2023 SCI Review Course

Endometabolic, Cardiovascular, Nutritional, and Immunological Health in SCI

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Miami, Florida

THE MIAMI PROJECT TO CURE PARALYSIS

UNIVERSITY OF MIAMI
MILLER SCHOOL of MEDICINE

Academy of Spinal Cord Injury Professionals, Inc.™
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DISCLOSURE

- Grant/research support from Craig H. Neilsen Foundation #878801

Learning Objectives

- At the conclusion of the *endometabolic dysfunction* presentation, the learner will:
  - Briefly review SCI and its comorbidities
  - Describe the causal relationship between energy metabolism, obesity, metabolic syndrome and endocrine Dysfunction
  - Review anabolic and catabolic dysfunction after SCI
- At the conclusion of the *cardiovascular dysfunction in SCI* presentation, the learner will:
  - Review the neurogenic consequences of SCI on cardiovascular function
  - Discuss risks of VTE/PE following SCI, including prophylaxis and management
  - Review risk factors for coronary artery / peripheral arterial disease following SCI
- At the conclusion of the *nutrition and immune dysfunction after sci* presentation, the learner will:
  - Review the neurogenic consequences of SCI on metabolism and body composition
  - Discuss energy balance and components required to promote fat loss
  - Review immunological consequences of SCI and management concerns

Endometabolic Dysfunction

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Comorbidities after SCI

- Anabolic deficiency
- Parasympathetic dominance
- Sympathetic dysfunction
- Autonomic dysreflexia
- Neurogenic hypotension/bradycardia
- Neurogenic cardiomyopathy
- Mechanical ventilation or pacing (intact phrenic n.)
- Neurogenic restrictive/obstructive lung disease
- Neurogenic bladder w/ detrusor sphincter dyssynergia
- Neurogenic bowel
- Neurogenic skin, pressure injury risk
- Neuropathic & nociceptive pain
- Obstructive sleep apnea
- Spastic or flaccid paralysis
- Sarcopenia/myopenia
- Heterotopic ossification
- Osteopenia/osteoporosis
- Upper extremity overuse syndrome
- Venous thromboembolism
- Pulmonary embolism
- Metabolic syndrome & its risk factors
- Neurogenic obesity
- Cardiovascular disease

Obesity-Related Risk Factors

- Hypertension
- Dyslipidemia
- Dysglycemia/insulin resistance
  - Type 2 diabetes mellitus
  - Glucose intolerance
  - Hyperinsulinemia
- Coronary heart disease
- Angina pectoris
- Congestive heart failure
- Stroke
- Gallstones
- Cholecystitis & Cholelithiasis
- Immunosuppression
- Gout / Osteoarthritis
- Obstructive sleep apnea
- Some types of cancer (e.g., breast, prostate, colon)
- Complications of pregnancy
- Poor female reproductive health
- Urinary stress incontinence
- Uric acid nephrolithiasis
- Psychological disorders

Neurogenic Obesity after SCI

- Obesity is at **pandemic** proportions in SCI[1,2]
- Neurogenic obesity reflects excess body fat (♂ > 22%, ♀ > 35%) due to[1,2]
  - Motor Paralysis
  - Obligatory Sarcopenia/Myopenia
  - Sympathetic Dysfunction
  - Anabolic Insufficiency
  - Blunted Satiety
    - Energy Intake > Energy Expenditure
- Obesity mediates metabolic syndrome via[1,2]
  - Dysglycemia/Insulin Resistance
  - Hypertension
  - Dyslipidemia
  - Thromboembolism
  - Coronary Artery Disease

Review

Neurogenic obesity and systemic inflammation following spinal cord injury: A review

Gary J. Farkas, David R. Gater

ASIA American Spinal Injury Association

UHealth Jackson Rehabilitation Care

Christine E. Lynn Rehabilitation Center for the Miami Project to Cure Paralysis

Pathophysiology of Neurogenic Obesity After Spinal Cord Injury

David R. Gater, Jr, MD, PhD, MS,[1,2] Gary J. Farkas, PhD,[1] and Eduard Tiozzo, PhD, MSCTI[1]

Journal of Personalized Medicine

MDPI

Review

The Diagnosis and Management of Cardiometabolic Risk and Cardiometabolic Syndrome after Spinal Cord Injury

Gary J. Farkas [1,2,*], Adam M. Burton [3], David W. McMillan [2,4], Alicia Sneij [1,2] and David R. Gater, Jr. [1,2,3]

Metabolic Syndrome

Clustering of component metabolic risk factors

↑ risk for CVD, CVD mortality, diabetes, stroke, and mortality

Early warning sign & silent killer

https://jamestownspine.com/metabolic-syndrome/

Farkas GJ et al, J Personalized Med, 2022.

Metabolic Syndrome Defined

Table 1. The most recognized definitions for identifying and diagnosing cardiometabolic syndrome and its component risk factors.

		International Diabetes Federation [22,23]	National Cholesterol Education Project Adult Treatment Panel III [17]	National Heart, Lung, and Blood Institute/American Heart Association [18,19]	World Health Organization [20]	European Group for the Study of Insulin Resistance [21]
Required Criteria/Emphasis		Obesity Plus, any 2 of the following risk factors	None. Any 3 of the following risk factors	None. Any 3 of the following risk factors	Impaired fasting glucose, impaired glucose tolerance (prediabetes) or type 2 diabetes mellitus, and/or insulin resistance * Plus, any 2 of the following risk factors	Insulin resistance or fasting hyperinsulinemia (>75% percentile) Plus, any 2 of the following risk factors
			Component Risk Factors			
Central Obesity		Waist circumference ≥ 102 cm in US men or ≥88 cm in US women ‡,††	Waist circumference ≥ 102 cm in men ‡ or ≥88 cm in women	Waist circumference ≥ 102 cm in men or ≥88 cm in women	Waist-to-hip ratio > 0.90 in men; Waist-to-hip ratio > 0.85 in women; and/or body mass index > 30 kg/m^2	Waist circumference ≥ 94 cm in men or ≥80 cm in women
Dyslipidemia	Elevated triglycerides	Triglycerides ≥ 150 mg/dL, or on treatment for dyslipidemia	Triglycerides ≥ 150 mg/dL	Triglycerides ≥ 150 mg/dL, or on treatment for evaluated triglycerides	Triglycerides ≥ 150 mg/dL	Triglycerides > 150 mg/dL, HDL-C < 39 mg/dL in men and women, or on treatment for dyslipidemia
	Reduced HDL-C	HDL-C < 40 mg/dL in men or <50 mg/dL in women, or on treatment for dyslipidemia	HDL-C < 40 mg/dL in men or <50 mg/dL in women	HDL-C < 40 mg/dL in men or <50 mg/dL in women, or on treatment for reduced HDL-C	HDL-C < 35 mg/dL in men or <39 mg/dL in women	
Hypertension		Systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mmHg, or on treatment previously diagnosed hypertension	Systolic blood pressure ≥ 130, or diastolic blood pressure ≥ 85 mmHg	Systolic blood pressure ≥ 130, diastolic blood pressure ≥ 85 mmHg, or on treatment for or previously diagnosed with hypertension	Blood pressure ≥ 160/90 mmHg § Blood pressure ≥ 140/90 mmHg §	≥140/90 mmHg, or on treatment for hypertension
Dysglycemia		Fasting plasma glucose ≥ 100 mg/dL, or previously diagnosed type 2 diabetes mellitus	Fasting plasma glucose ≥ 100 mg/dL **/≥ 110 mg/dL **	Fasting plasma glucose ≥ 100 mg/dL, or on treatment elevated glucose	Impaired fasting glucose, impaired glucose tolerance (prediabetes), or type 2 diabetes mellitus	Fasting glucose ≥ 110 mg/dL (but not diabetes, <126 mg/dL)
Insulin Resistance		None.	None.	None.	Insulin resistance *	Insulin resistance or fasting hyperinsulinemia (>75% percentile)
Other		None.	None.	None.	Microalbuminuria: urinary albumin excretion rate ≥ 20 μg/min, or albumin:creatinine ratio ≥ 20 mg/g	None.

Farkas GJ et al, J Personalized Med, 2022.

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Dyslipidemia	Elevated triglycerides	Triglycerides ≥ 150 mg/dL, or on treatment for dyslipidemia	Tri cerides ≥ 0 mg/dL	Triglycerides ≥ 150 mg/dL, or on treatment for evaluated triglycerides	Triglyceride 150 mg/dL
	Reduced HDL-C	HDL-C < 40 mg/dL in men or <50 mg/dL in women, or on treatment for dyslipidemia	HDL < 40 mg/dL in men or 50 mg/dL in women	HDL-C < 40 mg/dL in men or <50 mg/dL in women, or on treatment for reduced HDL-C	HDL-C < 35 men or <39 women
Hypertension		Systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mmHg, or on treatment previously diagnosed hypertension	Systolic blood pressu ≥ 130, or diastolic blood pressure ≥ 85 mmHg	Systolic blood pressure ≥ 130, diastolic blood pressure ≥ 85 mmHg, or n treatment for or viously diagnosed wit pertension	Blood press 160/90 mml Blood press 140/90 mml
Dysglycemia		Fasting plasma glucose ≥ 100 mg/dL, or previously diagnosed type 2 diabetes mellitus	Fasting plasma glucose ≥ 100 mg/dL **/≥ 110 mg/dL **	Fasting sma glucose ≥ 100 mg/ or on treatment elev d glucose	Impaired fas impaired glu tolerance (pr type 2 diabe
Insulin Resistance		None.	None.	None.	Insulin resis
Other		None.	None.	None.	Micr bumi urinary rate ≥ 20 µ albumin:crea 20 mg/g

		International Diabetes Federation [22,23]
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	Reduced HDL-C	HDL-C < 40 mg/dL in men or <50 mg/dL in women, or on treatment for dyslipidemia
Hypertension		Systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mmHg, or on treatment previously diagnosed hypertension
Dysglycemia		Fasting plasma glucose ≥ 100 mg/dL, or previously diagnosed type 2 diabetes mellitus
Insulin Resistance		None.
Other		None.

Farkas GJ et al, J Personalized Med, 2022.

Metabolic Syndrome in Veterans with SCI?

- N = 473 veterans with SCI
- Age: 56.0 ± 13.1 y
- 49.6% tetraplegia

- Obese
  - 26.9% BMI ≥ 30 kg/m^2
  - 76.7% BMI_{SCI} > 22 kg/m^2
- 69.7% HDL-c < 40 ♂/ < 50 ♀ mg/dL or Dx
- 37.2% TG > 150 mg/dL or Dx
- 49.8% FBG > 100 mg/dL or Dx
- 55.1% HTN or Dx

- **57.5% IDF Metabolic Syndrome**

Research Article

Prevalence of metabolic syndrome in veterans with spinal cord injury

David R. Gater Jr.[1], Gary J. Farkas[1], Arthur S. Berg[2], Camilo Castillo[3]

[1]Department of Physical Medicine and Rehabilitation, Penn State College of Medicine, Hershey, Pennsylvania, [2]Department of Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania, [3]Division of Physical Medicine and Rehabilitation, Department of Neurosurgical Surgery, University of Louisville School of Medicine, Louisville, Kentucky

Metabolic Syndrome in SCI?

- n=72, C5-L2 motor complete SCI
  - 59 males, 13 Females
  - 72.2% paraplegia
- Age: 44.4 ± 11.3 y
- Time Since Injury: 14.4 ± 11.0 y
- BMI: 27.3 ± 5.9 kg/m^2

- Obesity
  - 82% BMI_{SCI} > 22 kg/m^2
  - 97% by 4C model %BF (> 22%BF ♂ or > 35%BF ♀)
- Dyslipidemia or Rx (83%)
  - 83% All
  - 85% HDL-c < 40 mg/dL for men
  - 77% HDL-c < 50mg/dL for women
- Dysglycemia/T2DM or with Dx
  - 32% FBG > 100 mg/dL
- Hypertension
  - 43% SBP ≥ 130 or DBP ≥ 85 mmHg or Rx

ASIA
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Rehabilitation Care
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For the Miami Project to Cure Paralysis

Body Composition and Metabolic Assessment After Motor Complete Spinal Cord Injury: Development of a Clinically Relevant Equation to Estimate Body Fat

David R. Gater, Jr, MD, PhD, MS,[1,2] Gary J. Farkas, PhD,[1] David R. Dolbow, DPT, PhD,[3] Arthur Berg, PhD,[4] and Ashraf S. Gorgey, PhD[5]

- **IDF Metabolic Syndrome**
  - **59.4% by 4C model %BF**
  - **55.7% by BMI_{SCI} > 22 kg/m^2**

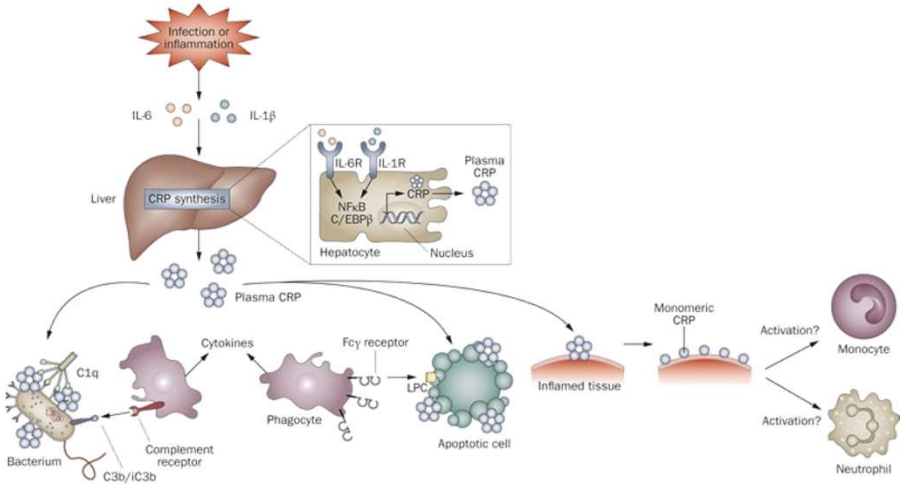
Adipocytes are Proinflammatory

- Adipocytes secrete
  - Proinflammatory adipokines (cytokines)
  - Anti-inflammatory adipokines (cytokines)
  - Other factors

- Systemic inflammation
  - PIC → ↑ nuclear factor κ β (NFκβ) → C-reactive protein (CRP)
  - CRP → ↓ nitric oxide → vasoconstriction
  - ↑ leukocyte adhesion
  - Endothelial cell apoptosis

- Mediate cardiometabolic dysregulation
  1. Hypertension/vascular dysfunction
  2. Dyslipidemia
  3. Dysglycemia/insulin resistance

→ ↑ cardiometabolic risk

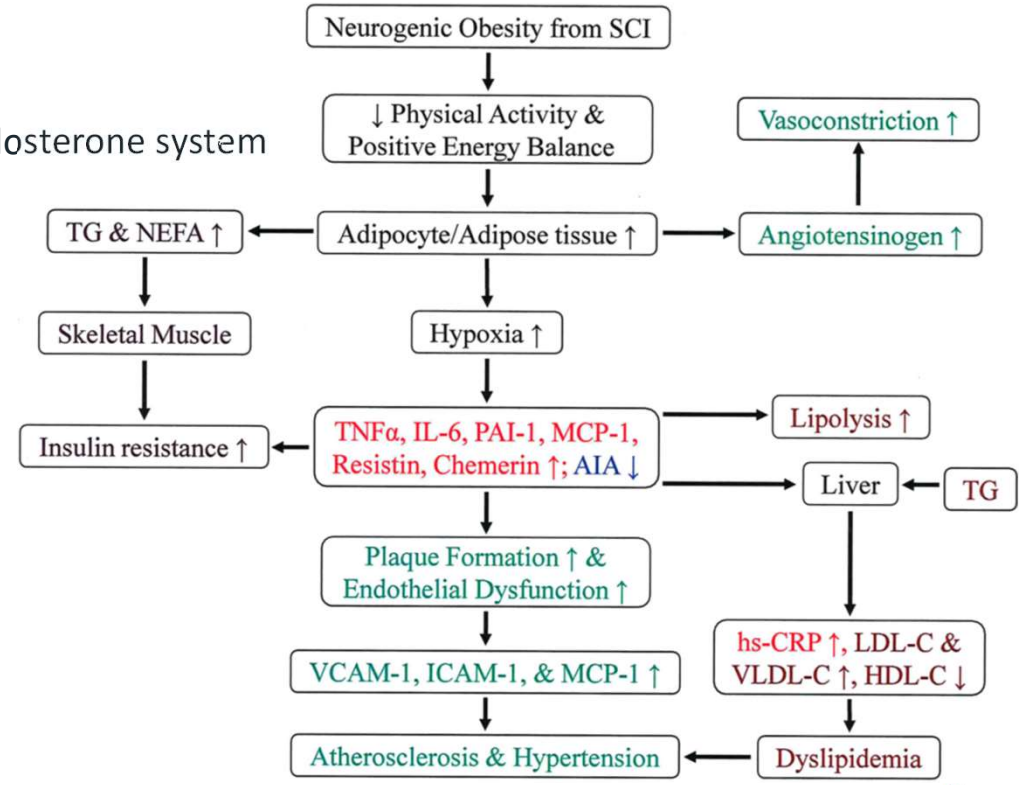


Rhodes et al, Nat Rev Rheumatol, 2011

Farkas et al , JSCM, 2018; Chen J et al, Diabetes Care, 2004; Kriketos et al, Diabetes Care, 2004; Devaraj et al, Circulation, 2003

