

# Anatomic Patterns of Peripheral Neuropathies

Clinicopathologic localization through distribution, mechanism, and selected disease examples

**Mononeuropathy**

**Polyneuropathy**

**Mononeuritis  
multiplex**

**Polyradiculoneuropathy**

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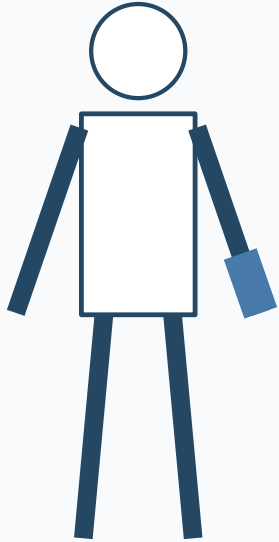
## **Localize the pattern before naming the disease**

- Describe the number of nerves involved and the degree of symmetry.
- Identify whether deficits favor distal lengths or include proximal regions.
- Use the distribution to prioritize plausible mechanisms and causes.

# Four anatomic patterns of neuropathy

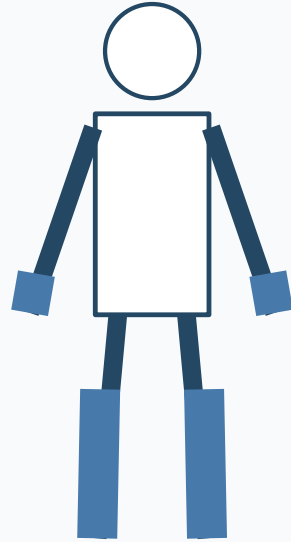
## One nerve

Schematic distribution



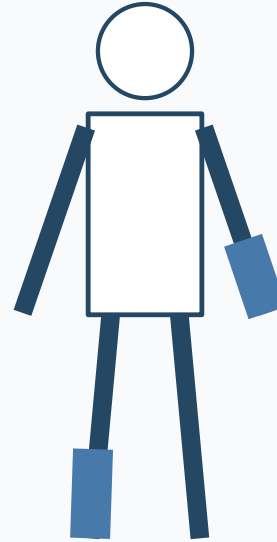
## Many symmetric nerves

Schematic distribution



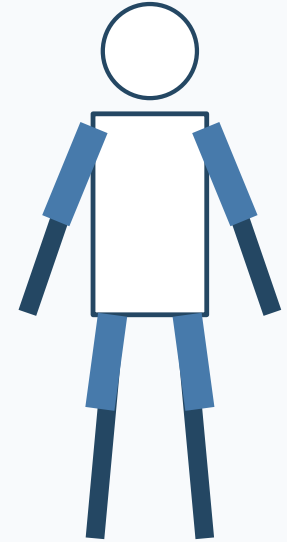
## Scattered individual nerves

Schematic distribution



## Roots + peripheral nerves

Schematic distribution



# Distribution and tissue target answer different questions

## **ANATOMIC DISTRIBUTION**

One nerve · symmetric multiple nerves · scattered nerves · roots and nerves

## **PRIMARY INJURY COMPARTMENT**

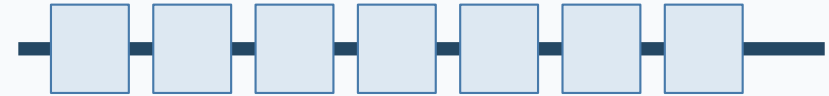
Axon · Schwann cell/myelin · neuronal cell body

*A distribution may arise from more than one microscopic mechanism.*

# The peripheral nerve contains several fiber populations

- Most peripheral nerves contain both sensory and motor fibers.
- Small unmyelinated fibers convey some pain, temperature, and autonomic functions.
- Large myelinated axons conduct proprioceptive, light-touch, and motor signals.

**Nerve fiber and myelin**



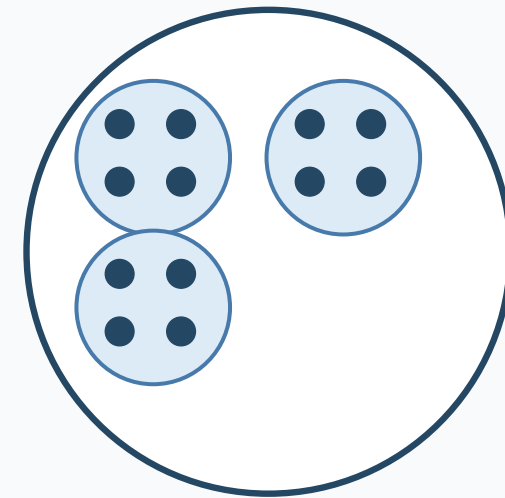
**Myelin internodes**

**Nodes of Ranvier = gaps**

# Connective tissue layers organize the nerve

- Endoneurium surrounds individual nerve fibers.
- Perineurium wraps groups of fibers into fascicles.
- Epineurium encloses the whole nerve in fibrovascular tissue.

Peripheral nerve cross-section

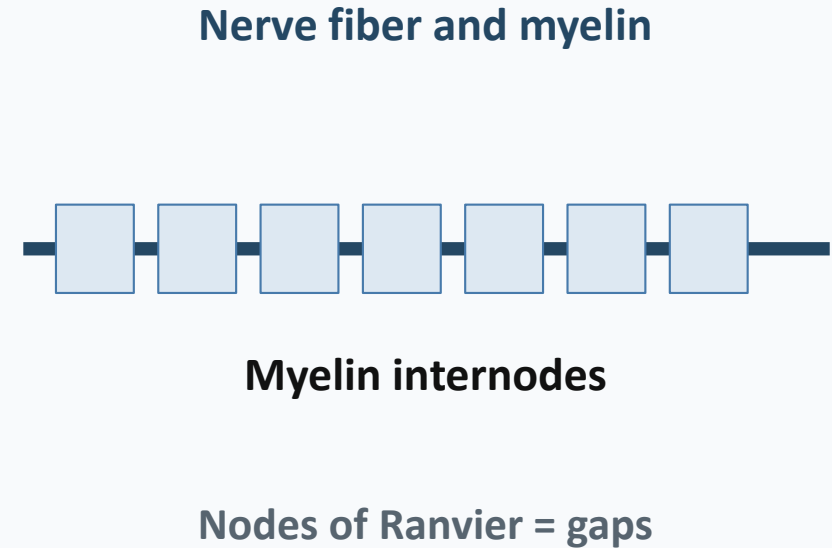


Epineurium → nerve

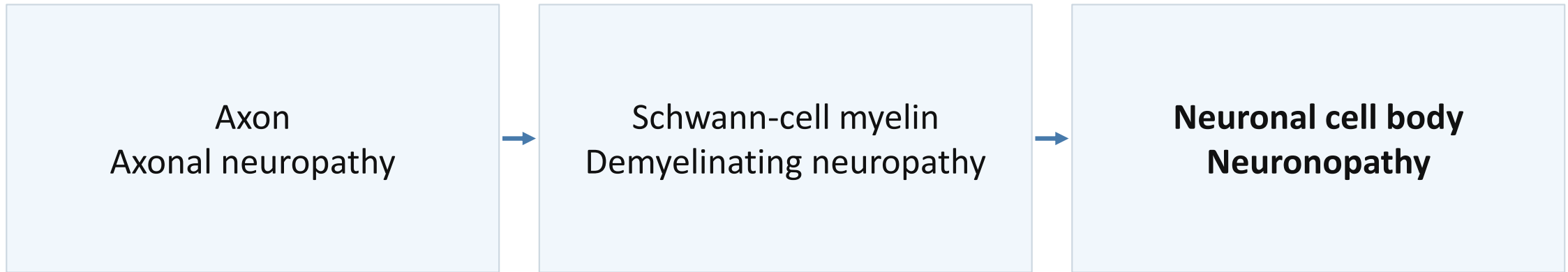
Perineurium → fascicles

# Schwann-cell myelin enables rapid impulse conduction

- One Schwann cell produces one myelin internode for a single axon.
- Nodes of Ranvier separate myelinated segments.
- Internodal integrity is important for saltatory conduction.



