

Atrophy

Cellular adaptation • Morphology • Clinicopathologic interpretation

Reduced tissue mass • Cellular adaptation • Functional consequences

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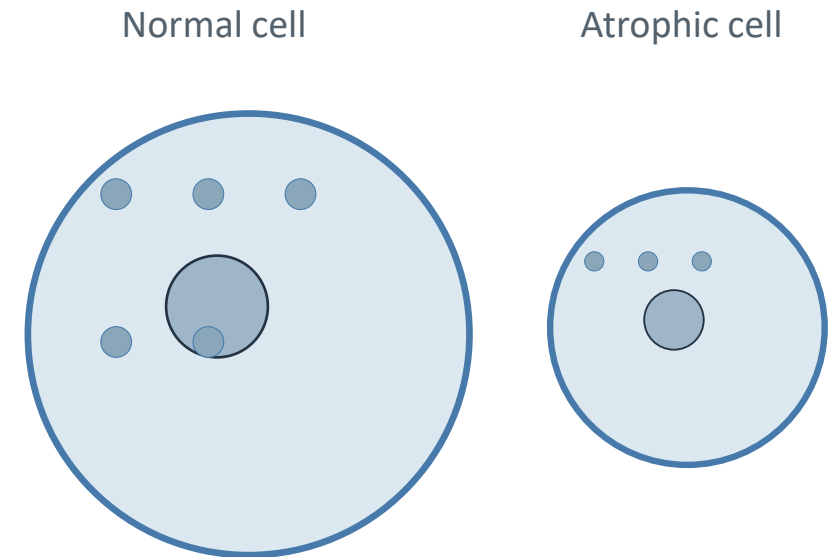
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Learning objectives

- Define atrophy and distinguish reduced cell size from loss of cells.
- Explain the six major causes of pathologic atrophy.
- Relate cellular shrinkage to reduced synthesis, degradation and autophagy.
- Interpret tissue morphology and determine when cell loss becomes irreversible.

Atrophy within the spectrum of cellular adaptation

- Adaptations alter cell size, number or phenotype in response to changed demands.
- Atrophy reduces organ mass, whereas hypertrophy and hyperplasia increase it.
- An adaptive response can preserve surviving cells but compromise organ function.



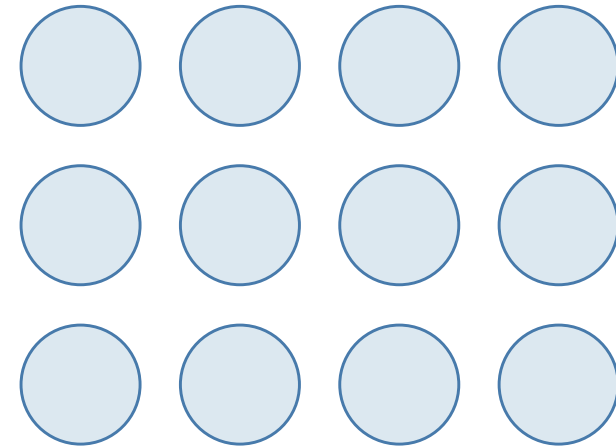
Reduced cytoplasmic volume and organelles

Schematic — not histology

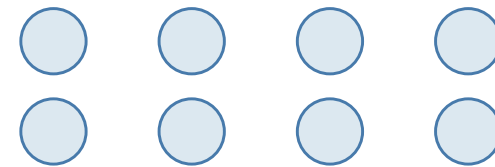
What is atrophy?

- An organ or tissue becomes smaller because its constituent cells shrink and/or decrease in number.
- The word describes a morphologic response, not a single disease or molecular pathway.
- Atrophy may occur during normal development or under pathologic stress.

Preserved cellular mass



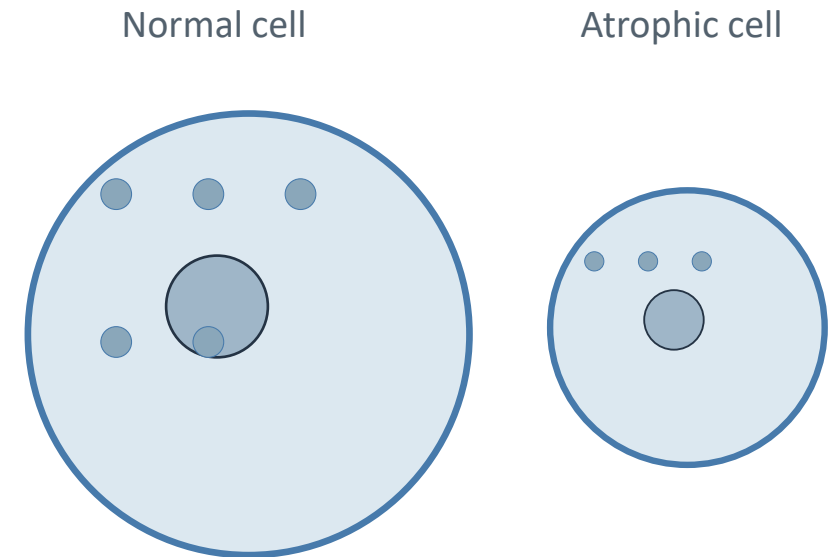
Reduced tissue volume



Schematic: Cell-size and cell-number effects

Cell shrinkage and cell loss are distinct components

- Loss of cytoplasm and intracellular structures decreases individual cell volume.
- Cell loss, including apoptosis in some settings, further reduces tissue mass.
- The relative importance of these components depends on cause and duration.

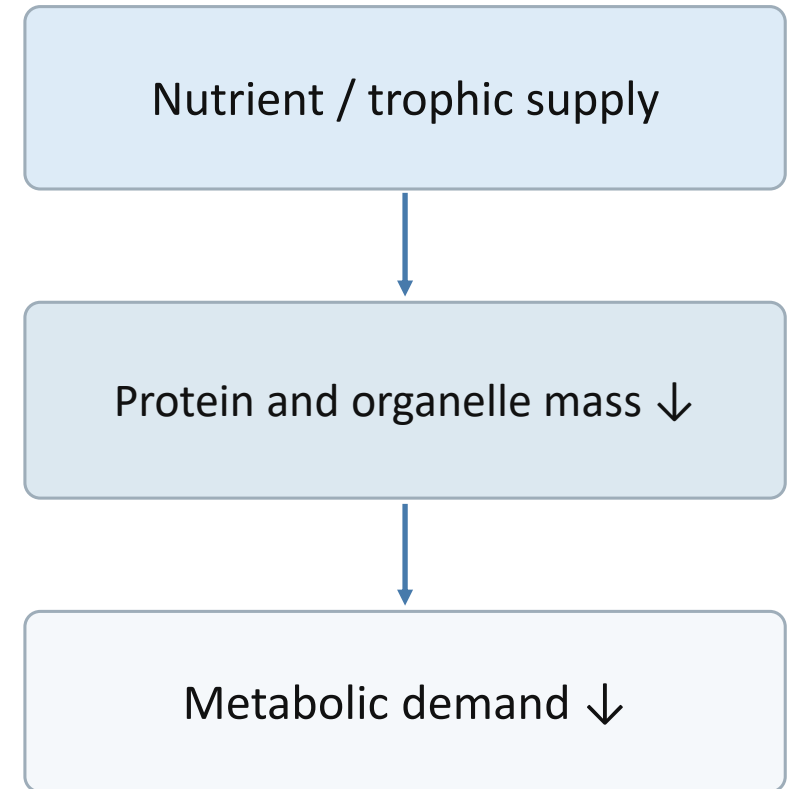


Reduced cytoplasmic volume and organelles

Schematic — not histology

Atrophy is an active adaptation

- Cells facing fewer resources can reduce their biosynthetic and maintenance demands.
- Smaller cells require less energy and fewer intracellular components.
- Early atrophy can preserve cell survival despite diminished specialized function.

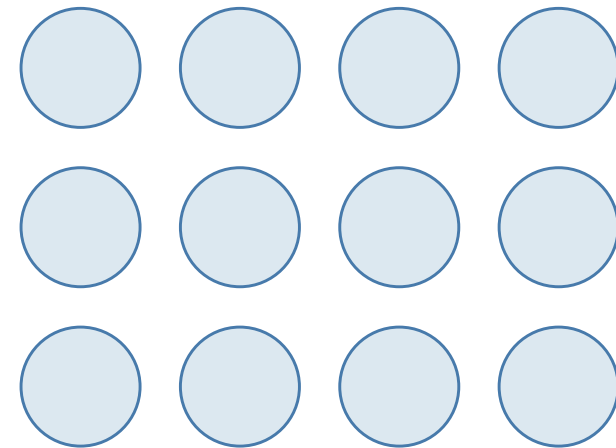


Adaptation can sustain viability despite loss of function

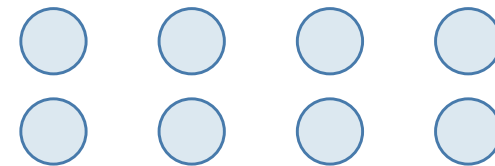
Atrophy can be physiologic or pathologic

- Physiologic atrophy accompanies programmed changes in normal development.
- Pathologic atrophy follows loss of workload, blood supply, nutrition or trophic support.
- Interpret size reduction in its developmental, clinical and tissue context.

Preserved cellular mass



Reduced tissue volume



Schematic: Cell-size and cell-number effects

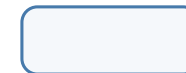
Physiologic regression during development

- Normal embryonic structures are not all retained in mature anatomy.
- The notochord and thyroglossal duct as examples of developmental atrophy.
- Regression in the expected developmental period is not itself evidence of disease.

Transient embryonic structure



Expected developmental regression



Generic schematic — not embryologic anatomy

Local and generalized patterns of atrophy

- A local insult may selectively affect one muscle, organ or compressed tissue region.
- Systemic nutrient deficiency or prolonged inactivity can affect multiple muscle groups.
- Distribution is often a stronger etiologic clue than organ size alone.

Disuse

Denervation

Chronic ischemia

Malnutrition

Hormone loss

Pressure

Six cause groups

The six causes of pathologic atrophy

- Disuse and denervation reduce support for skeletal muscle.
- Chronic ischemia and malnutrition limit metabolic resources.
- Endocrine withdrawal and sustained pressure remove trophic input or impair perfusion.