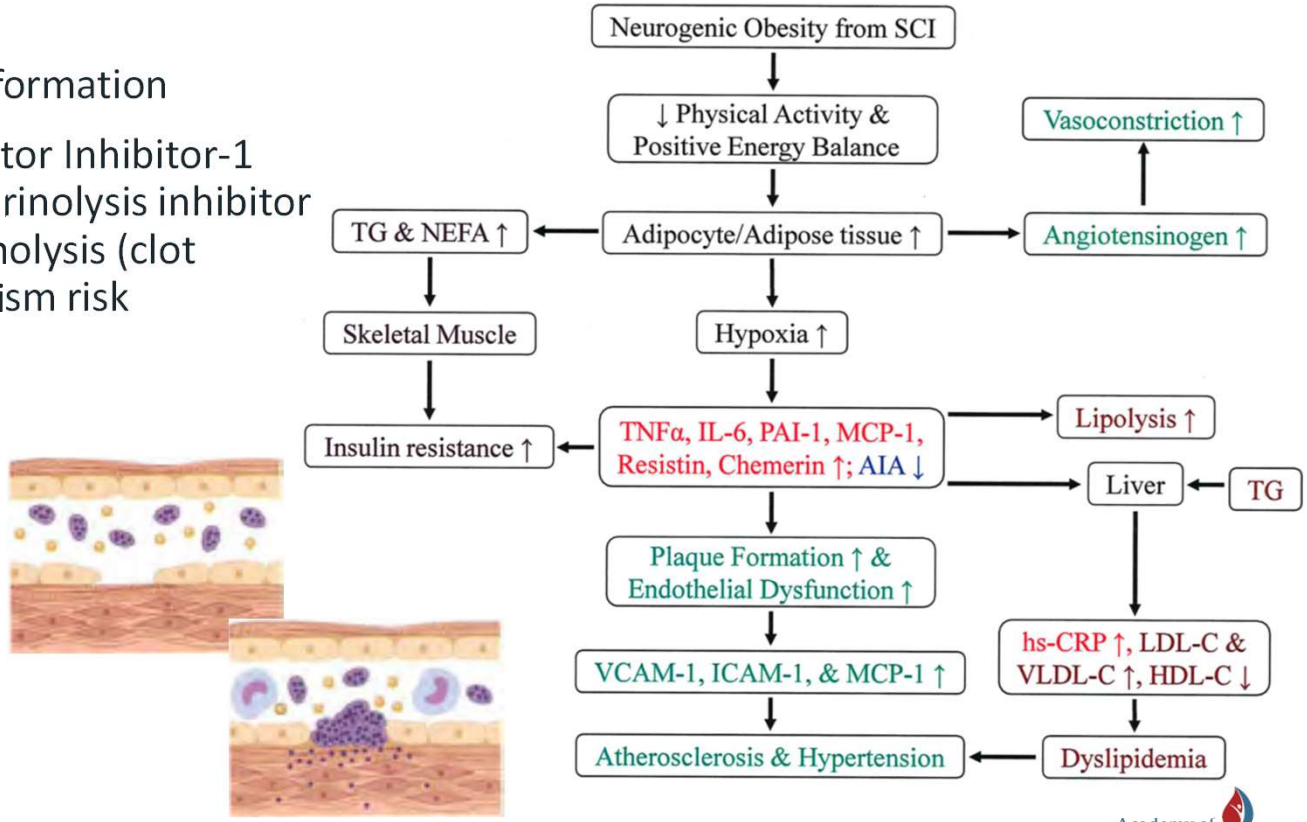
1. Adipocytes Mediate Hypertension

- Adipocytes
  - Angiotensinogen → triggers renin-angiotensin-aldosterone system → systemic vasoconstriction
  - IL-6 → CRP → ↓ NO → ↓ vasodilation
  - ICAM-1, VCAM-1, MCP-1
- Excess body fat → adrenal compression (RAAS)
- Atherogenesis
  - Poor Compliance Arterioles



Adipocytes Impair Fibrinolysis

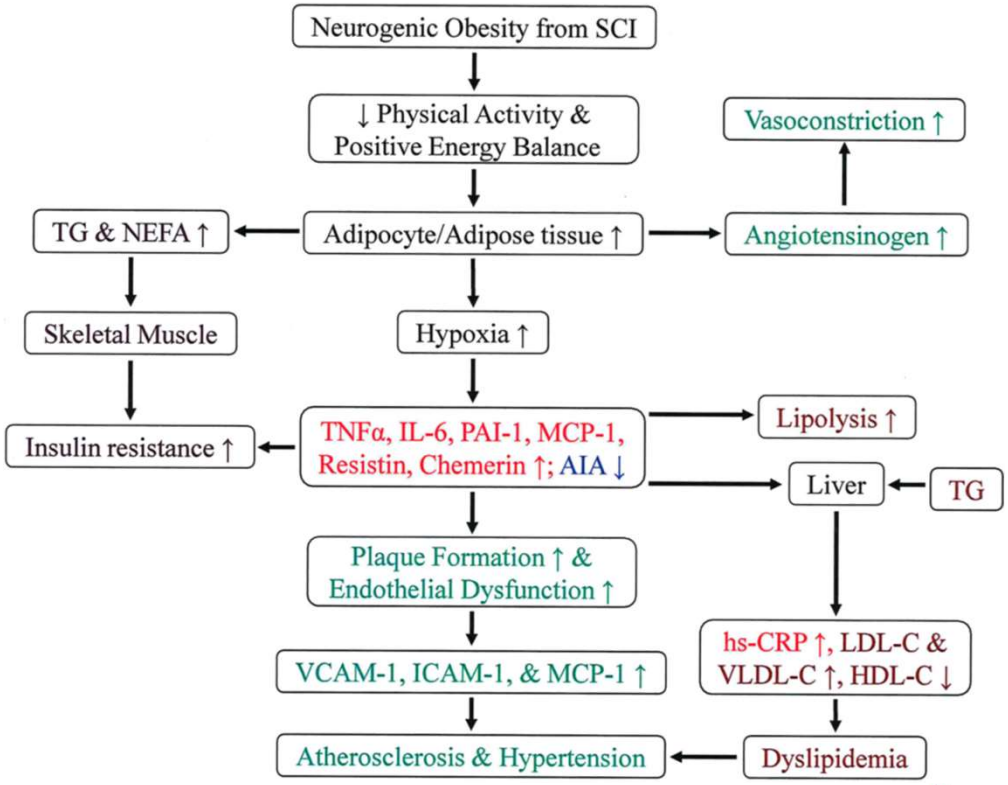
- Adipocytes → prevent thrombus formation
- Adipocytes → plasminogen activator Inhibitor-1 (PAI-1) & thrombin-activatable fibrinolysis inhibitor (TAFI) → TAFI & PAI-1 impair fibrinolysis (clot breakdown) → ↑ thromboembolism risk



Aso et al, Diabetes Care, 2005

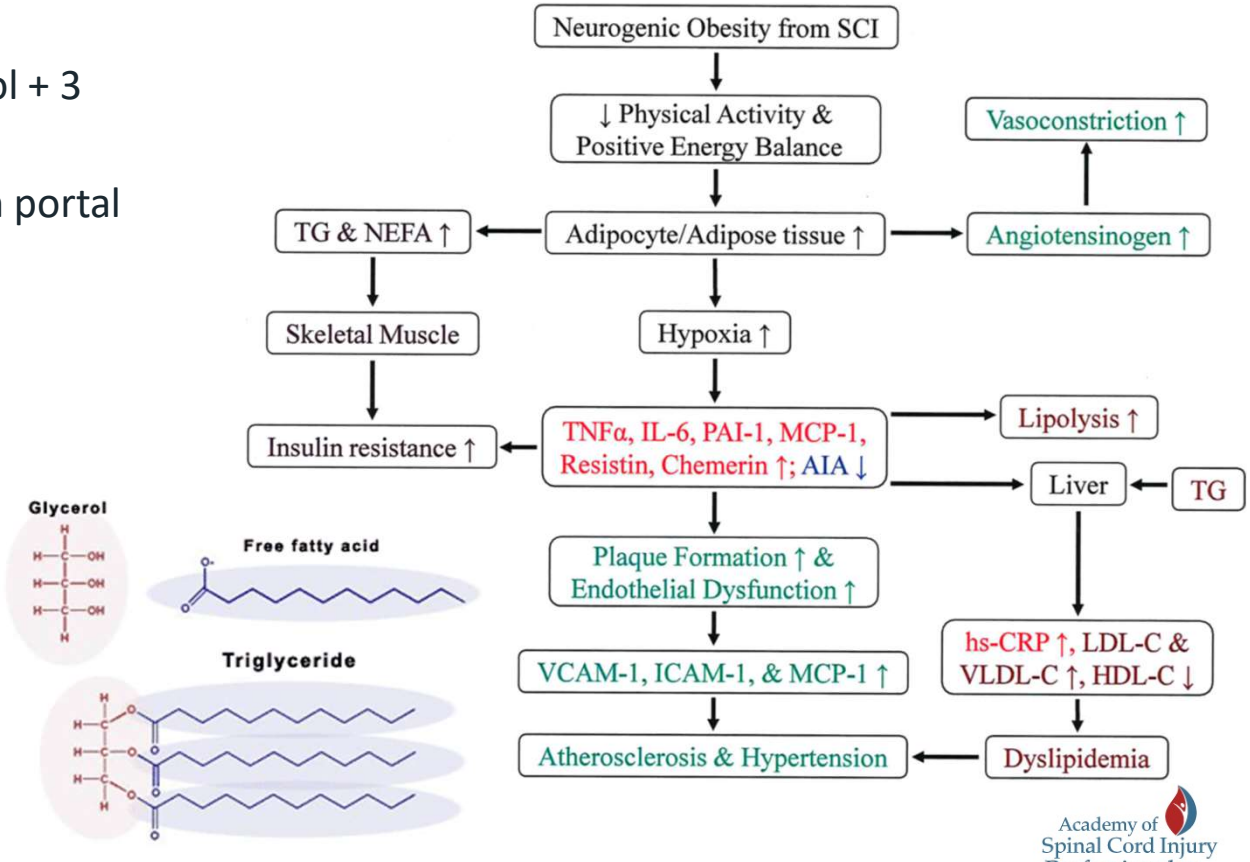
Hypertension/Vascular Inflammation in SCI

- Weaver et al, AJPMR, 2007
  - Hypertension?
  - n=7,959 veterans with SCI/D
  - 39% BP 120/79-139/89
  - 3% BP >140/90
- Manns et al, APMR, 2005
  - Abdominal sagittal diameter associated with CRP in SCI
- Frost et al, APMR, 2005
  - ↑CRP in SCI vs. Controls
- Lee et al, JSCM, 2005
  - CRP elevated in SCI
  - CRP ↑ in those with metabolic syndrome



2. Visceral Adipocytes Mediate Dyslipidemia

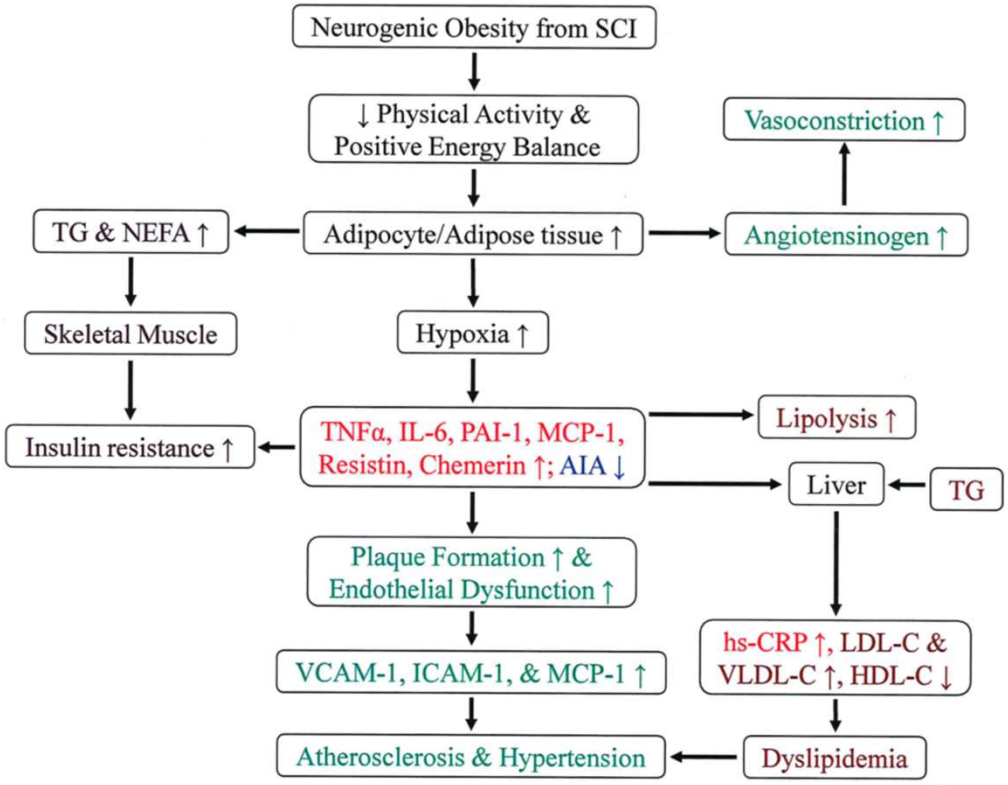
- Adipocytes → triglycerides → glycerol + 3 non-esterified fatty acids (NEFA)
- Adipocytes → NEFA → accumulate in portal circulation → liver overwhelmed → cholesterol dysregulation
  - ↑ LDL-c
  - ↑ VLDL-c
  - ↓ HDL-c



Farkas, Gater, JSCM, 2018

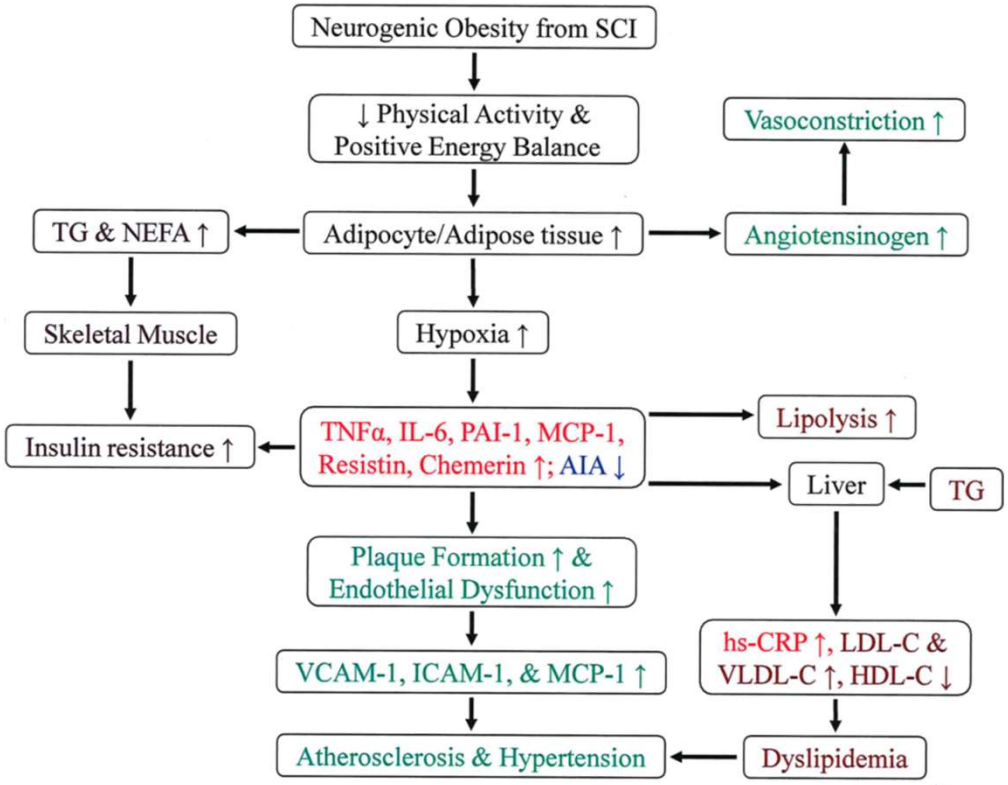
Dyslipidemia in SCI

- Bauman et al, Paraplegia, 1992
  - Tetraplegia: TC: 188, HDL-c: 40±1
  - Paraplegia: TC: 191, HDL-c: 37±1
  - AB Controls TC: 210, HDL-c: 48±2
- Zlotolow et al, J Am Paraplegia Soc, 1992
  - Serum HDL-c, SCI veterans 35±2 vs. age-matched AB 49±2
- Tharion et al, Spinal Cord, 1998
  - ↓ HDL in 58% with SCI
  - ↑ TC in 2% with SCI
- Bauman & Spungen, TSCIR, 2007
  - 63% SCI had HDL < 40mg%
  - 44% SCI had HDL < 35 mg%
  - 19% SCI had HDL < 30mg%
- Gater et al, JSCM, 2019 (n=477 veteran, 50% tetra)
  - 69.7% HDL < 40 mg%
- Gater et al, TSCIR, 2021 (n=72, 72% para)
  - ♂: 85% HDL-c < 40 mg%
  - ♀: 77% HDL < 50mg%



3. Adipocytes Mediates Insulin Resistance

- Adipocytes → ↑ IL-6 + TNF-α → SOCS → ↓ PI3K → ↓ glucose uptake → IR
- Adipocytes → ↑ NEFA → deposited in muscle, liver, pancreas → ↓ SI → IR
- Resulting CRP ↑ associated with insulin resistance
- PI-3 kinase cascade inhibition
  - Fatty acyl CoA
  - Diacylglycerol
  - Ceramides



Chen et al, Diabetes Care, 2004

Adipocytes Cause Insulin Resistance

A. Adipocyte → NEFA → FA metabolites → PKC → serine/threonine kinases → ↓ insulin signaling

B. Adipocyte → proinflammatory adipokines → ↓ insulin signaling

C. Adipocyte Tissue Macrophages (ATM) → ↑ proinflammatory cytokines → ↓ insulin signaling & glucose uptake

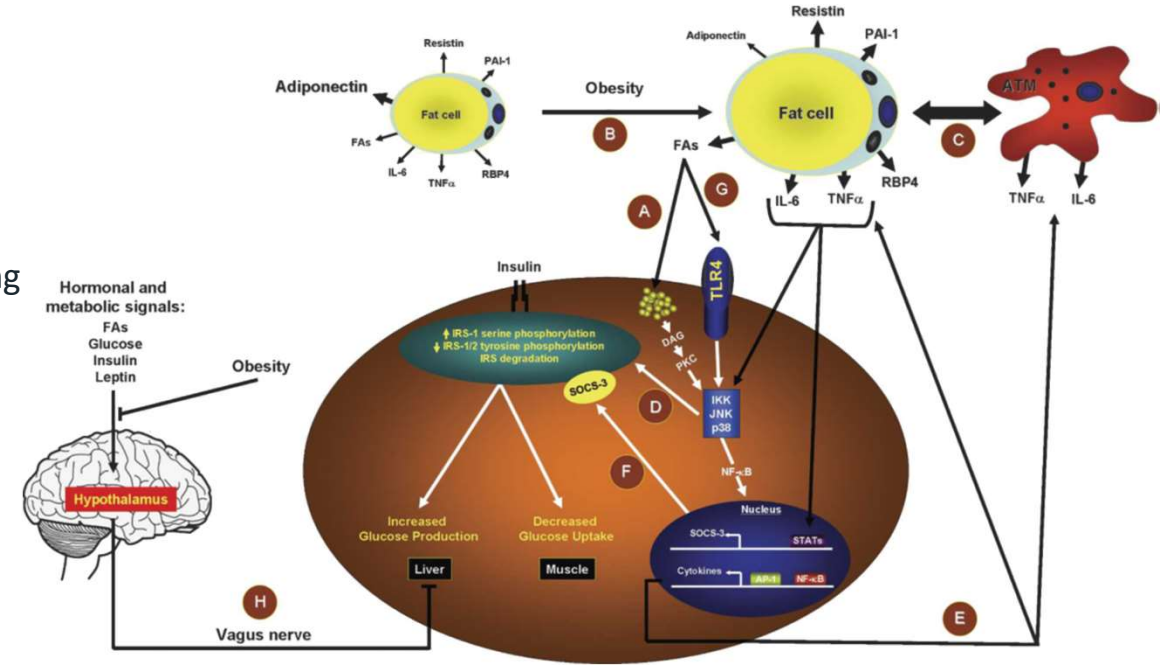
D. Adipocyte → FA metabolites & adipokines → ↑ → kinases (JNK, IKK, p38 MAPK) → ↓ IRS-1 & IRS-2 → ↓ insulin signaling