# Axon, myelin, and neuron can be injured separately



*These are pathobiologic categories—not four anatomic distribution patterns.*

# Axonal neuropathy reduces the number of functioning axons

- Degeneration affects the axon first; Myelin breaks down secondarily.
- Degeneration and regeneration may coexist during ongoing injury.
- Nerve signal amplitude falls as axons are lost; Conduction speed is relatively preserved.

## Wallerian degeneration: Severed axon

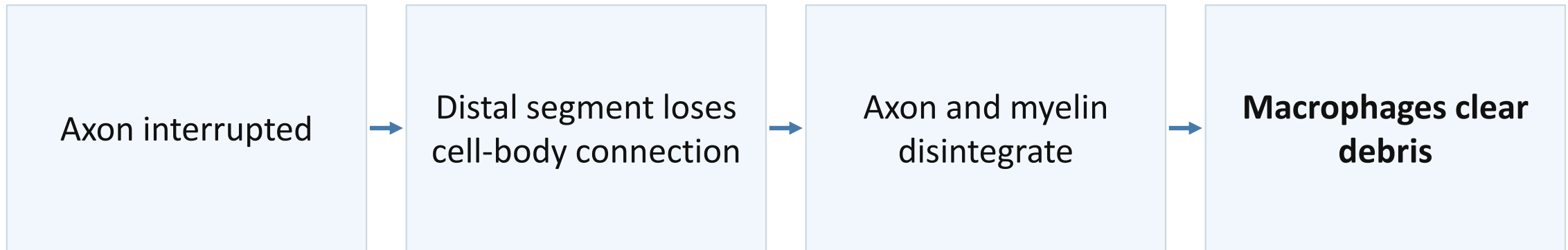


**Proximal stump**

**Distal fragmentation**

**Macrophages clear axon/myelin debris**

# Wallerian degeneration links focal injury to distal loss



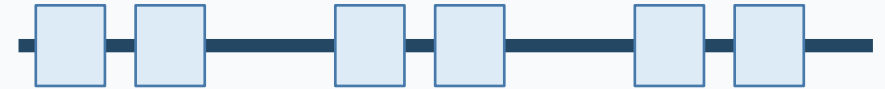
## **Morphologic consequence**

Fragments of degenerated myelin (“ovoid” profiles) mark an injured axon.

## Segmental demyelination may spare the axon

- Myelin internodes are lost discontinuously along otherwise preserved axons.
- Remyelination creates shorter and thinner new internodes.
- Slower nerve conduction is the characteristic electrophysiologic effect.

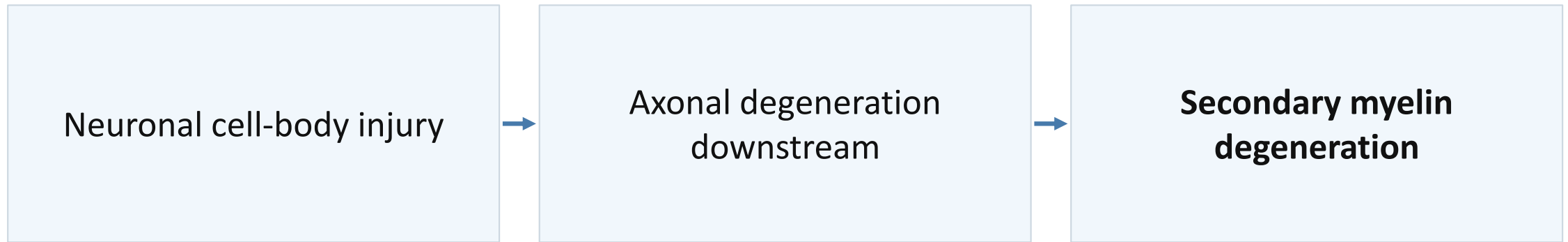
**Axon intact; Individual internodes injured**



**Discontinuous myelin loss**

**Repair creates short, thin sheaths**

# Neuronopathy can disrupt both distal and proximal territories



## **Localization distinction**

Cell-body injury need not preferentially affect the longest axons.

# What electrodiagnostic patterns imply

| Predominant injury | Characteristic physiology                | Pathologic interpretation                           |
|--------------------|------------------------------------------|-----------------------------------------------------|
| Axonal             | Lower response amplitude                 | Reduced functioning axon population                 |
| Demyelinating      | Reduced conduction velocity              | Loss of myelin and saltatory efficiency             |
| Neuronopathic      | Distribution may not be length-dependent | Cell-body loss with downstream process degeneration |

# Pattern recognition narrows—but does not prove—etiology

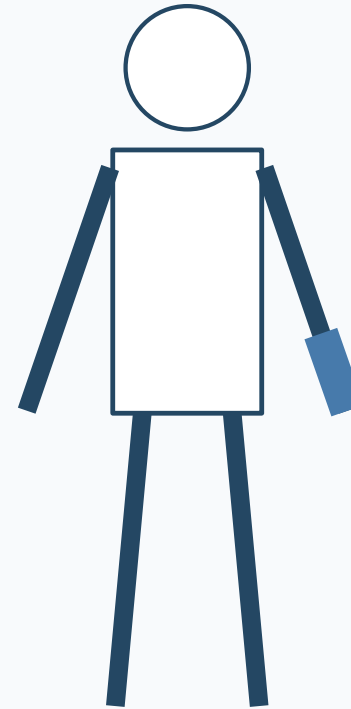


*Overlap exists; A single disease may produce several anatomic patterns.*

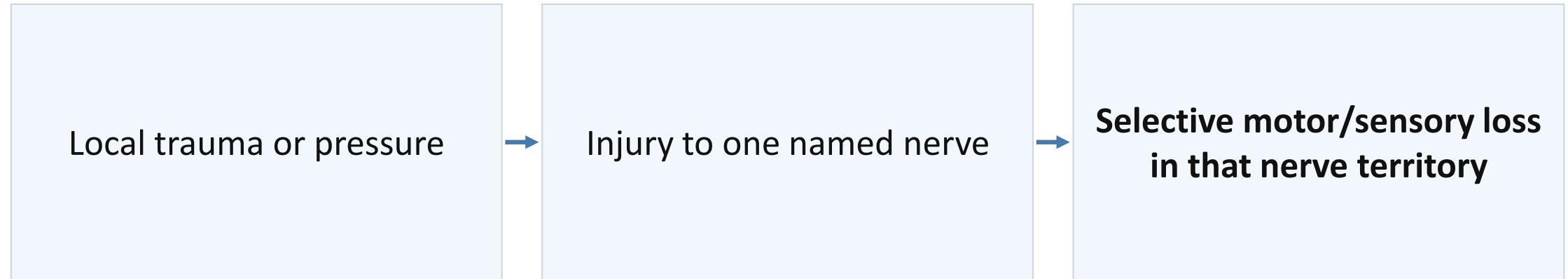
# Mononeuropathy follows one named peripheral nerve

- Motor and/or sensory deficits occupy a circumscribed nerve territory.
- The involved nerve's anatomy defines the deficit distribution.
- Trauma, entrapment, compression, and infection are recognized causes.

