

Is it deconditioning ?

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QEH



Deconditioning – introduction

- used rather loosely and inconsistently
- no objective diagnostic criteria for deconditioning so far
- 'mobility and functional decline secondary to prolonged bed rest that is unrelated to the underlying medical condition or injury'
- secondary to disuse muscle atrophy, leading to a decline in skeletal muscle strength, endurance and aerobic capacity
- the lower extremity extensor muscle groups seem to be most affected

Case 1

- Mr. X
- M/73
- Premorbid functional state (8/o8)
 - live with relatives at home
 - walk unaided
 - ADLI
- become chair bound and live in OAH since 10/o8

Past medical history

- Ischemic CVA in 2/08
 - presented with L hemiparesis
 - CT brain showing right periventricular and left basal ganglia infarct
 - good recovery
- DM Diagnosed since 2/08
- ACS in 2/08
 - coro 20/5/08 : significant left main and triple vessel disease
 - dLMN 80%, mLAD 100%, LCX dLCX 80%, pRCA 100%
 - plan for CABG
- CHF
 - Echocardiogram : impaired LV systolic function EF 30-35%, dilated LV, akinetic apex / anterior wall, other region grossly hypokinetic too, thickened calcified AV, 3-4/4 MR, severe TR with PHT, mild AR, no AS, no pericardial effusion

Deconditioning ?

- Admitted to hospital in 8/08 for hypoglycemia
- Later transferred to convalescence hospital for rehabilitation
- Poor mobility despite rehabilitation (frame + 1 assistance) and arranged OAH
- gradually become bed/chairbound in OAH
- Referred from CGAT to GDH for rehabilitation and comprehensive assessment

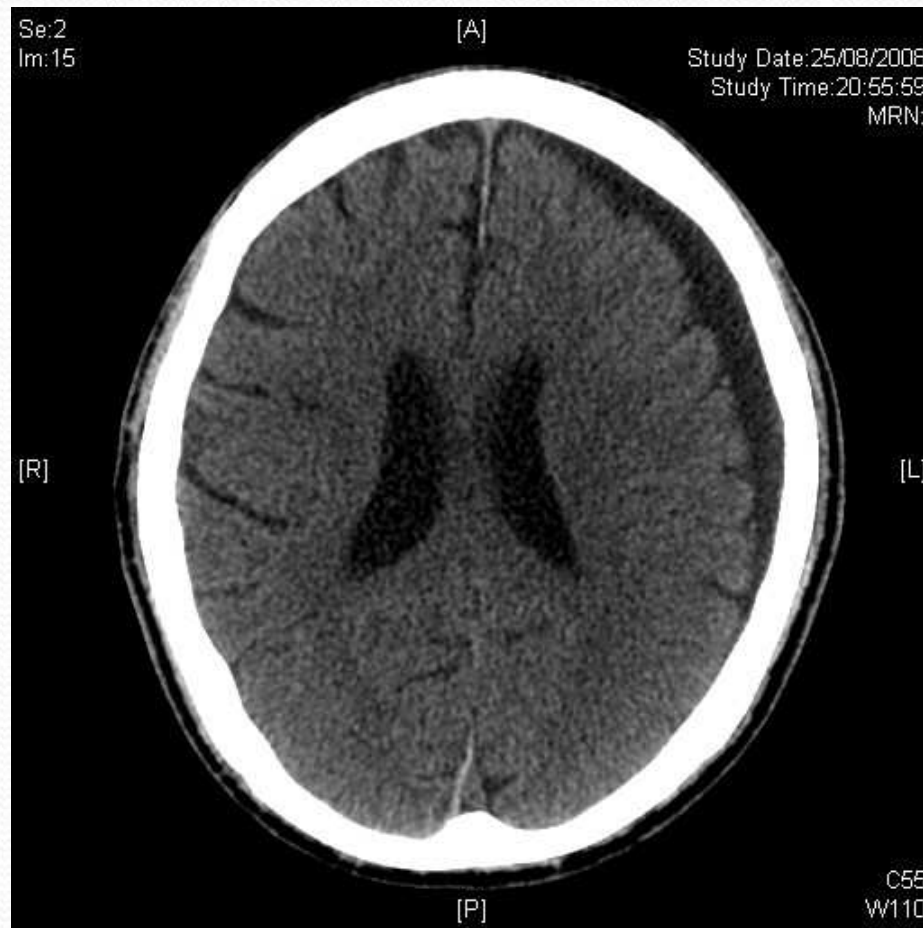
Is it just deconditioning ?