E. NFκB → ↑ proinflammatory cytokines → ↓ insulin signaling

F. Adipocyte → ↑ proinflammatory cytokines → SOCS proteins → ↓ insulin signaling

G. Adipocyte → FA → ↑ TLR4 → ↓ insulin signaling

H. CN X → ↑ gluconeogenesis

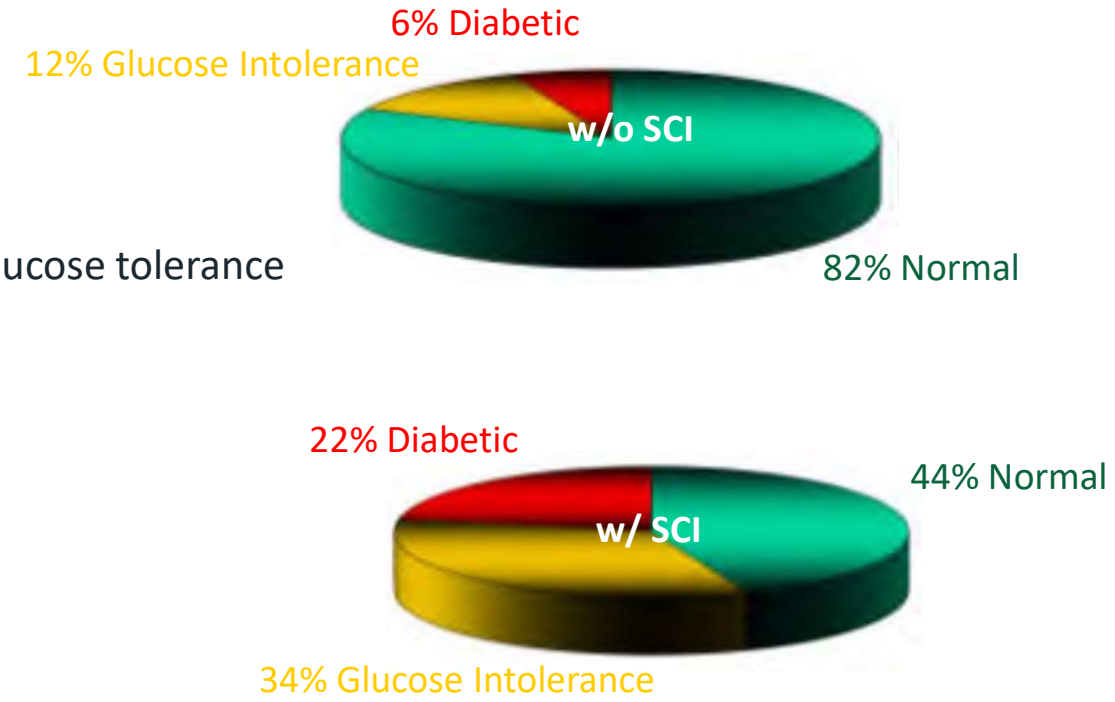


Qatanani et al, Genes Dev, 2007

Chen et al, Diabetes Care, 2004

Dysglycemia/Glucose Intolerance in SCI

- Bauman & Spungen, 1994
  - 34% SCI, impaired glucose tolerance
  - 22% SCI, diabetes
- Bauman et al, Spinal Cord, 1999; impaired glucose tolerance
  - 73% Tetra Complete
  - 44% Tetra Incomplete
  - 24% Para Complete
  - 31% Para Incomplete
- LaVela et al, JSCM, 2006
  - 20% diabetes (self-report) in SCI/D veterans

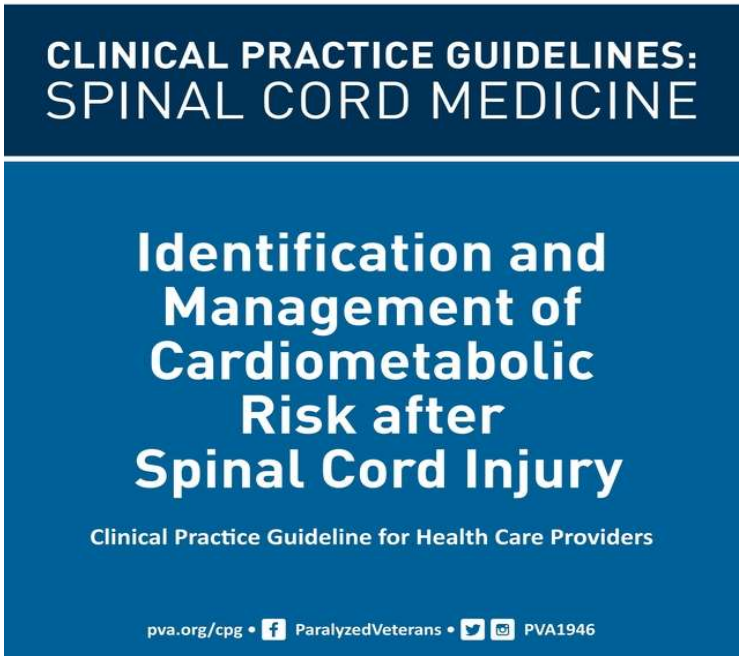


Cardiometabolic Risk after SCI

- Cardiometabolic Risk
  - Obesity
  - Pre-diabetes & Diabetes
  - Hypertension
  - Dyslipidemia
- Recommendations
  - Nutrition
  - Physical Activity
  - Pharmacotherapy

Paralyzed Veterans of America

consortium for SPINAL CORD MEDICINE CLINICAL PRACTICE GUIDELINES



Nash et al, JSCM, 2019

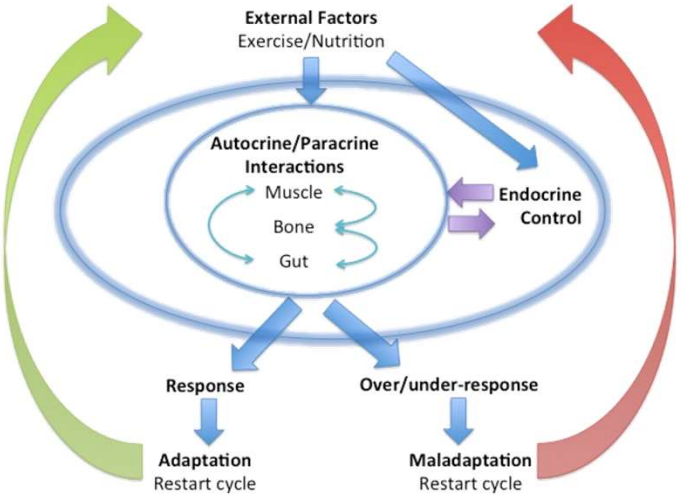
Management of Metabolic Syndrome & its Component Risk Factors

- Diet and Exercise → ↓ Obesity
- Sibutramine (Withdrawn, CV Events)
  - Appetite suppressant
  - ↓ (inhibit) norepinephrine reuptake (serotonin-norepinephrine reuptake inhibitor)
  - Like tricyclic antidepressants (SSRI)
- Noradrenergic drugs
  - Phentermine, Diethylpropion, Phendimetrazine, Benzphetamine
  - Used for short-term (~12 weeks)
  - ↓ (inhibit) noradrenaline synaptic reuptake → ↑ adrenergic stimulus
  - Dangerous in SCI
- Orlistat
  - ↓ (inhibit) pancreatic lipase (for fat digestion)
  - ↓ (blocks) intestinal lipid absorption → ↑ weight loss
- Antihypertensives
  - Thiazide-type diuretic, Ca channel blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker (ARB) in non-black population
  - Thiazide-type diuretic or Ca channel blocker in black population
- Lipid-lowering agents
  - Statins (e.g., rosuvastatin 10-20 mg/d)
- Insulin Resistance / Dysglycemia
  - Metformin (Biguanide)
    - 1st tx line
    - ↑ hepatic insulin sensitivity
      - ↓ Hepatic gluconeogenesis & glycolysis
    - ↑ Muscle GLUT4 & glycogenesis
  - Glitazones (Thiazolidinediones: Avandia)
    - ↑ insulin sensitivity @ liver, muscle, fat → ↑ glucose uptake & ↓ hepatic output
    - ↑ HDL-c, ↓ LDL-c & TG

Endocrine Responses in SCI

Catabolic Hormones after SCI

- Blunted catecholamine (E, NE, dopamine) response
- Blunted corticosteroid release
- ↓ glucagon release



Anabolic Hormones after SCI

- Blunted growth hormone & somatomedin response
- Blunted testosterone release
- Blunted (?) erythropoietin release
- Insulin resistance ↑ with exercise

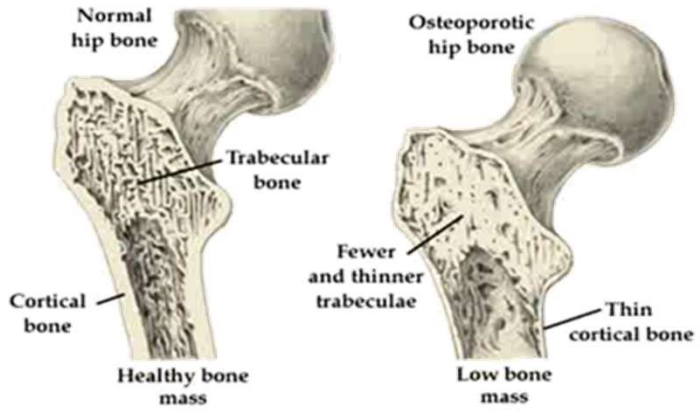
Anabolism with SCI

- ↓ Testosterone after SCI
  - Kostovski et al, Spinal Cord, 2008 (n=6)
  - Schopp et al, AJPMR, 2006 (n=92)
    - Age, Hct, & TSI ≈ Testosterone
- Testosterone replacement therapy
  - Bhasin et al, J Clin Endocrinol Metab, 2006
    - CPG on TRT
  - Nash & Gater, 2007
    - TRT to optimize exercise training if deficient
    - Muscle Mass: Protein Stores
  - Clark et al, 2008
    - TRT ≈ motor recovery incomplete sci
- Cautions
  - Contraindications
    - Benign prostatic hyperplasia
    - Prostate & breast cancers
  - May ↓ endogenous testosterone production
  - May ↓ HDL-c, ↑ LDL-c

Bone & Bone Metabolism after SCI

- Hormones
  - ↓ anabolic (T, E2, GH)
  - ↑ parathyroid hormone
  - Thyroid → ↓ calcitonin
- Obesity-related cytokines
  - IL-1, IL-6, TNF-α
  - Stimulate osteoclastic activity

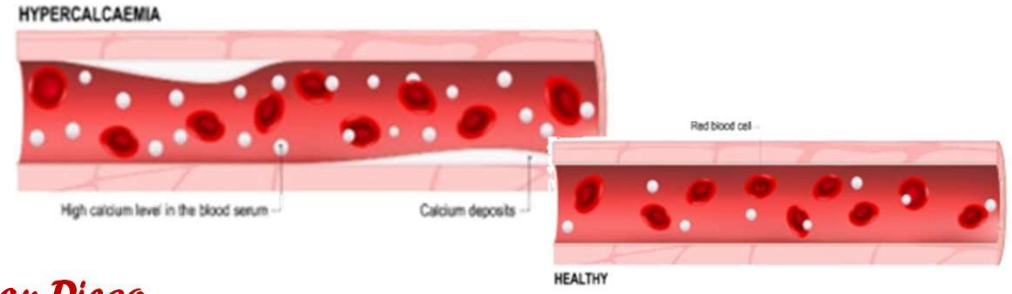
- Neuronal Changes
  - ↓ afferent signal conduction
  - Sympathetic blunting
    - Mechanical unloading →↓ adrenergic receptors in bone
    - Sympathetic blunting →↓ vascular perfusion
    - AD → stimulates osteoclasts



Immobilization Hypercalcemia

Etiology & Pathophysiology

- Paralysis → sudden/profound immobilization → mechanical unloading → immobilization hypercalcemia
  - Mechanism poorly understood
- ↓ muscle activity → ↓ bone mech. stimulus → ↑ osteoclast bone resorption → hypercalcemia
- ↑ Ca → ↓ PTH → ↑ [phosphate] → ↓ Vit,25-dihydroxy vitamin D synthesis
- Ca resorption → develops within 1st week, continues for 6-18 months post-injury
- Dangers: untreated → Ca deposit in kidneys (nephrocalcinosis)



Signs & Symptoms

- Insidious, be suspicious
- No association with LOI
- Serum [Ca] > 11.5-12 mg/dL
- S/S
  - Fatigue
  - Lethargy
  - Apathy
  - Abdominal pain
  - Constipation
  - Anorexia
  - Nausea
  - Vomiting
  - Polydipsia, polyuria
  - Dehydration

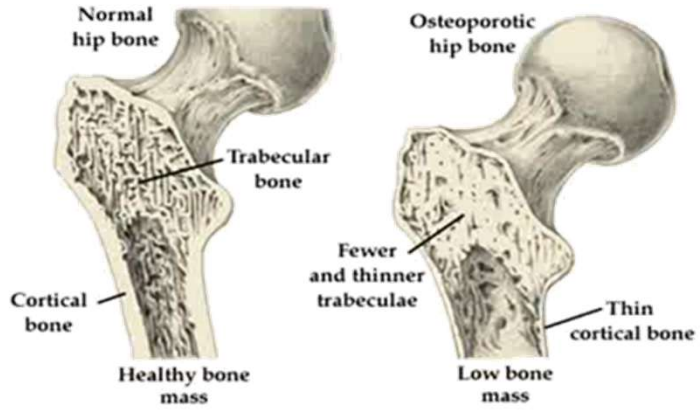
Immobilization Hypercalcemia Management

- Management
  - Calcitonin – 1st line, temporary ↓ activity
  - IV normal saline (100-150 cc/h) → volume repletion & hydration → diuresis
  - IV normal saline w/ or w/o furosemide as needed and/or pamidronate (30-90 mg IV over 4-24 hrs) (both bisphosphonates) → ↓ osteoclast-mediated resorption via ↓ osteoclast viability → ↓ bone breakdown
  - Mithramycin – blocks osteoclastic function
- Important Considerations
  - Don't ↓ Ca intake → ↓ Vit D → ↓ Ca intestinal absorption
  - Monitor K, hypokalemia can develop with management
- Osteopenia & Osteoporosis

Osteoporosis in SCI & Treatment

Osteoporosis in SCI is due to a combination of…

- Mechanical Unloading
- Hormonal Deficiency
- Impaired Neural Signaling
- Obesity-related cytokines

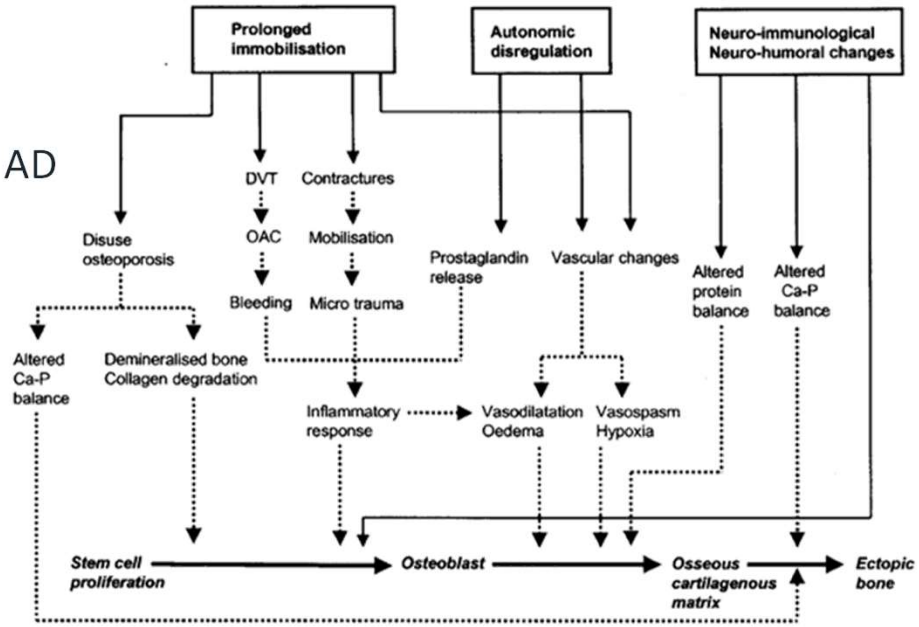


Optimal treatment strategies have yet to be fully characterized

- Likely will include a combination of:
  - Mechanical loading
  - Diet 1st → Vit D / Ca supplements
  - Bisphosphonates
  - ↓ obesity

Neurogenic Heterotopic Ossification

- Defined as formation of extraskeletal mature, lamellar bone in soft tissues (i.e., muscle)
- S/S: Pain, ↓ROM, swelling/warmth, fever, spasticity, AD
- Etidronic acid (etidronate)
  - Class of bisphosphonate
  - 20 mg/kg/d PO x 3 months
- Special Considerations
  - Normal creatine phosphokinase → etidronic acid 10 mg/kg/d PO x 3 months
  - ↑ creatine phosphokinase → etidronic acid + NSAID



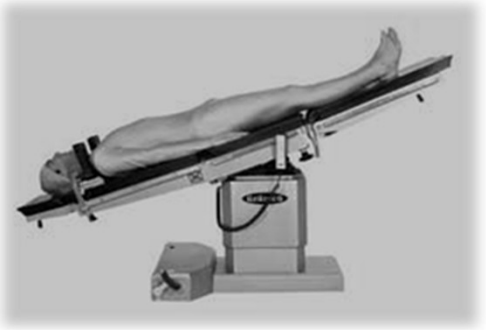
Cardiovascular Dysfunction in SCI

Learning Objectives

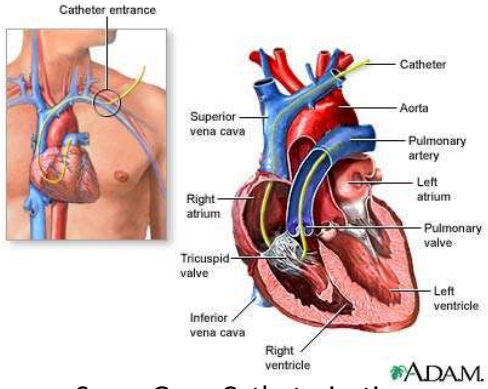
- At the conclusion of the *endometabolic dysfunction* presentation, the learner will:
  - Briefly review SCI and its comorbidities
  - Describe the causal relationship between energy metabolism, obesity, metabolic syndrome and endocrine Dysfunction
  - Review anabolic and catabolic dysfunction after SCI
- At the conclusion of the *cardiovascular dysfunction in SCI* presentation, the learner will:
  - Review the neurogenic consequences of SCI on cardiovascular function
  - Discuss risks of VTE/PE following SCI, including prophylaxis and management
  - Review risk factors for coronary artery / peripheral arterial disease following SCI
- At the conclusion of the *nutrition and immune dysfunction after sci* presentation, the learner will:
  - Review the neurogenic consequences of SCI on metabolism and body composition
  - Discuss energy balance and components required to promote fat loss
  - Review immunological consequences of SCI and management concerns

Neurogenic Hypotension

- Hypovolemic shock
  - Hypotension
  - Hypothermia
  - Tachycardia
- Neurologic shock
  - Hypotension
    - Judicious fluids to prevent neurogenic pulmonary edema
    - Trendelenburg positioning
  - Vasopressors with Swan-Ganz cathing & monitoring (MAP>85)
    - Dopamine 2.5-5 ug/min (α & β1-agonist)
    - Levophed 0.01-0.2 ug/min
- Hypothermia
- Bradycardia
  - Atropine
  - Temporary cardiac pacing