Schematic distribution



# Why a single focal nerve lesion causes restricted deficits



## **Localization principle**

The distribution should be anatomically coherent rather than simply “one limb.”

# Mechanical injuries are important focal causes

## **Laceration**

Direct cutting of a peripheral nerve

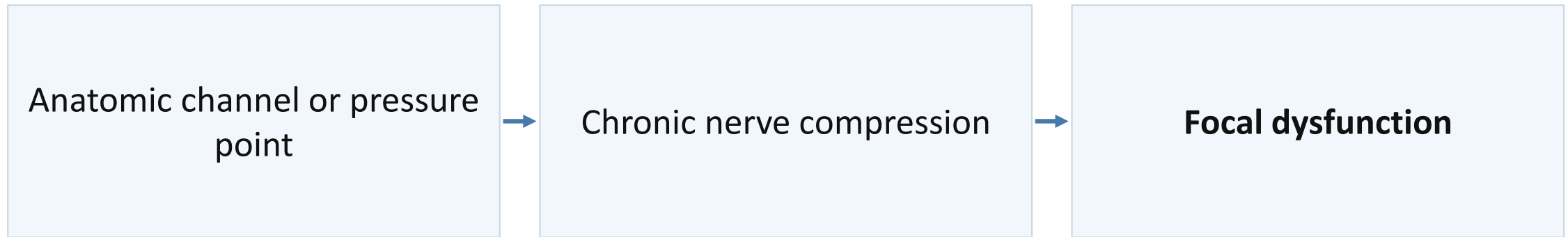
## **Avulsion**

Traction separates or damages nerve

## **Chronic compression**

Persistent pressure within an anatomic compartment

# Entrapment reflects pressure at a vulnerable site

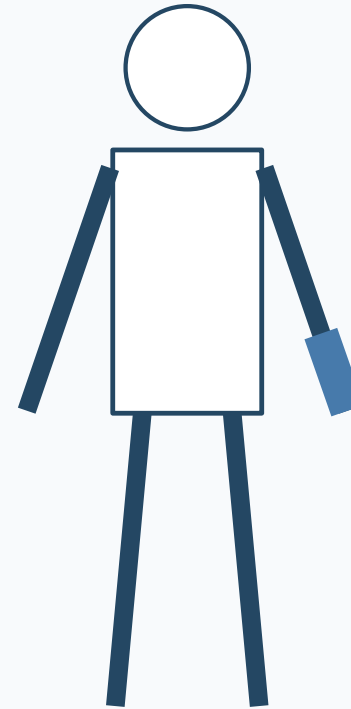


*The site of compression predicts the affected named nerve.*

# Median nerve compression: Carpal tunnel syndrome

- The median nerve is compressed at the wrist beneath the transverse carpal ligament.
- Symptoms include paresthesias and numbness in the thumb and first two digits.
- Hypothyroidism, diabetes, tissue edema, and other conditions may be associated.

Schematic distribution



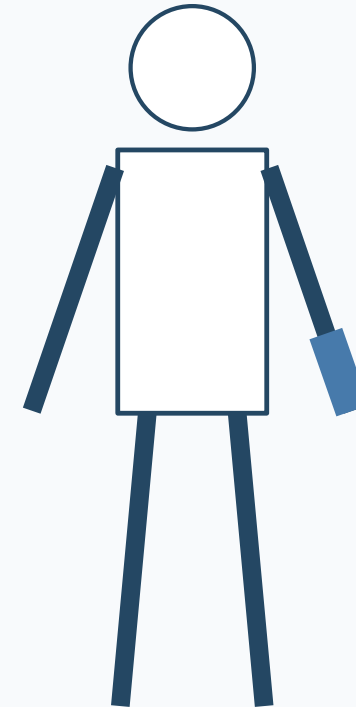
## Other typical entrapment locations

- The ulnar nerve may be compressed at the elbow.
- The common peroneal nerve is vulnerable around the knee.
- The radial nerve may be compressed in the upper arm, causing a focal palsy.

# Radial nerve palsy illustrates a focal motor deficit

- An illustrative right wrist drop can arise from right radial-nerve involvement.
- Deficits are restricted to the affected nerve rather than a symmetric distal pattern.
- Upper-arm compression is a recognized cause of radial nerve injury.

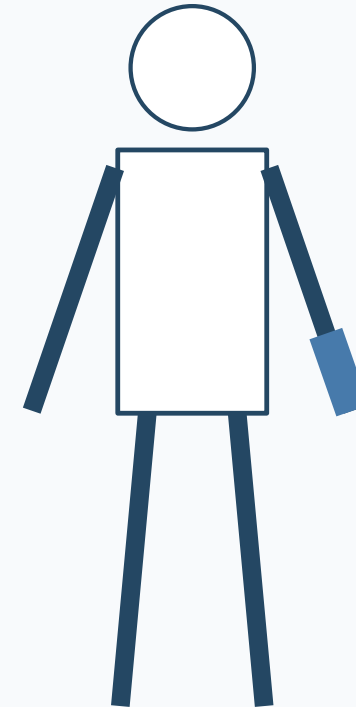
Schematic distribution



# Peroneal nerve involvement can cause foot drop

- Common peroneal nerve injury can produce a focal foot drop.
- The characteristic deficit is on the same side as the injured nerve.
- A foot drop alone should not automatically be called polyneuropathy.

Schematic distribution



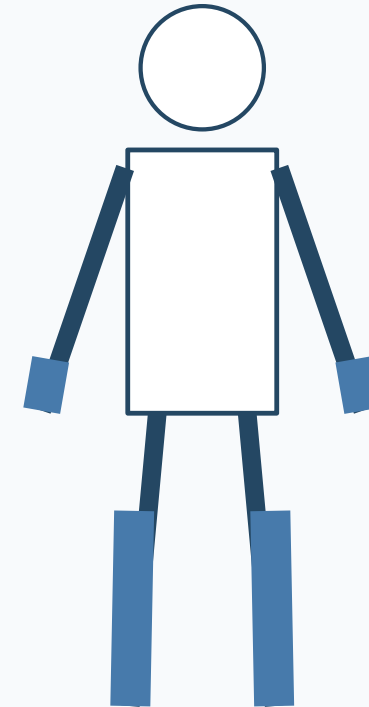
# How to recognize an isolated mononeuropathy

| Observation    | Favors mononeuropathy         | Would prompt reconsideration           |
|----------------|-------------------------------|----------------------------------------|
| Nerve count    | One named nerve               | Multiple unrelated nerves              |
| Distribution   | Restricted nerve territory    | Length-dependent bilateral distal loss |
| Laterality     | Often unilateral or focal     | Symmetric distal progression           |
| Possible cause | Entrapment, injury, infection | Diffuse metabolic or immune cause      |

# Polyneuropathy affects many nerves, often symmetrically

- Multiple peripheral nerves are impaired rather than one discrete nerve.
- The most common arrangement is bilateral and approximately symmetric.
- Many axonal polyneuropathies preferentially affect long distal processes.