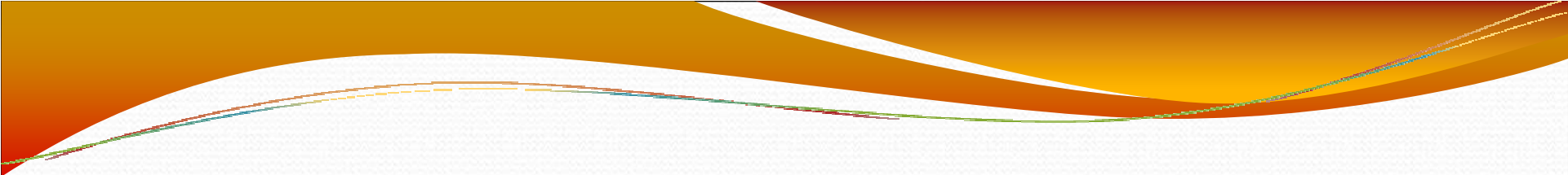
- First assessment in GDH
 - Significant deterioration over the past months in mobility and ADL function
 - On discharge from convalescence hospital : UL 4+/5, LL 4/5
 - In GDH 1st assessment : UL 4+/5, LL 1-2/5
 - Upper limb weakness as well
 - Clinically admitted for workup in 11/08 after the first assessment

What happened initially ?

- Initially present to hospital for hypoglycemia in 8/o8
 - Generalized weakness leading to fall
 - H'stix at ambulance 2.7, given glucose water, recheck at AED 3.2
 - fall 1 day prior to the admission, sustained elbow abrasion
- Actually he had lower limb weakness for few days prior to admission
- Lower limb power 4+/5

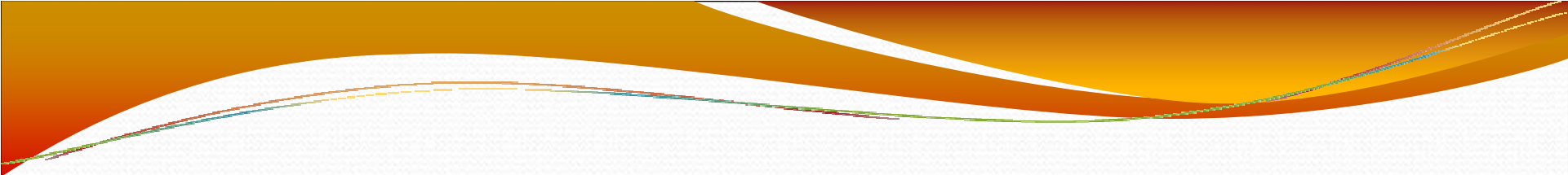
CT brain scan 8/08



- 
- CT brain (day 4 after admission) found L CSDH
 - consulted NS for conservative management
 - transferred to convalescence hospital for rehab
 - received 1/12 training
 - on discharge after rehabilitation : frame walker + 1 mod assistance
 - FU CT brain showed resolving CSDH
 - arranged OAH on D/C

Further history

- further deterioration since discharged from hospital in 10/08
- Progressive increase in limb weakness and with involvement of upper limb as well
- gradually become bed/chairbound
- denied use of any herbs / proprietary preparation
- received flu vaccine in OAH 2 weeks before the clinical admission

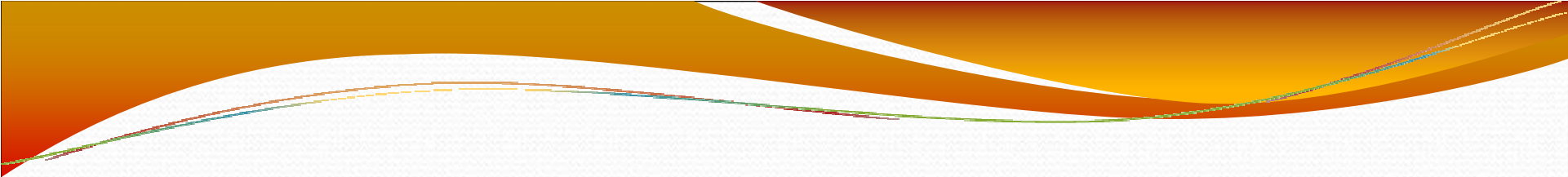
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- Suicidal attempt
 - Feel depressed and useless as he is not very dependent
 - Wanted to jump out of the window in OAH
 - Felt down when he just stepped out of his bed, too to even get close to window
 - GDS 8/15

