Occipitotemporal location
- Age >55 years
- Associated symptoms: worse with movement of the head, waking a patient from sleep at night
- Abnormal neurologic examination

Imaging Findings Sudden onset headache:



19 year old teenager who fell off his bicycle



78 year old man who fell on the ice.

Case 4:

A 25-year-old woman with a 5-year history of multiple sclerosis has a 2-day history of leg weakness and urinary incontinence. Temperature is 100.6 °F. Results of physical and neurologic examinations are otherwise normal. Her urine is positive for nitrites and leukocyte esterase.

Which of the following should be done next?

- A. Intravenous methylprednisolone
- B. Ciprofloxacin
- C. Interferon-beta-1a
- D. Oral prednisone
- E. Plasmapheresis

Multiple Sclerosis (MS)

- Episodes of dysfunction due to demyelinating lesions (plaques) in CNS at different times
- 3 patterns
 - Relapsing-remitting → Episodes of neurologic dysfunction lasting weeks before remission and may lead to the accumulation of disability
 - Secondary progressive disease → Follows relapsing-remitting; no evidence of remission following exacerbations, only progressive disability
 - Primary progressive → Not preceded by relapsing-remitting phase
 - Devic's Disease or Neuromyelitis optica. Disease involving optic nerves and spinal cord. Antibodies are made to Aquaporin 4. Treatment options different from MS

MS Diagnosis

- Sensory loss or paresthesias (especially elicited by neck flexion)
- Internuclear ophthalmoplegia, optic neuritis
- Ataxia, hyperreflexia, spasticity
- Heat sensitivity that causes worsening fatigue or neurologic symptoms (pseudo-relapse)
- MRI of the brain and spinal cord → Ovoid white matter lesions

MS Therapy

- Corticosteroids
 - IV methylprednisolone followed by oral
 - Speeds recovery from acute exacerbations (e.g., optic neuritis)
 - Treat fever and look for underlying infection before beginning corticosteroids (pseudo-relapse)
- Interferon- β
 - Following 1st attack of a clinically isolated syndrome (optic neuritis, spinal cord syndrome, or brain stem–cerebellar syndrome)
- Interferon- β or glatiramer acetate
 - For confirmed relapsing-remitting MS
- For MS relapses with no or minimal impact on function → Observe
- Newer agents: Fingolimod (Gilenya); Natalizumab (Tysabri): Beware of side-effects.
- Dimethyl Fumarate: Tecfidera (new oral agent) with a reasonable safety profile

Things to watch out for:

- Interferon agents are contraindicated in patients with liver disease or depression
- When starting the dose, monitor the liver function tests every 2 weeks and then monthly for 3 months
- Corticosteroids shorten exacerbation time but have no impact on natural history of MS
- As primary care physicians, please watch the vitamin D levels.