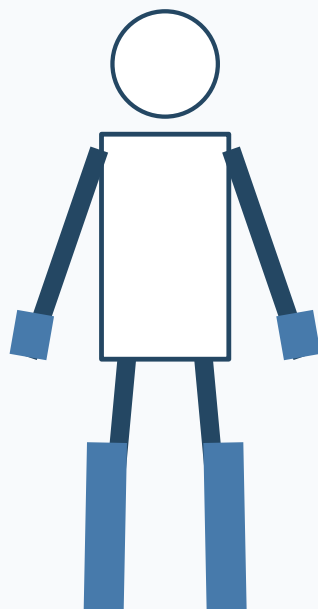
Schematic distribution



# Symmetry is a powerful initial discriminator

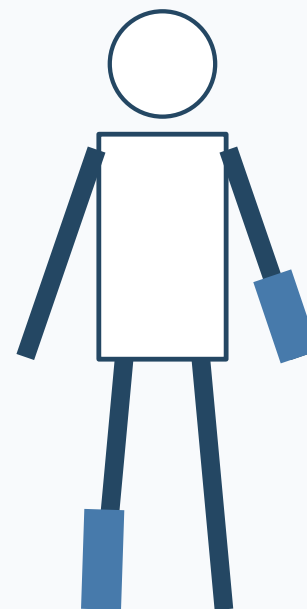
## Symmetric distal pattern

Schematic distribution



## Asymmetric multifocal pattern

Schematic distribution



# Length-dependent axonal loss starts in the longest nerves

Long distal axons are  
vulnerable



Distal degeneration begins in  
feet



**Deficits ascend with  
progression**

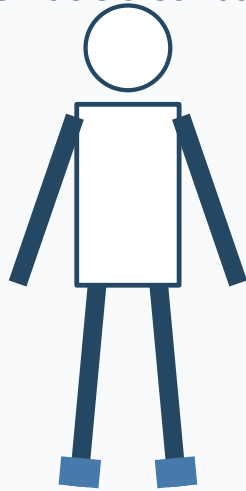
## **Pathology term**

A progressive distal-to-proximal axonal process is often called “dying back.”

# Distal polyneuropathy progresses in recognizable stages

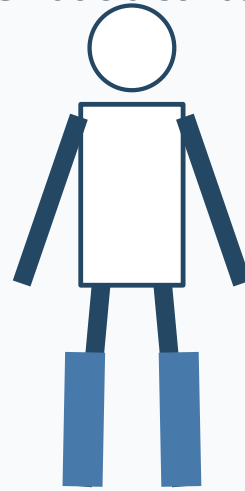
## Early: Feet

Schematic distribution



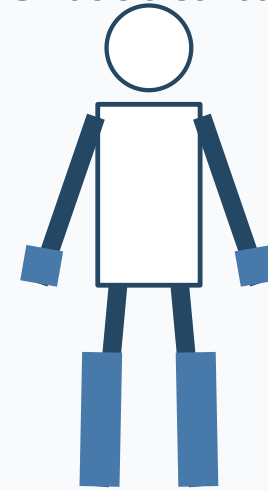
## Progression: Lower legs

Schematic distribution



## Later: Hands + legs

Schematic distribution

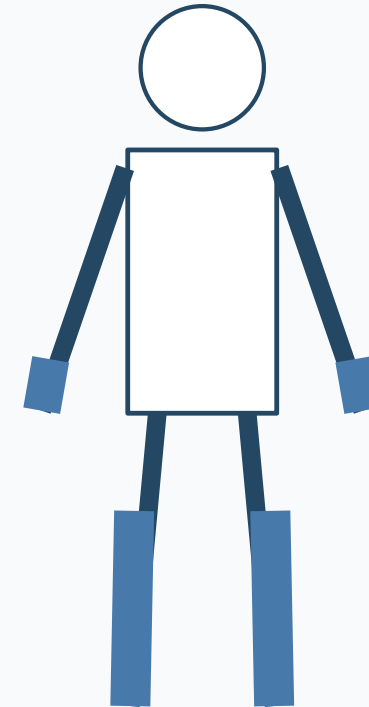


*Conceptual stages: Hand symptoms appear as leg deficits approach the knees.*

# The “stocking-and-glove” pattern is anatomically distal

- Sensory deficits ascend from the feet in a length-dependent neuropathy.
- Hand involvement generally follows substantial ascending leg involvement.
- The term describes territory, not a unique cause or tissue mechanism.

Schematic distribution



# Dying-back degeneration explains the distal gradient

- The longest axons are most vulnerable to chronic toxic or metabolic disturbances.
- Degeneration occurs distally while the neuronal cell bodies remain comparatively preserved.
- Progressive loss of distal fibers produces the distal clinical deficit.

## Wallerian degeneration: Severed axon



**Proximal stump**

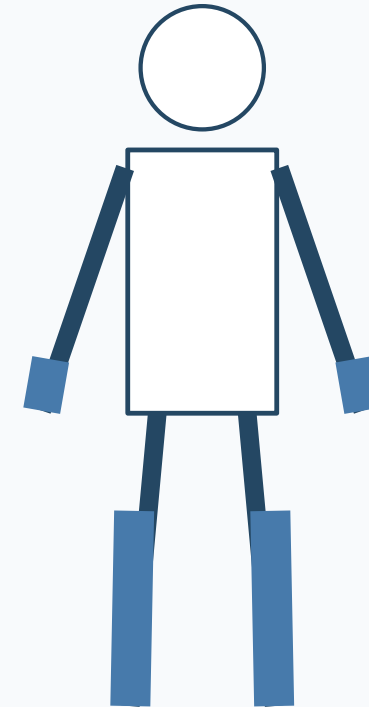
**Distal fragmentation**

**Macrophages clear axon/myelin debris**

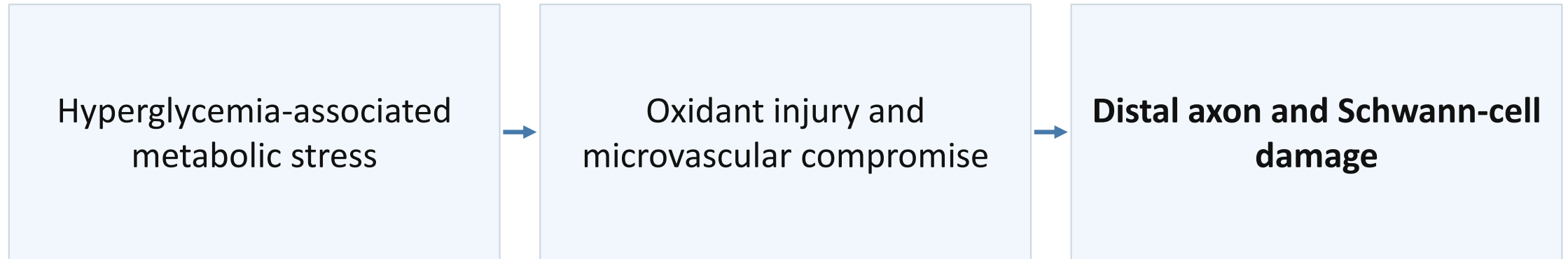
# Diabetes is a prototype of distal symmetric polyneuropathy

- Diabetic peripheral neuropathy most often has an ascending distal symmetric sensorimotor distribution.
- Sensory axons are prominently involved; Autonomic and motor fibers can also be affected.
- The typical morphologic pattern is loss and regeneration of peripheral axons.