Physical examination

- Neurological examination
 - Significant generalized muscle wasting
 - generalized hypotonia and hyporeflexia
 - Power :
 - Upper limbs proximal 3/5 distal 2/5
 - Lower limbs proximal 2/5 distal 0/5
 - Impaired distal pinprick sensation
 - no definite sensory level
 - no cranial nerve palsy

Investigations

- Blood test
 - CBP / RLFT normal
 - Hba1c 6.1
 - ESR 43
 - TSH normal
 - B12 / folate normal
 - VDRL NR
 - CK normal
 - Ig pattern normal no paraprotein
 - CRP < 3.2
 - AFP / CEA / PSA normal
 - ANA / antiENA / RF / ANCA -ve

- 
- Lumbar puncture
 - total protein ↑ 0.96
 - glucose 3.6
 - Normal white cell count
 - Microscopy and C/ST –ve
 - VDRL –ve
 - AFB smear and culture –ve
 - Viral study unremarkable



- CT brain :

- Hypodense area noted in right periventricular white matter and right occipital lobe; can be old infarcts.
- A lacunar infarct in left basal ganglia.
- There is no hydrocephalus or extraaxial collection.
- No midline shift is demonstrated

- NCT :

- severe sensorimotor axonal neuropathy with element of demyelination

Outcome

- Diagnosis : CIDP
- Neurology team suggested :
 - IVIg for 5/7
 - Prednisolone 50mg
 - later added azathioprine
- Psychiatry review : situational reaction, for support counselling

Outcome after initial treatment

- IVIg + steroid + azathioprine + rehabilitation in conv. Hospital
 - Self care in seated position
 - Still chair bound
 - Mod assistance in ADL
- Reviewed in GDH 1/09
 - LL power static 2/5
 - UL power improved : prox 4/5 distal 3/5
 - Restored some UL function but still chairbound
 - Suffered from depression due to the residual neurological deficit
 - Started prozac since 1/09



Chronic inflammatory demyelination polyneuropathy

CIDP

- an acquired peripheral neuropathy, presumably of immunological origin
- Clinical presentation and course are extremely variable
- One of the few peripheral neuropathies amenable to treatment

CIDP

- Incidence : 0.15 / 100000
- Prevalence : 1.29-1.9 / 100000
- A slight male preponderance
- age of onset ranged from 10 to 82 years
- mean age of onset 47.6 years

Gérard Said Chronic inflammatory demyelinating polyneuropathy
Neuromuscular Disorders - May 2006 (Vol. 16, Issue 5, Pages 293-303)

pathophysiology

- Considered to be immune mediated
 - Evidence of both cellular and humoral response are involved
 - specific provoking antigens have not been identified
- reaction along with interstitial and perivascular infiltration of the endoneurium
- segmental demyelination of peripheral nerves

Histological feature

- Characteristic features consist of patchy regions of demyelination and edema with variable inflammatory
- The spectrum of abnormalities in the nerve biopsy includes
 - endoneurial edema
 - Demyelinated fibers
 - macrophage mediated demyelination
 - Remyelination
 - Schwann cell proliferation with onion bulb formation
 - inflammatory infiltration with mononuclear cells
 - Axonal degeneration and axon loss

Associated conditions

- Vaccination
- Prior infection (URTI or GE)
- Vasculitis
- HIV infection
- Hodgkin's lymphoma
- Paraproteinemia
- Multiple sclerosis
- SLE
- Chronic active hepatitis B or C
- Inflammatory bowel disease
- DM
- pregnancy

Diagnosis

- Different diagnostic criteria
 - AAN
 - INCAT
- Definite diagnosis to be made with
 - typical clinical feature (peripheral neuropathy for > 2 months)
 - typical electro-diagnostic test (demyelination)
 - +/- nerve biopsy (demyelination)
 - CSF : normal WCC +/- protein elevation