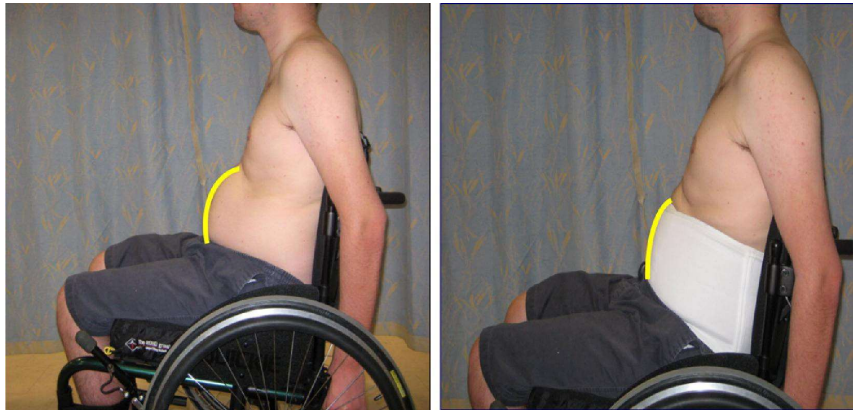
Trendelenburg positioning



Swan-Ganz Catheterization

Neurogenic Hypotension

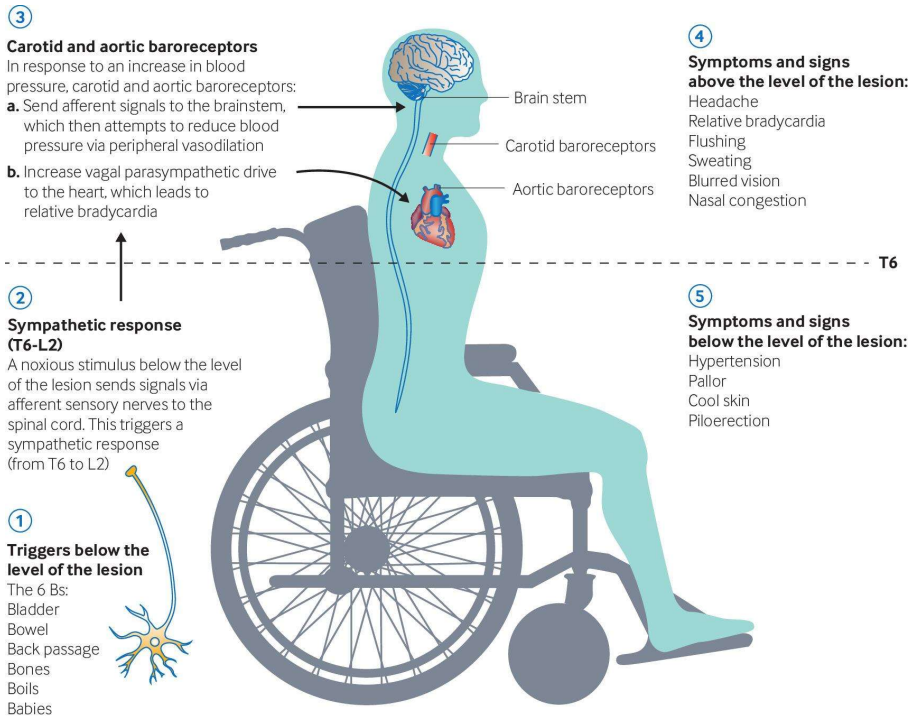
- Gradual incline
  - Recline wheelchair
  - Tilt table (therapy)
- Mechanical support
  - Abdominal binder
  - Elastic Stockings
  - Adequate Hydration
- Pharmacological Interventions
  - Salt tablets 1g qid
  - Ephedrine 20-30 mg qid
  - Midodrine Chloride 2.5-10 mg tid
  - Fludrocortisone 0.05-0.1 mg qid



Wadsworth BM et al. Arch Phys Med Rehabil, 2012.

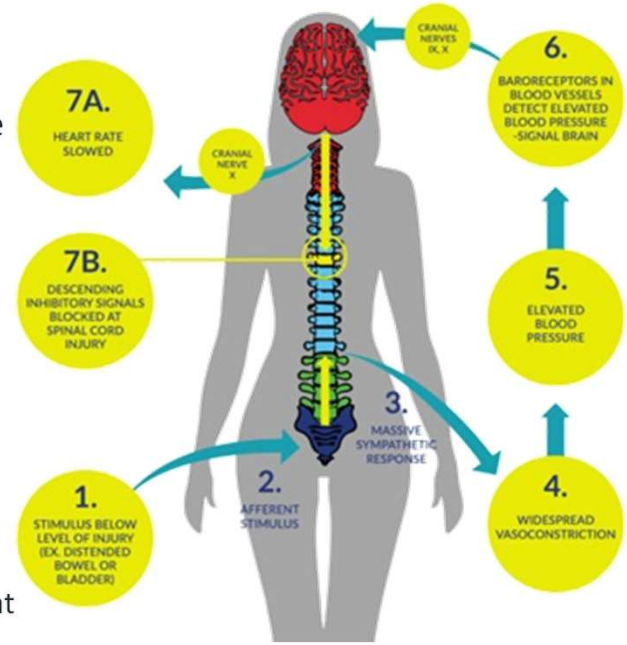
Autonomic Dysreflexia (AD)

- Anthony Bowlby first reported in 1890
- Definition: Massive sympathetic outflow in response to strong/noxious stimuli below the level of SCI in lesions above T6 (sometimes T7 or T8)
- Complications
  - Cerebrovascular accident
  - Seizures
  - Organ failure
  - Death



Autonomic Dysreflexia

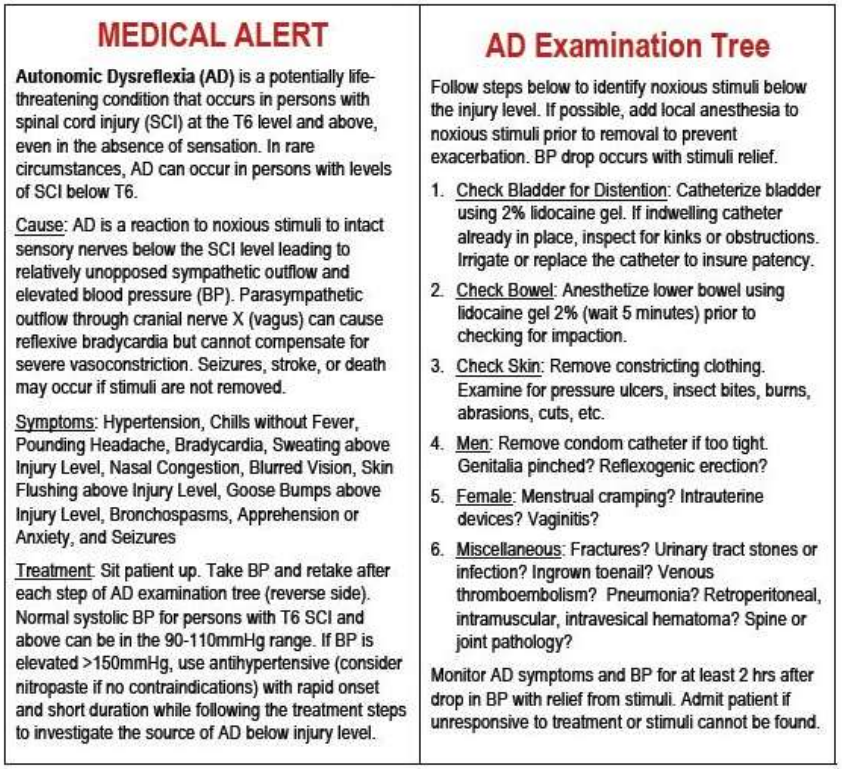
1. Strong sensory input (not necessarily noxious)
   - 6 Bs: bowel (#1), bladder (#2), back passage, bones, boils, babies
2. Strong sensory input → carried to SC via afferent fibers
3. Sensory input travels up SC below LOI → evokes a massive (reflex) sympathetic surge from thoracolumbar sympathetic nerves (≈T 6 to L2) →
4. Sympathetic surge → causes widespread vasoconstriction, most significantly in the sub-diaphragmatic vasculature ("splanchnic bed"/foregut – celiac trunk).
5. Widespread peripheral vasoconstriction → peripheral arterial hypertension
6. Carotid & aortic baroreceptors detect ↑ BP → afferent signal sent via CN 9 & 10 (reflex) to brainstem to detect this hypertensive crisis
7. Brain does 2 maneuvers to ↓ BP
   A. Brain → ↑ afferent signal via CN 10 to ↓ HR → ↑ relative bradycardia* → ↓ peripheral BP
      - This compensatory bradycardia (*not always present) is inadequate → hypertension continues
   B. Brain → sends descending inhibitory impulses → ↓ sympathetic surge → because of SCI at or above T6 most impulses are unable to traverse most sympathetic outflow levels → inhibitory impulses are blocked in SC
8. ↑ sympathetic outflow → ↑ sweating & vasodilation (flushed, red cheeks) ↑ LOI



Autonomic Dysreflexia Sign & Symptoms

- Summary:
  - ↓ LOI sympathetic NS prevail
  - ↑ LOI parasympathetic NS prevail
  - Inciting stimulus removed → reflex hypertension resolves

- Signs/Symptoms
  - Slowed pulse, chest tightness, anxiety
  - ↑ LOI: headache, bradycardia, flushing, sweating, blurred vision, seeing spots, nasal congestion
  - ↓ LOI: sudden hypertension, pallor, cool skin, piloerection



MEDICAL ALERT

Autonomic Dysreflexia (AD) is a potentially life-threatening condition that occurs in persons with spinal cord injury (SCI) at the T6 level and above, even in the absence of sensation. In rare circumstances, AD can occur in persons with levels of SCI below T6.

Cause: AD is a reaction to noxious stimuli to intact sensory nerves below the SCI level leading to relatively unopposed sympathetic outflow and elevated blood pressure (BP). Parasympathetic outflow through cranial nerve X (vagus) can cause reflexive bradycardia but cannot compensate for severe vasoconstriction. Seizures, stroke, or death may occur if stimuli are not removed.

Symptoms: Hypertension, Chills without Fever, Pounding Headache, Bradycardia, Sweating above Injury Level, Nasal Congestion, Blurred Vision, Skin Flushing above Injury Level, Goose Bumps above Injury Level, Bronchospasms, Apprehension or Anxiety, and Seizures

Treatment: Sit patient up. Take BP and retake after each step of AD examination tree (reverse side). Normal systolic BP for persons with T6 SCI and above can be in the 90-110mmHg range. If BP is elevated >150mmHg, use antihypertensive (consider nitropaste if no contraindications) with rapid onset and short duration while following the treatment steps to investigate the source of AD below injury level.

AD Examination Tree

Follow steps below to identify noxious stimuli below the injury level. If possible, add local anesthesia to noxious stimuli prior to removal to prevent exacerbation. BP drop occurs with stimuli relief.

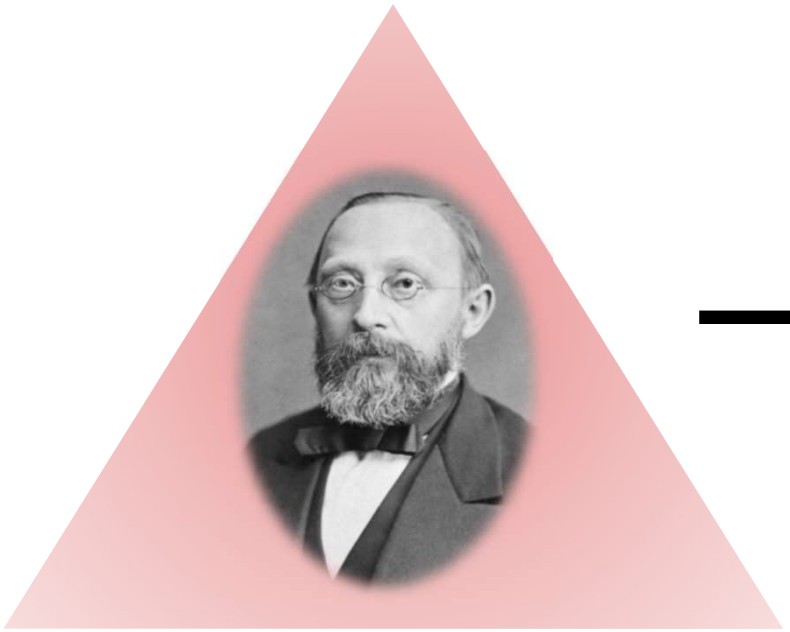
1. Check Bladder for Distention: Catheterize bladder using 2% lidocaine gel. If indwelling catheter already in place, inspect for kinks or obstructions. Irrigate or replace the catheter to insure patency.
2. Check Bowel: Anesthetize lower bowel using lidocaine gel 2% (wait 5 minutes) prior to checking for impaction.
3. Check Skin: Remove constricting clothing. Examine for pressure ulcers, insect bites, burns, abrasions, cuts, etc.
4. Men: Remove condom catheter if too tight. Genitalia pinched? Reflexogenic erection?
5. Female: Menstrual cramping? Intrauterine devices? Vaginitis?
6. Miscellaneous: Fractures? Urinary tract stones or infection? Ingrown toenail? Venous thromboembolism? Pneumonia? Retroperitoneal, intramuscular, intravesical hematoma? Spine or joint pathology?

Monitor AD symptoms and BP for at least 2 hrs after drop in BP with relief from stimuli. Admit patient if unresponsive to treatment or stimuli cannot be found.

https://msktc.org/sci/factsheets/autonomic-dysreflexia

Virchow's Triad (1856)

1. Venous Stasis



2. Hypercoagulability

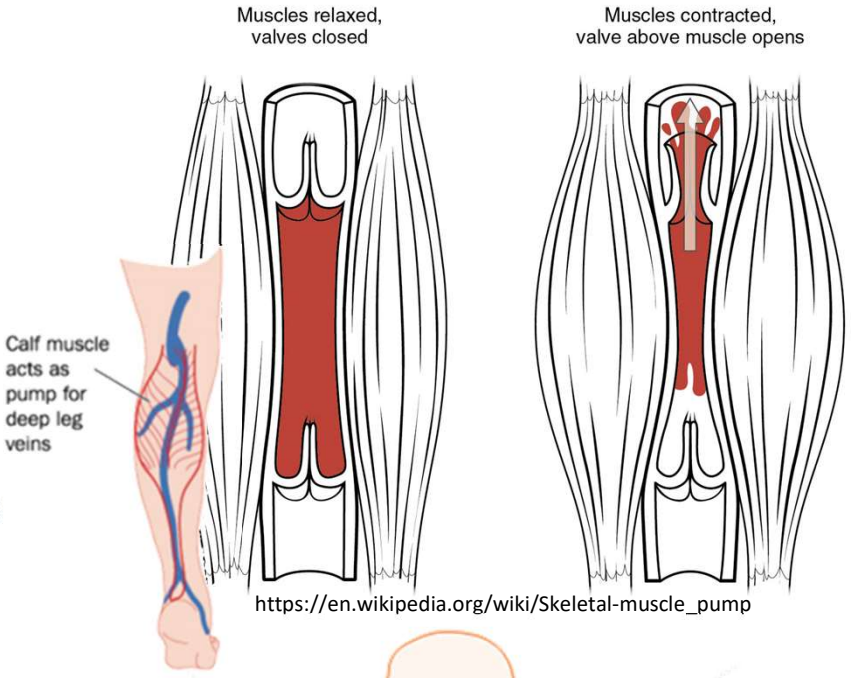
3. Vessel wall / endothelial damage

4. Venous Thrombosis (VT)
and/or
5. Pulmonary Embolism (PE)

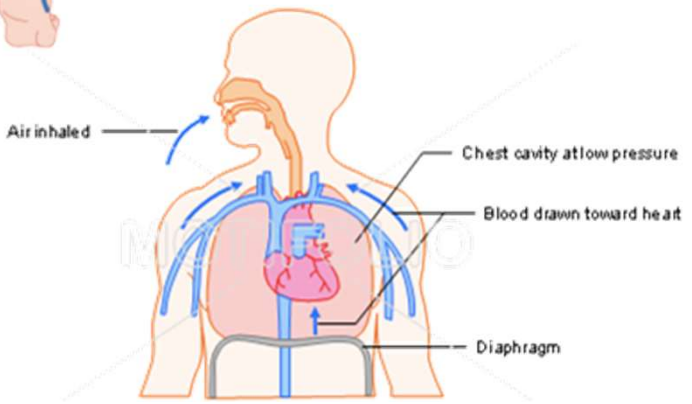
Kushner A et al, Virchow Triad. In: StatPearls [Internet]. Treasure Island (FL)