Schematic distribution



# Diabetic neuropathy reflects multiple injury pathways



## Interpretation

The text describes a multifactorial mechanism—not a single established initiating defect.

## Loss versus abnormal gain of sensory signals

| Clinical description     | Functional interpretation               | Illustrative manifestation         |
|--------------------------|-----------------------------------------|------------------------------------|
| Negative sensory symptom | Normal input is reduced                 | Numbness or reduced pain sensation |
| Positive sensory symptom | Abnormal firing of injured nerve fibers | Pins-and-needles or dysesthesia    |

## **Distal sensory neuropathy may have systemic consequences**

- Loss of protective pain sensation increases vulnerability to unnoticed injury.
- Impaired balance and distal sensation contribute to functional morbidity.
- Chronic foot ulcers and fractures may occur in diabetic neuropathy.

## **Autonomic involvement can coexist with distal polyneuropathy**

- Diabetic autonomic neuropathy commonly accompanies distal sensorimotor neuropathy.
- Postural hypotension, impaired bladder emptying, and sexual dysfunction are described manifestations.
- A mixed sensory–autonomic presentation does not imply a different anatomic nerve-count pattern.

## **Uremia provides another symmetric distal example**

- Renal failure may be associated with distal symmetric peripheral neuropathy.
- Possible symptoms include distal dysesthesias, muscle cramps, and diminished reflexes.
- Axonal degeneration predominates, although secondary demyelination may occur.

## Metabolic and nutritional causes can converge on a pattern

| Example                | Clinical distribution described in Robbins            | Dominant lesion or qualification             |
|------------------------|-------------------------------------------------------|----------------------------------------------|
| Hypothyroidism         | Distal symmetric neuropathy or focal carpal tunnel    | Predominantly sensory axonal, or compression |
| Vitamin B12 deficiency | Peripheral nerve dysfunction with spinal tract injury | Mixed peripheral and central involvement     |
| Other deficiencies     | Peripheral neuropathy                                 | B1, B6, vitamin E, folate, copper, zinc      |

## **Toxic neuropathy is an etiologic—not anatomic—label**

- Alcohol, heavy metals, organic solvents, and some medications can damage peripheral nerves.
- Cancer chemotherapy may injure axons or neuronal processes; Some drugs disrupt axonal transport.
- The observed distribution must still be separately determined for each patient.

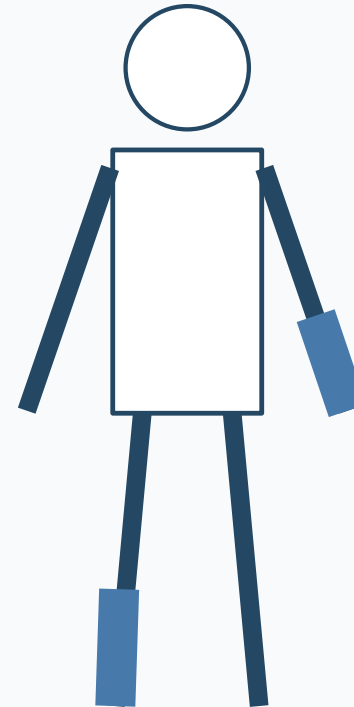
## One metabolic disease can produce multiple patterns

- Although diabetes commonly causes symmetric distal polyneuropathy, focal presentations also occur.
- Examples include mononeuropathies, cranial neuropathies, and painful radiculoplexus neuropathy.
- The anatomic pattern should therefore be described rather than inferred from the known diagnosis.

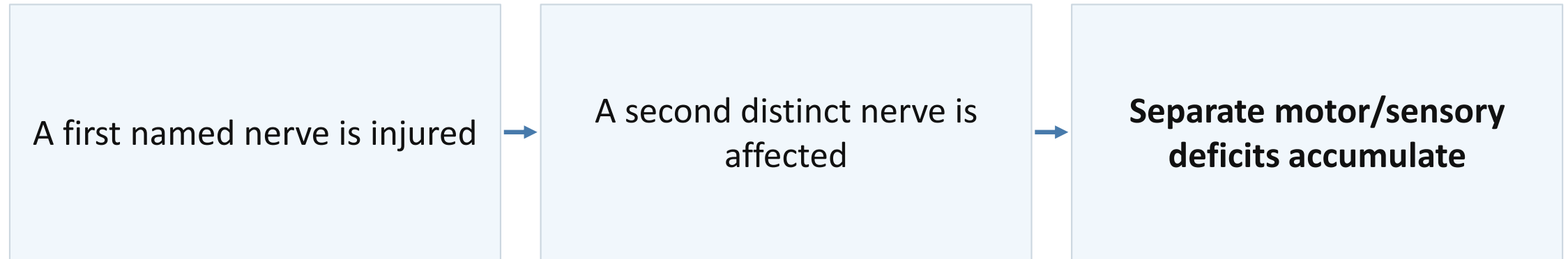
# Mononeuritis multiplex damages separate nerves patchily

- Different named nerves are affected in a nonuniform, seemingly random pattern.
- Clinical findings are usually asymmetric and multifocal.
- The combination is not explained by one nerve lesion or one uniform distal gradient.

Schematic distribution



# Multiplicity plus asymmetry is the key logic



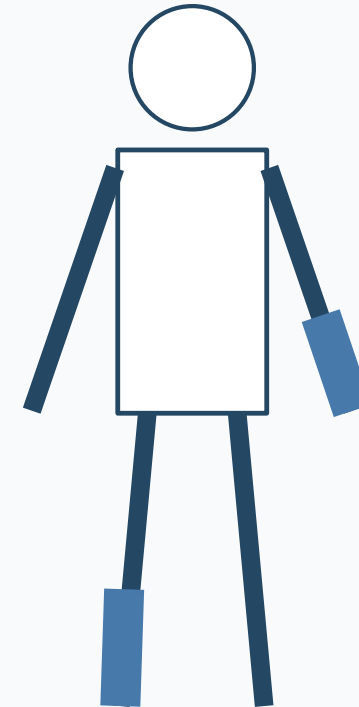
## **Contrast**

Not the same as a symmetric length-dependent polyneuropathy.

# Two noncontiguous deficits can identify multiplex injury

- A right radial lesion can cause right wrist drop.
- A separate left peroneal lesion can cause left foot drop.
- The combined pattern implies multifocal injury rather than a single continuous nerve territory.

Schematic distribution



# Vasculitis is a classic cause of mononeuritis multiplex

Inflamed peripheral-nerve  
vessels



Focal ischemic nerve injury



**Uneven axonal degeneration  
among fascicles**

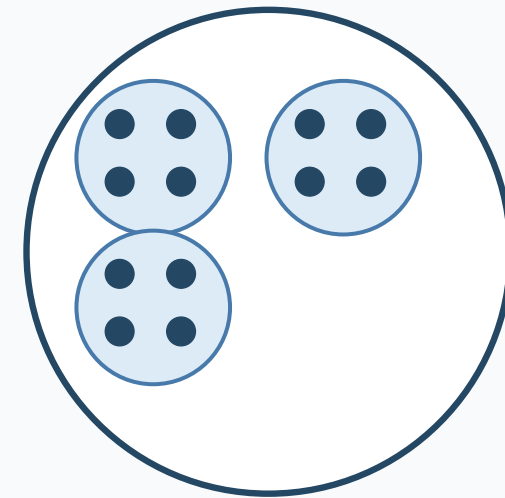
## **Distributional implication**

Patchy vascular involvement can produce different deficits in different nerves.