Disuse

Denervation

Chronic ischemia

Malnutrition

Hormone loss

Pressure

Six cause groups

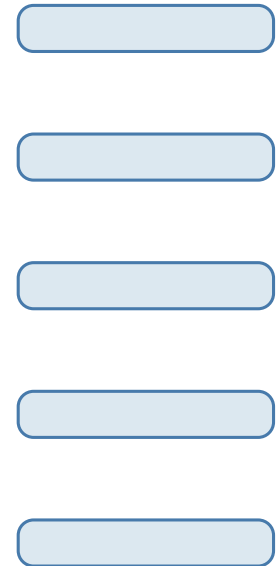
Disuse atrophy: A falling mechanical demand

- Immobilization in a cast removes usual workload from skeletal muscle.
- Complete bed rest similarly reduces the stimuli sustaining muscle mass.
- The resulting decrease in fiber size is an adaptive response to disuse.

Normal fibers



Atrophic fibers



Schematic — not a muscle biopsy

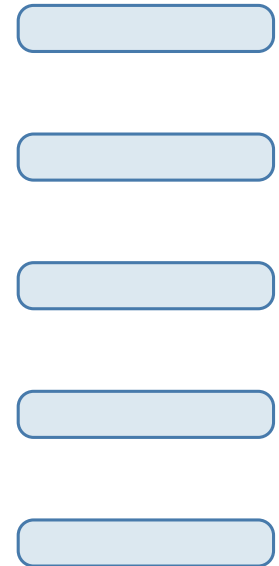
Disuse: The early structural response

- Skeletal muscle fibers become smaller before substantial fiber loss develops.
- This early decrease in cell size is reversible after activity resumes.
- Reversibility depends on timing and the persistence of underlying conditions.

Normal fibers



Atrophic fibers

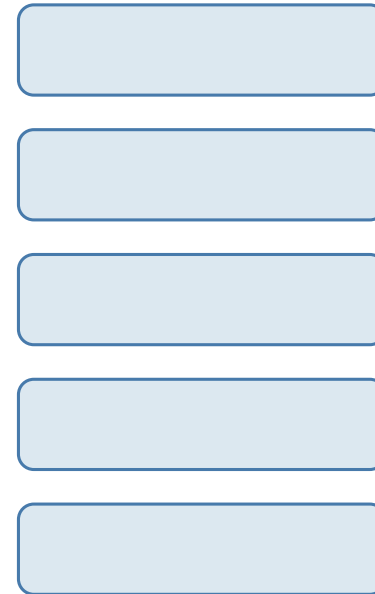


Schematic — not a muscle biopsy

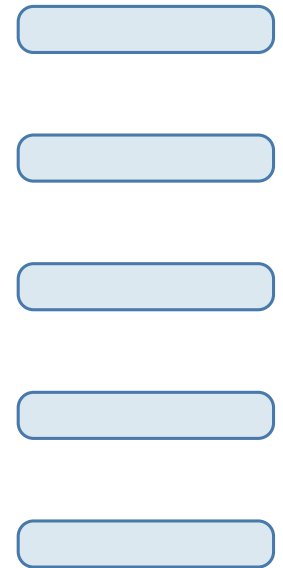
Disuse: Progression with prolonged inactivity

- Persistent unloading can reduce the number of muscle fibers as well as their size.
- Apoptosis contributes to the fiber loss described with prolonged disuse.
- Structural loss limits the assumption that all muscle wasting is promptly reversible.

Normal fibers



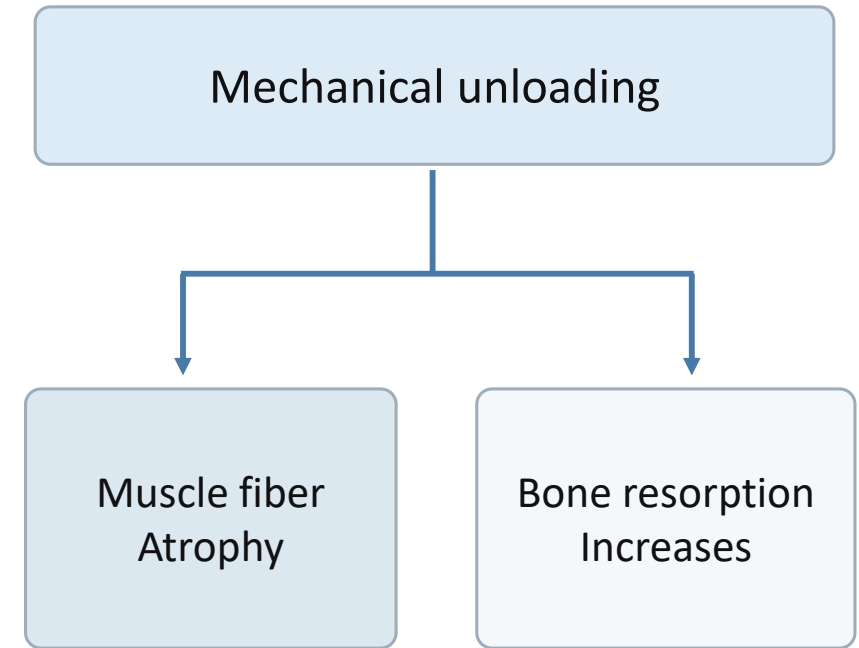
Atrophic fibers



Schematic — not a muscle biopsy

Disuse also affects bone

- Loss of mechanical loading increases bone resorption in the disuse setting.
- Muscle wasting and disuse osteoporosis can therefore coexist.
- A casted limb may show coupled consequences in muscle and bone rather than an isolated muscle response.

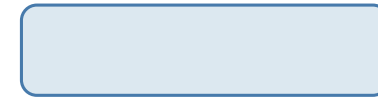
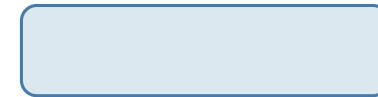
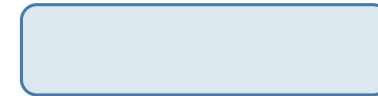


Two consequences of sustained disuse

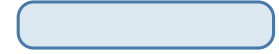
Cast immobilization and bed rest: Shared principles

- A cast causes regional reduction of mechanical work in immobilized muscles.
- Bed rest affects a broader distribution because many muscles are unloaded.
- Both share reduced demand, but the anatomic distribution differs.

Normal fibers



Atrophic fibers



Schematic — not a muscle biopsy

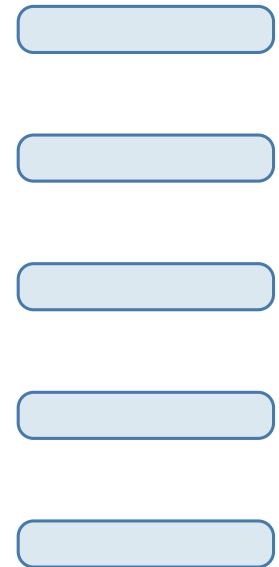
Disuse atrophy: Consequences for function

- Reduced muscle fiber mass lowers the tissue available for contraction.
- Weakness may become evident during remobilization after prolonged unloading.
- Functional recovery is a separate question from restoration of gross muscle size.

Normal fibers



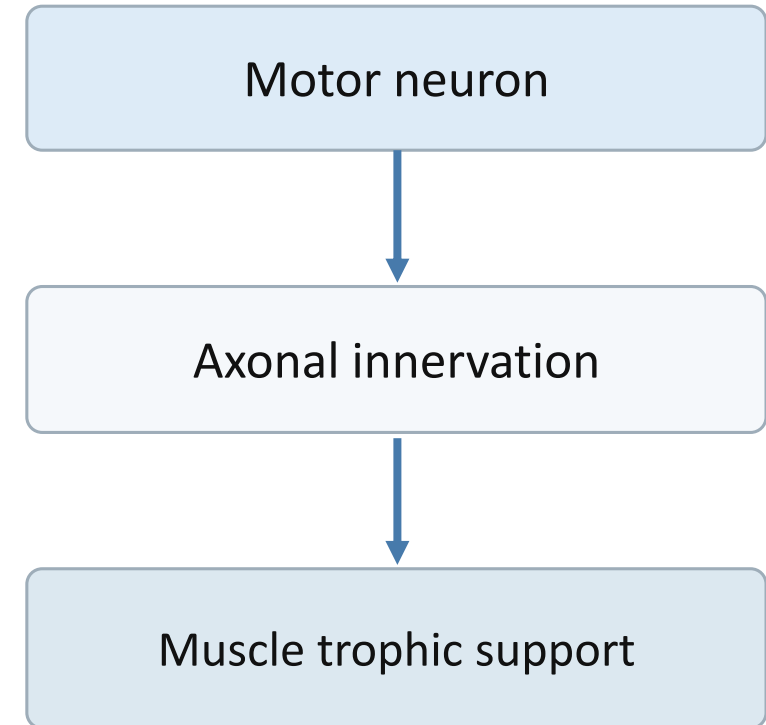
Atrophic fibers



Schematic — not a muscle biopsy

Denervation atrophy: Lost neural support

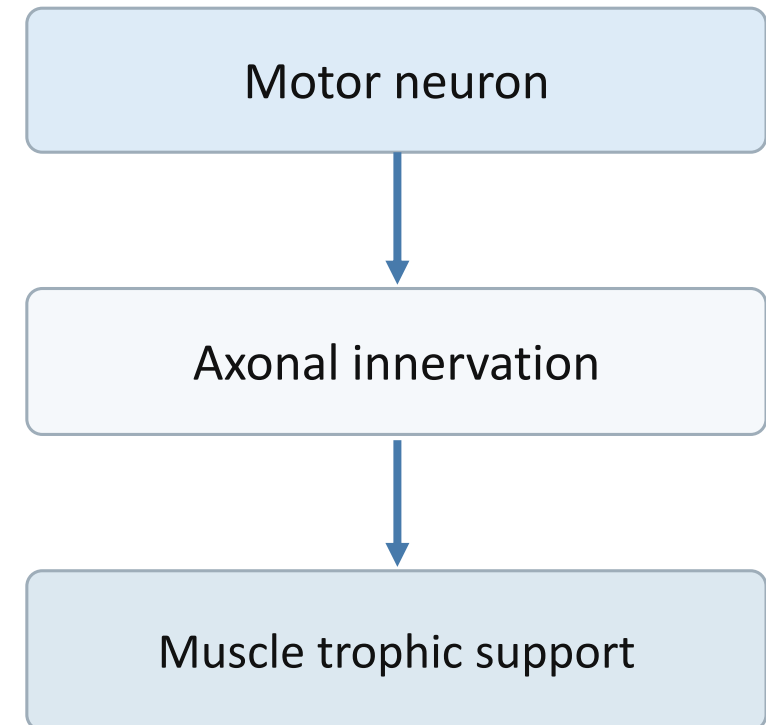
- Skeletal muscle metabolism and function depend on an intact nerve supply.
- Damage to the supplying nerve can produce atrophy in its target fibers.
- The primary insult is neural rather than a direct loss of muscle workload.