1. Venous Stasis in SCI

- Normal Venous Return
  - Muscle pump (positive pressure)
  - Respiratory pump (vacuum)
  - Smooth m. pump around veins – sympathetic constricts
- Following SCI
  - Chronic venous insufficiency
  - Impaired muscle pump (somatic disruption)
  - Venodilation (sympathetic blunting)
  - Impaired ventilation (somatic disruption)



https://en.wikipedia.org/wiki/Skeletal-muscle_pump

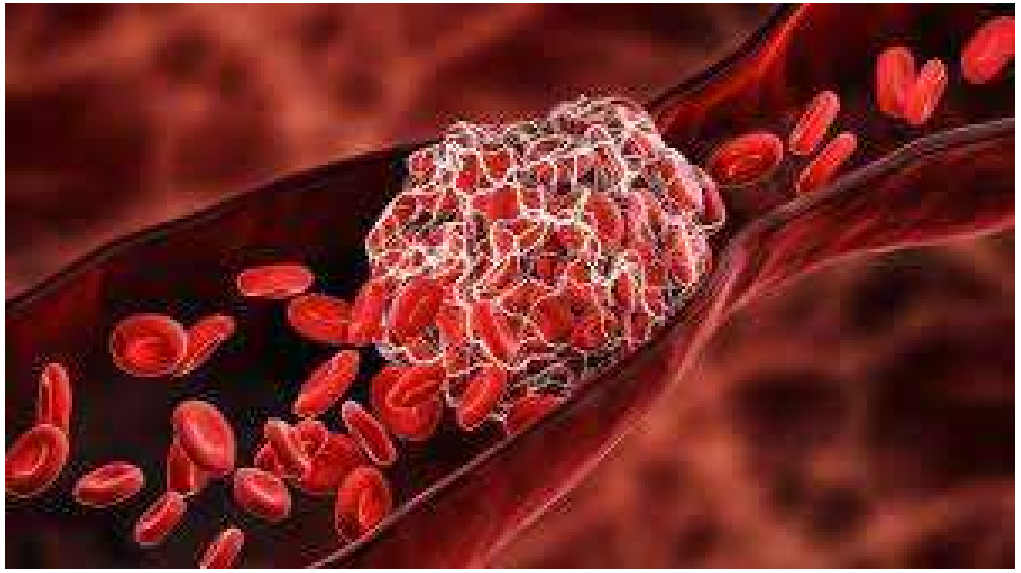


http://alignmentyoga.blogspot.com/2016/10/stuff-i-learned-7.html

2. Hypercoagulability in SCI

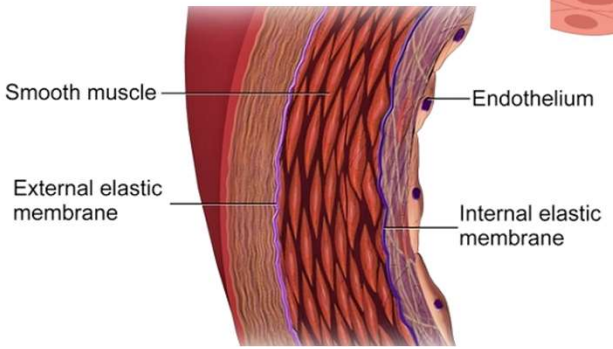
- Thrombophilia

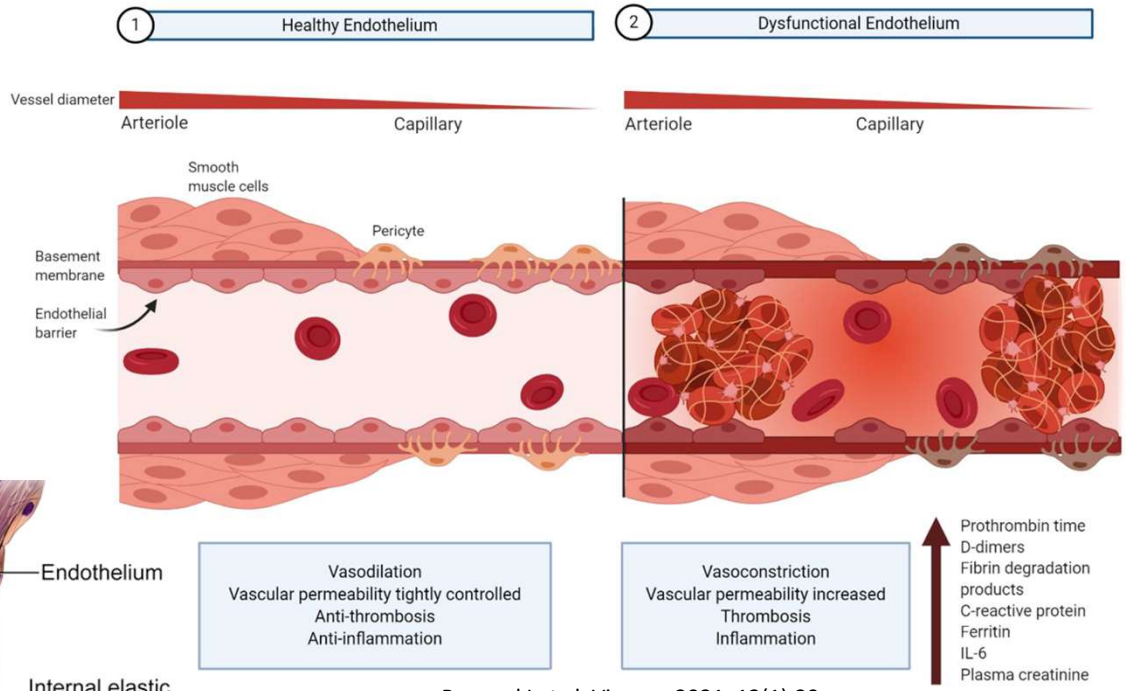
- ↑ Factor VIII:C
  - Procoagulant Glycoprotein
  - Hepatic production
- ↑ Factor VIII:Ag
  - Von Willebrand factor Ag
  - From Endothelial Cells
- ↑ Factor VIII:Ag to VIII:C
  - ↑ collagen-induced platelet aggregation
  - Thrombus formation



3. Vessel wall/Endothelial Damage

- Intimal and/or endothelial injury
- Trauma
  - Venipuncture
  - Fracture
- Inflammation
- Infection
- Tumor





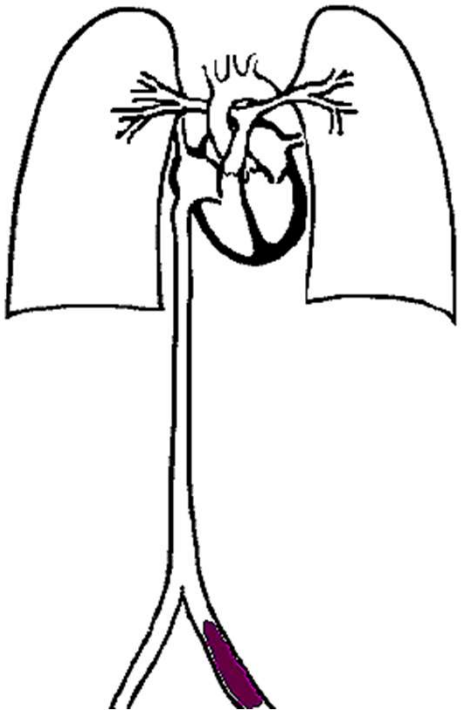
Bernard I et al, Viruses. 2021; 13(1):29.

4. Venous Thrombosis

- Venous thrombosis (deep venous thrombosis)
- Thrombosis
  - Blood clot attached to endothelial wall of deep veins
  - venous stasis → platelet aggregation → hypercoagulability → intimal injury
- Additional risk factors
  - Smoking
  - Oral contraceptives
  - Cancer, diabetes, fractures
- Symptoms
  - Thigh, calf, popliteal area pain
  - Lower extremity swelling
  - Tenderness, warmth, blushing, & vein thickening (cords)
  - + Homan sign (Squeeze test)
    - Knee flexion with passive dorsiflexion → pain in popliteal region
- Postphlebitic syndrome
  - Develops post-VT
  - Vein blood clot → chronic venous insufficiency

5. Pulmonary Emboli

- Thrombus dislodges from venous wall → "traveling" clot
- Emboli → inferior vena cava → R atrium → R ventricle → pulmonary a. (lodged) → O_2-rich blood flow through pulmonary v. is blocked
- Symptoms
  - Acute cough, SOB, chest pain
  - Tachycardia, Tachypnea
  - ↓ breath sounds, wheezing, friction rub
  - Syncope, cyanosis
  - Anxiety, restlessness, Δ mental status
- Differential Dx:
  - Pericarditis, MI, Heart Failure
  - Pleuritis, Pneumonia



VT/PE Diagnostic Workup

Venous Thrombosis

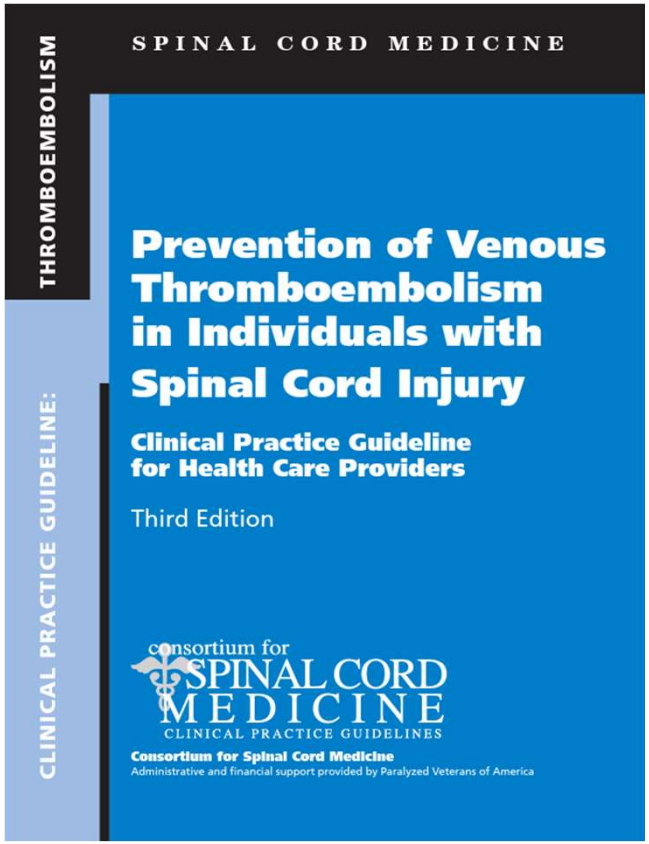
- Impedance Plethysmography
- Compression Ultrasound
- Venous Doppler Imaging
- Venography

Pulmonary Emboli

- Arterial Blood Gas (PaO_2< 80)
- Spiral CT
- Ventilation (V)/Perfusion (Q) scan
- Pulmonary Angiogram

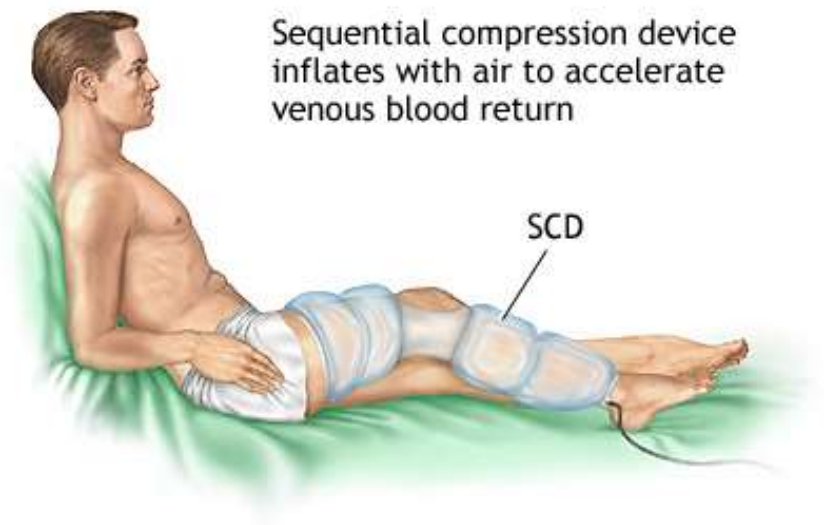
VT Prophylaxis (Revision 2016)

- Mechanical Prophylaxis
  - TED Hose (+/-)
  - Pneumatic Compression Devices (PCDs)
  - Inferior Vena Caval Filter - NOT recommended as 1° prophylaxis
- Anticoagulant prophylaxis
  - If NO bleeding risk
    - Low Molecular Weight Heparin
    - Direct Oral Anticoagulants (DOACs) – may be considered as thromboprophylaxis during acute SCI
    - Adjusted Dose Unfractionated Heparin – NOT recommended unless Low Molecular Weight Heparin is not available
    - Oral Vitamin K antagonists (warfarin) – NOT recommended in early, acute care setting
  - If bleeding risk
    - Assess risk daily and begin LMWH when appropriate
- Prophylaxis Duration
  - Uncomplicated incomplete & complete SCI → 8 weeks
  - Complete + Risk(s) → 12 weeks



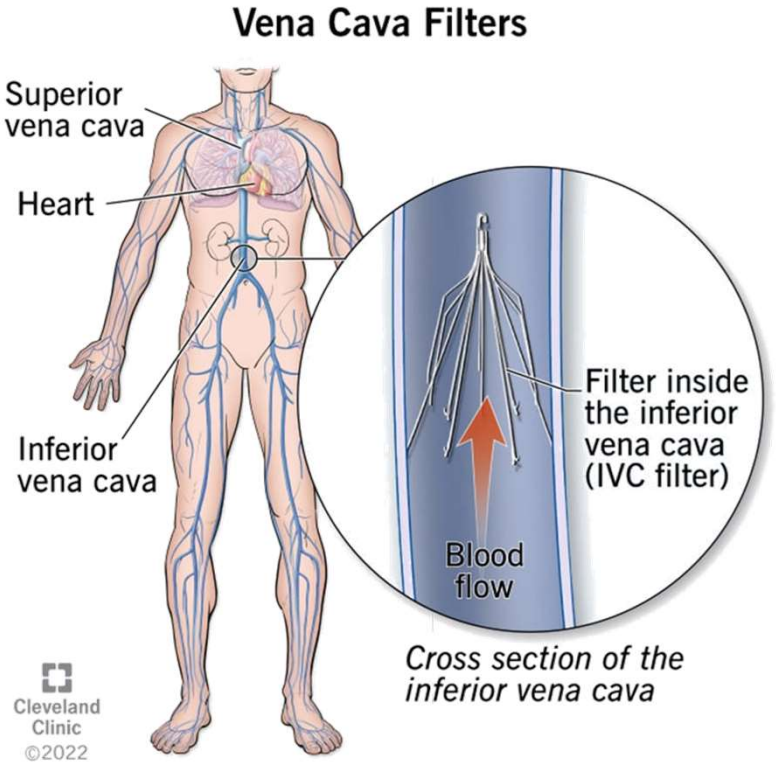
Sequential Compression Devices

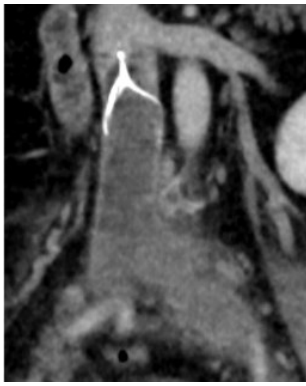
- TED (thromboembolic deterrent) hose: First 2 weeks
  - Thigh-high = knee-high
  - No literature to support independent efficacy
- Pneumatic Compression Devices (PCDs) → first 2 weeks
  - Blood expulsion from LE
  - ↑ antithrombin III
- Lower limb Doppler US → not recommended

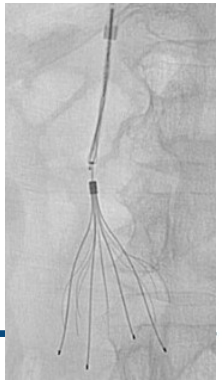


Inferior Vena Cava Filter

- NOT recommended as 1° prophylaxis
- Indications
  - Anticoagulants contraindicated
  - Recurrent PE despite anticoagulation
  - PE with hemodynamic compromise
  - Compromised cardiopulmonary function
  - Undergoing pulmonary embolectomy
- Complications
  - Prohibits “Quad” coughing
  - Lower extremity and IVC VT
  - Filter migration
  - Vena caval perforation







PVA Consortium Clinical Practice Guidelines, 2016

Anticoagulation Prophylaxis

- Low Molecular Weight Heparin
  - Enoxaparin: 30 mg SC q 12°
  - Dalteparin: 2500 IU SC qd
  - Alternatives (e.g., heparin-induced thrombocytopenia):
    - Argatroban
    - Lepirudin
- Unfractionated Heparin (low dose or adjusted-dose)
  - NOT recommended, unless Low Molecular Weight Heparin unavailable
  - SCI Injury Severity
    - Incomplete SCI: 5000 u SC q 12°
    - Complete SCI: 3500 u SC q 8 to Activated Partial Thromboplastin Clotting Time (aPTT)* 1.5-2x normal
- Warfarin: Not indicated

VT/PE Management

- Pharmacological treatment if USING Direct Oral Anticoagulants (DOAC)
  - Anticoagulation (w/o cancer)
    - Direct Oral Anticoagulants (DOAC; e.g., dabigatran, rivaroxaban, apixaban or edoxaban) > Vit. K antagonists
    - Vit. K antagonists > Low molecular weight heparin
  - Anticoagulation (w/ cancer)
    - Low molecular weight heparin > Vit. K antagonists or Direct Oral Anticoagulants (DOAC)

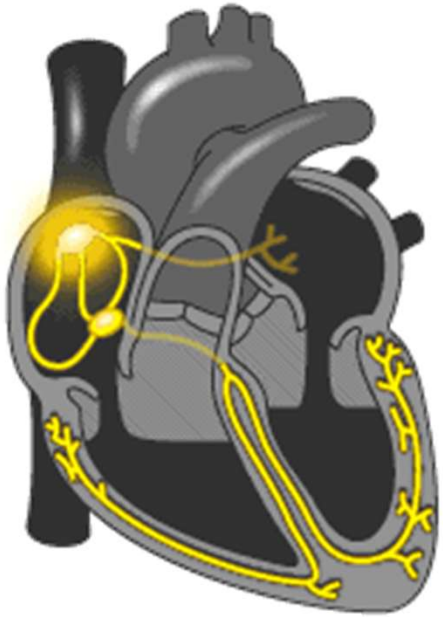
Treatment period
- 1st idiopathic VT: 3-6 months
- 2nd VT: extended

- Pharmacological treatment if NOT using Direct Oral Anticoagulants (DOAC)
  - Enoxaparin sodium 1 mg/kg q12h or 1.5 mg/kg/d SC
    - Single dose not > 180 mg/day
  - Day 1: start warfarin at 5 mg, adjust subsequent daily dose according to the International normalized ratio (INR)
  - Days 3-5: check platelet count
  - Stop LMWH after at least 4 to 5 days of combined therapy when INR is > 2.0
  - Anticoagulate with warfarin for at least 3 months at an INR range of 2.0–3.0
- IVC filter as indicated

Kearon et al, Chest, 2016

CV Responses in SCI

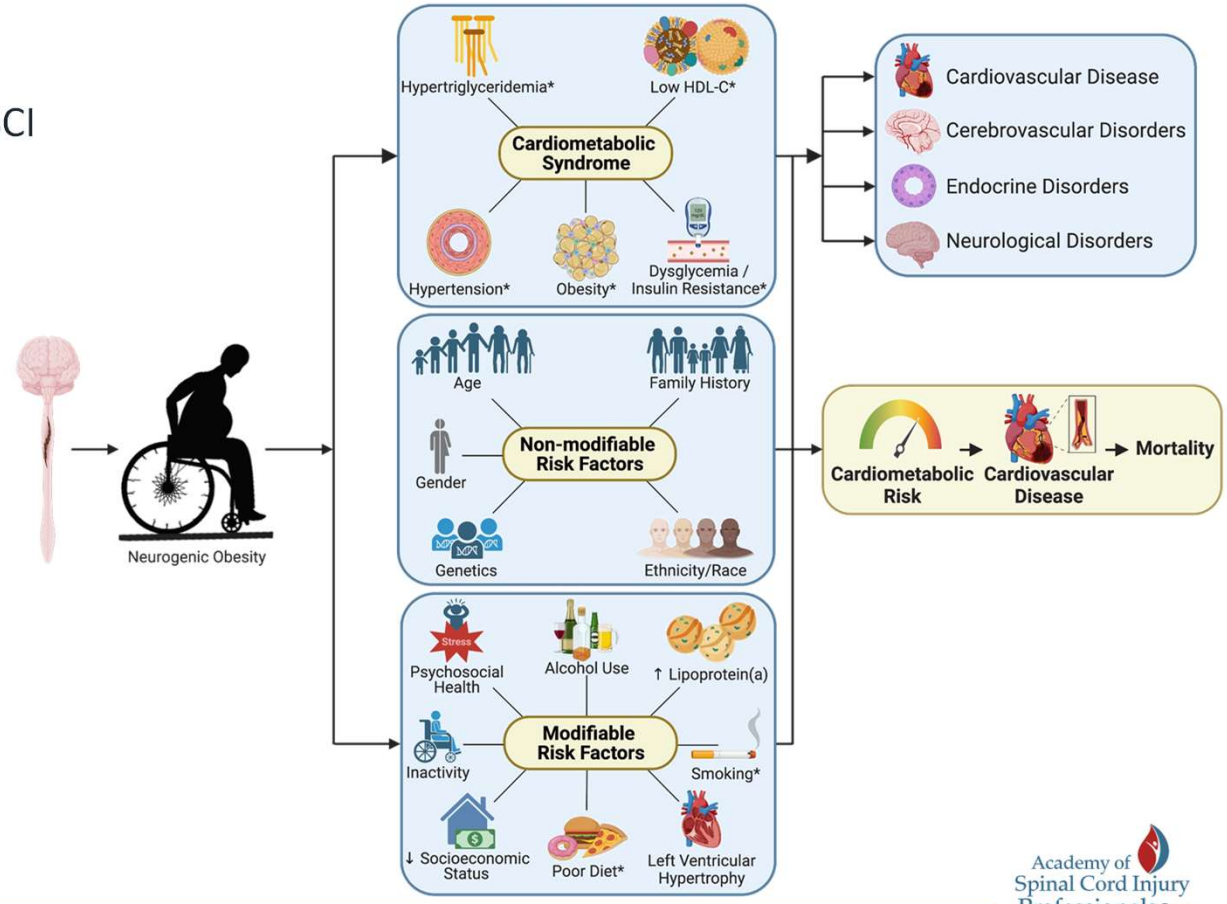
- Circulatory hypokinesis = hypotension on exertion due to blunted sympathetic response (with parasympathetic dominance)
  - ↓ sympathetic response → ↓ vasoconstriction / ↑ vasodilation
  - ↓ venoconstriction / ↑ venodilation → ↑ blood pooling
  - Impaired venous pump → ↑ blood pooling
- Impaired cardiac output (Q = HR*SV)
  - Adaptive myocardial atrophy → ↓ SV
  - ↓ LVEDV → ↓ SV
- Blunted HR chronotropic response due to
  - Incomplete sympathetic drive
  - SCI above T3 rarely achieve HR > 120 bpm
  - Dysrhythmias (heart block)