# Vasculitic nerve injury is often fascicularly uneven

- Some nerve fascicles exhibit greater axonal loss than adjacent fascicles.
- Perivascular inflammation can accompany the axonal injury.
- Damage to vessel walls supports a vasculitic process when demonstrated histologically.

Peripheral nerve cross-section



Epineurium → nerve

Perineurium → fascicles

## **Systemic autoimmune disease is a related differential**

- Rheumatoid arthritis, Sjögren syndrome, and systemic lupus erythematosus may be accompanied by neuropathy.
- They may cause distal sensory or sensorimotor polyneuropathies.
- Vasculitic neuropathy may also occur as a distinct manifestation of these disorders.

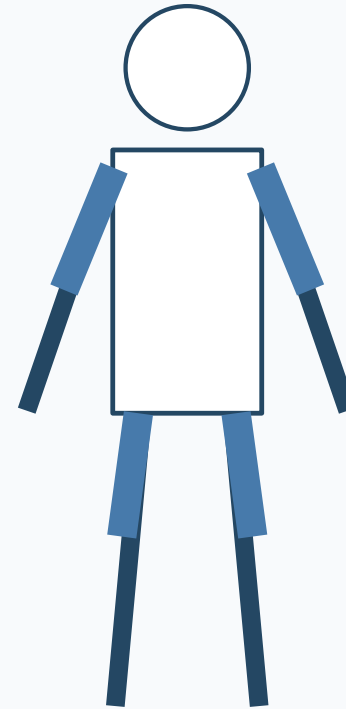
# Polyneuropathy versus mononeuritis multiplex

| Feature         | Polyneuropathy (typical)    | Mononeuritis multiplex           |
|-----------------|-----------------------------|----------------------------------|
| Nerves          | Multiple                    | Multiple, independently affected |
| Symmetry        | Usually bilateral/symmetric | Patchy and asymmetric            |
| Spatial pattern | Often length-dependent      | Scattered nerve territories      |
| Example         | Diabetic distal neuropathy  | Vasculitic neuropathy            |

# Polyradiculoneuropathy extends from roots into peripheral nerves

- Both spinal nerve roots and peripheral nerves participate in the injury.
- Proximal and distal portions of the body can be symptomatic.
- Diffuse symmetric involvement is a characteristic clinical presentation.

Schematic distribution



# Root involvement changes the expected distribution

Nerve-root involvement



Peripheral nerve involvement



**Deficits include proximal +  
distal regions**

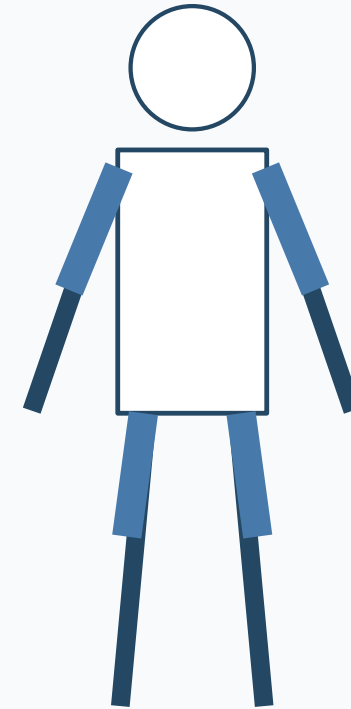
## **Localization implication**

Prominent proximal deficits argue against assuming a pure dying-back distal axonopathy.

# Proximal and distal findings suggest a broader process

- A symmetric combination of proximal and distal weakness can support polyradiculoneuropathy.
- Isolated distal symptoms are less specific and commonly occur in polyneuropathy.
- Anatomic pattern remains distinct from the underlying immune or myelin injury mechanism.

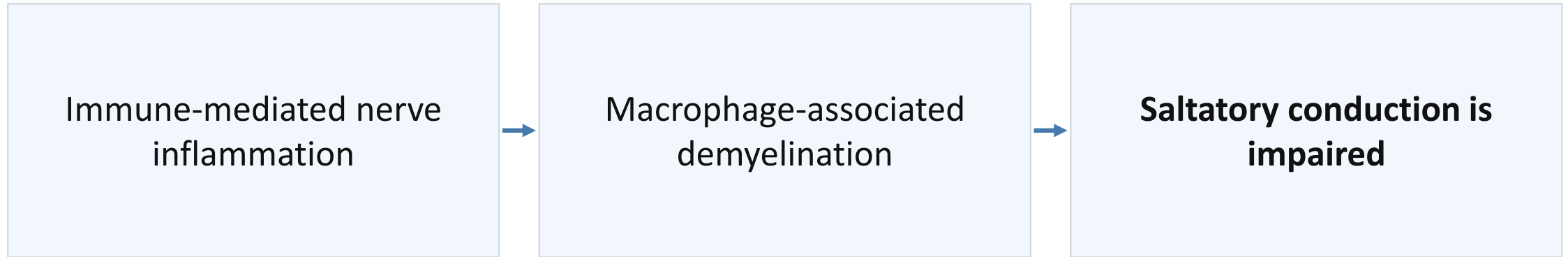
Schematic distribution



# Guillain–Barré syndrome demonstrates an acute root–nerve process

- The common inflammatory form is acute inflammatory demyelinating polyradiculoneuropathy.
- Classically there is ascending weakness with early loss of deep tendon reflexes.
- Root and peripheral nerve inflammation damages myelin; Severe injury may also involve axons.

# Immune damage to myelin explains typical GBS physiology



## **Electrophysiology**

Multifocal destruction of internodes commonly slows nerve conduction.

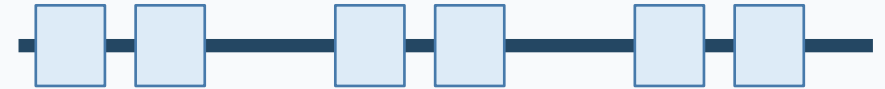
# **CIDP is a chronic inflammatory polyradiculoneuropathy**

- CIDP usually produces a symmetric mixed sensorimotor neuropathy.
- Symptoms persist for at least two months and may evolve with relapses or remission.
- Both proximal and distal deficits, including weakness and sensory disturbance, may be present.

# Repeated demyelination can remodel peripheral nerves

- Schwann cells repeatedly form replacement myelin around affected axons.
- Concentric Schwann-cell proliferation may form onion bulbs.
- Onion bulbs indicate recurrent demyelination but are not specific for CIDP.

