

CRITICAL ILLNESS POLYNEUROPATHY (CIP) & MYOPATHY (CIM)

“Spontaneous weaknesses indicate disease.” Hippocrates, 460-377 B.C.

- First report: motor loss in the wake of prolonged sepsis in critically ill patients. (Bolton, 1984 A.D.)
 - Last 15 years:
 - CIP often associated with myopathy (CIM)
 - CIM and CIP often coexist, & cannot differentiate
 - Most patients have sepsis, multiple organ dysfunction syndrome, and a catabolic state before the onset
 - manifestation of the systemic inflammatory response syndrome (SIRS) or sepsis, and the multiple organ failure syndrome
 - muscle weakness and prolonged respiratory failure in critically ill patients
- de Seze M, et al. Critical illness polyneuropathy. A 2-year follow-up study in 19 severe cases. Eur Neurol 2000, 43: 61--9.

CIP

- Acute axonal sensory-motor polyneuropathy mainly affecting the lower limb nerves

CIM

- Acute primary (i.e. not due to denervation) myopathy causing muscle weakness and paralysis in critically ill patients
- Pure functional impairment and normal histology
- Atrophy/necrosis, may need EM to see
- CK usually normal
- Often coexists with CIP

As many as:

- 80% of patients with septic shock and multiple organ failure have evidence of CIP/CIM by neurological exam and electromyographic studies.
- 80% of these may be detected within 72 hours after the onset of sepsis.

Systemic Inflammatory Response Syndrome

- Definition (the FLU!)
 - Fever
 - WBC
 - Tachypnea
 - Tachycardia
- Sepsis: SIRS + Infection + Organ Dysfunction: Nerves and muscles are organs too!

Sepsis: Organ Dysfunction

- Brain: encephalopathy
- Lung: capillary leak (“pulmonary edema, pneumonia, aspiration, heart failure”)
- Heart: hyperdynamic, decreased EF, hypocontractility
- GI: stress ulcers, ileus, non-occlusive mesenteric ischemia
- Renal: decreased GFR

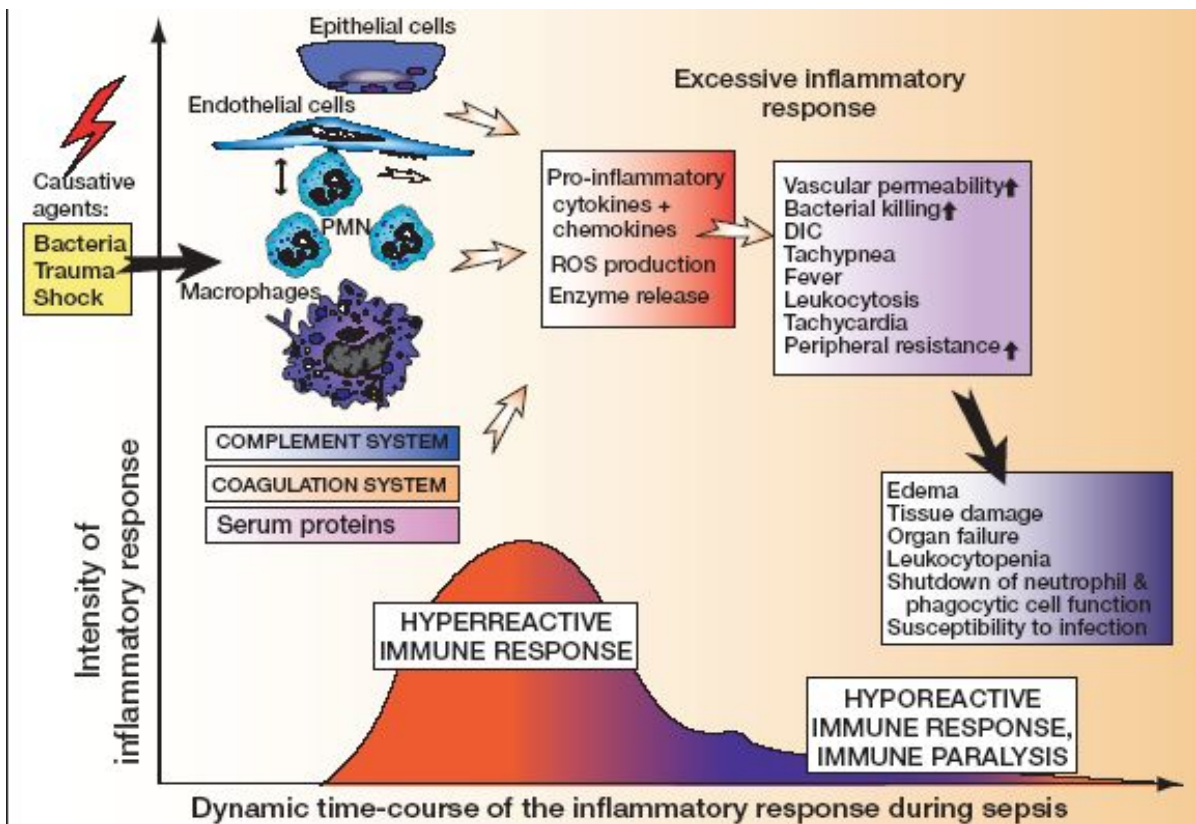
- Blood: thrombocytopenia, coagulopathy, DIC
- Muscles: weakness; peripheral and or central (respiratory)