Interruption of this chain may cause atrophy

The distribution of denervation is informative

- Muscles supplied by an injured nerve are preferentially affected.
- Mapping weakness and wasting to a nerve distribution can identify the level of pathology.
- This contrasts with the more load-related distribution expected in disuse.



Interruption of this chain may cause atrophy

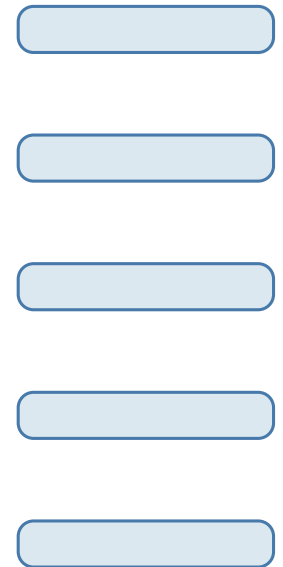
Disuse and denervation: Similar outcome, different origin

- Both can produce smaller skeletal muscle fibers and reduced strength.
- Disuse begins with reduced mechanical activation; Denervation begins with disrupted nerve supply.
- The clinical context determines which mechanism should be investigated.

Normal fibers



Atrophic fibers

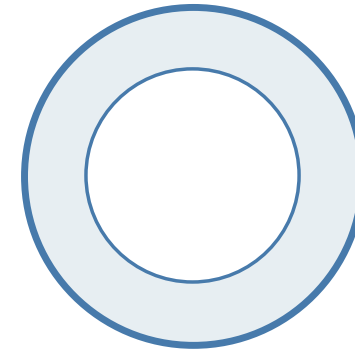


Schematic — not a muscle biopsy

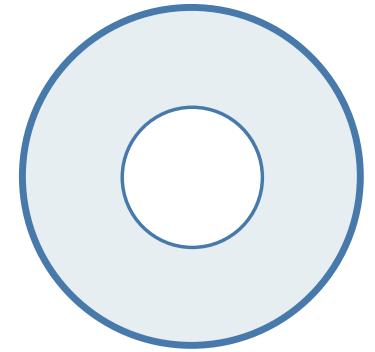
Chronic ischemia: Slow nutrient and oxygen limitation

- Gradually progressive arterial occlusive disease may chronically limit tissue perfusion.
- Cells reduce their metabolic requirements in response to sustained supply restriction.
- Tissue atrophy may precede irreversible ischemic injury when the reduction is gradual.

Uncompromised
lumen



Narrowed lumen

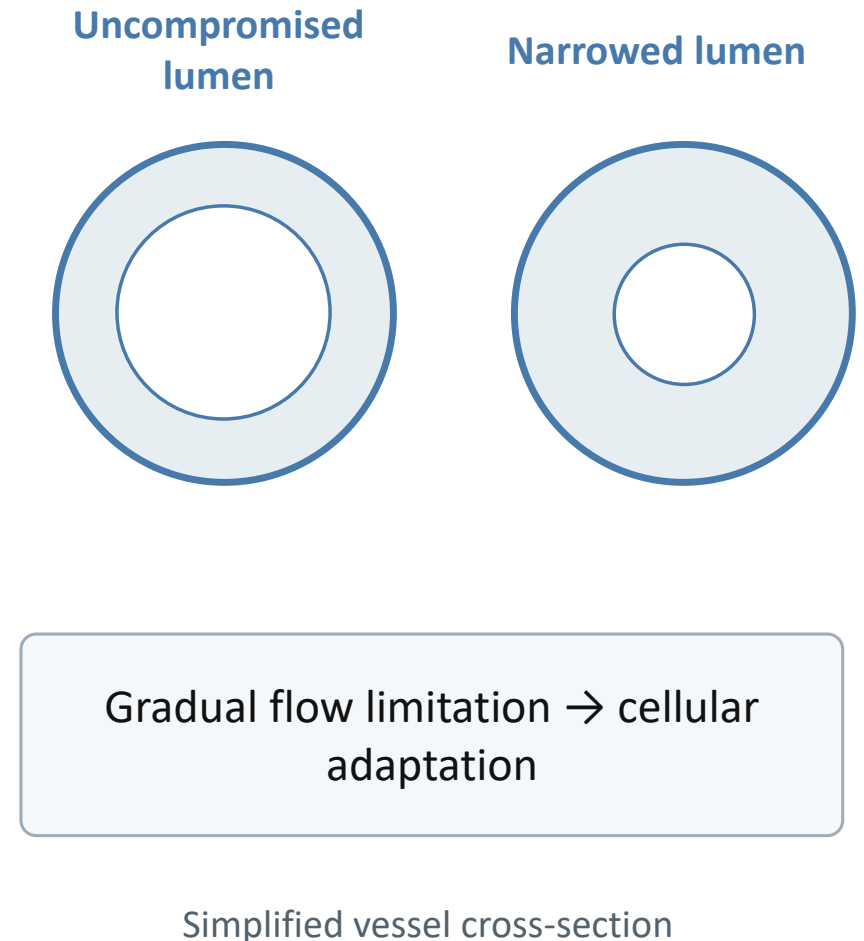


Gradual flow limitation → cellular
adaptation

Simplified vessel cross-section

Chronic ischemia differs from acute destructive injury

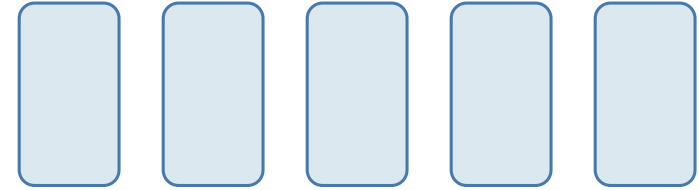
- Atrophy represents a slower process in which reduced cell mass can temporarily permit survival.
- A sufficiently severe or persistent perfusion deficit eventually overwhelms adaptation.
- Cell death may then contribute to permanent loss of tissue substance.



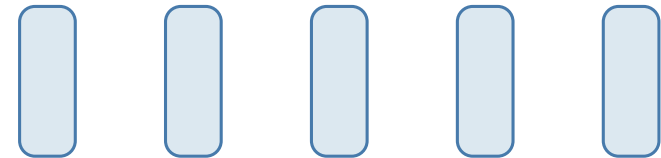
Brain atrophy in chronic vascular disease

- An atrophic brain associated with atherosclerotic cerebrovascular disease.
- Reduced blood supply is the proposed underlying stress in that textbook example.
- This illustration should not be interpreted as proof that every atrophic brain has one cause.

Normal cortical folds



Atrophy: Narrowed gyri, widened sulci

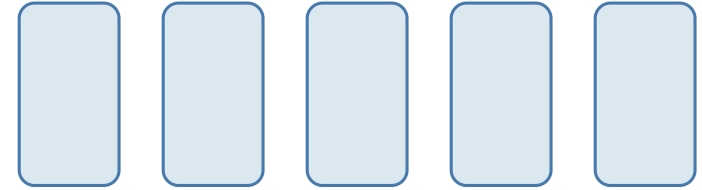


Schematic — not a brain specimen

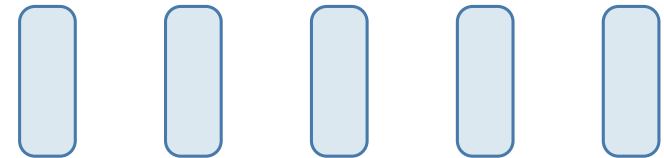
Macroscopic appearance of cerebral atrophy

- Loss of cerebral substance makes cortical gyri narrower.
- Sulci become wider as the intervening brain parenchyma is lost.
- These surface changes are morphologic signs; Cause requires clinical correlation.

Normal cortical folds



Atrophy: Narrowed gyri, widened sulci

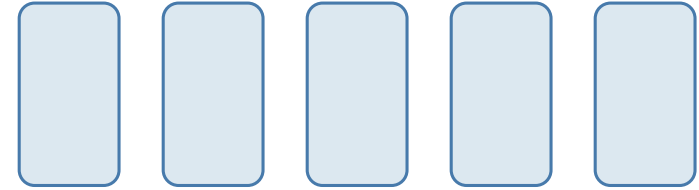


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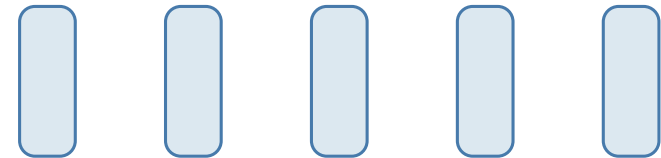
Why widened sulci matter morphologically

- Sulci occupy the spaces between adjacent cortical gyri.
- When gyri lose tissue volume, intervening grooves appear more prominent.
- Morphologic interpretation relies on changed relationships, not on color or texture alone.

Normal cortical folds



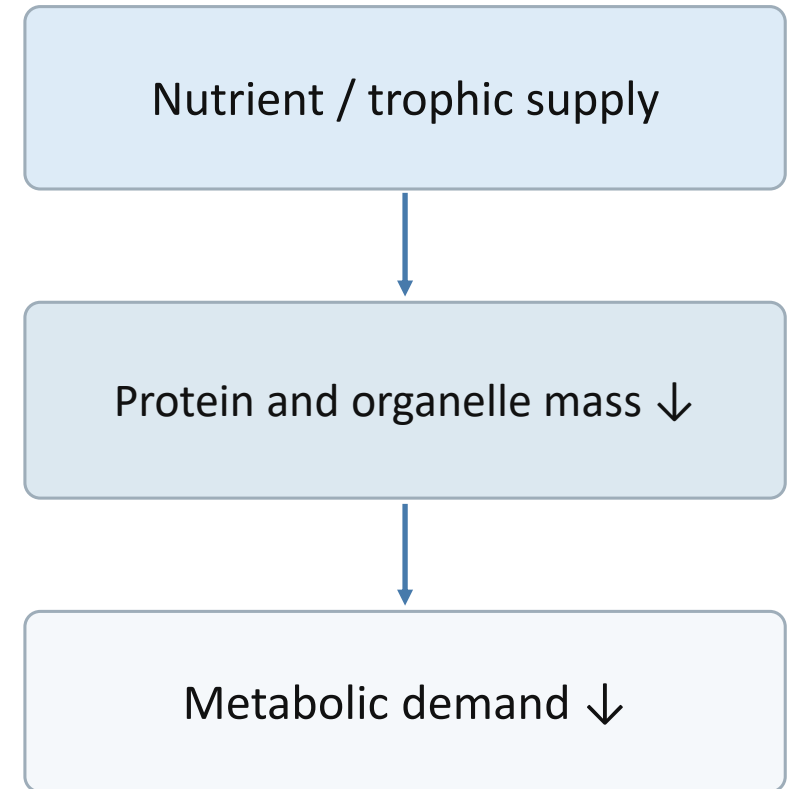
Atrophy: Narrowed gyri, widened sulci



Schematic — not a brain specimen

Nutritional atrophy: An energy-deficit response

- Profound protein–calorie malnutrition eventually depletes stored energy reserves.
- Skeletal muscle proteins can be mobilized for energy when other reserves diminish.
- Sustained catabolism produces pronounced muscle wasting.



