The Quest for an Underlying Cause

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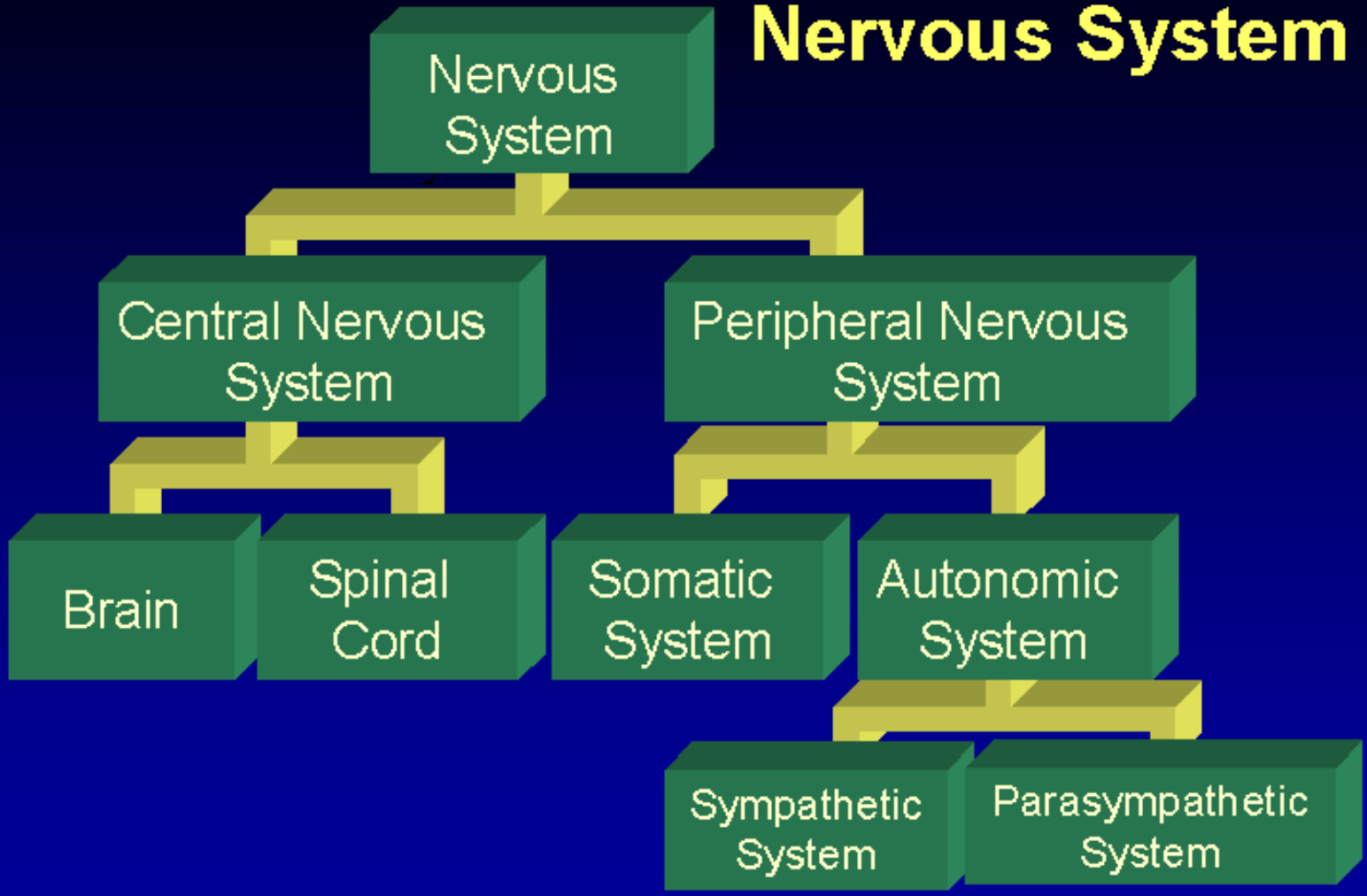