CIDP vs GBS

- CIDP time course > 2 months
- In GBS, neurological deterioration is usually completed by 4 weeks from initial presentation and a slow (although may be incomplete) recovery can be expected
- Patients with CIDP have a more slowly progressive weakness and a protracted course either monophasic or relapsing
- a history of viral infection is more commonly obtained with Guillain-Barré syndrome
- relapses are much more common with CIDP

Prognosis

- Clinical course
 - Remitting and relapsing
 - Progressing
- Elderly and diabetes may have poorer outcome

Treatment

- No single 'best' treatment regimen
- Proven effective treatment
 - Steroid
 - Data come from old studies, most are non-randomized studies
 - IVIg
 - A few randomized study had proven it's effectiveness
 - Relatively well tolerated with few side effects
 - Repeated doses may be required in maintaining remission or during relapses
 - plasma exchange

IVIg in CIDP

- Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. Eftimov F; Winer JB; Vermeulen M; de Haan R; van Schaik IN Cochrane Database Syst Rev. 2009 Jan 21;(1):CD001797.
- 7 randomised controlled trials including 287 participants
- Conclusion :
 - A significantly higher proportion of participants improved in disability within one month after IVIg treatment as compared with placebo
 - NNT = 3
 - IVIg improves disability more than placebo over 24 and 48 weeks

Other treatment

- Other agent
 - Azathioprine : may be useful as a steroid sparing agent
 - MMF
 - Etanercept
 - Interferon
 - Cyclosporin
- Rehabilitation
- Psychosocial impact

Table 2. Therapeutic regimes for chronic inflammatory demyelinating poly(radiculo)neuropathy (CIDP)

Proven effective treatments	Regimen
Prednison	Induction: 60 mg prednison daily or 1.5 mg/kg on alternate days in a single morning dose Maintenance: slowly tapering over months-years
IVIg	Induction: 2 g/kg, divided over 2–5 days Maintenance: 0.4–1 g/kg each 2–6 weeks
PE	Induction: 3–5 PE sessions (2–2.5 l/session) Maintenance: one PE session/1–3 weeks
Not-proven effective treatments	Regimen
IV methylprednisolon	Induction: 500 mg daily for 5 days, or 1 g daily for 3 days Maintenance: not determined
Azathioprine	1.5–3 mg/kg per day
Mycophenolate mofetil	1.0–2.0 g/day divided into two oral doses
Cyclosporin	2.5–5.0 mg/kg per day divided into two oral doses
Methotrexate	7.5–15 mg once a week orally; see [11•]
Other treatments	See [13•]

IV = intravenous; IVIg = intravenous immunoglobulin; PE = plasma exchange.

Further progress of our patient

- On maintenance steroid (prednisolone 50mg daily) and azathioprine therapy after the initial course of IVIg
- No further improvement neurologically since on steroid and azathioprine
- Repeated admission for poor DM control
- Sputum grow atypical mycobacterium 1/09 (admitted for fever), CXR clear, for monitoring
- Steroid was tailed off as clinically not responding well but complicated with hyperglycemia
- Azathioprine was also stopped later because of leucopenia and derranged LFT
- On regular IVIg every month since 4/09

Further progress of our patient

- Latest assessment
 - Upper limb
 - Shoulder abduction 4+/5
 - Elbow flexion and extension 5/5
 - Wrist extension 5/5
 - Wrist flexion 4/5
 - Finger abduction 4/5
 - Lower limb
 - Hip flexion 3/5
 - Knee flexion 3/5
 - Knee extension 3-4/5
 - Ankle dorsi- and plantar flexion 3-4/5
- On prozac for depression, mood stable
- Still chairbound, but need less assistance in ADL