Adaptation can sustain viability despite loss of function

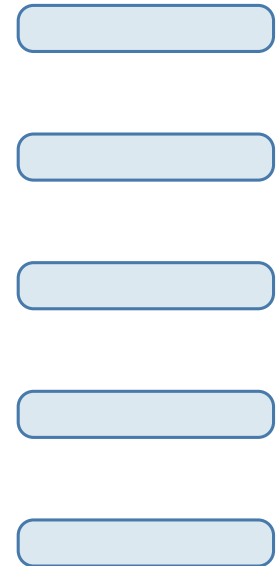
Marasmus and skeletal muscle loss

- Marasmus is the severe undernutrition example specified.
- Adipose reserve depletion is followed by use of skeletal muscle protein as fuel.
- The principal visible consequence is reduced skeletal muscle mass.

Normal fibers



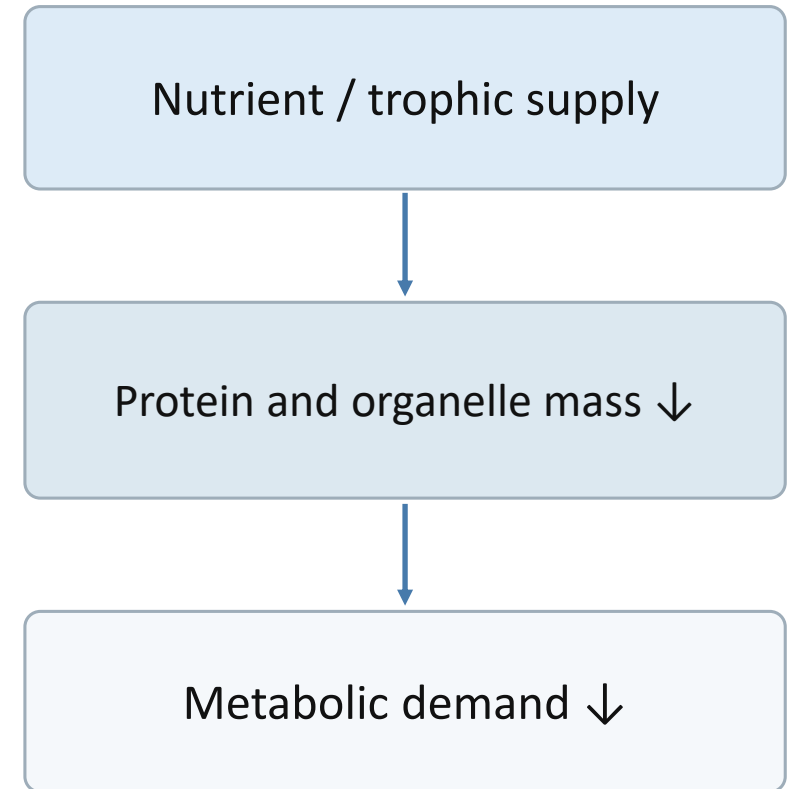
Atrophic fibers



Schematic — not a muscle biopsy

Wasting in chronic inflammatory disease

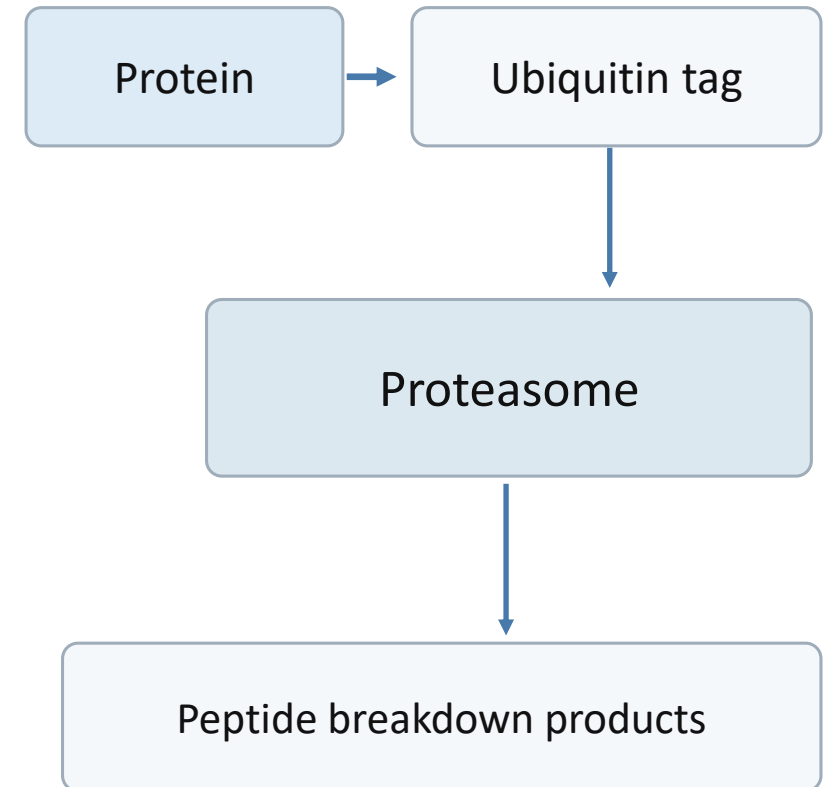
- Cachexia may accompany chronic inflammatory diseases and malignancy.
- Muscle loss cannot automatically be explained by reduced food intake alone.
- Systemic catabolic signals can contribute to loss of muscle proteins and energy reserves.



Adaptation can sustain viability despite loss of function

Cancer-associated cachexia as an atrophy setting

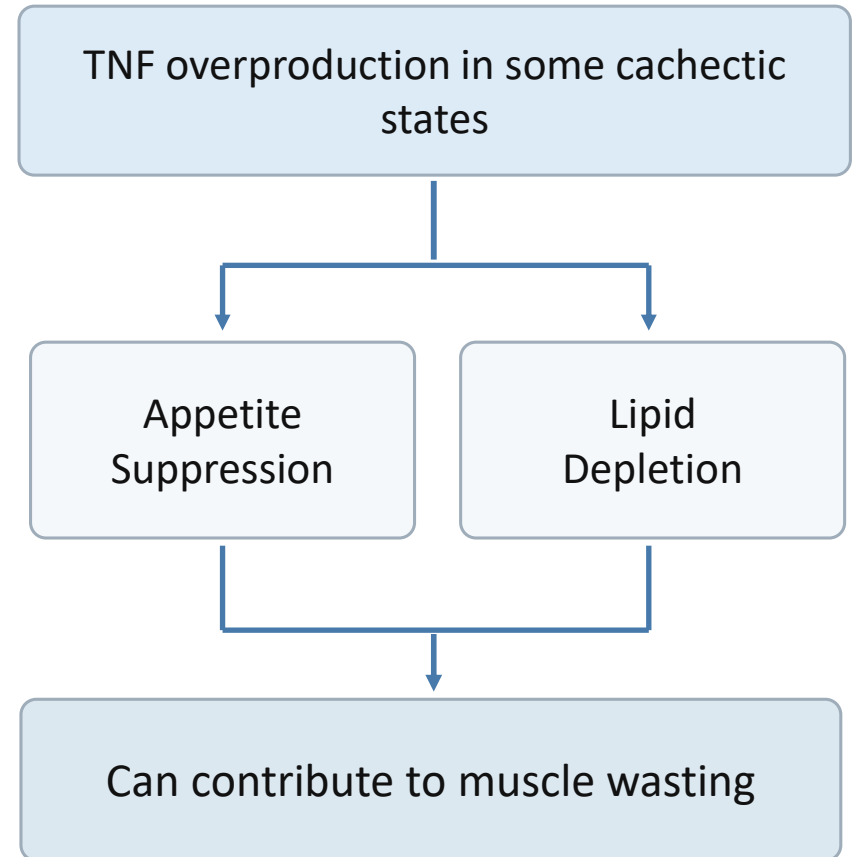
- Cancer-related wasting is one of the catabolic conditions linked to accelerated proteolysis.
- Robbins implicates the ubiquitin–proteasome pathway in breakdown of muscle proteins.
- A single organ may not adequately represent the systemic burden of tissue wasting.



Simplified ubiquitin–proteasome pathway

TNF in selected cachectic states

- Chronic TNF overproduction as a proposed mediator in some cases.
- Reported downstream effects include appetite suppression and lipid depletion.
- This is a qualified mechanism, not an assertion that TNF alone explains all cachexia.



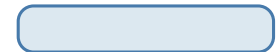
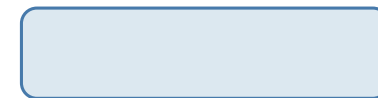
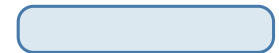
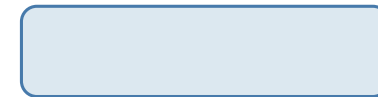
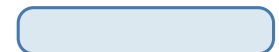
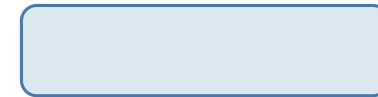
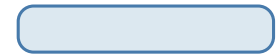
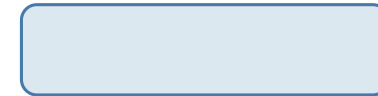
Proposed mechanism; Not applicable to every cachexia

Nutrition-related loss versus disuse

- Nutritional atrophy follows inadequate fuel and protein availability.
- Disuse atrophy follows loss of normal mechanical demand.
- Both can accelerate protein breakdown; The trigger and management context differ.