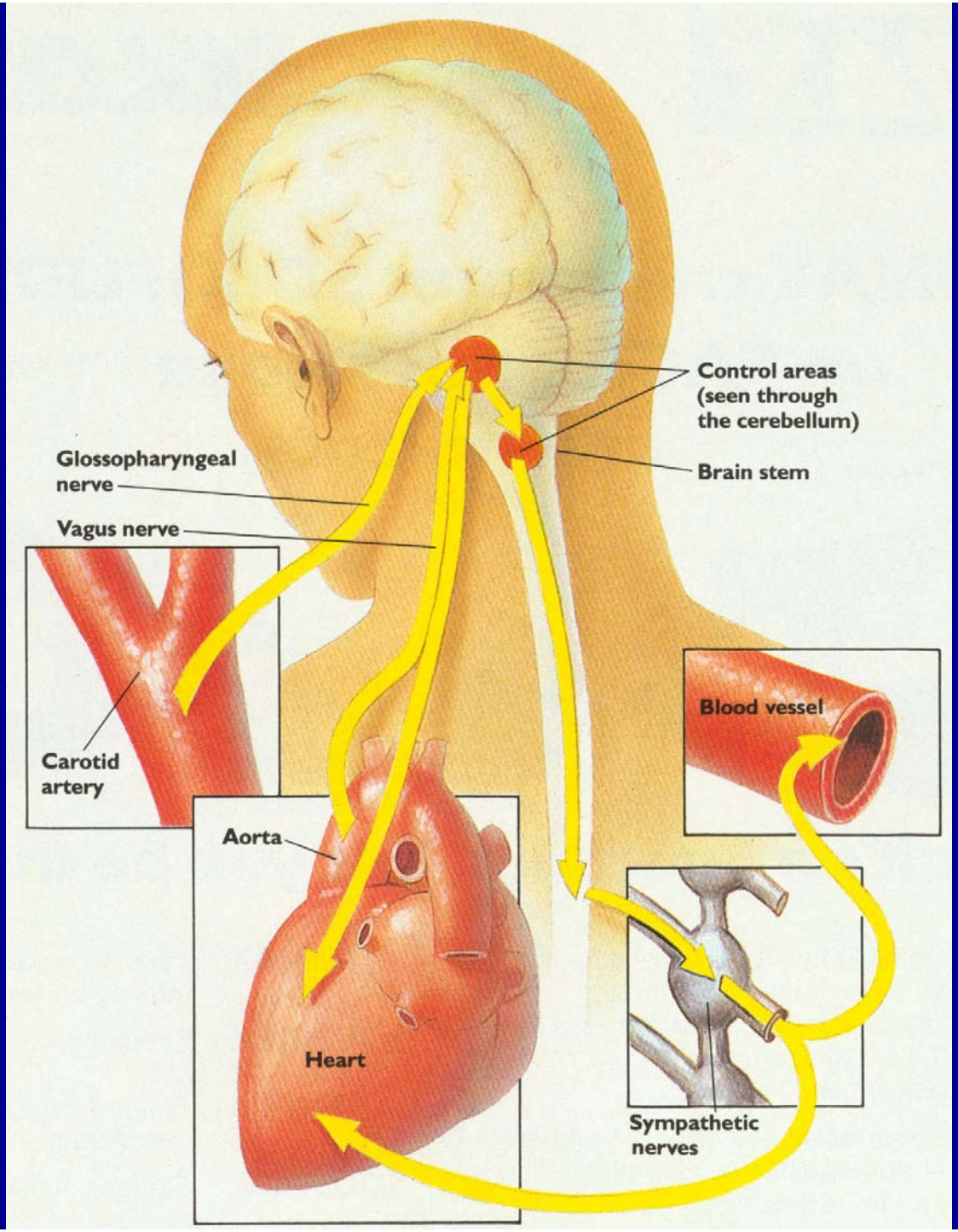
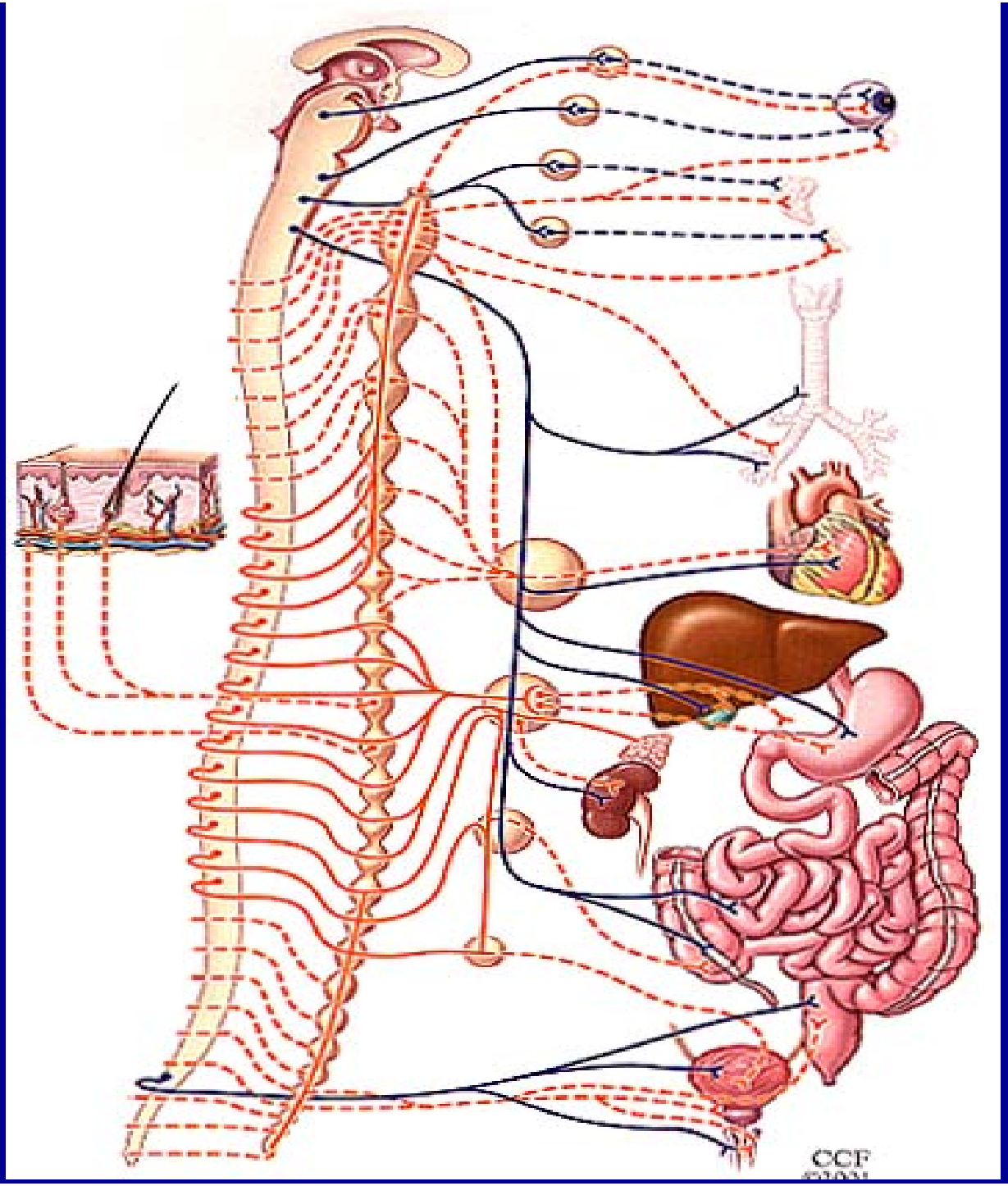
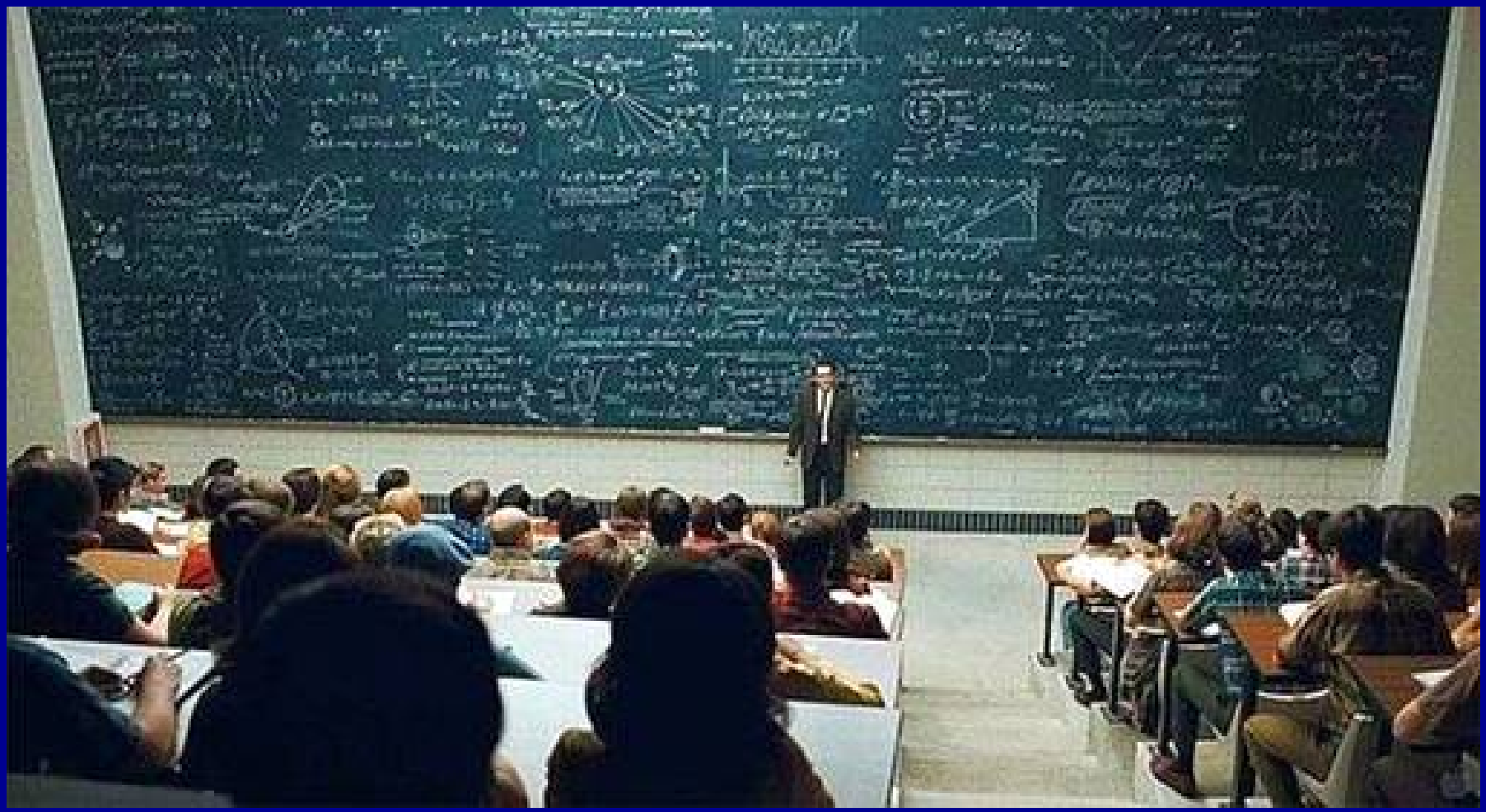
Structure of the Nervous System