Cardiovascular Disease in SCI

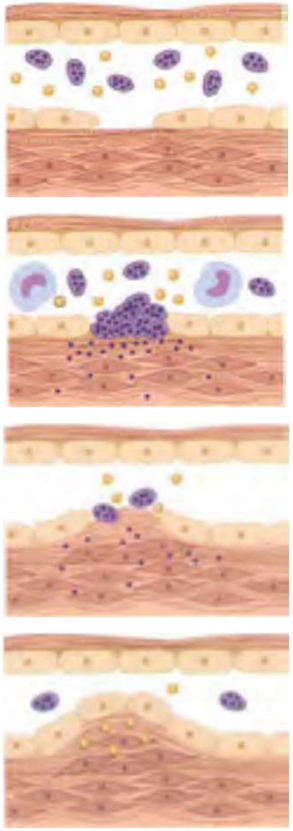
- Leading cause of mortality in chronic SCI
- Silent Ischemia

- Risk Factors
  - Modifiable*
  - Non-modifiable



Farkas et al, Curr Opin Neurol, 2023

Pathophysiology of Atherosclerosis

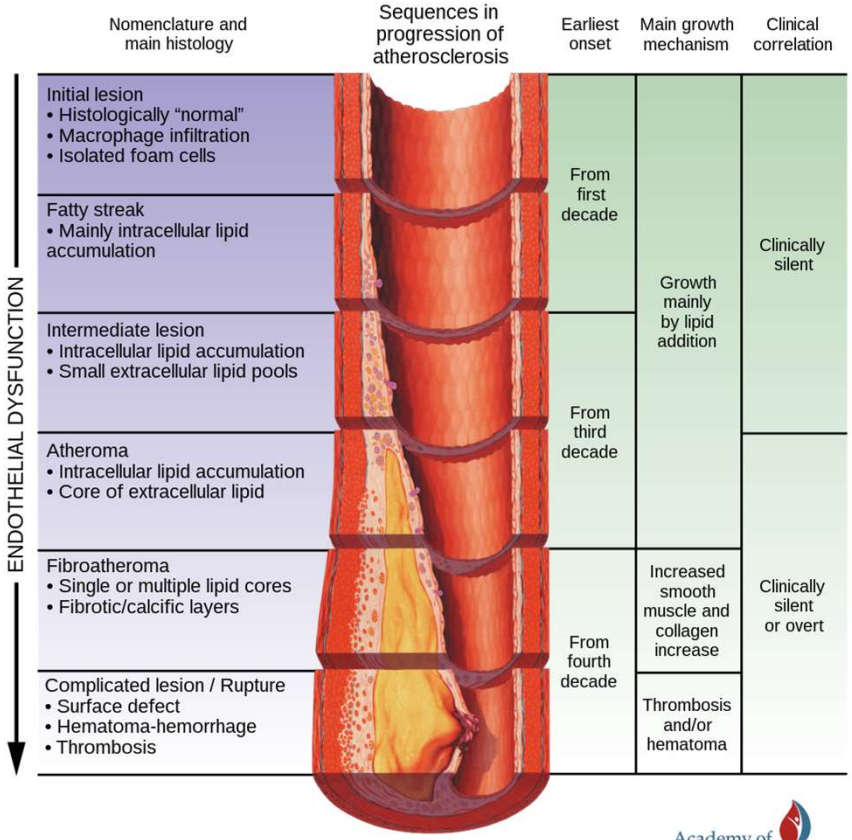


1. A blood-borne irritant → injures arterial wall → exposes underlying connective tissue

2. Platelets & monocytes adhere to exposed connective tissue → platelets release platelet-derived growth factor (PDGF) → PDGF promotes smooth muscle migration & proliferation from tunica media to intima

3. A plaque composed of smooth muscle, connective tissue, and debris is formed at injury site

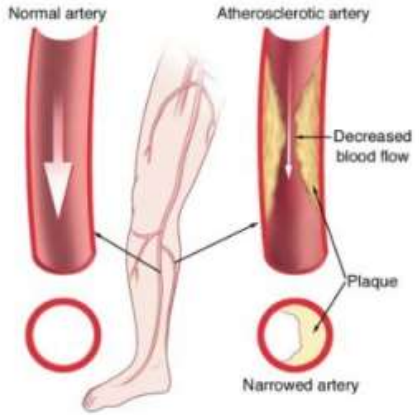
4. Lipids (LDL-c) are deposited into plaque → narrows arterial lumen → impedes blood flow → ↑ BP



Peripheral Vascular Disease

- Venous
- Lymphatic
- Arterial (PAD)
  - Hazard = 1.4 in SCI vs. w/o SCI
  - Hazard = 3.1 in SCI + DM vs. w/o SCI + DM
  - Risk factors
    - Hypertension
    - Diabetes
    - Cigarette smoking
    - ↑ LDL-c
    - Family history

- Management
  - ↓ risk factors
  - Antiplatelet agents
  - Pentoxifylline (Trental)
  - Foot & skincare
  - Exercise
  - Diet?
  - Revascularization
  - Amputation



https://www.cdc.gov/heartdisease/PAD.htm

Su et al, 2015, Medicine (Baltimore)

Coronary Artery Disease

Risk Factors

- Family Hx
  - ♂ 1° relative < 55 y
  - ♀ 1° relative < 65 y
- Cigarette Smoking
- Hypertension
  - SBP ≥ 135 or DBP ≥ 85 (>2x) or antihypertensive Rx
- Hypercholesterolemia/dyslipidemia
  - TC > 200 mg/dL
  - HDL < 40 mg/dL
  - LDL > 130 mg/dL
  - Or on lipid-lowering agent
- Diabetes
  - Fasting Glucose > 126 mg/dL, HbA1C ≥ 6.5%
- Obesity
  - BMI > 30 kg/m^2 or $WC_{♂}$ > 102 cm or $WC_{♀}$ > 88 cm
- Sedentary lifestyle/inactivity

Diagnostics

- Multi-gated Acquisition (MUGA) Scan
  - Tagged RBCs
- Persantine/Adenosine Thallium Scan
  - Thallium Chloride-201 Coronary Perfusion
  - Technetium-99m Sestamibi (Cardiolite)
- Dobutamine Echocardiogram
- Angiography
- Graded Exercise Test (GXT)
  - Limited in Dx capability by GXT intensity
    - Sensitivity [TP/TP+FN] 74-97%
    - Specificity [TN/TN+FP] 64-94%
  - Bauman et al, 1994; n=20 paraplegia, GXT & SPECT
    - 5/13 had ECG evidence of ischemia on GXT*
    - 13/13 single photon emission CT (SPECT) evidence of ischemia (including 5 above*)
    - 8 undiagnosed without SPECT imaging

ACSM Guidelines, 2021

ACSM GXT Exercise Screening

CAD Risk Factors

- Family Hx
  - ♂ 1° relative < 55 y
  - ♀ 1° relative < 65 y
- Cigarette Smoking
- Hypertension
  - SBP ≥ 135 or DBP ≥ 85 (>2x) or antihypertensive Rx
- Hypercholesterolemia/dyslipidemia
  - TC > 200 mg/dL
  - HDL < 40 mg/dL
  - LDL > 130 mg/dL
  - Or on lipid-lowering agent
- Diabetes
  - Fasting Glucose > 126 mg/dL, HbA1C ≥ 6.5%
- Obesity
  - BMI > 30 kg/m^2 or $WC_{♂}$ > 102 cm or $WC_{♀}$ > 88 cm
- Sedentary lifestyle/inactivity

Major Signs / Symptoms

- Anginal equivalent at chest, neck, jaw, arms
- Dyspnea on exertion
- Dizziness or syncope
- Orthopnea or Paroxysmal Nocturnal
- Dyspnea
- Ankle Edema
- Palpitations or tachycardia
- Intermittent claudication
- Known heart murmur
- Unusual fatigue or dyspnea with usual activities

ACSM Recommendations for GXT

Planned Exercise Intensity / GXT	Risk Stratification		
	Low Risk	**Moderate Risk**	**High Risk**
Current Physical Examination & GXT			
Moderate (3-6 METs)	Unnecessary	Unnecessary	**Recommended**
Vigorous (>6 METs)	Unnecessary	**Recommended**	**Recommended**
Physician Supervision During GXT			
Submaximal GXT	Unnecessary	Unnecessary	**Recommended**
Maximal GXT	Unnecessary	**Recommended**	**Recommended**

Low Risk: Younger (M < 45 y, W < 55 y) persons who are asymptomatic and meet no more than 1 risk factor threshold from the previous slide.
Moderate Risk: Older persons or those who meet the threshold of 2 risk factors.
High Risk: Individuals with signs/symptoms listed on the previous slide or known cardiovascular, pulmonary, or metabolic disease.

Management in CAD Risk: Lipids & Diabetes

Lipid Profiles

- Risk of CAD with
  - ↑ TC, ↑ LDL-c, ↑ VLDL-c, ↑TG, ↓HDL-c
- Modifying variables
  - Exercise
    - ↓ TC, ↓ LDL-c, ↓ VLDL-c, ↑HDL-c
  - Diet/Nutrition (AHA Step II Diet)
    - Fat < 30%, sat fat < 7%, <200 mg Chol/d
    - 6-12 g/d soluble fiber
    - Vit B6, B12, & folate → ↑ homocysteine
  - Pharmacological agents
    - Statins (HMG-Co-A reductase Inhibitors)

Diabetes

- Risk of CAD with
  - Poor lipid profile → stimulates platelet activity → glycosylation → endothelium injury
- Diabetes management
  - Diet
  - Exercise
  - Pharmacological
    - AOM?

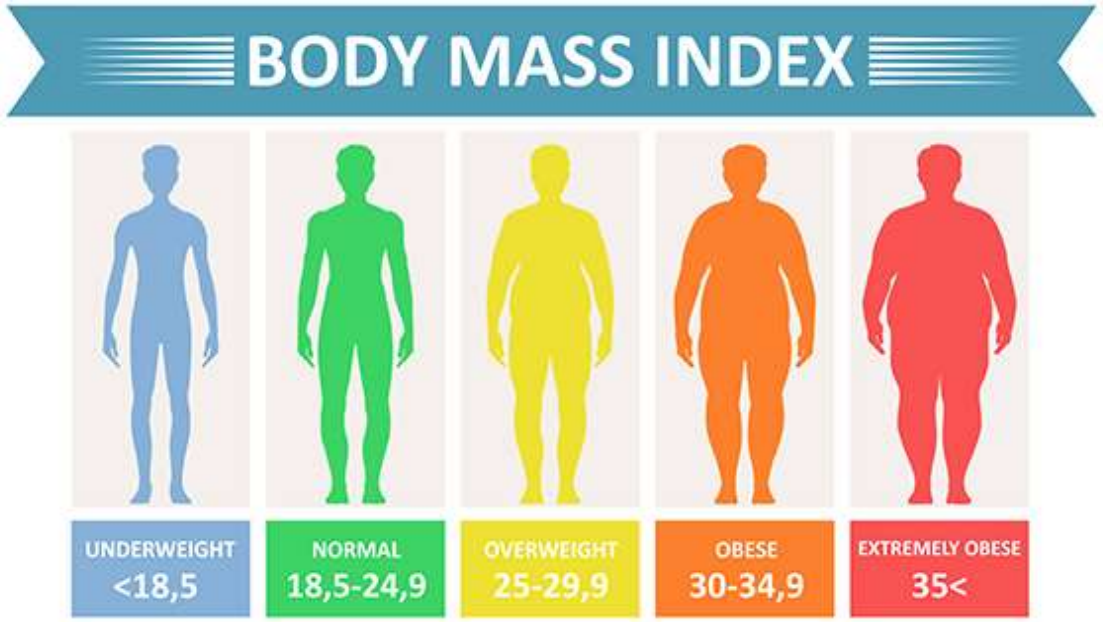
Nash, Gater, PM&R Clin NA, 2020

Nutrition and Immunological Factors

Learning Objectives

- At the conclusion of the *endometabolic dysfunction* presentation, the learner will:
  - Briefly review SCI and its comorbidities
  - Describe the causal relationship between energy metabolism, obesity, metabolic syndrome and endocrine Dysfunction
  - Review anabolic and catabolic dysfunction after SCI
- At the conclusion of the *cardiovascular dysfunction in SCI* presentation, the learner will:
  - Review the neurogenic consequences of SCI on cardiovascular function
  - Discuss risks of VTE/PE following SCI, including prophylaxis and management
  - Review risk factors for coronary artery / peripheral arterial disease following SCI
- At the conclusion of the *nutrition and immune dysfunction after sci* presentation, the learner will:
  - Review the neurogenic consequences of SCI on metabolism and body composition
  - Discuss energy balance and components required to promote fat loss
  - Review immunological consequences of SCI and management concerns

BMI Underestimates Obesity after SCI



https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

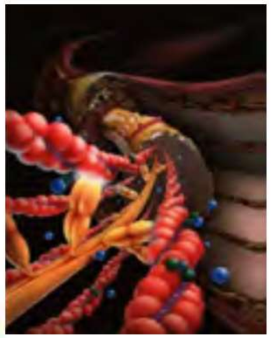
$BMI_{SCI} > 22\ kg/m^2$

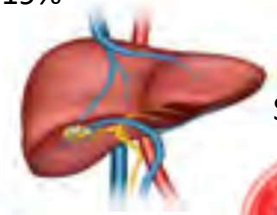
Laughton et al, Spinal Cord, 2009; Nash et al, JSCM, 2019

Essential Clinical Measurements

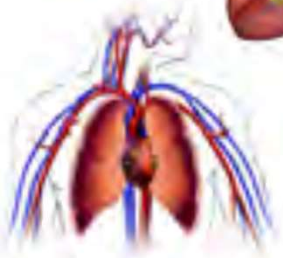
- Body Composition
  - Body weight = fat mass + fat-free mass
  - Fat mass
    - Estimation %BF = 23.484 + 0.118 (age) – 10.725 (sex) + 0.181 (weight) + 0.141 (ABD_{SF})
  - Fat-free mass
    - Estimation FFM = 0.288×body weight+26.3
- Total Energy Expenditure
  - Resting metabolic rate, resting energy expenditure (requirements)
  - RMR x 1.15
- Total energy intake


Brain 19%


Skeletal Muscle 18%


Liver 29%


Kidney 7%


Heart 29%

Farkas et al, AJPMR, 2019

Energy Expenditure after SCI

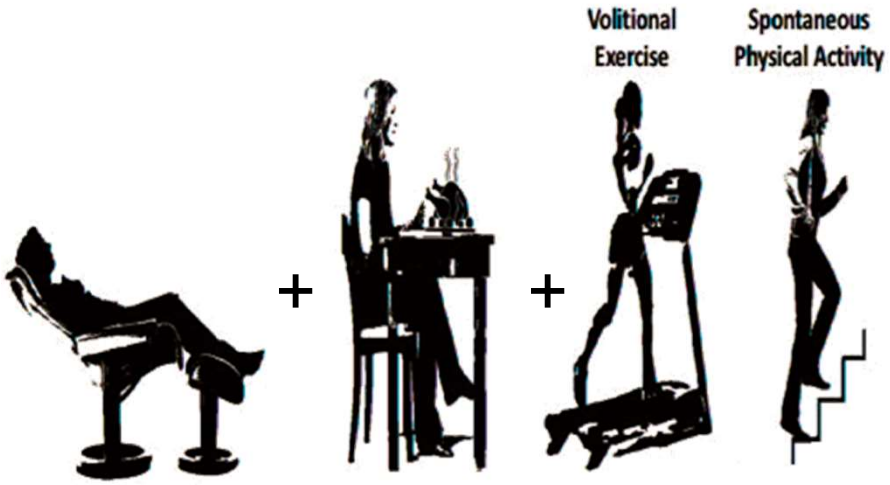
- Blunted Sympathetic Response
  - Hyperinsulinemia
  - Impaired Gluconeogenesis
  - Impaired Lipolysis
- Reduced Anabolism/Catabolism
  - Testosterone
  - Growth Hormone
  - Corticosteroids
  - Thyroxine

↓ Energy Expenditure

- RMR is 12-54% less in SCI vs. AB
- UE work utilizes 20-26% ↓ energy vs. LE work despite a similar rate pressure product (RPP=HRxSBP)

Farkas et al, Int J Sports Nutr Exerc Metab, 2019

Total Energy Expenditure



Resting/Basal Metabolic Rate 60-75%

Thermic Effect of Food 7-10%

Thermic Effect of Physical Activity 15-30%

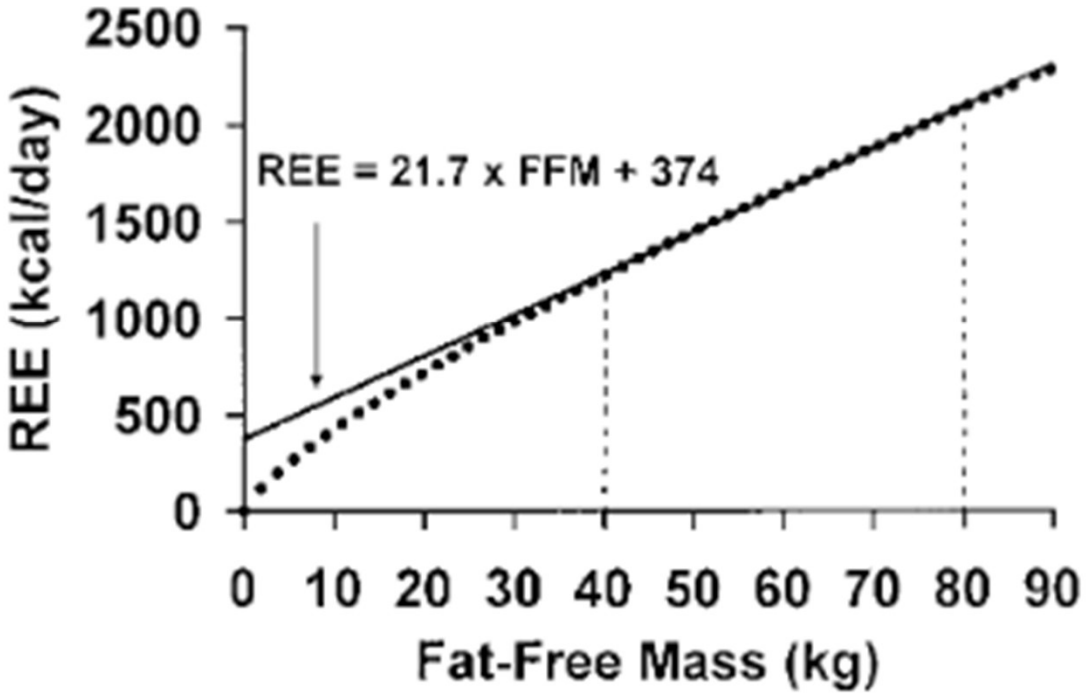
= Total Energy Expenditure

AB (TEE ≈ 2800 kcal/d) >
Paraplegia SCI (TEE ≈ 2240 kcal/d) >
Tetraplegia SCI (TEE ≈ 1200 kcal/d)