Normal fibers

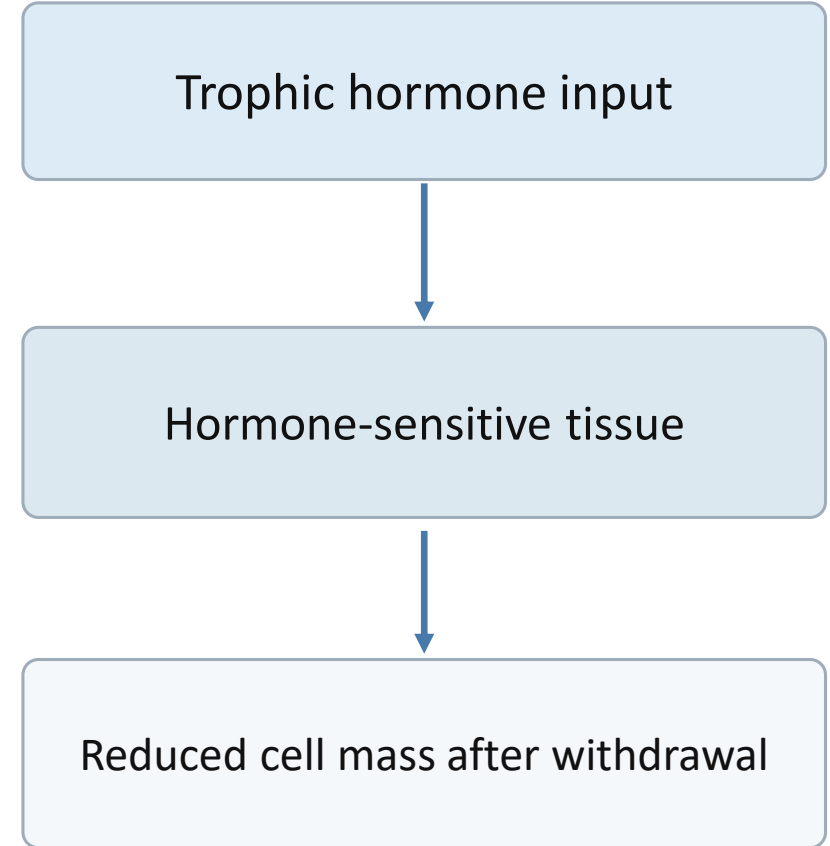
Atrophic fibers



Schematic — not a muscle biopsy

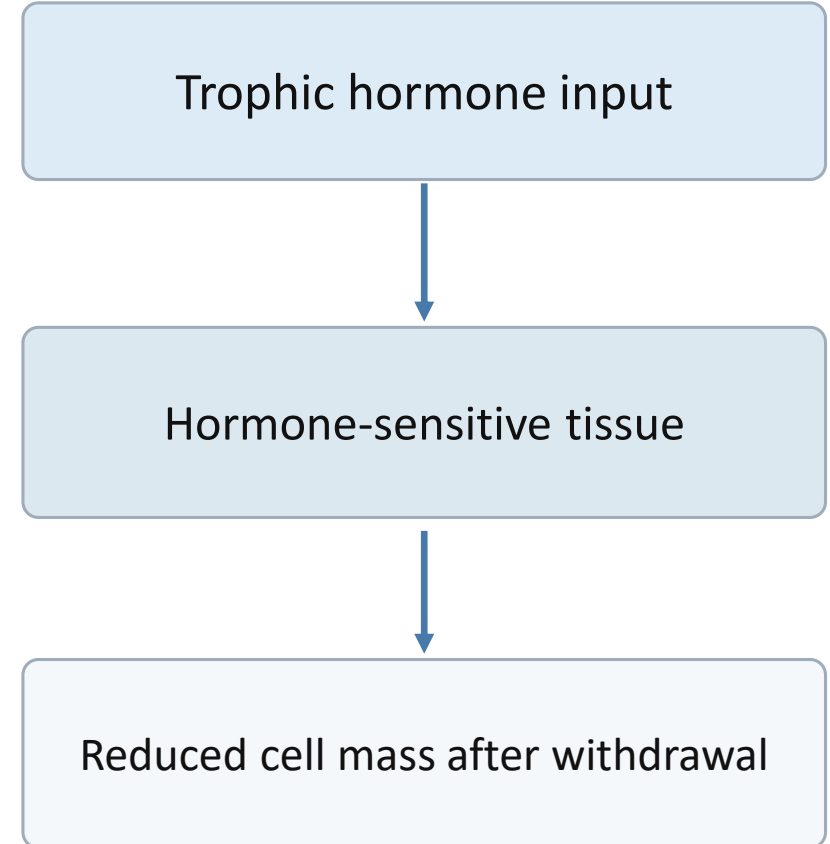
Endocrine withdrawal removes trophic support

- Hormone-dependent tissues require stimulation to maintain normal cellular metabolism.
- Removing endocrine input can reduce tissue mass and specialized function.
- Reproductive tissues and the breast as examples.



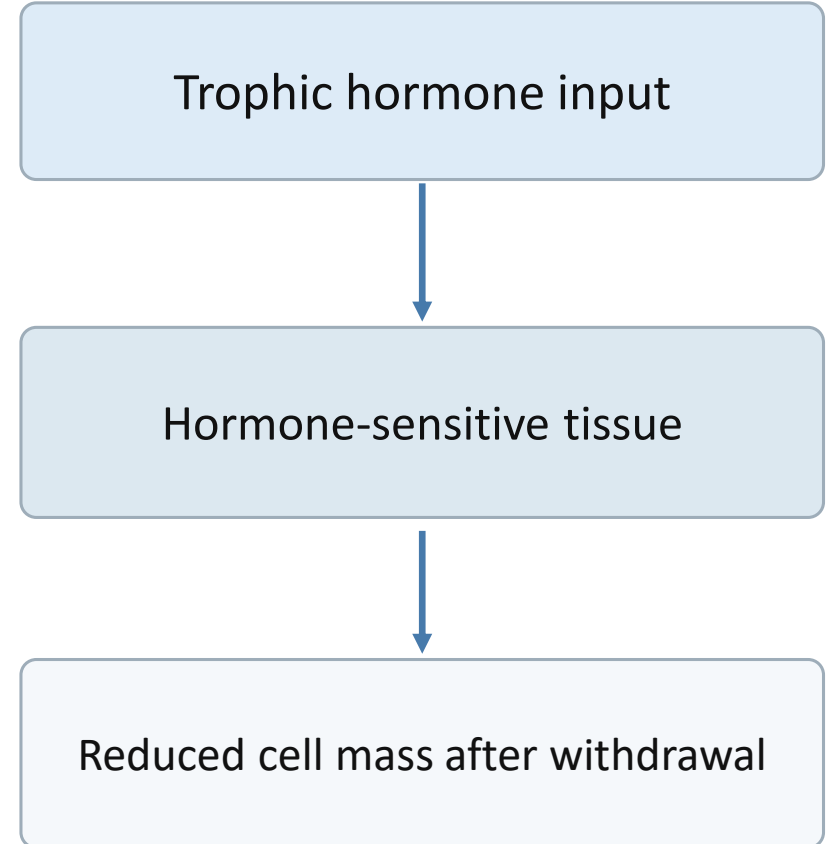
Postmenopausal atrophy of hormone-responsive tissues

- Loss of estrogen stimulation follows the menopausal transition.
- Atrophy may affect the endometrium, vaginal epithelium and breast.
- This reflects trophic withdrawal, not necessarily a primary vascular lesion.



Androgen deprivation and prostatic atrophy

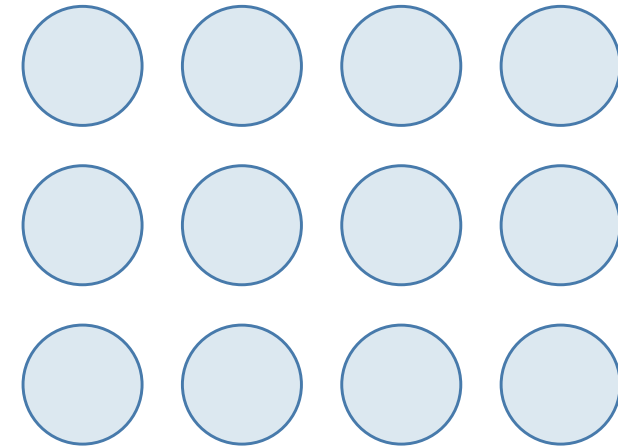
- Prostatic tissue responds to androgenic stimulation.
- Chemical or surgical castration removes androgen support.
- Prostatic atrophy after androgen deprivation in the treatment context of prostate cancer.



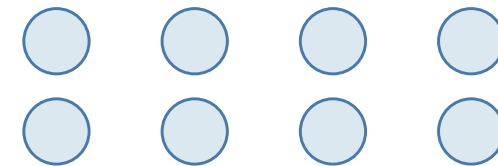
Apoptosis after endocrine withdrawal

- Trophic withdrawal can initially decrease cell size and activity.
- Apoptosis contributes to actual cell loss in some endocrine organs after hormone withdrawal.
- The resulting organ shrinkage may therefore involve both cellular dimensions and cellularity.