Control areas
(seen through
the cerebellum)
Brain stem
Glossopharyngeal
nerve
Vagus nerve
Carotid
artery
Blood vessel
Aorta
Heart
Sympathetic
nerves


CCF

POTS is an abnormal clinical state: There are a multitude of ways to get there.....



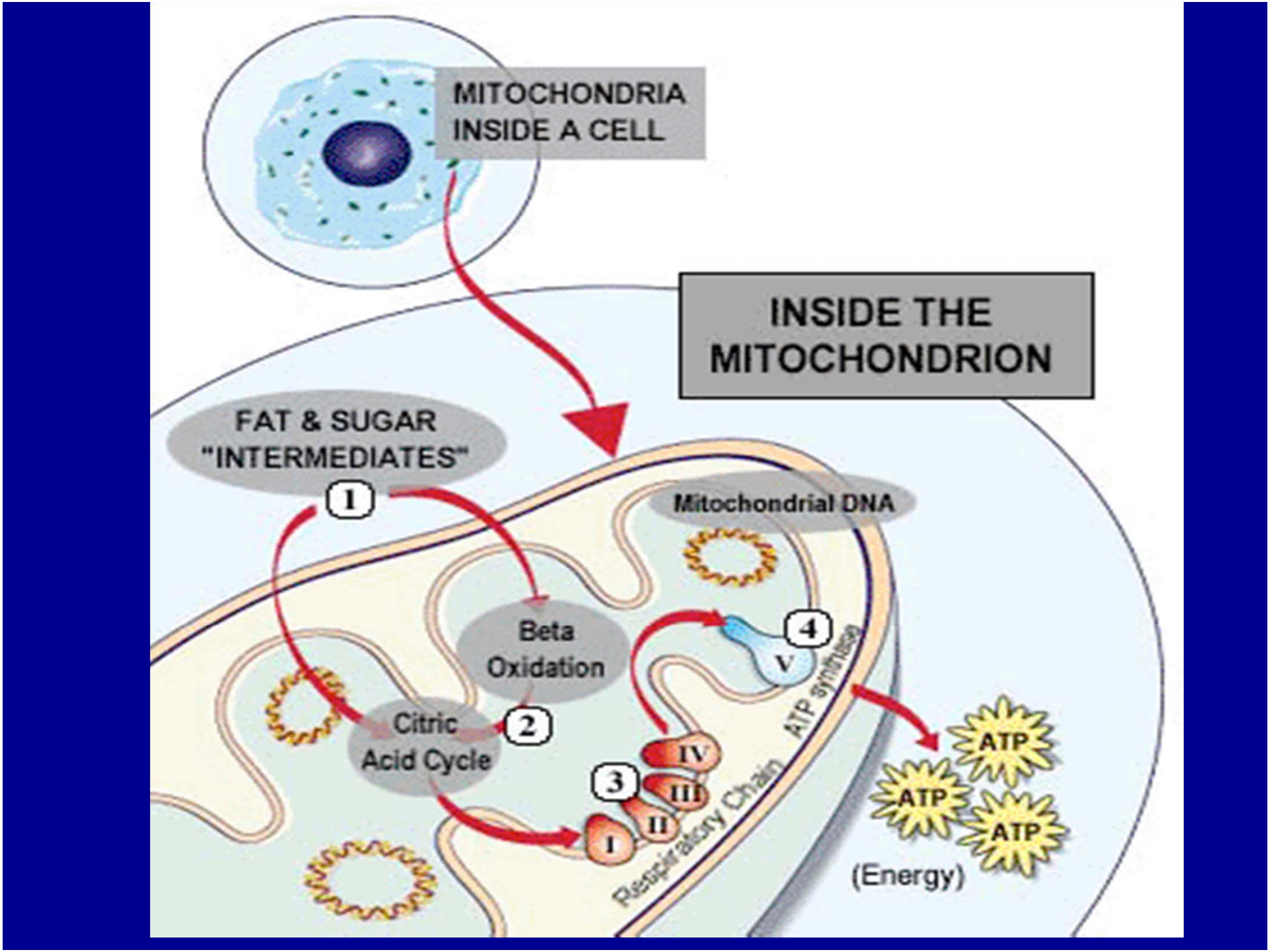
POTS may occur as a consequence of

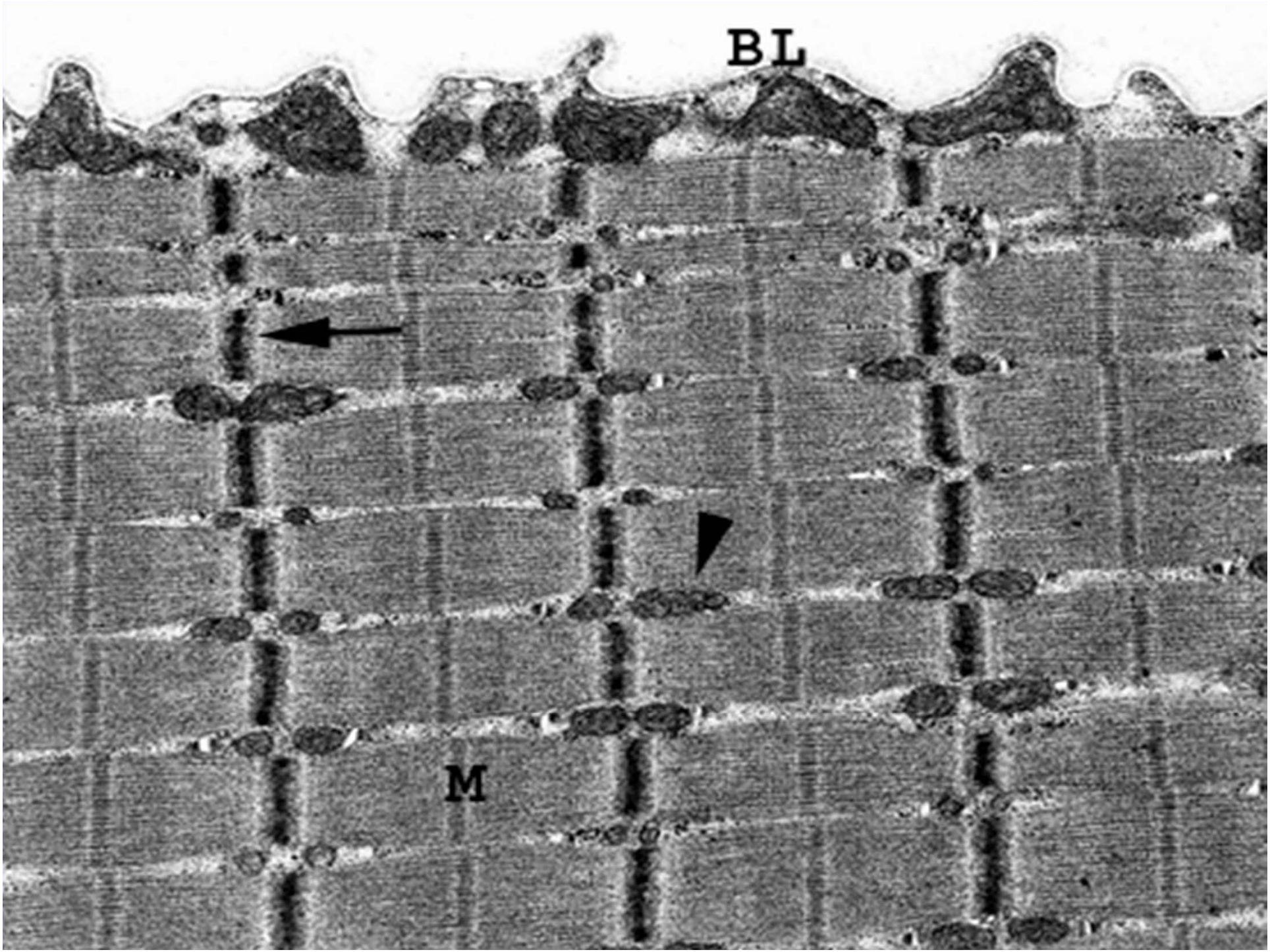
1. diabetes
2. joint hypermobility syndrome
3. chemotherapy
4. multiple sclerosis
5. amyloidosis
6. sarcoidosis
7. Lyme disease
8. Parkinson's disease
9. mitochondrial cytopathy
10. mast cell Instability