Case 2

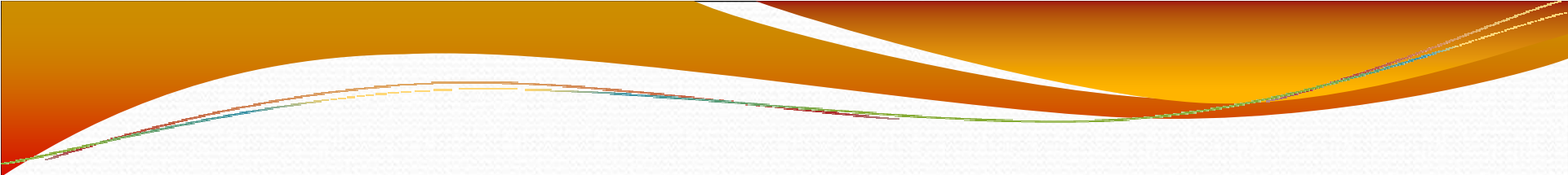
- Mr. Z
- M/85
- Premorbid functional state : (1/09)
 - live with wife and maid
 - walk with stick
 - ADLI

Past medical history

- DM on OHA
- HT
- AF
 - previously on digoxin
 - switched to amiodarone since 10/08
- iron deficiency anemia
 - OGD 16/12/08 : NAD
 - Sigmoidoscopy 18/12/08: rectal polyp
- cervical spondylosis
- gout
- recurrent syncope
 - Tilt table and carotid sinus massage : -ve
 - Echocardiogram 1/07 : satisfactory LV function, degenerative valves with mild MR
 - holter AF, HR 47 to 185; longest RR 2.54s (asymptomatic)
 - Repeated EEG : no epileptiform activities

Deconditioning ?

- Admitted to hospital 1/09
 - Initially presented with hypoglycemia
 - Hstix 1.7 with decreased consciousness and sweating
 - Free T₄ <5.2, TSH 24.09
 - Stopped amiodarone
- Transferred to convalescence hospital
 - thyroxine 25mcg daily
 - a course of rehabilitation was given
 - need assistance in transfer and stand, walk with frame
 - Discharged in 2/09 and referred GDH for further training

- 
- First assessment in GDH for training
 - bed /chairbound
 - ADLD
 - poor appetite
 - malaise sleep a lot

Physical examination

- alert
- GCS 15/15
- power proximal (shoulder / hip) 3-/5
- distal 4/5
- generalized hypotonia and hyporeflexia
- Cardiovascular, chest and abdominal exam unremarkable

Outcome

- Diagnosis : amiodarone induced hypothyroidism with myopathy
- Progress
 - TFT checked : TSH 16.09
 - Thyroid antibodies -ve
 - Thyroxine stepped up
 - Rehabilitation given
 - Progressive improvement in muscle power



- Outcome

- latest TSH 6.11
- power proximal 4+/5 distal 5-/5
- tone normal
- Able to walk with stick
- ADLI
- out-door activities daily (accompany with maid)

Amiodarone induced thyroid disease

Basaria S & Cooper DS. Amiodarone and the thyroid. *American Journal of Medicine* 2005 **118** 706–714

Amiodarone

- class III anti-arrhythmic drug
- Each amiodarone molecule contain 2 iodine atoms
- metabolism in the liver releases ~ 3 mg of inorganic iodine into circulation for every 100 mg of amiodarone
- very lipophilic and is concentrated in adipose tissue
- Elimination a half-life about 100 days
- may have a direct toxic effect on thyroid follicular cells resulting in a destructive thyroiditis