Preserved cellular mass



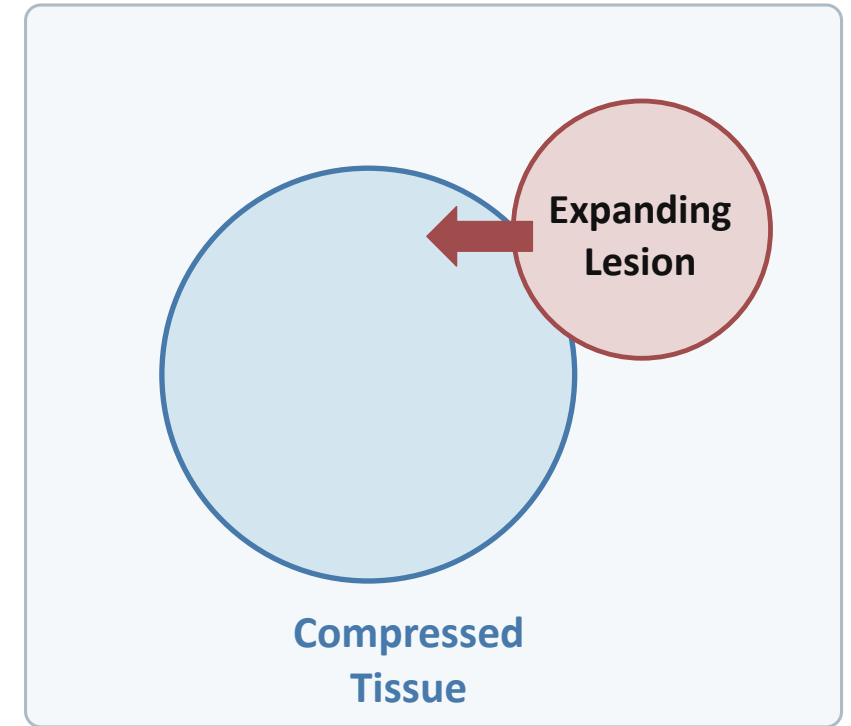
Reduced tissue volume



Schematic: Cell-size and cell-number effects

Pressure atrophy: An expanding mass compresses tissue

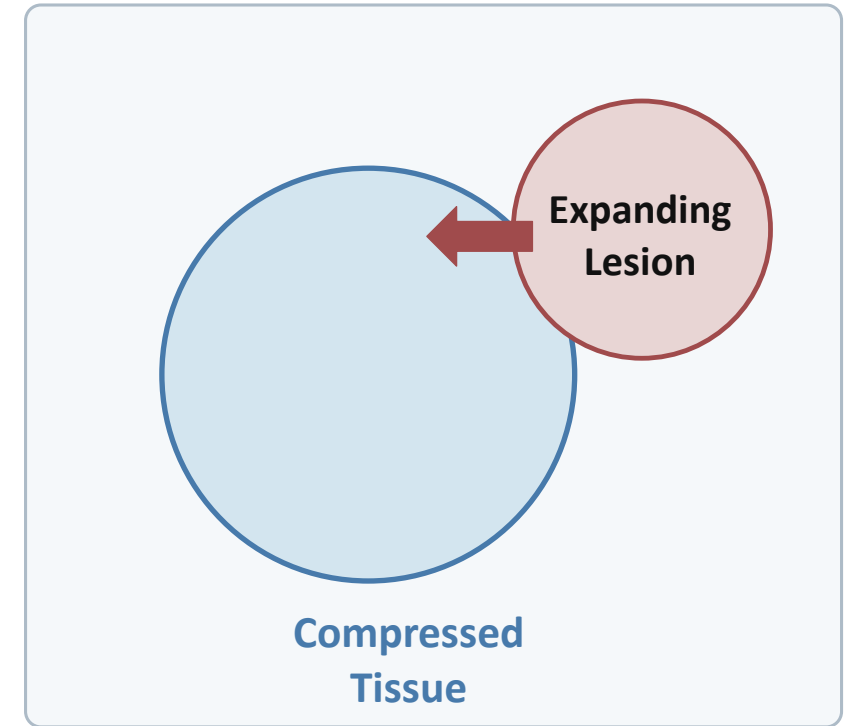
- A benign neoplasm can exert pressure on surrounding non-neoplastic tissue.
- Sustained compression may make the adjacent tissue smaller.
- The benign character of a lesion does not rule out local tissue damage.



Schematic — no specific diagnosis implied

A proposed vascular mechanism for pressure atrophy

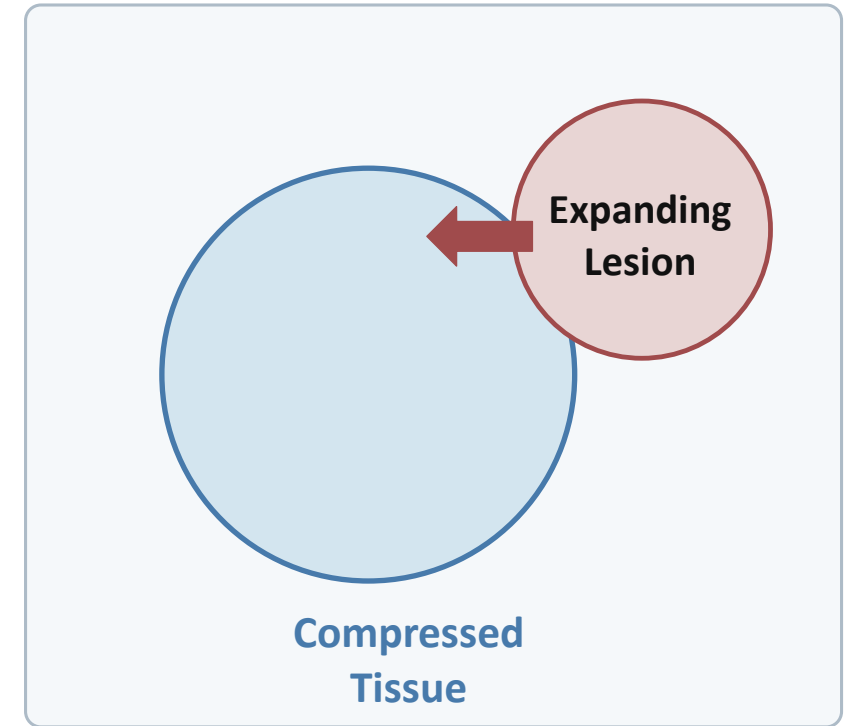
- Pressure can compromise perfusion of the compressed region.
- Consequent ischemic changes as a probable mechanism.
- This is a mechanism proposed for the setting, rather than a universal proven sequence.



Schematic — no specific diagnosis implied

Recognizing pressure atrophy in a specimen

- Evaluate tissue immediately adjacent to an enlarging lesion or structure.
- Consider whether the surrounding parenchyma has lost volume under sustained compression.
- Correlate the geometry with duration and with the expected local blood supply.



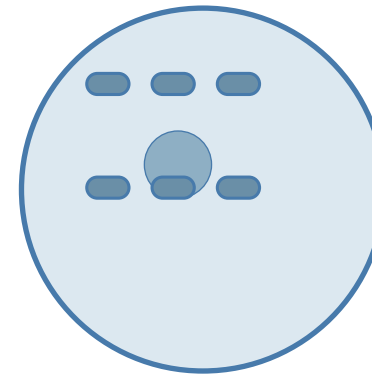
Schematic — no specific diagnosis implied

The six causes: Identify the initiating stress

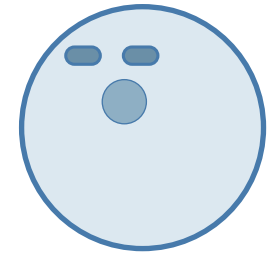
Cause	Initiating disturbance	Textbook example
Disuse	Reduced mechanical work	Cast / bed rest
Denervation	Loss of nerve supply	Nerve damage
Ischemia	Chronically reduced blood supply	Arterial occlusion
Nutrition	Insufficient energetic substrate	Marasmus
Endocrine loss	Withdrawal of trophic hormones	Postmenopause / castration
Pressure	Sustained tissue compression	Expanding benign mass

Common early cellular response

- Atrophic cells reduce their size and intracellular organelle content.
- This response is shared across diverse causes despite different initiating stresses.
- Reduced cell mass can bring metabolic demand closer to reduced supply.



More organelles

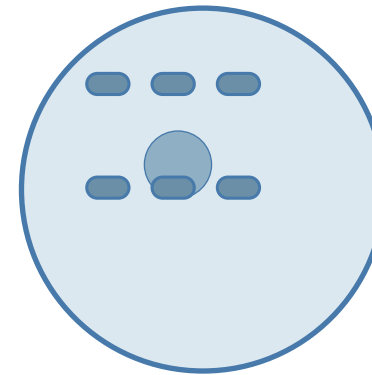


Fewer organelles

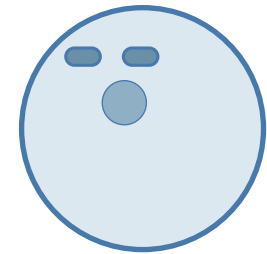
Schematic — not an electron micrograph

Atrophic skeletal muscle: Subcellular simplification

- Atrophic muscle cells contain fewer mitochondria.
- The quantity of contractile myofilaments is decreased.
- Rough endoplasmic reticulum is also reduced, reflecting lower synthetic demand.



More organelles

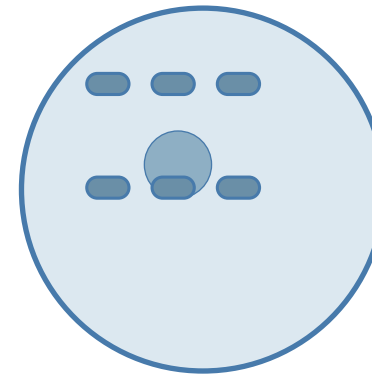


Fewer organelles

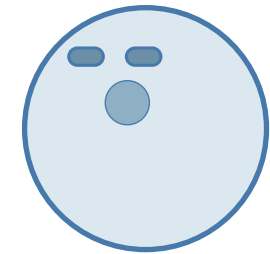
Schematic — not an electron micrograph

Why organelle loss changes cell physiology

- Fewer mitochondria accompany a reduction in the cell's energy-handling machinery.
- Fewer myofilaments correspond to less contractile apparatus.
- Reduced rough ER is consistent with attenuated protein biosynthesis.



More organelles

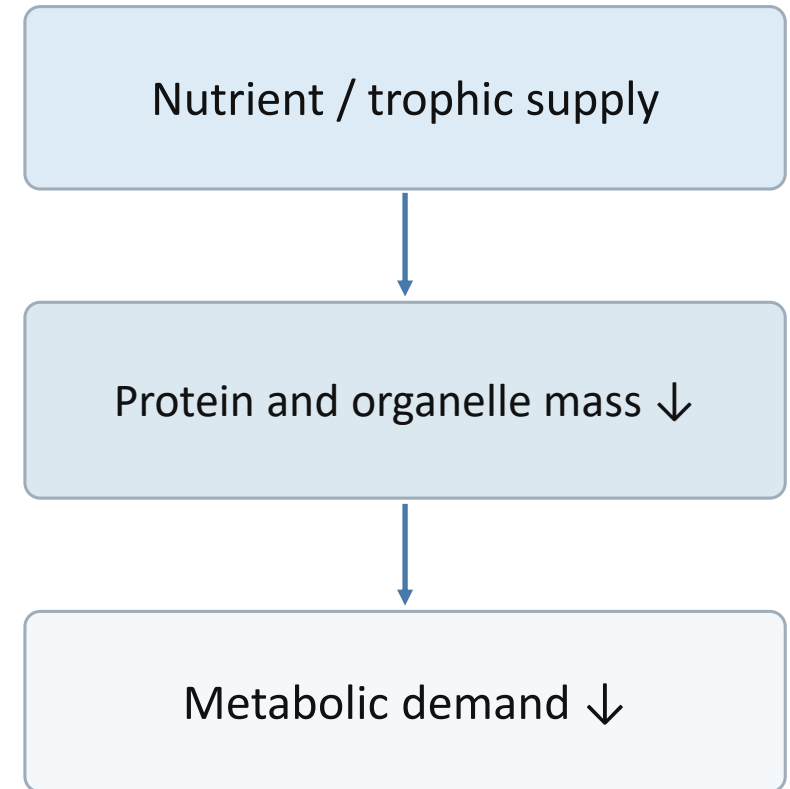


Fewer organelles

Schematic — not an electron micrograph

A new supply–demand equilibrium

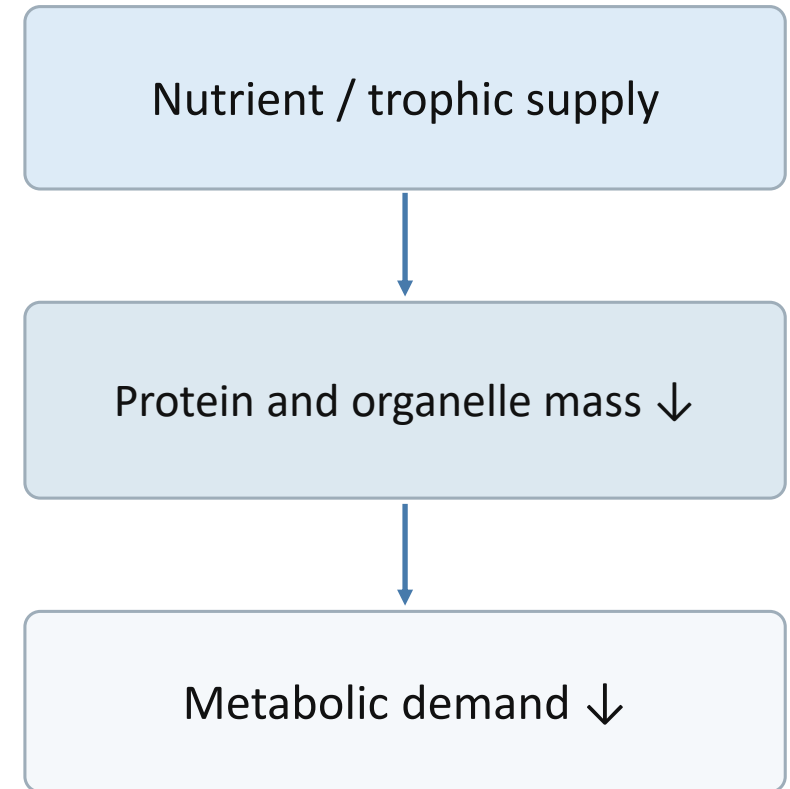
- The cell cannot sustain its previous biosynthetic and functional mass under constrained support.
- Shrinking intracellular structures lowers the resources needed to maintain viability.
- The resulting steady state preserves tissue only at diminished functional capacity.