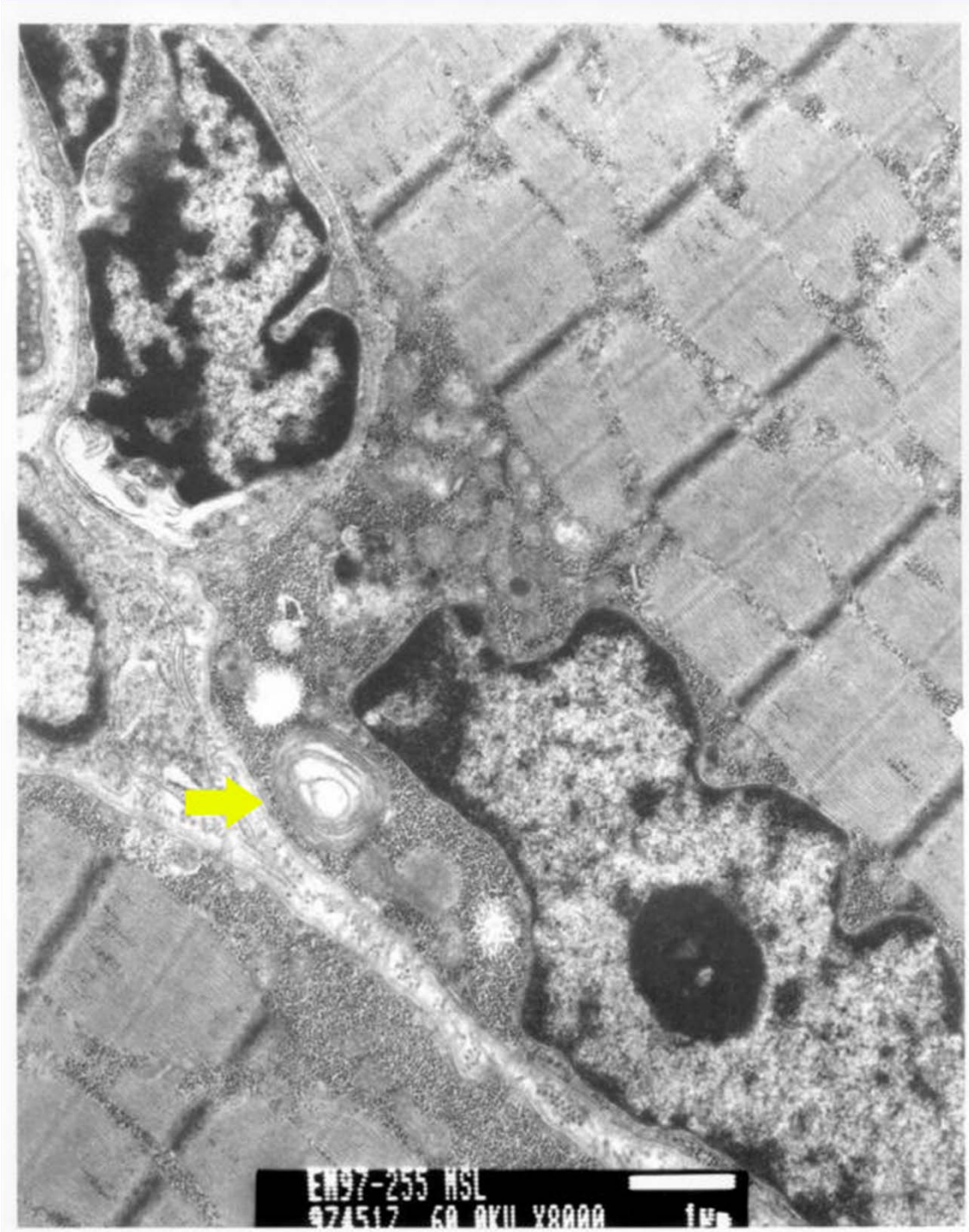
POTS in Mitochondrial Cytopathy

Background

- Autonomic dysfunction has been reported to occur in patients suffering from mitochondrial cytopathy. However there is paucity of literature on the occurrence of orthostatic intolerance (OI) in patients suffering from mitochondrial cytopathy. We report on a series of patients with mitochondrial cytopathy who developed features of autonomic dysfunction in the form of OI.


MITOCHONDRIA
INSIDE A CELL
INSIDE THE
MITOCHONDRION
FAT & SUGAR
"INTERMEDIATES"
1
Mitochondrial DNA
Beta
Oxidation
Citric
Acid Cycle
2
3
4
V
IV
III
II
I
Respiratory Chain
ATP synthase
ATP
ATP
ATP
(Energy)


BL
M



Note abnormal Arrangement of Cristae with Dense body formation

Autonomic Dysfunction Presenting as Orthostatic Intolerance in Patients Suffering From Mitochondrial Cytopathy

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ABSTRACT

Background: Disturbances in autonomic nervous system function have been reported to occur in patients suffering from mitochondrial cytopathies. However, there is paucity of literature on the occurrence of orthostatic intolerance (OI) in these patients. We report on a series of patients diagnosed with mitochondrial cytopathy who developed features of autonomic dysfunction in the form of OI.

Methods: This was a single-center report on a series of 6 patients who were followed in our clinic for orthostatic intolerance. All of these patients had a diagnosis of mitochondrial cytopathy on the basis of muscle biopsy and were being followed at a center specializing in the treatment of mitochondrial disorders. This study was approved by our local institutional review board. Each of the patients had suffered from symptoms of fatigue, palpitations, near syncope, and syncope. The diagnosis of OI was confirmed by head-up tilt test. Collected data included demographic information, presenting symptoms, laboratory data, tilt-table response, and treatment outcomes.

Results: Six patients (3 females) were identified for inclusion in this report. The mean age of the group was 48 ± 8 years (range, 40–60 years). All of these patients underwent head-up tilt table testing and all had a positive response that reproduced their clinical symptoms. Among those having an abnormal tilt-table pattern, 1 had a neurocardiogenic response, 1 had a dysautonomic response, and 4 had a postural orthostatic tachycardia response. All but 1 patient reported marked symptom relief with pharmacotherapy. The patient who failed pharmacotherapy received a dual-chamber closed-loop pacemaker and subsequently reported marked improvement in her symptoms with elimination of her syncope.

Conclusions: Orthostatic intolerance might be a significant feature of autonomic nervous system dysfunction in patients suffering from mitochondrial cytopathy.

Introduction

Autonomic nervous system dysfunction has been reported to occur in patients suffering from mitochondrial cytopathy. The most common manifestations of autonomic dysfunction in these patients include gastrointestinal dysmotility, central apnea, bladder dysfunction, and dysregulation of both heart rate and blood pressure during stress.[1] Herein we report a series of 6 patients suffering from a mitochondrial cytopathy who presented with autonomic dysfunction in the form of orthostatic intolerance (OI).

Methods

This is a single-center report on a series of 6 patients who were referred to our clinic due to persistent symptomatic orthostatic intolerance. All of these patients carried a diagnosis of mitochondrial cytopathy that was made on the basis of muscle biopsy results and were being followed at a center that specialized in the treatment of mitochondrial disorders. The Figure 1 demonstrates modified Gormori stain of the muscle biopsy in a patient with mitochondrial cytopathy. This study was approved by our local institutional review board. OI refers to a heterogeneous group of disorders of hemodynamic regulation characterized by excessive pooling of blood in the dependent areas of the body during upright posture resulting in insufficient cerebral perfusion causing symptoms during upright posture relieved by recumbency. Symptoms included syncope, near syncope fatigue, palpitations, exercise intolerance, lightheadedness, diminished concentration, and headache.[2] Collected data included demographic information, presenting symptoms, laboratory data, tilt-table response, and treatment outcomes. The protocol used for tilt-table testing has been described in detail elsewhere, but basically consisted of a 70-degree baseline upright tilt for a period of 30 minutes, during which time heart rate and blood pressure were monitored continually.[3] If symptomatic hypotension and bradycardia occurred reproducing the patient's symptoms, the test was ended. If no symptoms