Effect of amiodarone on thyroid function

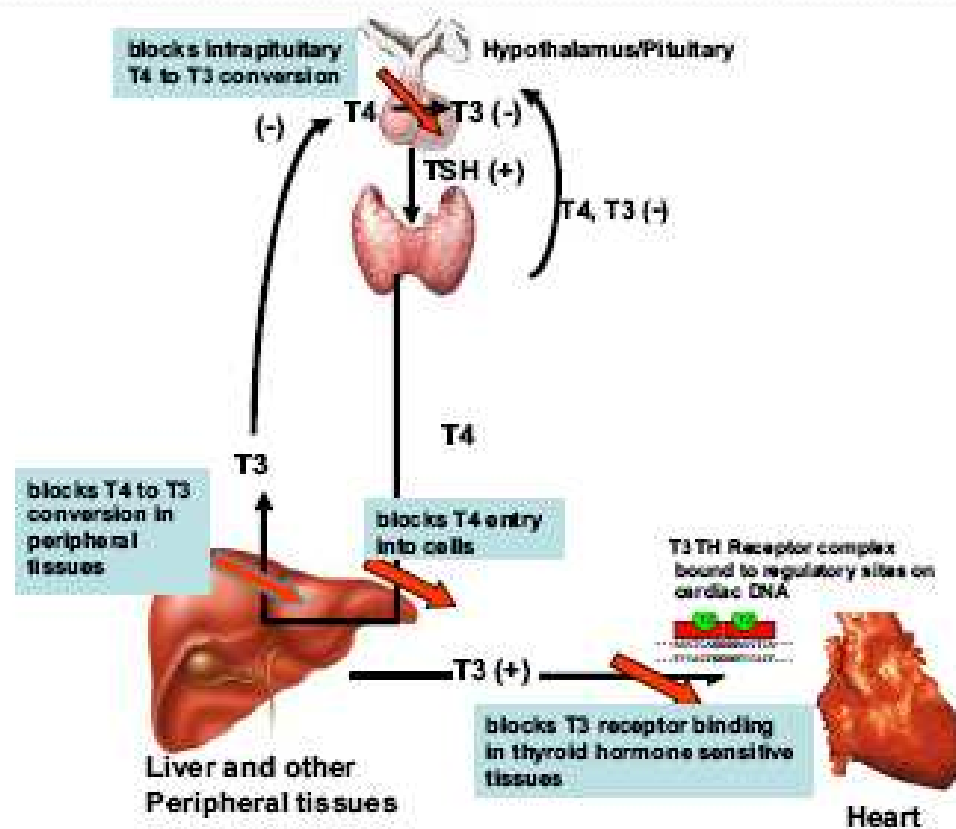


Figure 1 Mechanisms by which amiodarone affects thyroid hormone metabolism (TH = thyroid hormone).

Amiodarone induced hypothyroidism

Table 2 Effects of amiodarone on thyroid function tests in euthyroid subjects

Thyroid hormone	Acute effects (≤ 3 mos)	Chronic effects (≥ 3 mos)
Total and free T4	$\uparrow 50\%$	Remains $\uparrow 20-40\%$ of baseline
T3	$\downarrow 15-20\%$, remains in low-normal range	Remains $\downarrow 20\%$, remains in low-normal range
rT3	$\uparrow >200\%$	Remains $\uparrow >150\%$
TSH	$\uparrow 20-50\%$, transient, generally remains <20 mU/L	Normal

Amiodarone induced thyroid disease

- Amiodarone induced hypothyroidism
- Amiodarone induced thyrotoxicosis
 - type I AIT
 - type II AIT
- Effect of iodine intake in amiodarone induced thyroid disease
 - Higher prevalence of amiodarone induced thyrotoxicosis in iodine deficient region
 - Higher prevalence of amiodarone induced hypothyroidism in iodine sufficient region

Amiodarone induced hypothyroidism

- Female sex and thyroid antibodies are risk factor for developing AIH
- Higher prevalence of Hashimoto's thyroiditis in patient with AIH
- It is also possible that the release of autoantigens from the injured thyroid may lead to potentiation of autoimmunity, thereby accelerating the natural course of Hashimoto's thyroiditis
- Hashimoto's disease is associated with the development of AIH and persistence of hypothyroidism after stopping amiodarone

Amiodarone induced hypothyroidism

- Treatment

- For those who cannot stopped amiodarone
 - Replacement with T₄
 - Start with low dose eg. 25 ug/d
 - Higher than usual dose of T₄ may be need to render patient euthryoid (256 ug/d vs 136 ug/d)
- For those who have stopped amiodarone
 - Replacement if symptomatic
 - Regular monitoring and review the need for continuing replacement

Amiodarone induced thyrotoxicosis

- type I AIT
 - Increased thyroid hormone synthesis
 - Increased iodine provide substrate for thyroid hormone synthesis
 - Usually there is a latent thyroid disease like multinodular goiter or latent Grave's disease
- Type II AIT
 - Destructive thyroiditis
 - Initial hyperthyroid phase followed by hypothyroid phase
 - Most patient eventually recover

Amiodarone induced thyrotoxicosis

- Treatment for type I AIT
 - Stopping amiodarone ?
 - Anti-thyroid drugs
 - Radioactive iodine
 - Thyroidectomy
- Treatment for type II AIT
 - Steroid (prednisolone 40-60mg /day for 1-3 months then taper off), effective even continued amiodarone
 - Replacement may be necessary in hypothyroid phase



Deconditioning ? Deconditioning !