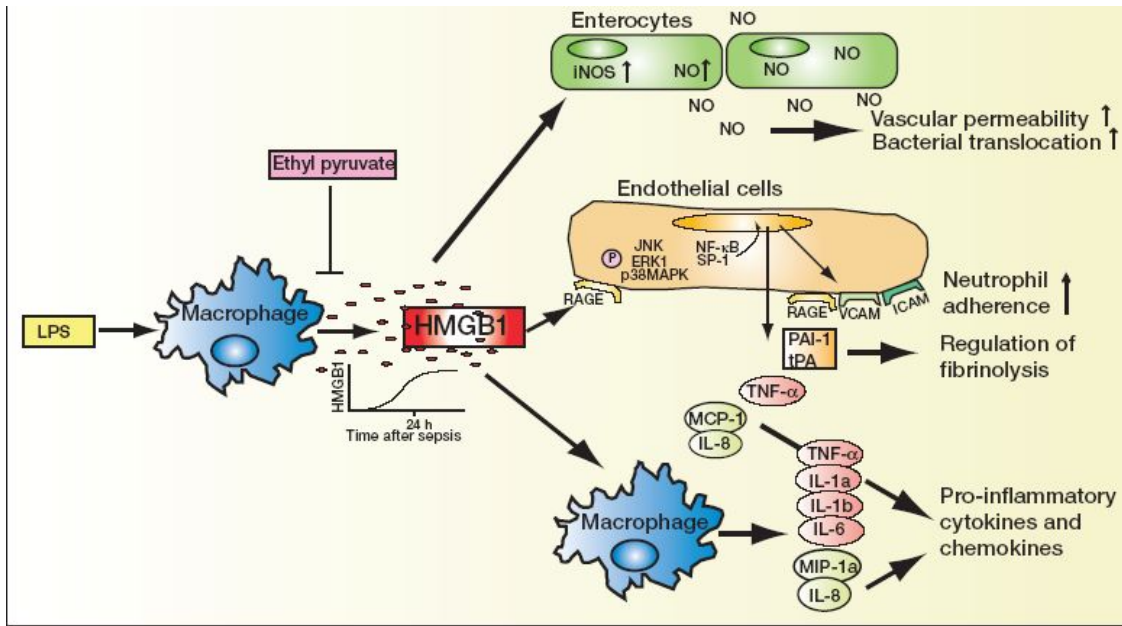
DDX: Weakness in Critically Ill Patient

- CIP or CIM
- CVA
- Encephalopathy
- Spinal compression, infarct
- Transverse myelitis
- Guillian-Barre syndrome
- Myasthenia Gravis
- Botulism
- Severe electrolyte disturbances

