A 45yo man with a long history of asthma presents to hospital with acute shortness of breath, requiring intubation and ventilation for respiratory support. A chest X-ray reveals right upper lobe consolidation. He is treated with intravenous methylprednisolone, metronidazole and ceftriaxone with his clinical course complicated by renal and cardiac failure requiring inotropic support and a short period of dialysis. Attempts to wean ventilation support are unsuccessful. Nerve conduction studies reveal the following:

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Distal latency</th>
<th>Conduction velocity</th>
<th>Amplitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right peroneal motor</td>
<td>5.3ms [≤6.1]</td>
<td>40m/s [≥40]</td>
<td>0.5mV [≥2]</td>
</tr>
<tr>
<td>Right tibial motor</td>
<td>5.0ms [≤6.6]</td>
<td>42m/s [≥41]</td>
<td>1.0mV [≥4]</td>
</tr>
</tbody>
</table>

Needle examination reveals fibrillation potentials with small motor unit potentials in all muscles examined.

The most likely diagnosis is:

A. Critical illness myopathy
B. Critical illness neuropathy
C. Acute polymyositis
D. Acute inflammatory demyelinating polyneuropathy
E. Steroid myopathy

- Conduction velocity is normal so demyelination is unlikely
- Amplitude is reduced in motor but not sensory axons – axonal degenerative neuropathy is unlikely to be purely motor
- Also, reduced amplitude is only seen when axonal degenerative neuropathy is advanced
- Earlier in axonal neuropathies collaterals develop to the muscle fibres so the amplitude is normal
- Small motor unit potentials suggest myopathy
- Fibrillations are common in neuropathies but can also occur in myopathy
- This is therefore most likely to be a myopathy
- Critical illness myopathy is the most common cause in ICU

DIFFERENTIAL DIAGNOSIS

- Critical illness myopathy and critical illness neuropathy are major causes (or combination of the 2)
- Other acute and subacute myopathies can occur including rhabdomyolysis, cachectic myopathy and rarely GBS

CRITICAL ILLNESS MYOPATHY

- Typically associated with IV glucocorticoids (rare if not exposed to IV steroids)
- Begins several days after treatment initiated
- Flaccid quadriplegesis, failure to wean from ventilation
- Sensation normal
- Facial muscle weakness can also occur but EOM weakness is rare
- NCS show reduced amplitude of motor pathways, sensory pathways normal
- EMG - fibrillation common, short duration, low amplitude and sometime polyphasic MUPs
- Can be distinguished from critical illness neuropathy by preservation of sensory function
- Treatment is supportive
- Recovery over weeks to months
- More common when non-depolarising neuromuscular blocking agents also used
- Muscle biopsy shows loss of thick filaments and atrophic fibres

Major Diagnostic Features:
- Sensory nerve amplitudes > 80% lower limit of normal in two or more nerves
- Needle EMG with short-duration, low-amplitude MUPs with early or normal full recruitment with or without fibrillation potentials
- Absence of a decremental response on repetitive nerve stimulation
- Muscle histopathologic findings of myopathy with myosin loss

Supportive Features:
- Motor amplitudes <80% lower limit of normal in 2 or more nerves without conduction block
- Elevated CK
- Demonstration of muscle inexcitability

Answer: A

CRITICAL ILLNESS NEUROPATHY
- Typically associated with prolonged illness, usually sepsis and MOF
- May be suspected when unable to wean from ventilator
- Exact mechanism unclear
- Diffuse weakness, decreased reflexes, distal sensory loss
- Cranial nerves intact
- NCS – diffuse symmetric, distal axonal sensorimotor neuropathy
- EMG/NCS - low amplitude motor and sensory action potentials
- Fibrillations develop over time
- CK normal
- Muscle biopsy shows neurogenic atrophy
- Treatment is supportive
- Spontaneous recovery usually occurs over weeks to months.

Diagnostic Criteria:
- Setting of critical illness, particularly if complicated by sepsis, MOF and SIRS
- Difficulty weaning from ventilator that is not related to cardiopulmonary causes
- Possible limb weakness
- Electrophysiologica evidence of axonal motor and sensory polyneuropathy

Electrophysiologica Studies:
- Sensory and motor nerve amplitudes <80% lower limit of normal in 2 or more nerves on NCS
- Absence of conduction block of F-waves
- Needle EMG with reduced recruitment of normal motor unit potentials (early) followed by fibrillation potentials and reduced recruitment of long-duration, high-amplitude MUPs (after weeks)
- Absence of decremental response on repetitive nerve stimulation

Supportive features
- Normal CSF protein and normal serum CK

C – Polymyositis is one of the inflammatory myopathies – others are dermatomyositis and inclusion body myositis. Usually present with progressive muscle weakness. Rare for respiratory muscles to be involved in acute cases. Likely autoimmune process. CK always elevated in PM. Diagnosis of exclusion. EMG shows short duration, low amplitude polyphasic potentials on voluntary action and fibrillations, complex repetitive discharges and positive sharp waves at rest.