LL weakness in elder

- Deconditioning is probably a diagnosis of exclusion
- warrant a thorough history and physical examination
- try to identify any particular cause leading to the symptoms
- especially any neurological cause
- appropriate investigation may be needed to establish the diagnosis
- early diagnosis may facilitate timely intervention and possibly better outcome
- maintain independency as far as possible

Deconditioning -- etiology -- bed rest

TABLE 1 Adverse effects of bed rest/immobility

System	Effect (s)
Musculoskeletal	Skeletal muscle atrophy, decreased muscle protein synthesis, decreased muscle strength and endurance (LExt > UExt, Extensors > Flexors) Joint contractures (Hip/knee flexion) Osteoporosis Impaired balance/fall risk
Cardiovascular	Decreased aerobic/cardiopulmonary function (e.g., VO ₂ max) due to decreased cardiac output from reduced venous return and stroke volume Orthostatic hypotension (secondary to reduced blood volume and increased venous compliance of lower extremities) Venous thromboembolism
Pulmonary	Atelectasis Hypostatic pneumonia
Gastrointestinal	Decreased appetite Constipation
Genitourinary	Urinary stasis, stones, and infection
Metabolic/endocrine	Glucose intolerance
Dermatological	Pressure ulcers
Psychological/behavioral	Sensory deprivation Disorientation/confusion Depression/anxiety

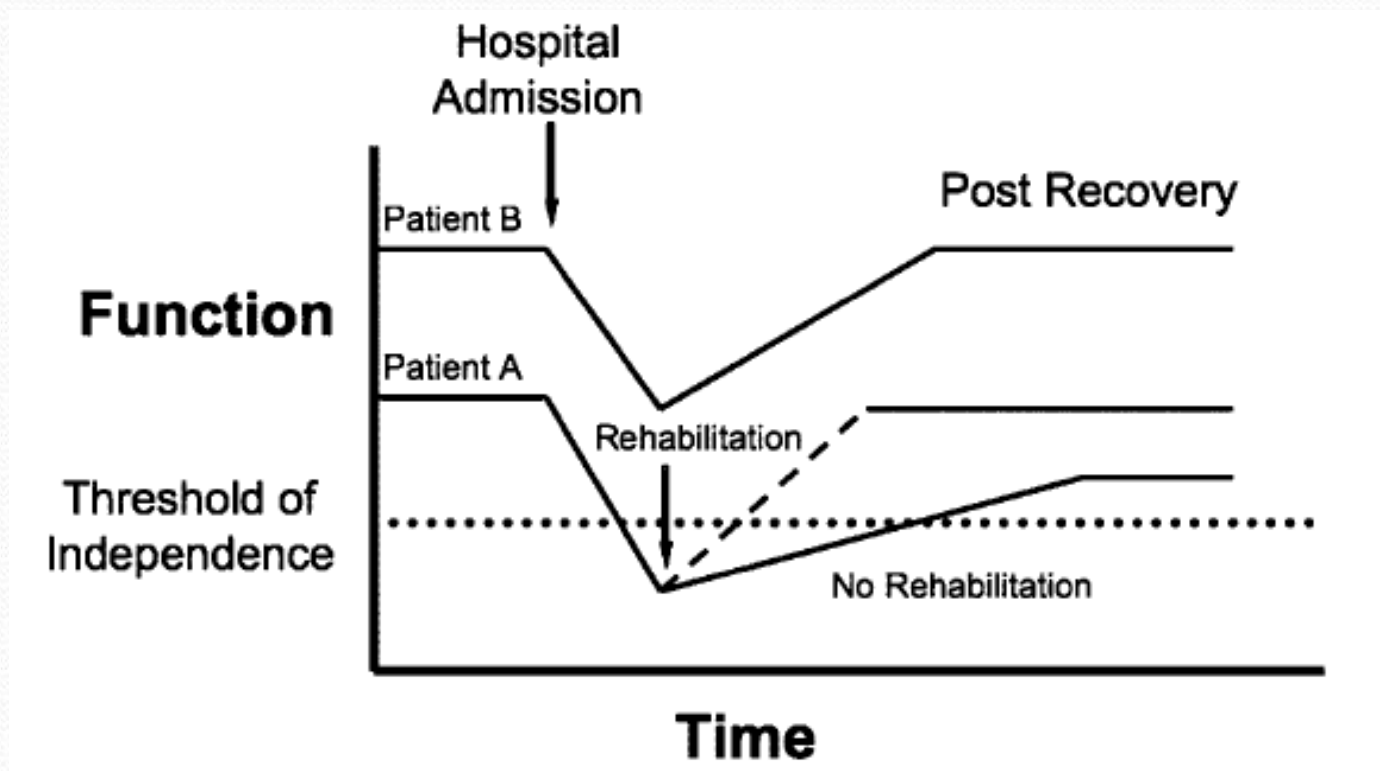
Adapted from Halar and Bell⁴ and Harper and Lyles.⁴³