Critical Illness Myopathy and Neuropathy

- Pathogenesis
 - Inflammatory
 - Metabolic
 - Bioenergetic
 - Organ dysfunction/failure without significant histological change



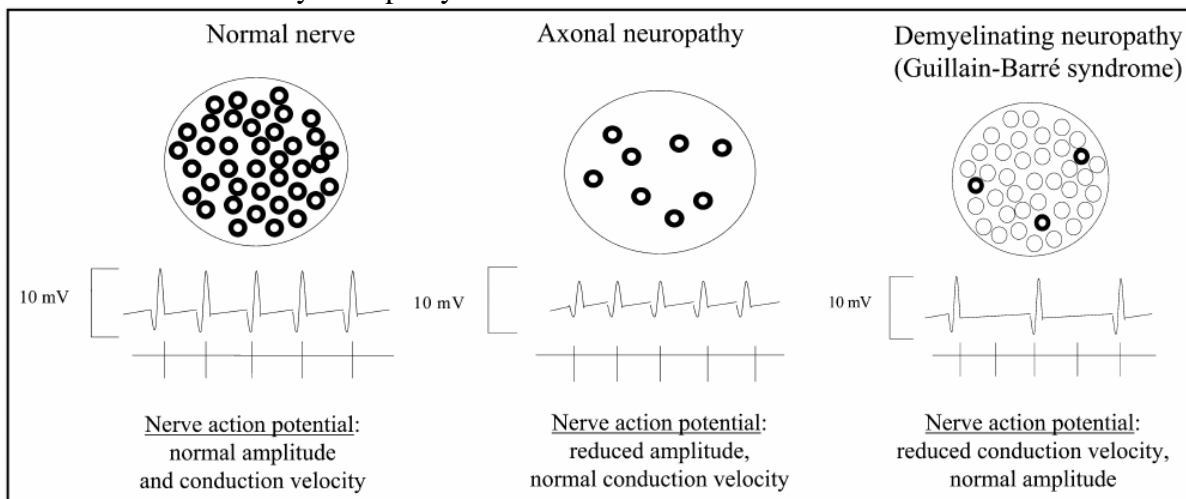


Science, 2005

Critical Illness CIP/CIM

- Microvascular changes in peripheral nerves
 - Increased endothelial expression of P-selectin
- Altered serum lipid profile
- Damage/inhibition of complex I of ETS
 - ATP depletion bioenergetic failure
- Activation specific proteolytic systems
 - Myofilament loss
 - Apoptosis

Dx: Critical Illness Polyneuropathy



History and clinical picture most important in making diagnosis!