**Axon intact; Individual internodes injured**



**Discontinuous myelin loss**

**Repair creates short, thin sheaths**

# Acute versus chronic inflammatory root–nerve disorders

| Attribute          | GBS / AIDP                             | CIDP                                   |
|--------------------|----------------------------------------|----------------------------------------|
| Course             | Acute, reaches nadir within four weeks | Symptoms persist at least two months   |
| Typical pattern    | Ascending weakness and areflexia       | Symmetric sensory and motor impairment |
| Predominant injury | Demyelination in common subtype        | Recurrent demyelination/remyelination  |
| Useful concept     | Acute polyradiculoneuropathy           | Chronic polyradiculoneuropathy         |

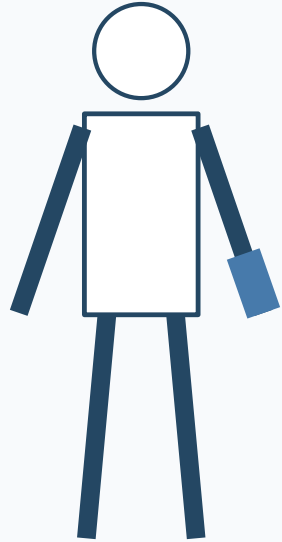
## Keep anatomic pattern and injury mechanism independent

| Clinical pattern      | Possible mechanism                   | Grounded example                    |
|-----------------------|--------------------------------------|-------------------------------------|
| Single-nerve focal    | Axonal injury from physical forces   | Carpal tunnel or radial compression |
| Symmetric distal      | Length-dependent axonal degeneration | Diabetes or uremia                  |
| Asymmetric multifocal | Patchy ischemic axonal injury        | Vasculitic neuropathy               |
| Root + nerve          | Immune demyelination                 | GBS (common subtype), CIDP          |

# Single, symmetric, scattered, or root-associated?

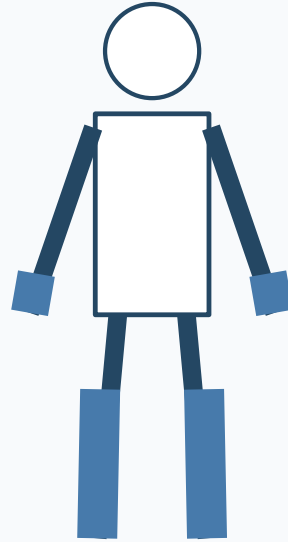
**One nerve**

Schematic distribution



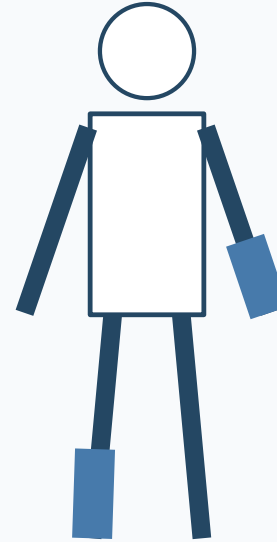
**Many symmetric nerves**

Schematic distribution



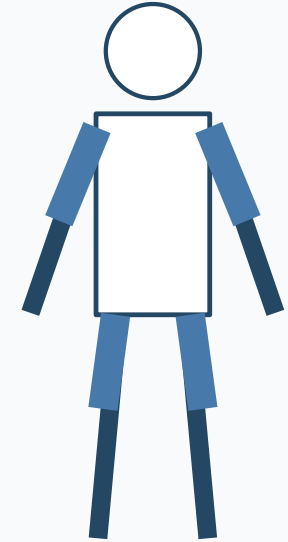
**Scattered individual nerves**

Schematic distribution

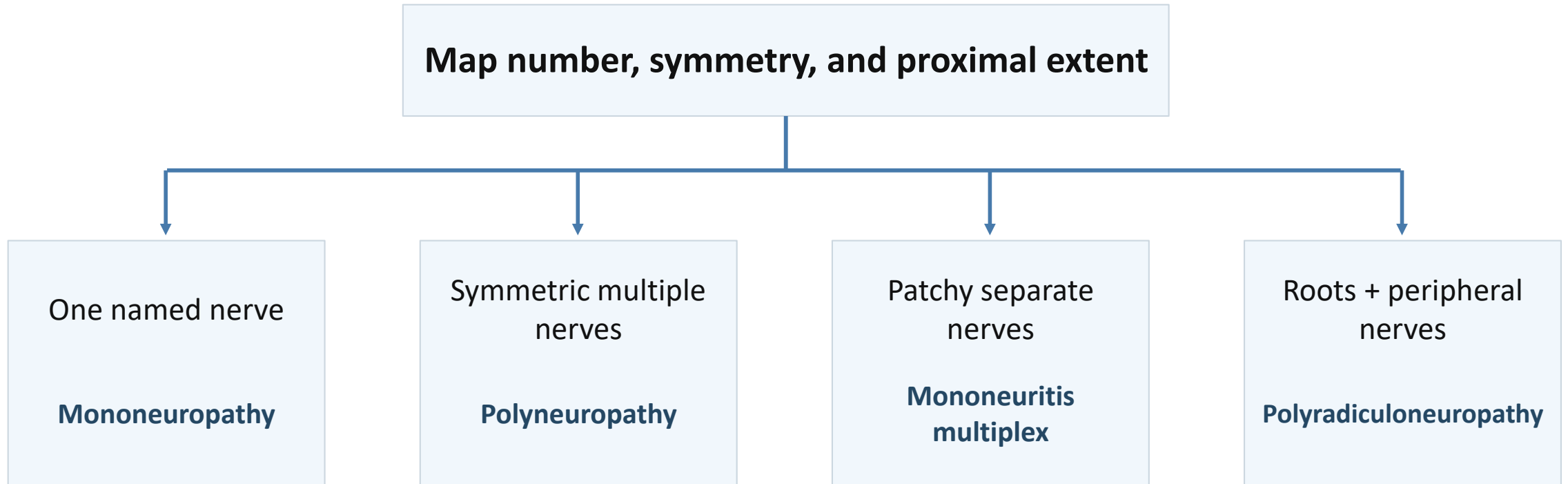


**Roots + peripheral nerves**

Schematic distribution



# A practical pattern-recognition pathway



*These are alternative patterns, not consecutive stages; Clinical presentations may overlap.*

## **Do not diagnose etiology from distribution alone**

- A neuropathic phenotype is a description of clinical anatomy, not a complete diagnosis.
- Metabolic, toxic, inflammatory, infectious, inherited, and physical causes can overlap.
- A mixed clinical pattern should prompt recognition of possible concurrent mechanisms.

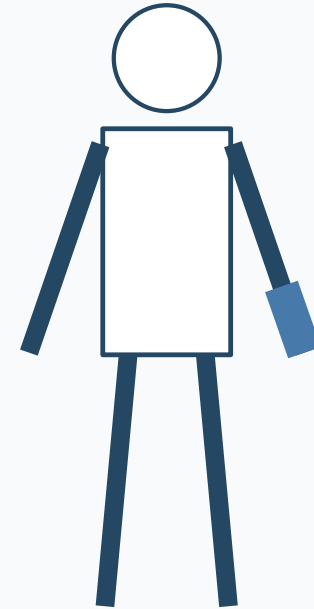
# Case 1: Focal hand symptoms

## Illustrative teaching case

Intermittent tingling and numbness are concentrated in the thumb and first two digits of one hand.

**Which anatomic pattern should be considered first?**

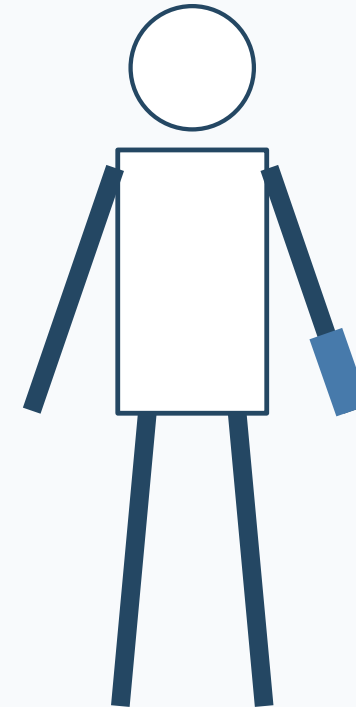
## Schematic distribution



## Case 1 interpreted: Median-nerve localization

- The symptoms occupy a restricted distribution compatible with one peripheral nerve.
- Wrist-level compression is one plausible lesion site.
- The unilateral focal pattern is different from a bilateral stocking-and-glove presentation.