D – GBS manifests as a rapidly ascending areflexic motor paralysis with or without sensory disturbance. Autoimmune basis. Rare in this setting.

E – Glucocorticoid-related myopathies can occur with chronic treatment or as “acute quadriplegic” myopathy secondary to high dose IV steroids (seems to be the same as A). In chronic setting, proximal muscle weakness develops, accompanied by cushingoid manifestations. EMG normal, muscle biopsy shows preferential type 2 muscle fibre atrophy.

SENSORY NERVE CONDUCTION STUDIES
- Sensory stimulus leads to generation of action potential = sensory nerve action potential (SNAP)
- Number of functioning neurons is estimated by the amplitude of SNAP
- State of myelin of axons is estimated by conduction velocity of SNAP
- In degenerative neuropathies, primary feature is reduced amplitude of SNAP (eg: diabetic neuropathy)
- In demyelinating disorders or nerve entrapment velocity is reduced (eg: GBS or carpal tunnel syndrome)
- In radiculopathies, both amplitude and conduction velocity are normal as the lesion in proximal to the cell bodies of the axons (in the dorsal root ganglion)

MOTOR NERVE CONDUCTION STUDIES
- The motor axon is stimulated and the action potential produced is measured in the muscle
- The amplitude of the muscle action potential indicates the number of activated muscle fibres
- Distal latency is the time taken for the action potential to result in muscle contraction – ie. AP travels down axon, acetylcholine released into neuromuscular junction and muscle action potential is generated
- Therefore slowing of the distal latency could be due to a problem in the axon or in the neuromuscular junction
- In axonal degenerative neuropathies, motor nerve conduction studies are not significantly abnormal until the process is moderately advanced
- There may be slight slowing of conduction and prolongation of distal latency due to loss of the largest axons
- Early in the disease collateral axons form to supply denervated muscle fibres – thus the action potential produced in the muscle remains normal
- Only when the disease is advanced and denervation is occurring faster than collaterals can develop does the amplitude decrease
- Important to test for sensory conduction in cases of possible degenerative neuropathy, otherwise many will be missed
- In demyelination, slow conduction and prolongation of distal latency is seen
- In radiculopathy the motor NCS is usually normal but if there is sufficient axonal loss there might be slight slowing of velocity
- Focal neurapraxic lesions (ie. compression of nerve such as in carpal tunnel) causes slower conduction and decreased amplitude, but nerves distal to the lesion will be normal
- Nerves proximal to the lesion will show normal velocity but reduced amplitude
- Note that myopathy can cause decreased muscle action potentials in motor NCS

EMG
- Best test to distinguish between neuropathic and myopathic processes

Myopathic:
- Small, short duration polyphasic muscle APs
- Motor units recruited in excessive numbers

Neuropathic:
- Muscle denervation – reduced number of motor units activated but increased rate of firing of remaining motor units
- Collateral supply leads to large polyphasic muscle APs
- Other features suggestive of denervation are fasciculations, positive sharp waves, complex repetitive discharges and fibrillations (but this can also occur in myopathy)

DEMYELINATION
- Slow nerve conduction velocity
- Marked prolongation of distal latencies
- Conduction block = major decrease in muscle AP on proximal stimulation compared to distal stimulation
- Dispersion of evoked muscle APs

AXONAL NEUROPATHY
- Decreased amplitude in sensory nerves and in motor nerves late in disease
- Relative preservation of velocity

NERVE COMPRESSION
- Decreased amplitude and velocity at site of lesion

RADICULOPATHY
- Normal

So my suggestion for this type of question is to:

1) Look at the EMG and decide whether it is neuropathic or myopathic
2) If myopathic – don’t need to worry about the NCS
3) If neuropathic – look at the velocity in particular
   a. Slow velocity suggests demyelination or nerve compression
      i. Amplitude reduced in compression
      ii. Amplitude normal in demyelination
   b. Normal velocity suggests axonal degenerative neuropathy
      i. Near normal amplitude may indicate mild to moderate disease
ii. Reduced amplitude may suggest severe disease
iii. Sensory amplitude should be low