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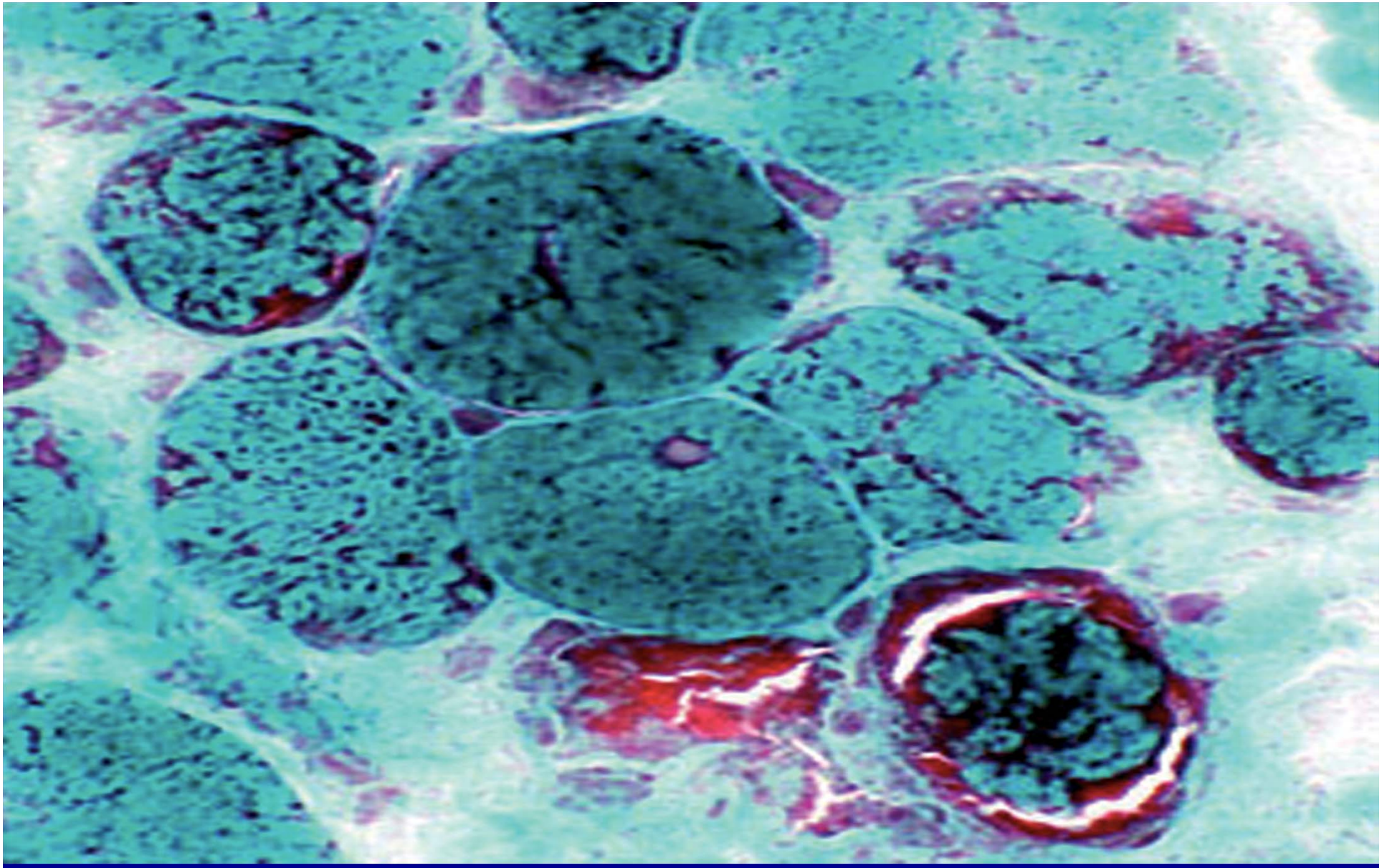
Methods:

- **6 Patients**
- **All had diagnosis of mitochondrial cytopathy on the basis of muscle biopsy.**
- **This study was approved by our local Institutional Review Board.**
- **These patients had suffered from symptoms of fatigue, palpitations, near syncope and syncope.**
- **The diagnosis of OI was confirmed by head up tilt test. Collected data included demographic information, presenting symptoms, laboratory data, tilt-table response, and treatment outcomes.**



Muscle biopsy in a POTS patient found to have a mitochondrial cytopathy

Kanjwal K et al Clin Cardiol 2010 ; 33: 626-629

Results:

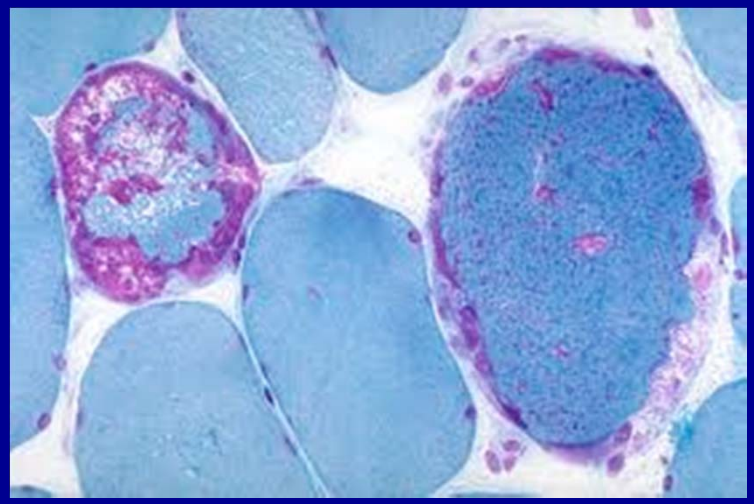
- Six patients, 3 females
- Mean age of the group was 48±8 (40-60) years.
- All patients had head-up tilt table testing (HUTT) and all had a positive tilt table study that reproduced their clinical symptoms. One had a neurocardiogenic response, one had a dysautonomic response, and 4 had a postural orthostatic tachycardia response.
- All but one patient reported marked symptom relief with pharmacotherapy.
- The patient who failed pharmacotherapy received a dual chamber closed loop pacemaker and subsequently reported marked improvement in her symptoms with elimination of her syncope.

Conclusion:

- Autonomic dysfunction in the form of POTS can occur in patients suffering from mitochondrial cytopathy.

Preliminary Data update 2015:

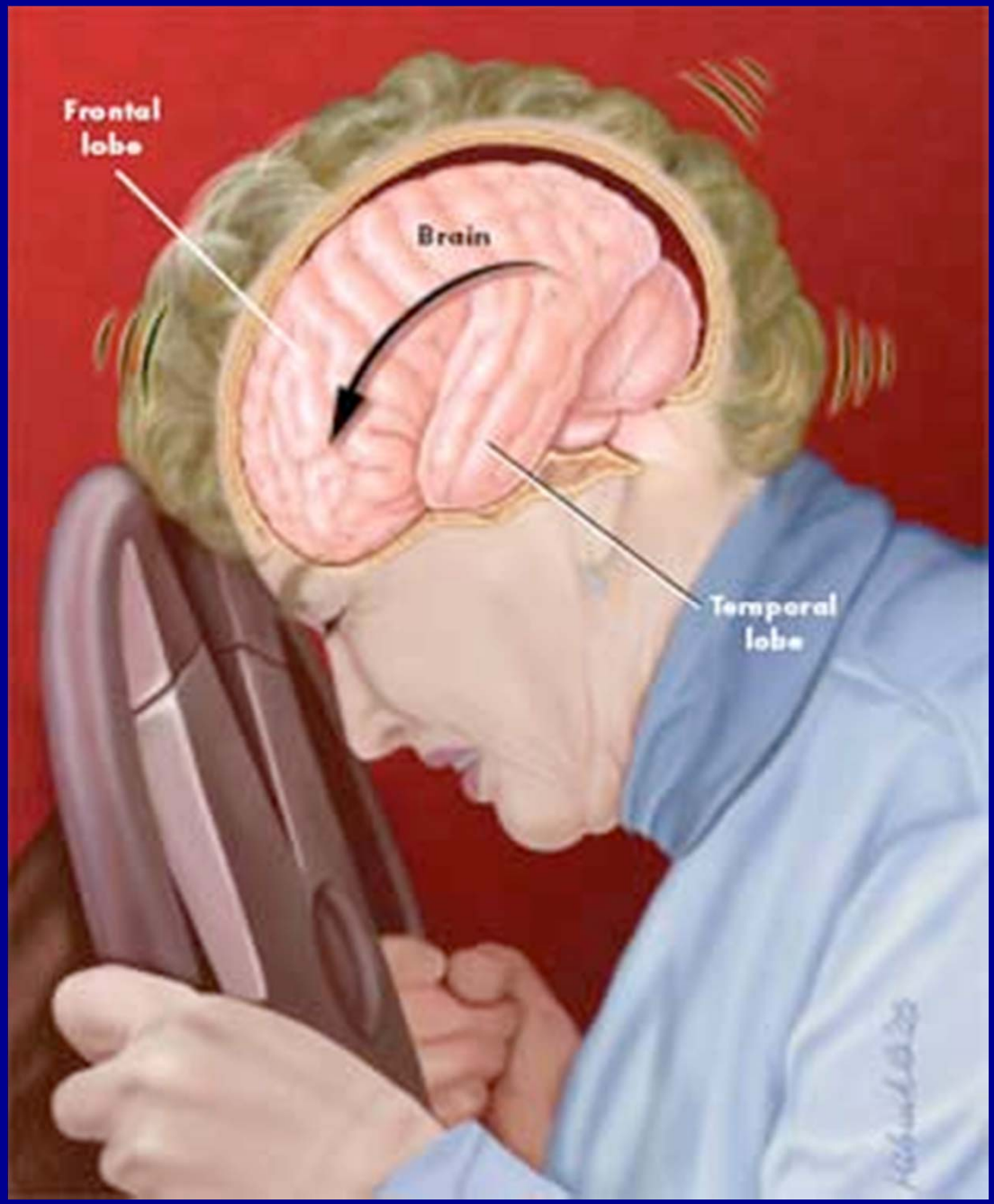
34 patients with Mitochondrial Disorders
(biopsy confirmed)
12 male, 22 female, age range 12- 59
(Mean age 25)
(includes patients from Israel, Canada and Honduras)