Schematic distribution



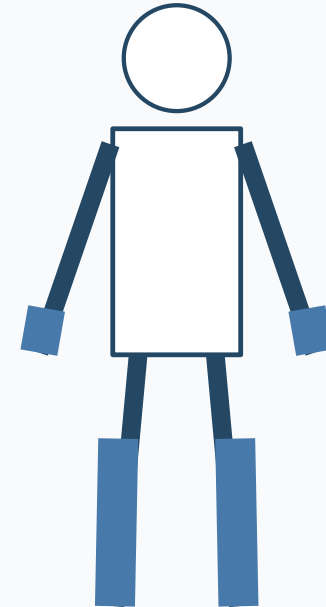
## Case 2: Distal bilateral sensory loss

### Illustrative teaching case

Sensory loss begins in both feet, then rises toward the lower legs; The fingertips become involved later.

**Which distribution describes this progression?**

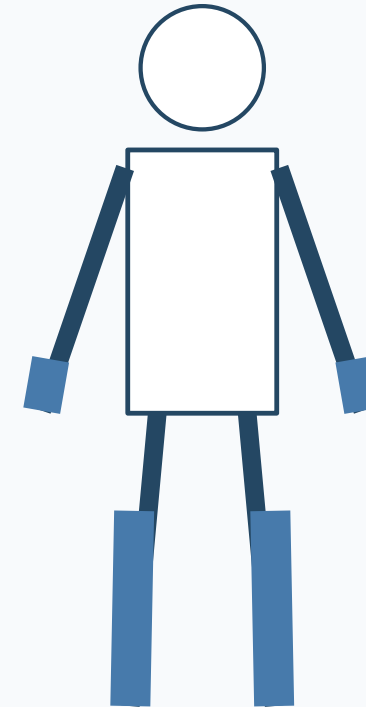
### Schematic distribution



## Case 2 interpreted: Length-dependent polyneuropathy

- The bilateral sensory loss implicates multiple nerves.
- Distal-to-proximal progression is characteristic of length-dependent axonal injury.
- Diabetes and other metabolic or toxic disorders are examples of etiologic categories.

Schematic distribution



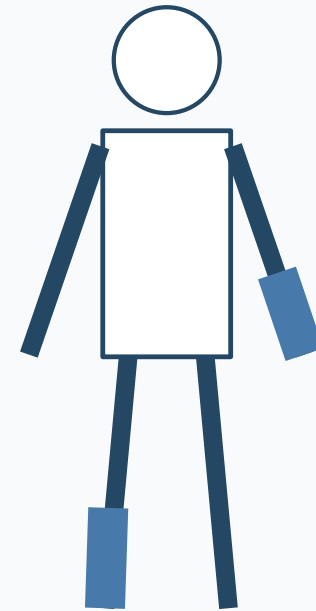
## Case 3: Unrelated focal motor deficits

### Illustrative teaching case

An individual develops right wrist drop and later develops left foot drop, affecting two different nerve territories.

**What distribution is suggested by the combined deficits?**

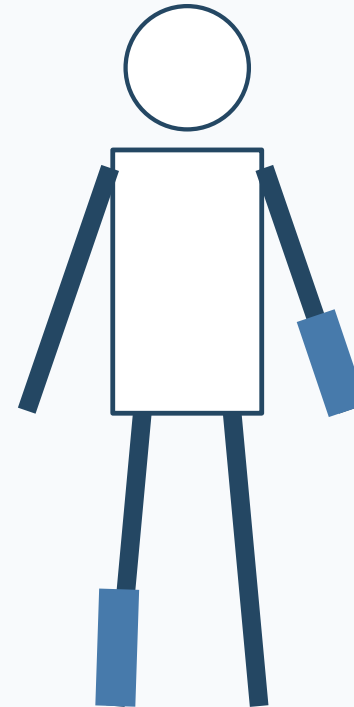
### Schematic distribution



## Case 3 interpreted: Mononeuritis multiplex

- The neurologic deficits localize to separate named nerves.
- Their asymmetric distribution cannot be explained by one focal nerve injury.
- Vasculitic injury is a relevant differential because it can affect fascicles patchily.

Schematic distribution



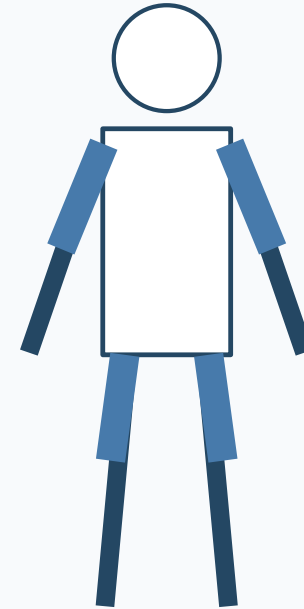
## Case 4: Weakness in proximal and distal limbs

### Illustrative teaching case

A patient develops symmetric weakness affecting proximal and distal portions of the limbs, with generalized nerve involvement.

**Which pattern should be evaluated?**

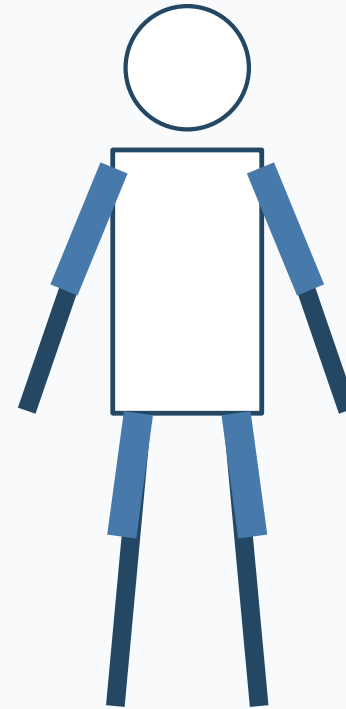
### Schematic distribution



## Case 4 interpreted: Roots and peripheral nerves

- The wide proximal–distal distribution suggests involvement beyond distal axon endings.
- A combined nerve-root and peripheral-nerve process is a key consideration.
- Immune-mediated demyelinating disorders such as CIDP fit this distribution.

Schematic distribution



## Synthesis: Pattern clues and typical examples

| Pattern                | Discriminating observation             | Illustrative cause   |
|------------------------|----------------------------------------|----------------------|
| Mononeuropathy         | Single named nerve                     | Entrapment or trauma |
| Polyneuropathy         | Symmetric, often length-dependent      | Diabetes or uremia   |
| Mononeuritis multiplex | Multiple nerves; patchy and asymmetric | Vasculitis           |
| Polyradiculoneuropathy | Roots and nerves; proximal + distal    | CIDP or GBS          |

## What to retain from the anatomic classification

- Count involved nerves and characterize symmetry before proposing a cause.
- Distal length dependence, focal territories, and proximal involvement convey different localizations.
- Separately classify whether the dominant injury affects axons, myelin, or neuronal cell bodies.
- Use disease examples to test the pattern—not to substitute for clinical localization.