Adaptation can sustain viability despite loss of function

Survival and function are not equivalent outcomes

- Atrophy can maintain the survival of stressed cells without normal performance.
- Early organ dysfunction may therefore exist while cell death remains minimal.
- Clinical interpretation should separate reduced function from frank tissue necrosis.

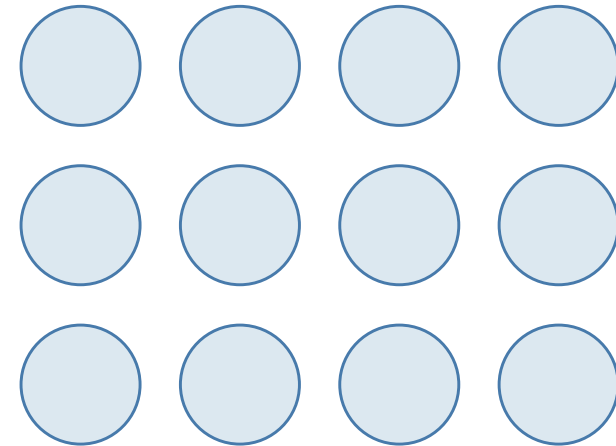


Adaptation can sustain viability despite loss of function

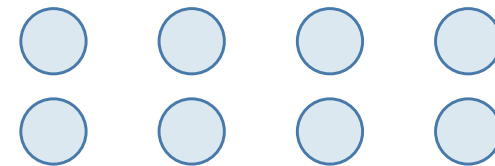
When adaptive atrophy becomes irreversible

- A progressive reduction in blood supply may eventually exceed adaptive capacity.
- Cells can become irreversibly injured and die, often by apoptosis' description.
- Late organ atrophy may incorporate permanent cell loss, not just reversible shrinkage.

Preserved cellular mass



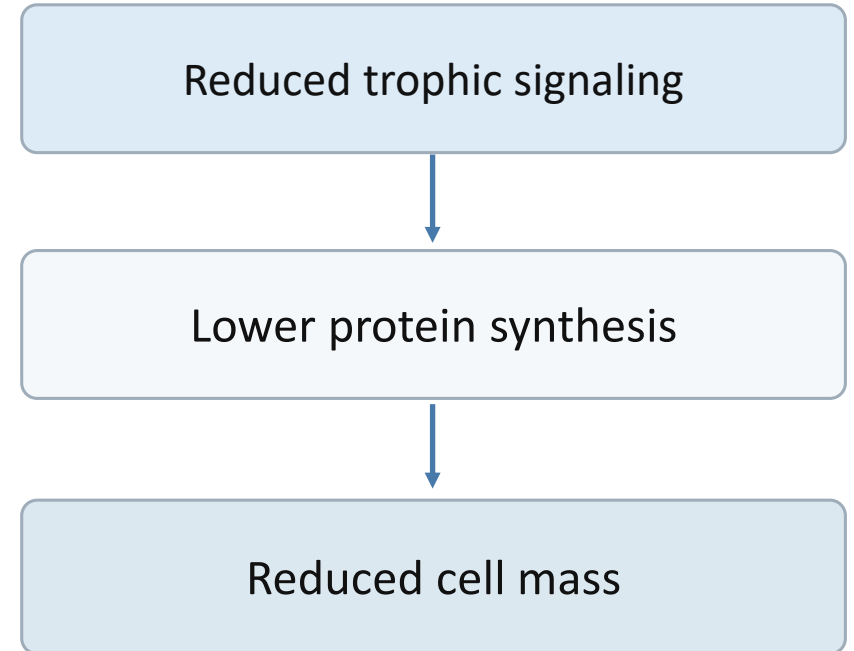
Reduced tissue volume



Schematic: Cell-size and cell-number effects

Protein homeostasis explains changes in cell mass

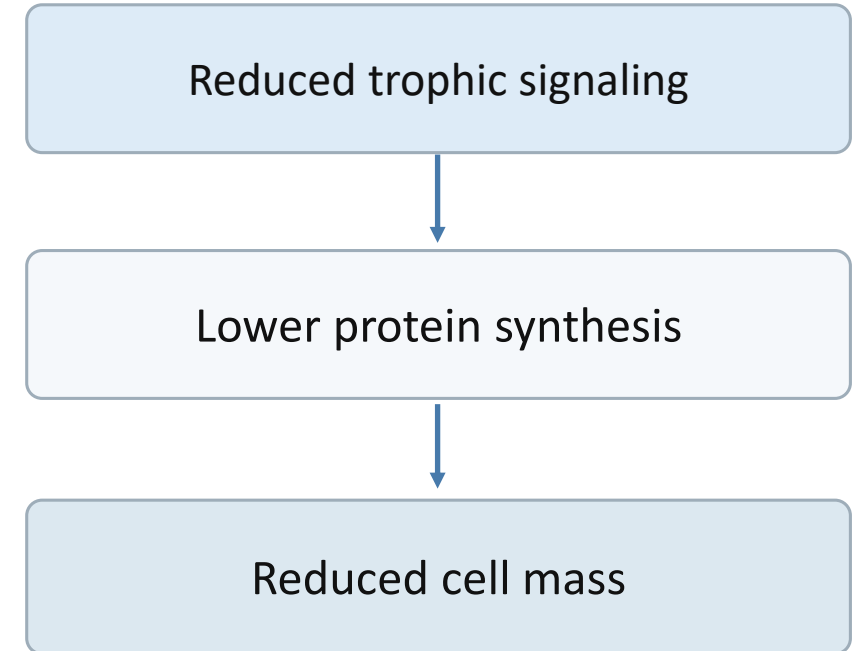
- Atrophy reflects reduced protein synthesis together with increased protein degradation.
- These processes shift the balance of cellular protein content toward net loss.
- Organellar turnover is an additional component of the atrophic response.



The anabolic side of the balance

Reduced trophic input decreases protein synthesis

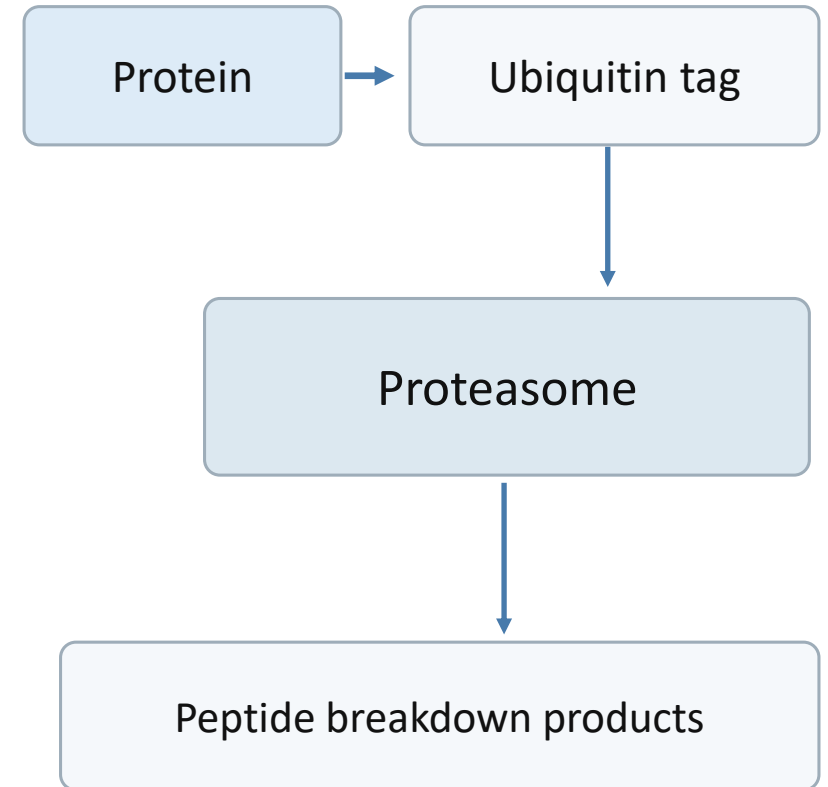
- Growth-related signals ordinarily promote nutrient uptake and mRNA translation.
- When stimulation falls, the anabolic drive to maintain cell proteins declines.
- The cellular proteome and structural mass decrease over time.