Benfato ID et al, Motriz: rev. educ, Fis 2017

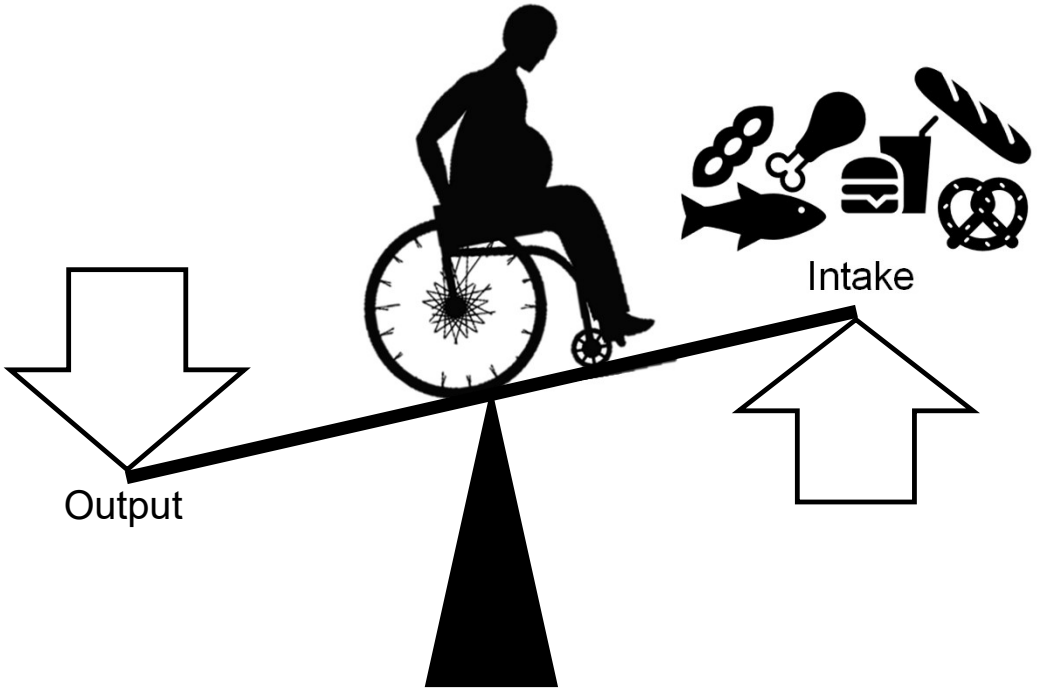
1. Veerman et al, Obesity. 2007; 2. Hill et al, Science. 2003; 3. Farkas, Spinal Cord, 2019.

Relationship between REE & FFM



Wang et al, Am J Physiol Endocrinol Metab, 2000

+ Energy Balance → Energy Balance

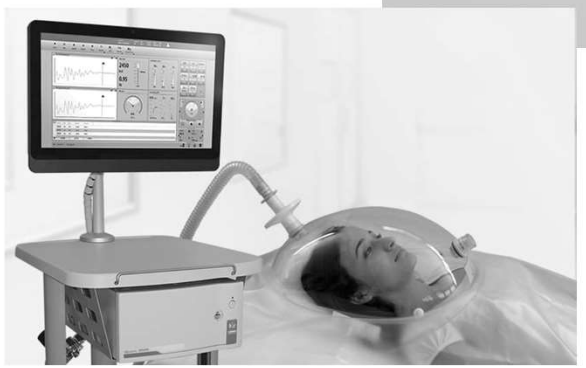


Energy Intake ≈ Energy Expenditure

Measuring Energy Expenditure

- Direct Calorimetry: measurement of heat generated by the body within a contained structure

- Indirect Calorimetry: estimating energy expenditure through O2 consumption & CO2 production
  - Conversion: 1 L VO_2 ≈ 5 kcal
  - Respiratory Quotient (RQ)
    - Ratio of VCO2 to VO2 consumed
    - Protein Oxidation RQ: 0.8
    - Lipids Oxidation RQ: 0.7
    - Carbohydrate Oxidation RQ: 1.0



Farkas et al, Int J Sports Nutr Exerc Metab, 2019

Estimated vs. Measured RMR in SCI

- 326 studies → 22 studies analyzed
- $RMR_{Measured}$: Range of 1,256-1,854 kcal/d
- $RMR_{Estimated}$: Range of 1,276.8-1,808 kcal/d
  - 7 overestimated 4-15% using RMR_{AB} equations
  - 2 underestimated 2-17% using RMR_{AB} equations

International Journal of Sport Nutrition and Exercise Metabolism, 2019, 29, 548-558
https://doi.org/10.1123/ijsnem.2018-0242

Human Kinetics
METHODOLOGY REVIEW

A Systematic Review of the Accuracy of Estimated and Measured Resting Metabolic Rate in Chronic Spinal Cord Injury

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University of California, San Francisco

Marika A. Pitot and David R. Gater Jr.
Penn State College of Medicine

Table 1. Prediction equations for estimating metabolic rate

Equation name/author(s), year		Sex	Equation
Nondisabled equations	Cunningham, 1980	M/F	= 500 + 22 (LBM)
	Harris-Benedict, 1919	M	= 66.4730 + (13.7516 × wt) + (5.0033 × ht) – (6.7550 × age) = (1.8496 × ht) + (9.5634 × wt) + 655.0955 – (4.6756 × age)
	Hayes et al., 2002	M/F	= K_{AT} × AT + K_{SM} × SM + K_{Bone} × Bone + K_{Brain} × Brain + K_{RM} × RM
	Mifflin, 1990	M	= 10 x wt + 6.25 x ht – 5 x age + 5 = 10 x wt + 6.25 x ht – 5 x age – 161
	Nelson et al., 1992	M/F	= (108 x FFM) + (16.9 x FM)
	Owen, 1987	M	= 290 + 22.3 (LBM)
		F	= 334 + 1.97 (LBM)
	Schofield, 1985	M	= 15.057 × wt + 692.2 *(age, 18 – 30 y)*, 11.472 × wt + 873.1 *(age, 30 – 60 y)*, 11.711 × wt + 587.7 *(age, > 60 y)*
		F	= 14.818 × wt + 486.6 *(age, 18 – 30 y)*, 8.126 × wt + 845.6 *(age, 30 – 60 y)*, 9.082 × wt + 658.5 *(age, > 60 y)*
SCI-specific equations	Buchholz et al., 2003	M/F	= -3618 – 795 x age – 731 x sex + 3170 x wt – 794 x T3 + 261 x metanephrine
		M/F	= 10682 – 1238 x age – 521 x sex – 24 x ht + 87 x FFM
	Chun et al., 2017	M/F	= 24.5 x FFM + 244.4
	Nightingale-Gorgey, 2018	M	= 23.469 × FFM + 294.330 *(FFM alone)*
		M	= 23.995 × FFM + 6.189 × SAD + 6.384 × TAD – 6.948 × TC + 275.211 *(FFM with circumferences and diameters)*
		M	= 19.789 × FFM + 5.156 × wt + 8.090 × ht – 15.301 × CC – 860.546 *(FFM with anthropometrics)*
		M	= 13.202 × ht + 11.329 × wt – 16.729 × TAD – 1185.445 *(anthropometrics alone)*

- SCI-specific equations →

Farkas et al Int J Sport Nutr Exercise Met (2019) 29(5):548-558

Estimating Total Energy Expenditure

- $TDEE_{AB}$ = BMR x 1.2
- $TDEE_{SCI}$ = (BMR x 1) + (BMR x 0.2)

- $TDEE_{SCI} = (BMR \times 1) + \left(BMR \times 0.2 \times \frac{2.5\ ml/kg/min}{3.5\ ml/kg/min}\right)$
- $TDEE_{SCI}$ = (BMR x 1) + (BMR x (0.2 x 0.77142))
- $TDEE_{SCI}$ = (BMR x 1) + (BMR x 0.15428)
- $TDEE_{SCI}$ = BMR x 1.15

Collins et al (2010) Med Sci Sport Ex 42(4):691-700

Farkas et al, AJPMR, 2019

Total Energy Intake

- Dietary Assessment
  - Ideal: Food prepared/packaged by a metabolic kitchen for controlled consumption
  - Practical (self-report)
    - 24-dietary recall
    - 1-, 3- or 7-day dietary records, RD-interview
    - Food-frequency questionnaire
- Energy densities (*macronutrients)
  - Carbohydrate 4 kcal/g
  - Protein* 4 kcal/g
  - Fat* 9 kcal/g
  - Alcohol* 7 kcal/g
  - Fiber 1.5-2.5 kcal/day

Gater et al, Topics in SCI Rehab, 2020

Nutritional Status in SCI

- 277 studies → 12 quantitative synthesis
- RMR (n=87): 1,492 kcal/d
- $TDEE_{SCI}$ = RMR x 1.15
  - $TDEE_{SCI}$ = 1,492 kcal/d x 1.15 = 1,715.8 kcal/d
- Energy Intake (n=606): 1,876 kcal/d
- Energy Excess: 160.2 kcal/d or 58,473 kcal/y
- 16.7 lbs body fat/year!

- Micronutrients
  - ↓ vitamin A, B5, B7, B9, D, E,
  - ↓ potassium and calcium

Spinal Cord (2019) 57:3–17
https://doi.org/10.1038/s41393-018-0218-4

ISCoS The International Spinal Cord Society

REVIEW ARTICLE

Nutritional status in chronic spinal cord injury: a systematic review and meta-analysis

Gary J. Farkas[1] · Marika A. Pitot[2] · Arthur S. Berg[3] · David R. Gater[4]

Received: 25 May 2018 / Revised: 16 October 2018 / Accepted: 23 October 2018 / Published online: 12 November 2018

Farkas et al (2019) Spinal Cord 57(1):3-17

Markers of Malnutrition

Short-term Nutrition Marker

- Prealbumin (transthyretin)
  - Normal = 16-40 mg/dL
  - Malnutrition = < 16 mg/dL
- BUT prealbumin → acute-phase reactant → subject to systemic inflammation → if hsCRP > 15 mg/dL → prealbumin NOT interpretable

Global Leadership Initiative on Malnutrition (GLIM)

- Dual diagnosis with at…
- ≥ 1 phenotypic indicator
  - Non-volitional weight loss, ↓ BMI, ↓ muscle mass (defined by FFMI)*
  - FFMI*
    - <17 kg/m2 for men
    - < 15 kg/m2 for women
- ≥ 1 etiological indicator
  - ↓ energy Intake, assimilation & disease Burden, or inflammatory condition, e.g., hsCRP > 15 mg/dL

Keller, J Clin Medicine, 2019

Mediterranean Diet for Weight Loss

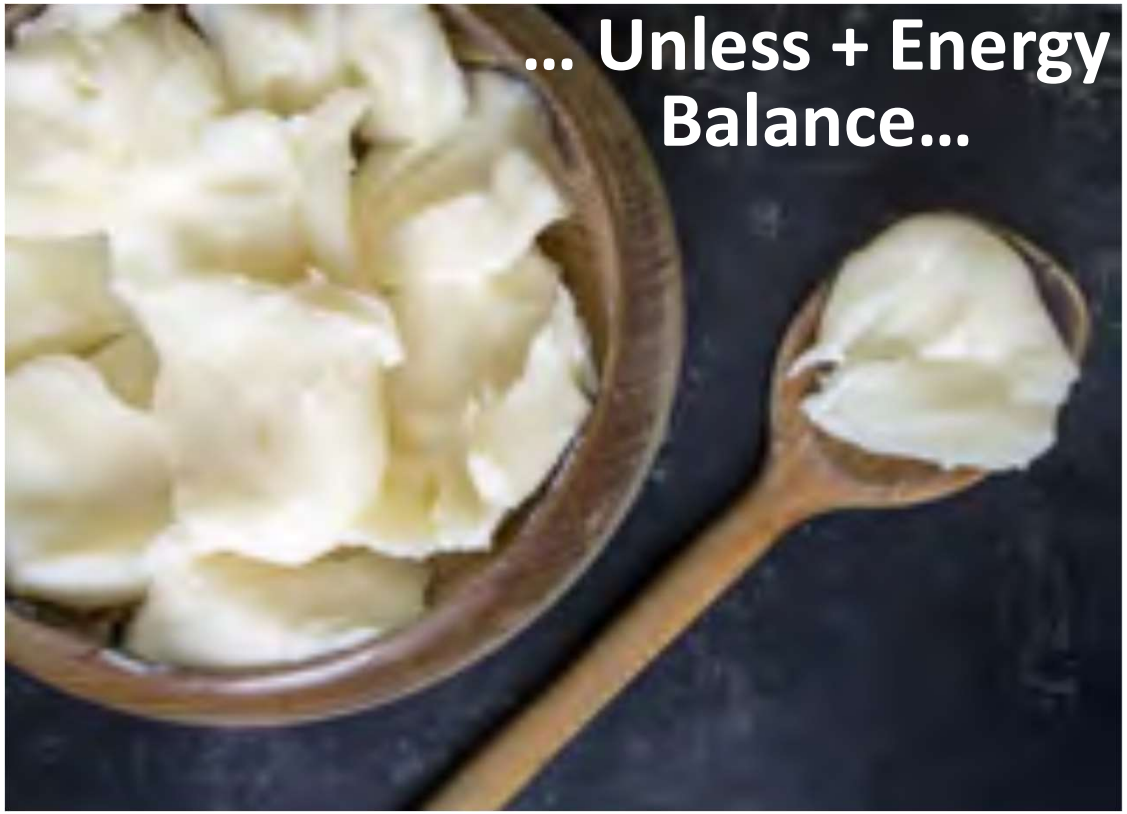
- Fewer meals & carbohydrates
- Plant-based, ↑ monosaturated fats
- Benefits
  - Stabilize blood sugar
  - ↓ cholesterol & triglycerides
  - ↓ heart disease risk
- Emphasize
  - Plant-based meals; ↓ lean meat & chicken amounts
  - ↑ whole grains, fresh fruits & vegetables, nuts, and legumes
  - Foods that naturally contain high amounts of fiber
  - Plenty of fish & other seafood
  - Olive oil (↑ monounsaturated fat), main fat source for preparing food. Olive oil is a healthy,
  - Food that is prepared and seasoned, without sauces/gravies
- Limit
  - Red meats
  - Desserts
  - Eggs
  - Butter

DASH Diet for Hypertension

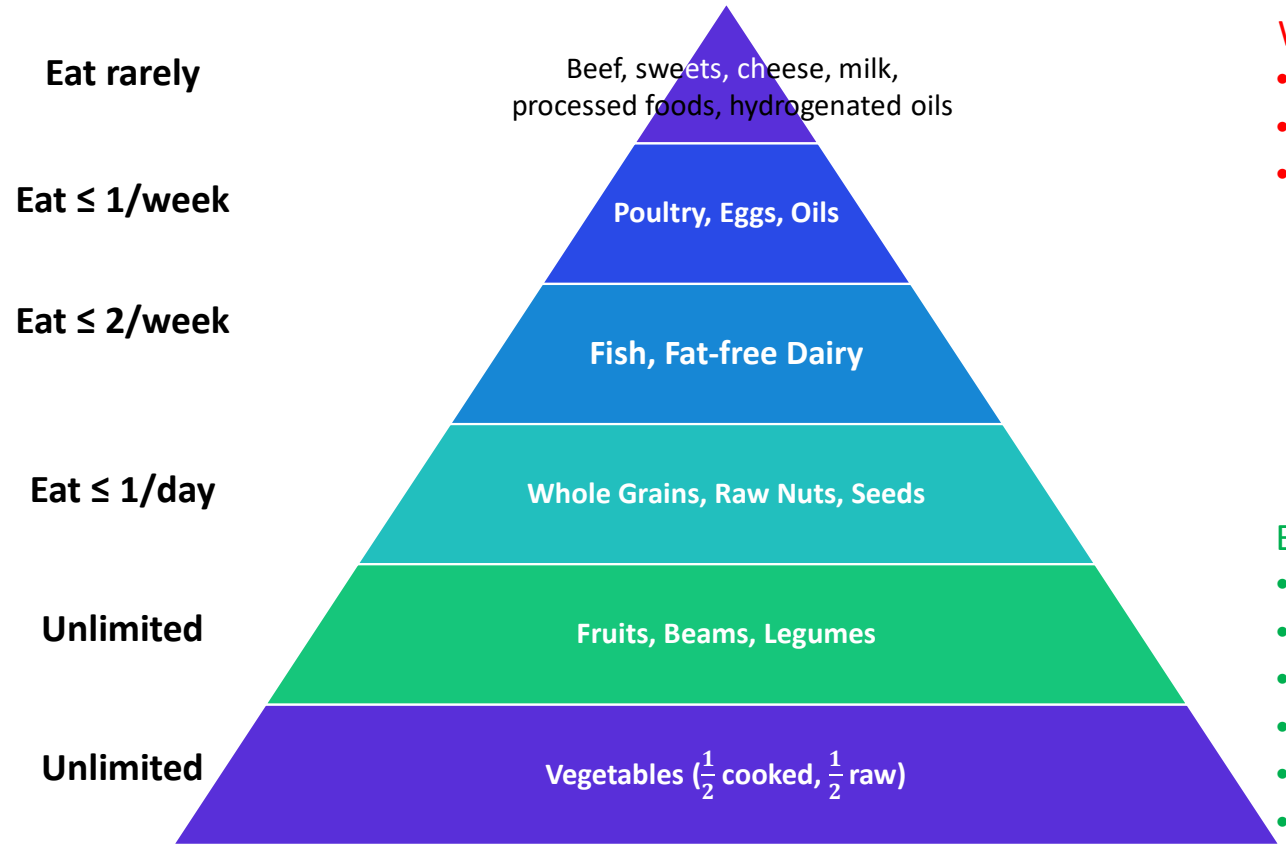
- **D**ietary **A**pproaches to **S**top **H**ypertension
- Low in salt
- Benefits
  - ↓ high BP
  - ↓ heart disease risk , heart failure, and stroke
  - Prevent/control type 2 diabetes
  - ↑ chol levels
  - ↓ chance of kidney stones