LExt, lower extremities; UExt, upper extremities; VO₂max, maximal aerobic capacity.

Effect of bed rest

- after 10 days of bedrest, elderly would :
 - lost of whole body and lower limb lean mass
 - lost of muscle strength (knee extension)
- however, no functional decline in those subjects who are healthy volunteers recruited from the community
- Kortebein P et. al. JAMA 2007;297:1772-4

Etiology -- functional reserve



Functional reserve

- decreasing functional reserve / capacity with age
- physiological phenomenon with age (sarcopenia)
- higher prevalence of co-morbidity with age
- decline in ADL function after hospital admission increases markedly with age
 - Higher rates of functional decline
 - lower rates of functional improvement
 - higher rate of incomplete recovery back to baseline
 - Covinsky KE et. al. J Am Geriatr Soc 2003;51:451

Other possible etiology

- other potential contributing factors
 - certain co-morbidity
 - cancer
 - cardiovascular disease (e.g., severe heart failure, cardiac transplantation)
 - chronic renal insufficiency
 - solid organ transplantation
 - individuals with severe, long-standing COPD
 - those surviving critical illness

Other possible etiology

- Other potential contributing factors (con't)
 - inflammation
 - nutrition
 - anemia
 - Pain
 - sleep deprivation
 - fatigue
 - depression

Deconditioning -- risk factor

- risk factor for deconditioning in elderly
 - increased age
 - deficits in baseline basic or instrumental ADL
 - cognitive deficits
 - use of a walking aids

Mahoney JE, Sager MA, Jalaluddin M: Use of an ambulation assistive device predicts functional decline associated with hospitalization. *J Gerontol A Biol Sci Med Sci* 1999;54A:M83-8

Rehabilitation

TABLE 2 Rehabilitation therapy for hospital-associated deconditioning

Physical therapy

- Bed mobility/transfers
- Gait and balance training
- Ambulatory endurance with/without gait aid/stair climbing
- Muscle strength and endurance training—hip and knee extensors primarily
- Range of motion and muscle flexibility/stretching of major joints and muscle groups of the lower extremities

Occupational therapy

- Activities of daily living (ADL) training, including fine motor skills and adaptive equipment needs
- Instrumental ADL/homemaking/community survival skills
- Cognitive and safety awareness assessment and remediation, if needed
- Range of motion and muscle flexibility/stretching of major muscle groups of the upper extremities to facilitate ADL training
- Energy conservation and joint protection principles, if needed
- Muscle strength and endurance training—shoulder abductors/adductors, elbow flexors/extensors, and finger flexors/grip strength

Contraindication for rehabilitation

TABLE 3 Contraindications to participation in therapeutic exercise/rehabilitation

Unstable angina or severe left main coronary disease
End-stage congestive heart failure
Severe valvular heart disease
Malignant or unstable arrhythmias
Elevated resting blood pressure (systolic, >200 mm Hg, diastolic, >110 mm Hg)
Large or expanding aortic aneurysm
Known cerebral aneurysm or recent intracranial bleed
Uncontrolled or end-stage systemic disease
Acute retinal hemorrhage or recent ophthalmologic surgery
Acute or unstable musculoskeletal injury
Acute illness with systemic features (e.g., pneumonia)
Severe dementia or behavioral disturbance

Bring Home Message

- thorough history taking and physical examination are essential when handling elderly with lower limb weakness
- try to establish a diagnosis, especially a neurological condition
- comprehensive assessment and rehabilitation
- risk factor of deconditioning



Thank you