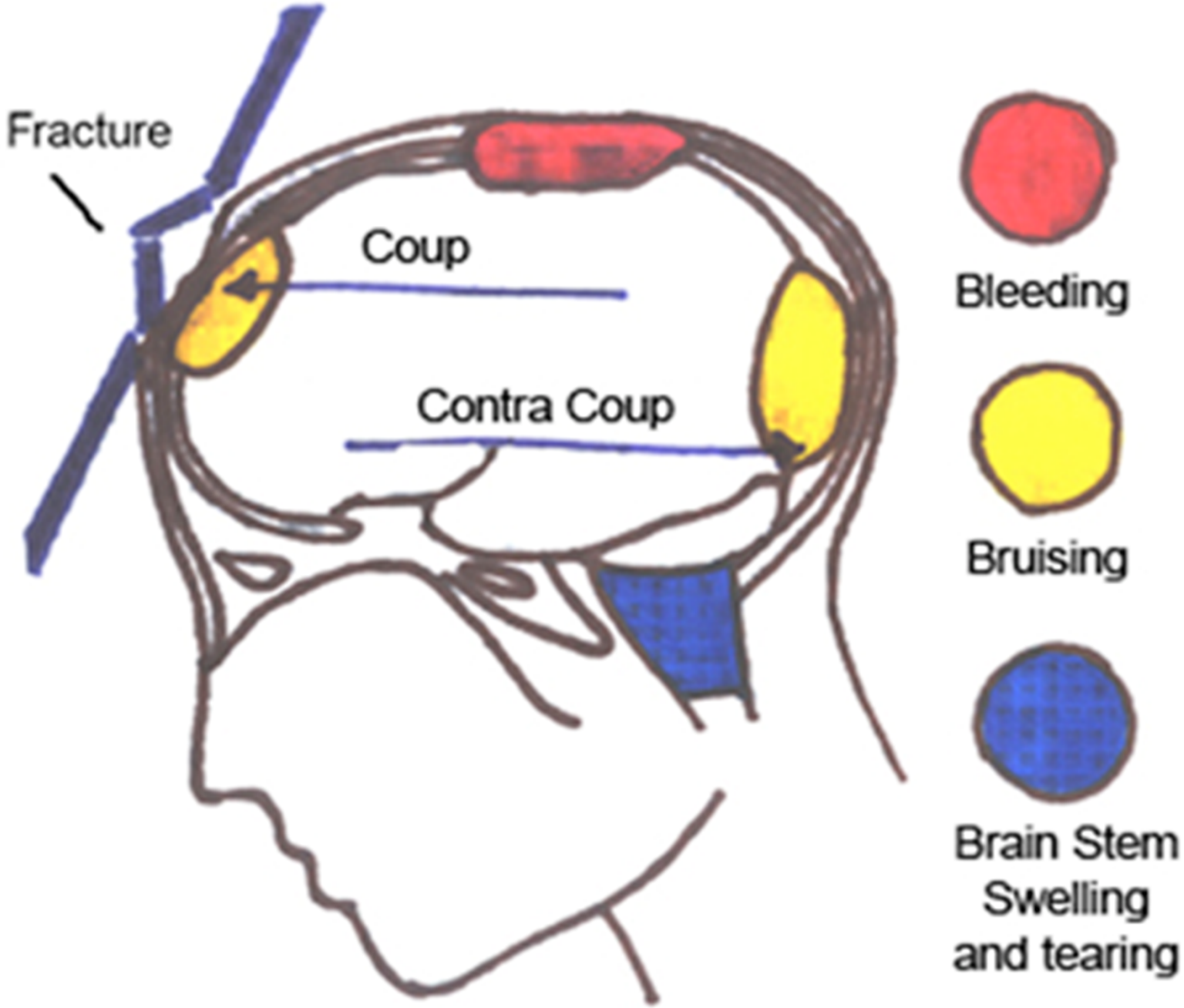


POTS and Trauma

Background

Autonomic dysregulation (called diencephalic epilepsy) has been reported to occur following traumatic brain injury (TBI). However, to date postural tachycardia syndrome (POTS) not been reported to occur as a long-term complication in patients having suffered from a TBI. We report on a series of patients who developed POTS after suffering TBI.


Frontal lobe
Brain
Temporal lobe


Fracture
Coup
Contra Coup
Bleeding
Bruising
Brain Stem
Swelling
and tearing

Methods

- Eight patients who were reffered to our center had suffered TBI and devoloped features of orthostatic intolerance following head trauma.
- Patients' neurological, neurosurgical and autonomic data (charts and/or physician letters) were then carefully reviewed for demographic characteristics, comorbid conditions, symptoms of orthostatic intolerance, medications and response to medication.
- These patients were diagnosed as having POTS primarily based on their clinical features and findings from the head up tilt test (HUTT). The data presented is observational and descriptive (percentages or means)

Results:

Eight patients (among them 7 women) aged 21-41 years suffered from TBI and developed features of POTS.

All had been normal with no symptoms prior to TBI.

All patients experienced orthostatic dizziness, fatigue, palpitations and near syncope. Six patients' suffered from frank syncope.

Six patients developed significant cognitive dysfunction and three developed a chronic pain syndrome following trauma.

Each of the patients reported severe limitations in activities of daily living, loss of employment and two were home bound.

Six patients demonstrated a good response to therapy with various combinations of medications.

The symptoms of orthostatic intolerance and syncope improved with initiation of medical therapy, as well as their reported quality of life.

Two patients failed to show any improvement with various combinations of medications and tilt training, and continued to experience orthostatic difficulties.