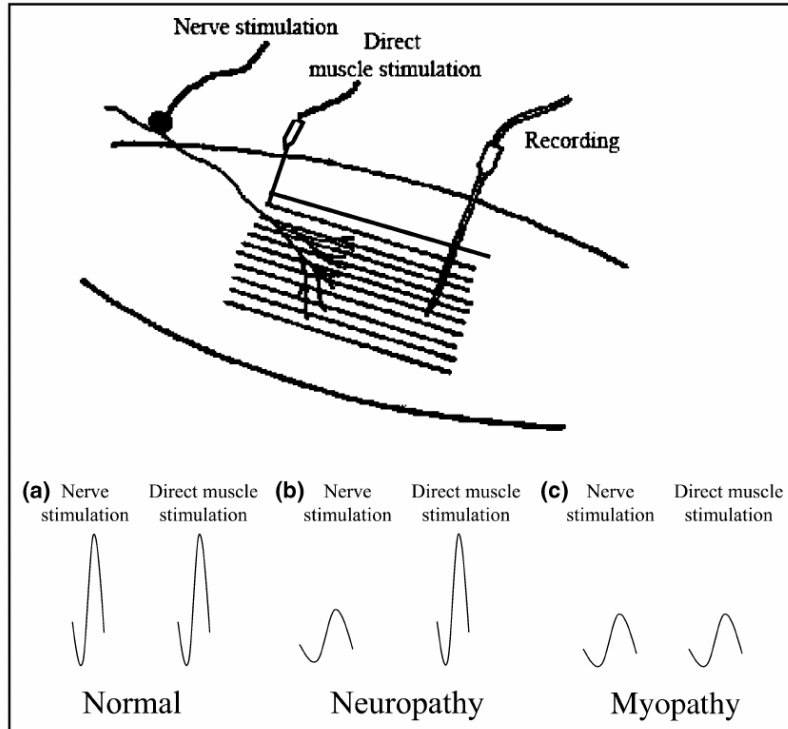
CIM: Pathogenesis

- Unexcitable while maintaining a normal structure
 - Shift in voltage dependence of sodium channel fast inactivation to more negative potentials (hyperpolarized) to reduce excitability
 - Steroids?
 - Mitochondrial dysfunction, ATP depletion
- Proteolytic systems; TGF-beta/MAPK pathway
 - Myofilament loss and apoptosis

Diagnosis: CIM

- Dx and Ddx vs CIP often not possible in ICU
- Uncooperative for accurate sensory and motor testing
- Limb edema
- DMS (direct muscle stimulation)
 - Stimulating and recording placed into muscle distal to end plate
 - Technically demanding, requires practice to obtain reliable results
- Muscle biopsy
 - Pathx, actin/myosin ratio? (1.37 nl, 0.37 CIM)
 - Inflammatory infiltrates: absent

Differentiating Neuropathy and Myopathy



Incidence of CIP?

- NeuroExam < Electrophysiologic
- 58%: prolonged ICU stay
- 70-80%: sepsis, septic shock, or MOF
- 100%: sepsis and coma
- Yet...
 - ONLY A SMALL NUMBER ARE D/C FROM ICU WITH CIP
- CIP only has clinical relevance if muscle is affected

Incidence of CIP/CIM?

- Timing of evaluation
- Methods of evaluation
- Total population not clearly defined/studied
- Reported examples from one institution: 0.09% (39/44,000) or 7% (7/100) liver transplants (van Koningsveld, et al. Lancet 2004; Campellone, et al. Neurology 1998)

CIP/CIM and Respiratory Failure

- Causal relationship?
 - ARF: Trach or reintubation
 - 79% of pt with CIP/CIM
 - 20% of Pt without(Garnacho-Montero J, et al. CCM 2005)
 - ARDS: Trach
 - Trach frequency equal between CIP/CIM and without CIP/CIM groups (Bercker S, et al. CCM 2005)

Critical Illness Neuropathy and Myopathy: Outcome

- Variable
- Dependent on severity of sepsis
- 2 year follow-up post-CIP
 - incomplete recovery within 1-2 years occurs frequently
 - The quality of life remains markedly impaired in all patients with abnormal nerve conduction studies.Zifko UA: Long-term outcome of critical illness polyneuropathy. *Muscle Nerve* 2000, 23: S49--S52

Critical Illness Myopathy and Neuropathy: Associations & risk factors

- Critical illness + sepsis
- + respiratory failure
- Multiple organ failure\ARDS
- Gender (female)
- Corticosteroids
- Severe asthma
- Malnutrition
- Immobility

- Hyperglycemia
- Paralytic agents

Prevention?

- Rapid treatment of sepsis
 - Don't let things fester
- Restricted use of paralytic agents?
- Avoiding (high dose) steroids if possible
- Glycemic control (insulin)
- ?

Conclusions

- CIP & CIM occur in most severely critically ill patients to some degree
- Need more prospective studies of all comers to ICU to more precisely gauge the impact of risk factors
- Simplified diagnostic techniques and devices for electrophysiological measurement of peripheral nerves and muscles in ICU patient

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