- Emphasizes foods
  - ↑ in Ca, K, Mg, fiber → when combined, help ↓ BP
  - Non-starchy fruits & vegetables
  - Whole grains
  - Low-fat dairy
  - Lean protein
- Limit
  - Added salt, adding salt to food
  - Sweets and sugar-sweetened beverages
  - Foods high in saturated fats (full-fat dairy, fatty meals, tropical oils, most packaged snacks
  - Alcohol intake

Mediterranean and DASH Diets…



High-Nutrient / Low-Energy Density



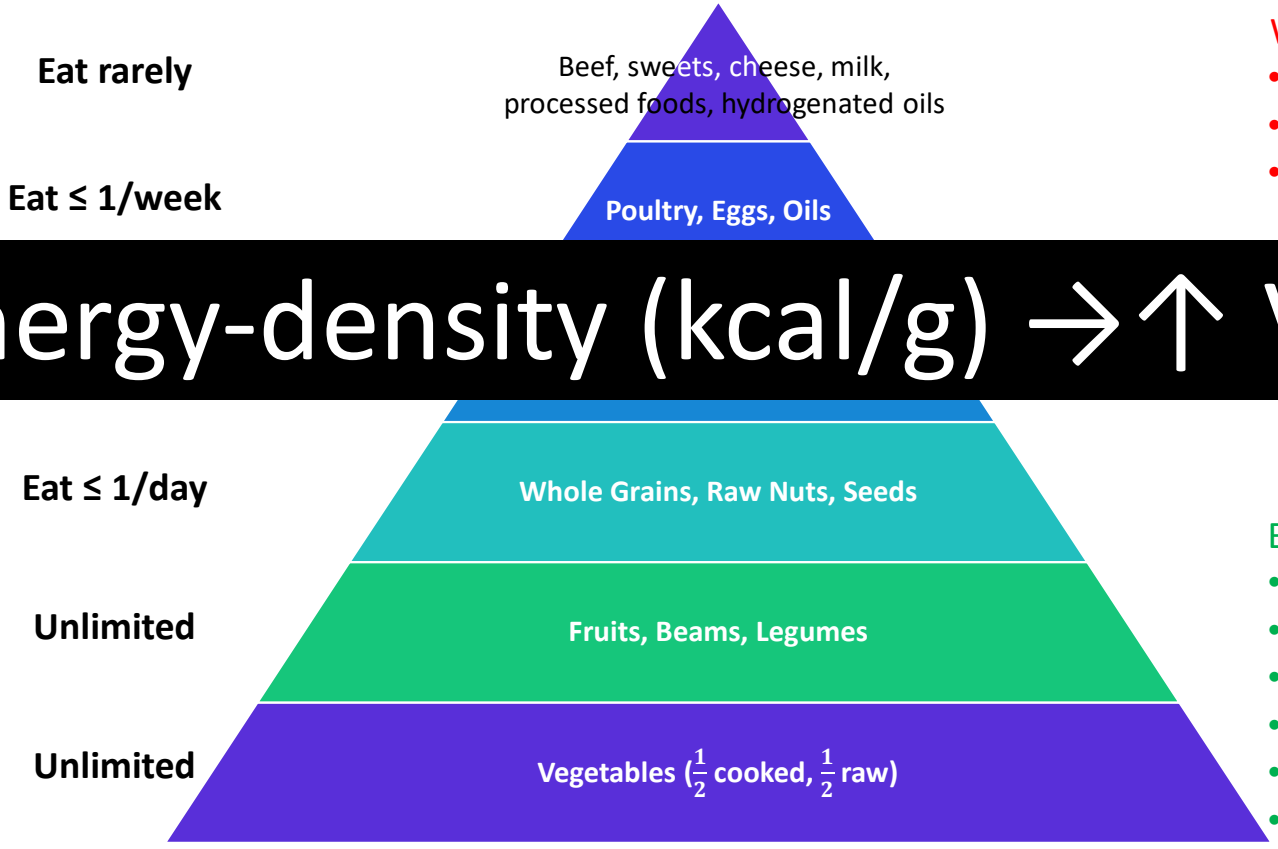
Worst Nutrient/Energy Ratio

- Flour & Sugar
- Oil
- Alcohol

Best Nutrient/Energy Ratio

- Green Vegetables
- Raw Vegetables
- Beans & Legumes
- Eggplant & Mushrooms
- Tomatoes & Peppers
- Fresh Fruit

High-Nutrient / Low-Energy Density



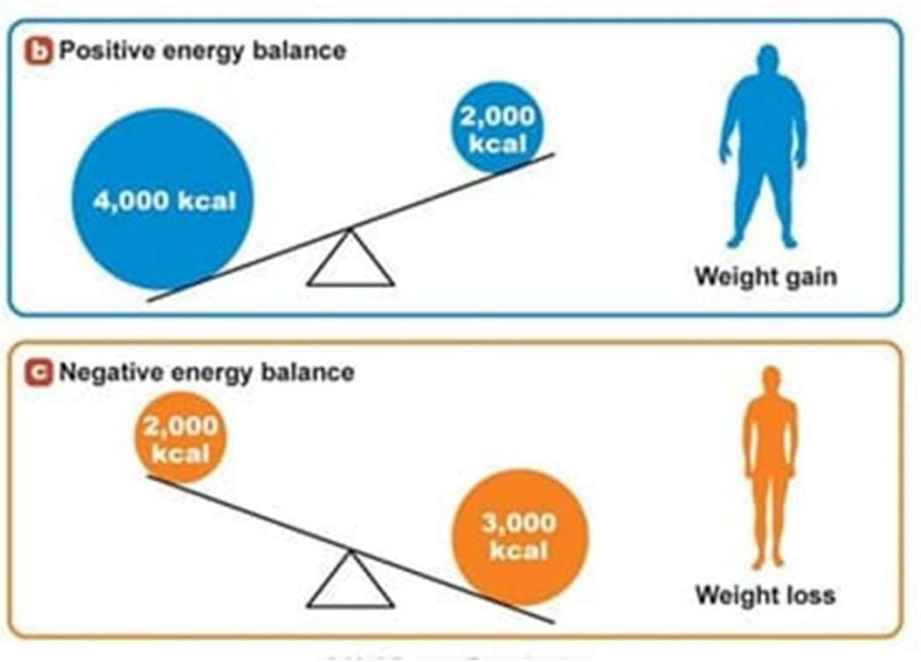
Worst Nutrient/Energy Ratio
- Flour & Sugar
- Oil
- Alcohol

↓ Energy-density (kcal/g) →↑ Volume

Best Nutrient/Energy Ratio
- Green Vegetables
- Raw Vegetables
- Beans & Legumes
- Eggplant & Mushrooms
- Tomatoes & Peppers
- Fresh Fruit

Clinical Take Away Points…

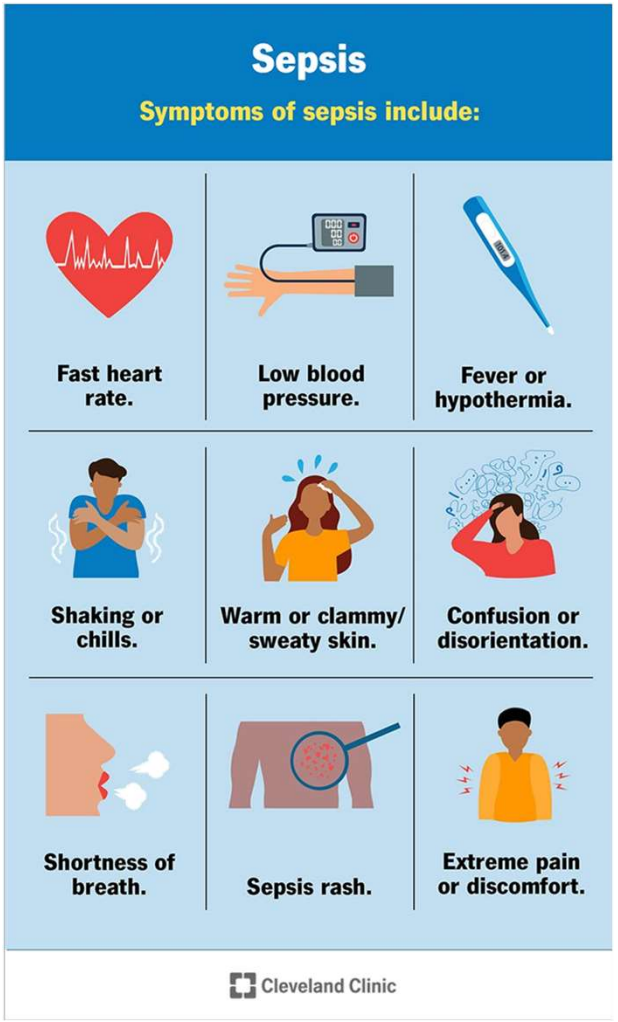
- To ↓ obesity in SCI
  - Determine body composition
  - Determine Total Energy Expenditure (TEE)
    - Resting Metabolic Rate x 1.15
- Monitor Caloric Intake
  - To achieve a NEGATIVE Energy Balance
    - Energy Expenditure > Energy Intake
- Modify diet and/or multivitamin to ensure micronutrients



Gater et al, Topics in SCI Rehab, 2020

Septicemia / Sepsis

- A leading cause of death in SCI
- Pneumonia & Septicemia
  - Leading cause of death in SCI since 1973 (NSCISC 2018)
- Pneumonia, Wound Infection, and Sepsis (PWS)
  - 14% SCI acute admissions (n=1299)
  - 36% AIS A
  - PWS ≈→ poor functional outcomes



Jaja et al, J Neurotrauma, 2019

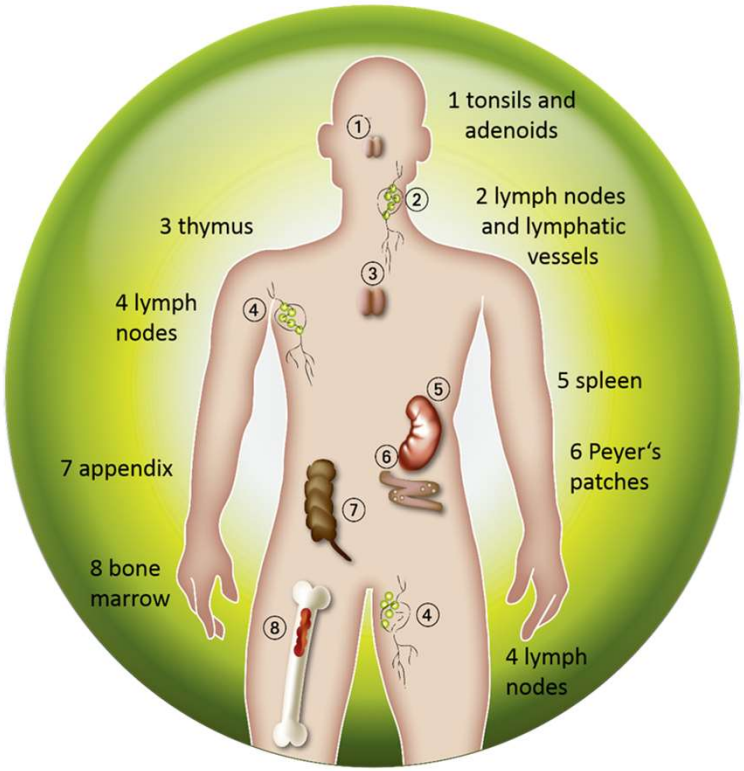
Pneumococcal / Influenza Vaccination

- Pneumococcal Vaccine Series (ACIP)
- 13-valent pneumococcal conjugate → 23-valent pneumococcal polysaccharide ≥ 1 year → > 65 y repeat 23-valent pneumococcal polysaccharide after 5 y

- Annual Influenza Vaccine Recommended
- COVID-19 Vaccine Recommended

Kobayashi et al, MMWR Morb Mortal Wkly Rep, 2015

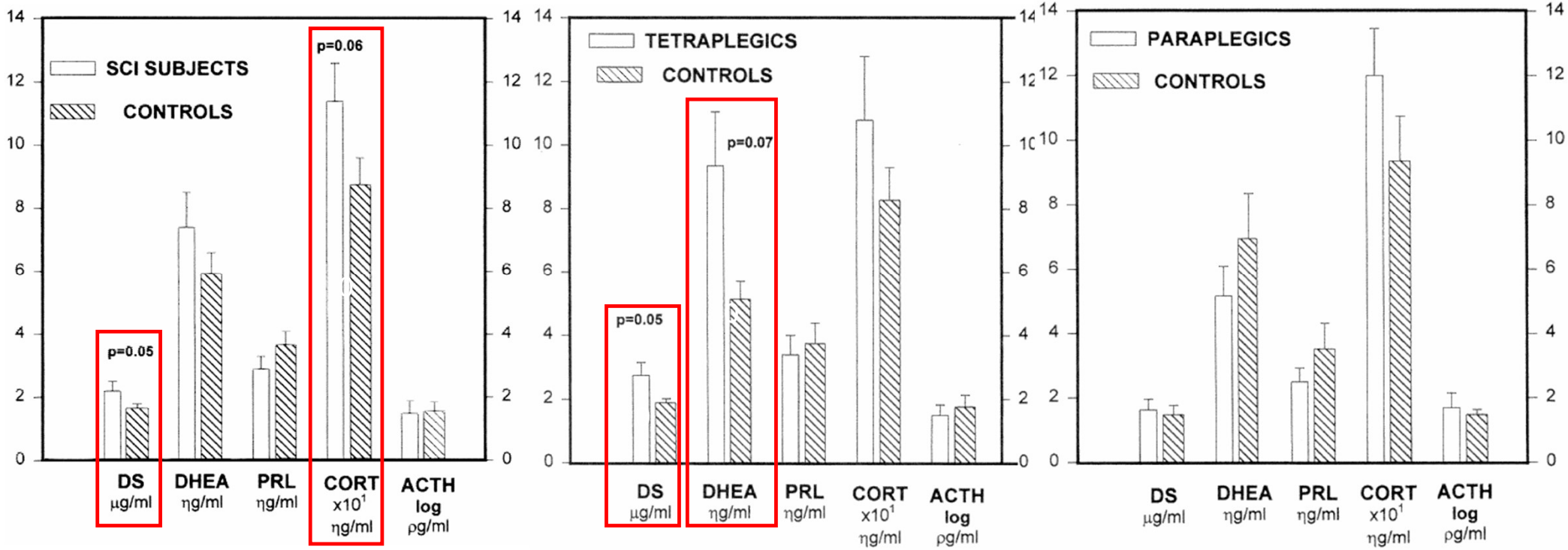
Immunosuppression after SCI



- Immune-CNS interface
  - Hypothalamus-pituitary-adrenal axis (HPA) (Glucocorticoids)
  - Sympathetic NS (Catecholamines)
  - Parasympathetic NS (Vagus n.)
- Acute SCI →
  - ↓ $CD14^+$ Monocytes
  - ↓ $CD3^+$ Lymphocytes
  - ↓ $CD19^+$ B-Lymphocytes
  - ↓ MHC Class II $(HLA\text{-}DR)^+$
  - Amplified by methylprednisolone administration
- Chronic SCI →
  - Immune Deficiency
  - Hypothalamus-pituitary-adrenal Axis (HPA) (Glucocorticoids)
  - Sympathetic NS (Catecholamines)
  - ↓ Natural Killer (T-cells)
  - Inflammation-mediated suppression (?)

Riegger et al, Neuroscience, 2009

Pituitary-adrenal Hormones after SCI

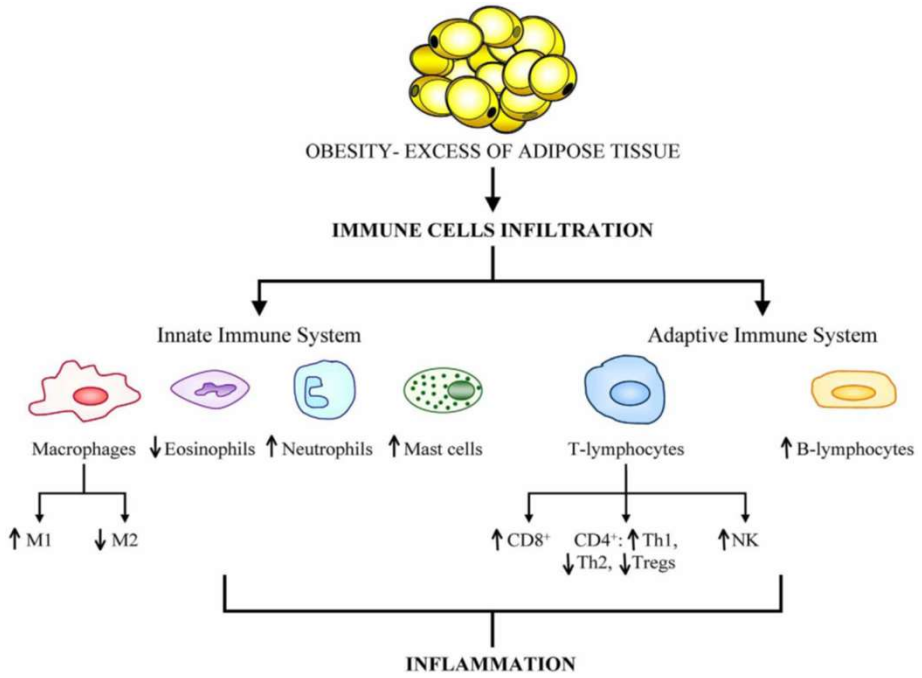


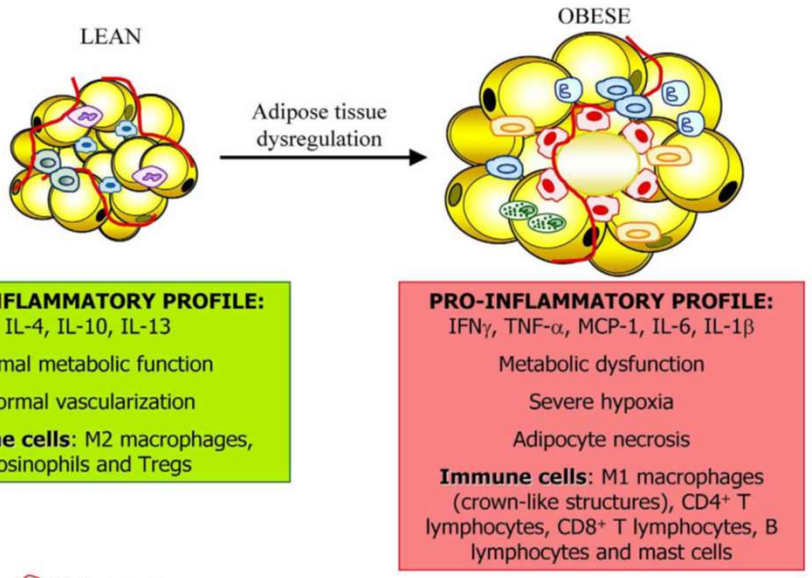
DS = Dehydroepiandrosterone sulfate
DHEA = Dehydroepiandrosterone
PRL = Prolactin
CORT = Cortisol
ACTH = Adrenocorticotropin

Academy of Spinal Cord Injury Professionals, Inc.
Many Minds. One Vision.

Campagnolo et al, APMR, 1999

Obesity, Adipose Tissue, & Immune Function





Catalan et al, Frontiers in Physiology, 2013

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THANK YOU!

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Q and A

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