Conclusion

- ***Postural tachycardia syndrome may, in some cases, be a late complication of traumatic brain injury.***

Preliminary Update:

2015

38 patients with POTS post TBI

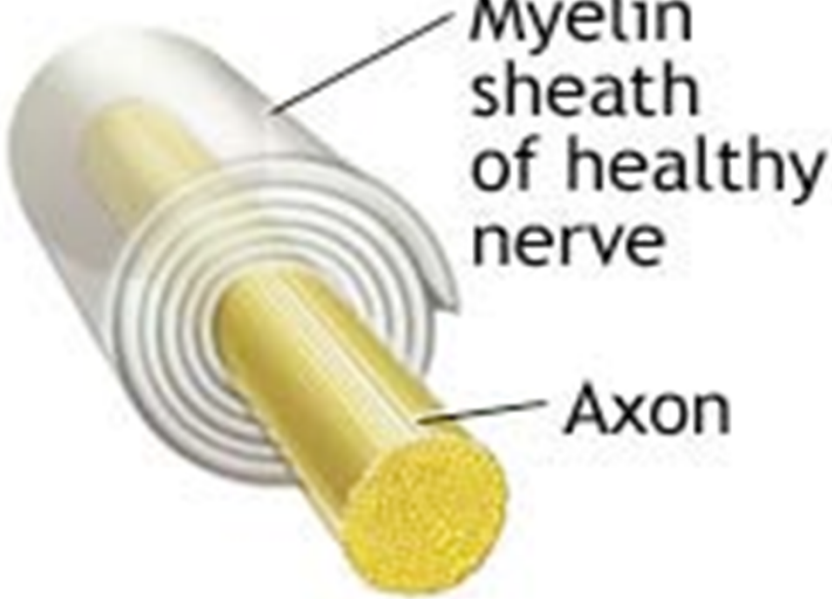
26 MVA, 7 post concussion, 5 Misc

POTS in MS

Background:

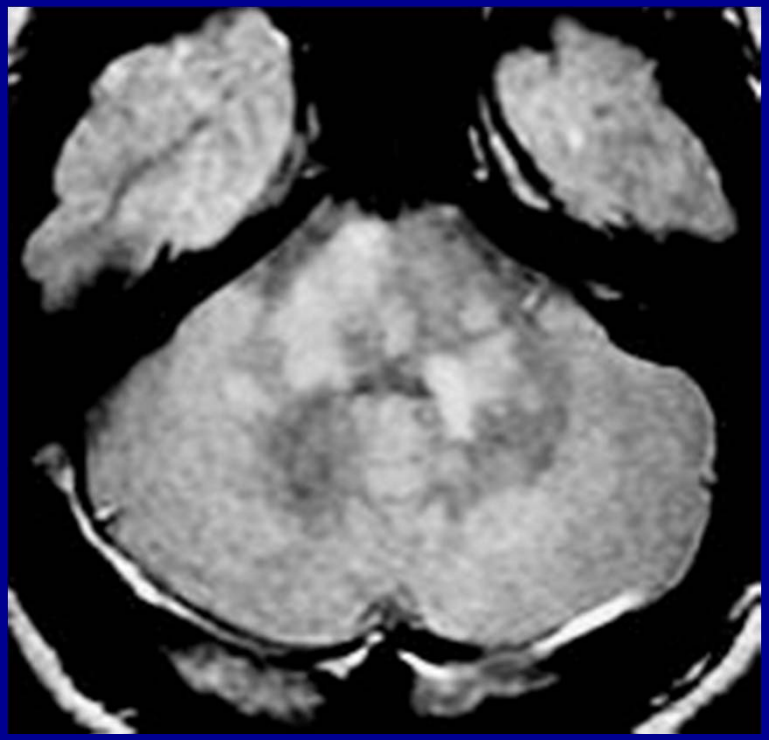
Autonomic dysfunction is common in patients suffering from multiple sclerosis (MS) and orthostatic dizziness occurs in almost 50% of these patients. However, there have been no reports on postural orthostatic tachycardia syndrome (POTS) in patients suffering from MS.

Central nervous system
(brain and spinal cord)



In multiple sclerosis
the myelin sheath,
which is a single cell
whose membrane wraps
around the axon,
is destroyed with
inflammation
and scarring

Could POTS be the presenting sign of MS?



MS plaques in the brainstem Area

Methods:

The patients were included for analysis in this study if they had POTS with either a prior history of MS or having developed MS while being followed for POTS.

Postural orthostatic tachycardia (POTS) is defined as symptoms of orthostatic intolerance(>6months) accompanied by a heart rate increase of at least 30 beats/min (or a rate that exceeds 120 beats/min) that occurs in the first 10 minutes of upright posture or head up tilt test (HUTT) occurring in the absence of other chronic debilitating disorders.

We identified nine patients with POTS who were suffering from MS as well. Each of these patients had been referred from various other centers for second opinions.

Results:

Age: 49±9 years

Eight of the 9 patients were women.

Five patients (55%) had hyperlipidemia,

3 (33%) migraine and 2 (22%) patients had coronary artery disease and diabetes each.

Fatigue and palpitations (9/9).

All patients also had orthostatic dizziness.

Syncope 5/9(55%) of patients.

Four patients (44%), episodes of near syncope.

The presence of POTS in our study population resulted in substantial limitation of daily activities.

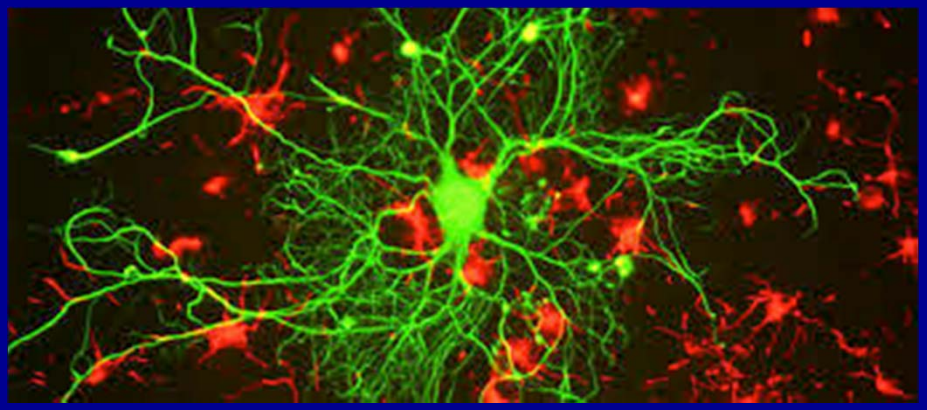
Following recognition and treatment of POTS, 6/9(66%), patients were able to resume daily activities of living.

Their symptoms (especially fatigue and orthostatic intolerance) improved. The frequency and severity of syncope also improved. Three (33%) patients failed to show a good response to treatment.

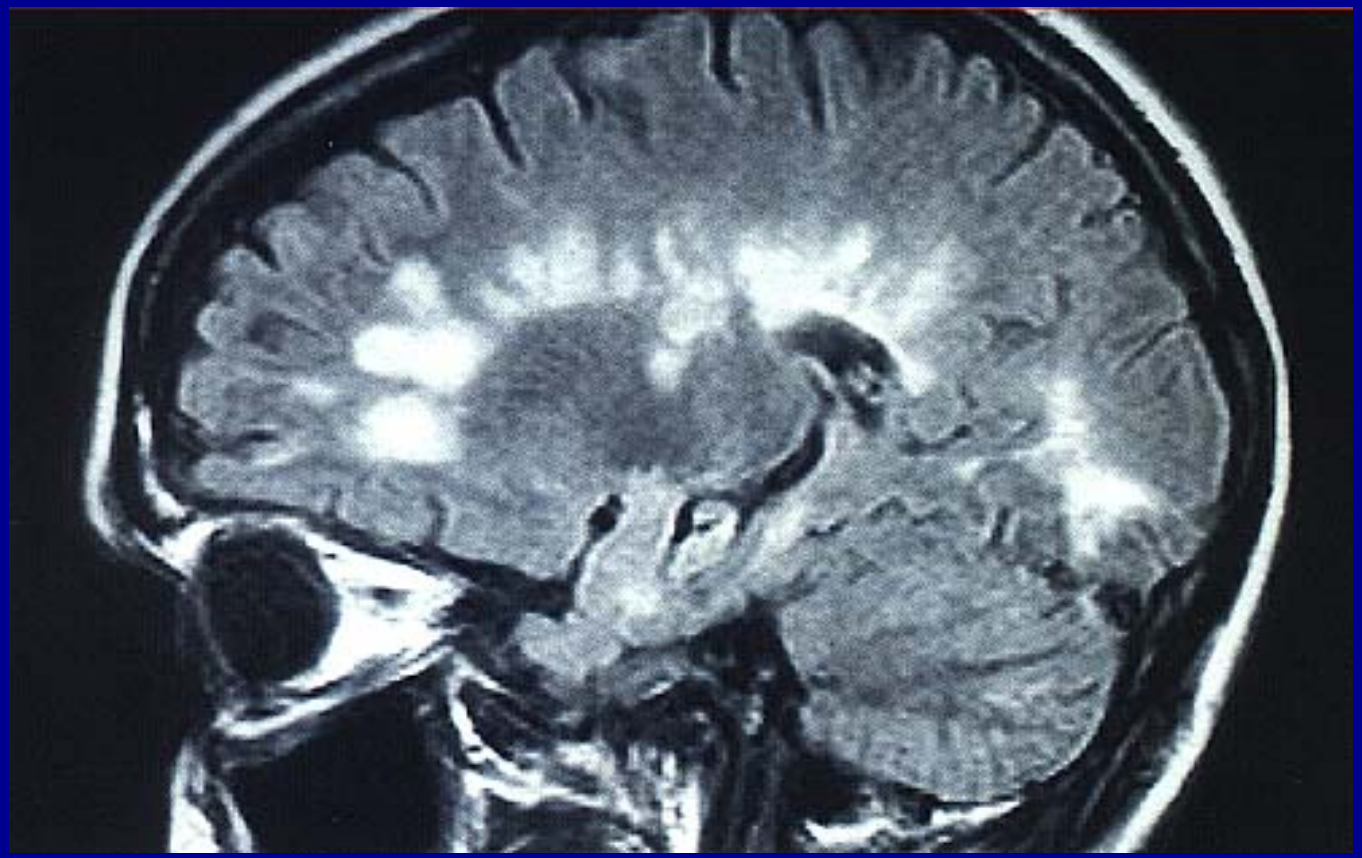
Conclusion:

- ***Patients suffering from MS may first manifest autonomic dysfunction by developing POTS. Early recognition and proper management may help improve the symptoms of POTS.***

We have identified 6 patients whose POTS preceded the diagnosis of MS by 1 to 5 years

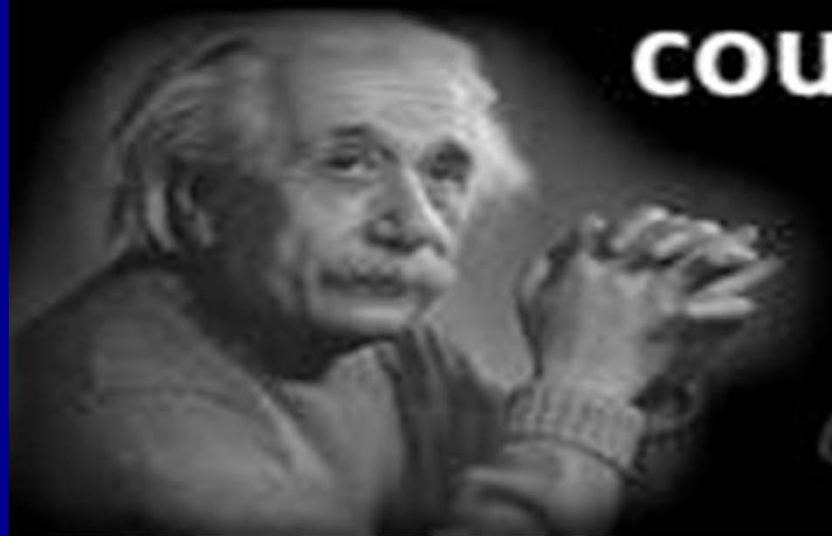


A 35 yr old physician (OB/GYN) from Harrisburg, PA with rapid onset progressive autonomic failure with severe OH. MRI of brain 12 months before was WNL. In MUO clinic had OH, ataxia, +Romberg. Had stopped work due to increasing cognitive impairment. MRI repeated.



Your Diagnosis?

Everything that can be counted does not necessarily count; everything that counts cannot necessarily be counted.

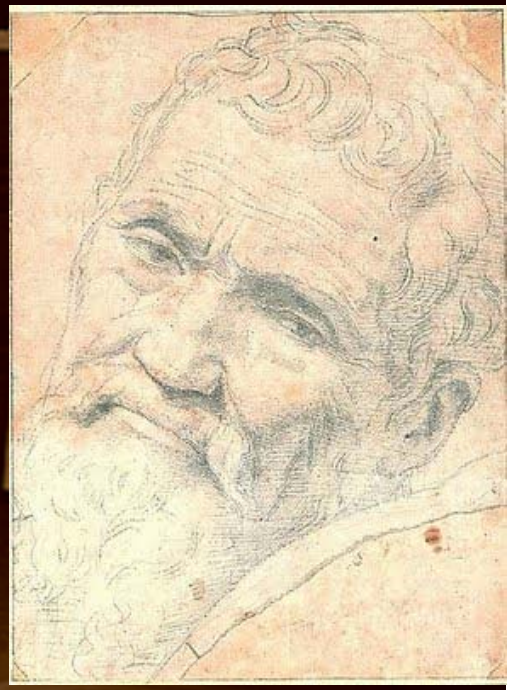


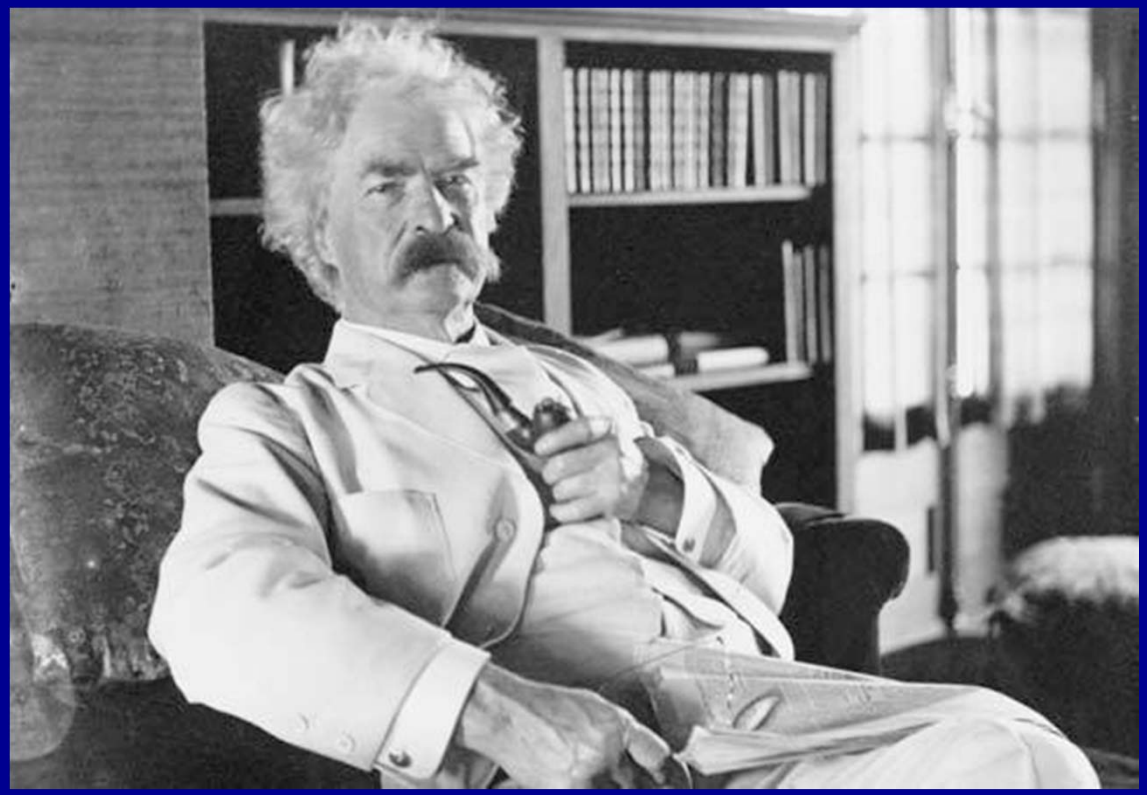
Albert Einstein

German Theoretical-Physicist

(1879-1955)

“Ancora Imparo...”
(I am still learning...)
Michelangelo age 87





"All you need in life is ignorance and confidence
And success is assured"

Mark Twain