The anabolic side of the balance

The ubiquitin–proteasome system

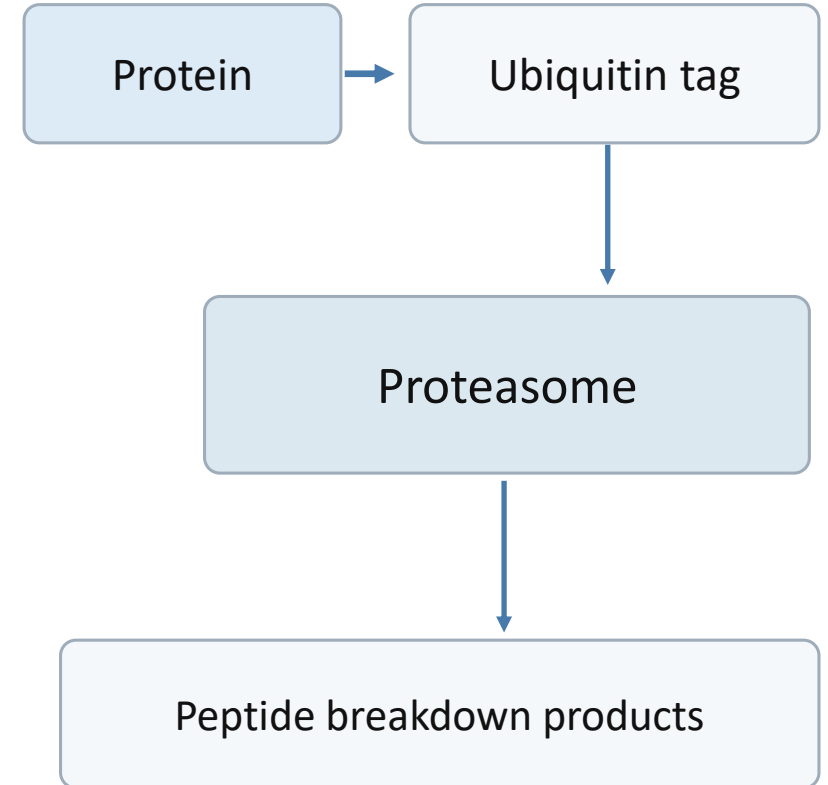
- Ubiquitin ligases attach ubiquitin to selected cellular protein substrates.
- Tagged proteins are targeted to proteasomes for degradation.
- Nutrient deficiency and disuse are triggers noted for this catabolic route.



Simplified ubiquitin–proteasome pathway

Proteolysis contributes to muscle wasting

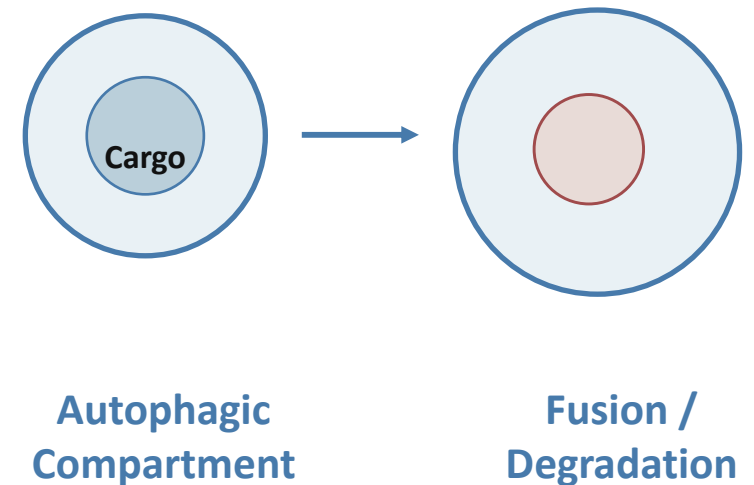
- Loss of skeletal muscle protein reduces the intracellular contractile apparatus.
- Enhanced proteasomal protein degradation is associated with multiple catabolic conditions.
- Cancer-related cachexia is specifically cited as a setting of accelerated proteolysis.



Simplified ubiquitin–proteasome pathway

Autophagy removes cellular components

- Atrophy can be accompanied by increased numbers of autophagic vacuoles.
- The pathway supports intracellular digestion of cytoplasmic components and organelles.
- This is distinct from proteasomal breakdown of ubiquitin-tagged proteins.



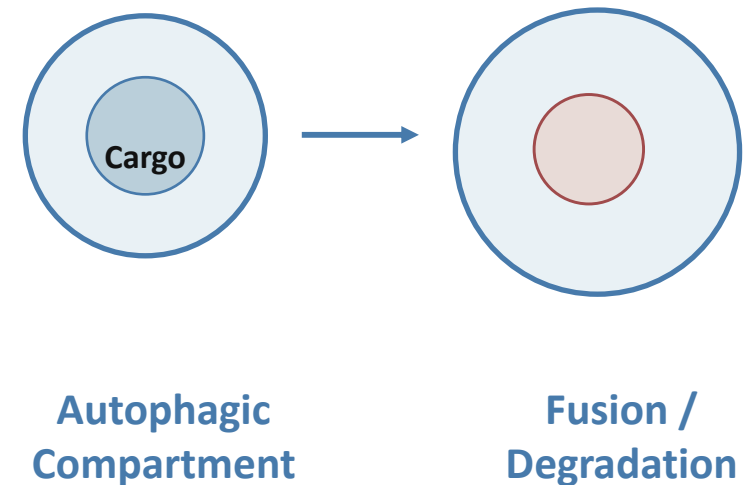
Schematic — not an ultrastructural image

Protein degradation and organelle recycling are complementary

Feature	Ubiquitin–proteasome	Autophagy
Typical cargo	Ubiquitin-tagged cellular proteins	Cytoplasmic structures and organelles
Atrophy association	Protein breakdown in disuse and catabolism	Increased autophagic vacuoles
Morphologic correlate	Less cellular protein mass	Vacuoles; possible residual bodies

Undigested residual bodies

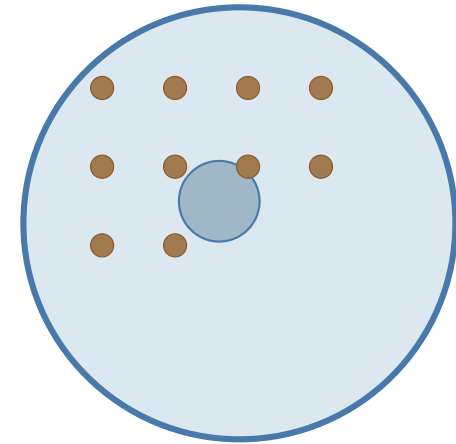
- Not all autophagic cargo is completely digested.
- Indigestible material may remain within membrane-bound cytoplasmic residual bodies.
- The residue can persist even when the tissue has otherwise shrunk.



Schematic — not an ultrastructural image

Lipofuscin and brown atrophy

- Lipofuscin is a pigment-containing example of persistent residual material.
- When the intracellular granules accumulate sufficiently, tissue may appear brown.
- “Brown atrophy” denotes this pigment-associated appearance, not a separate cause of tissue wasting.

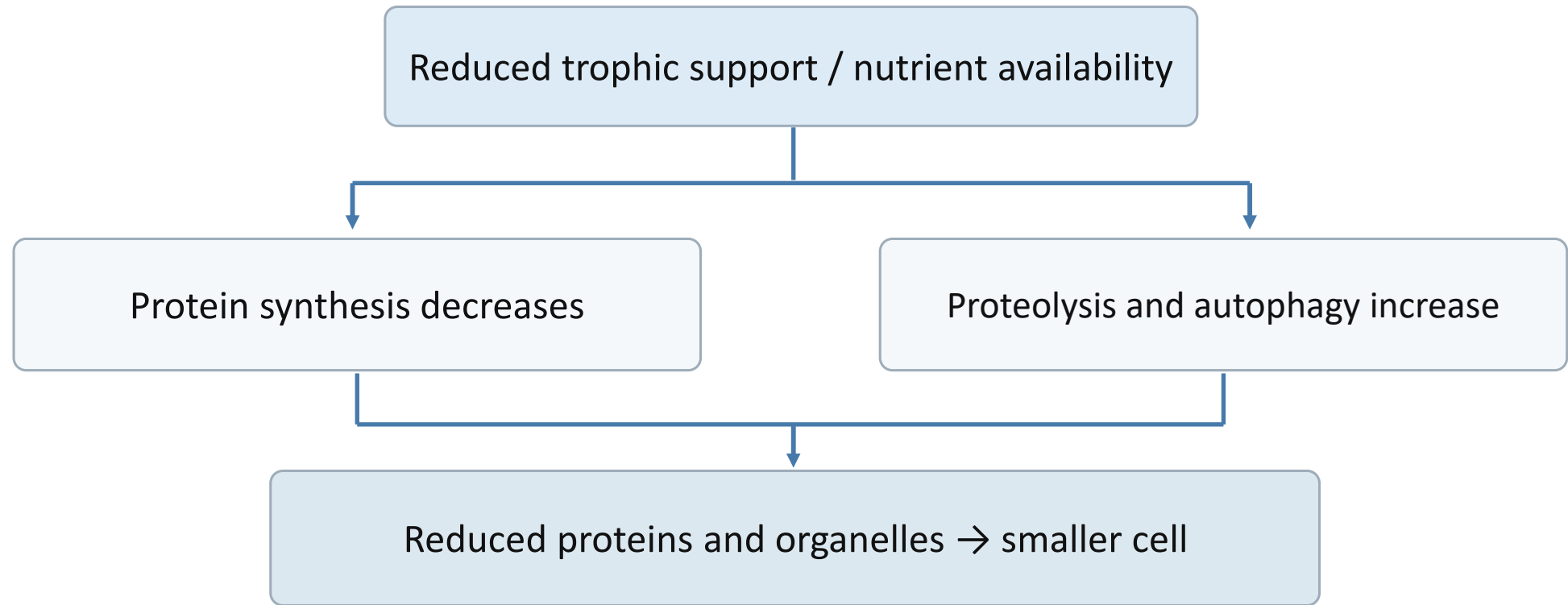


Residual brown granules

Schematic — not lipofuscin-stained tissue

Putting the intracellular mechanisms together

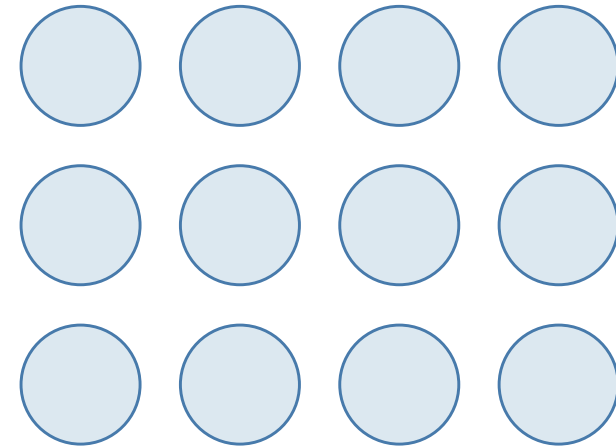
Two concurrent shifts in protein and organelle homeostasis reduce cellular mass.



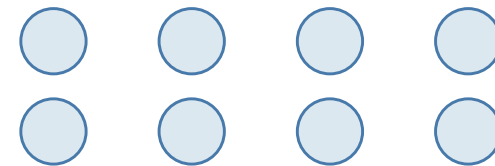
From cell biology to gross pathology

- Decreased cell size reduces organ volume even without immediate cell death.
- Additional apoptosis can further reduce cell number and tissue mass.
- Gross appearance depends on architecture: For example, narrowed gyri in cerebral atrophy.

Preserved cellular mass



Reduced tissue volume

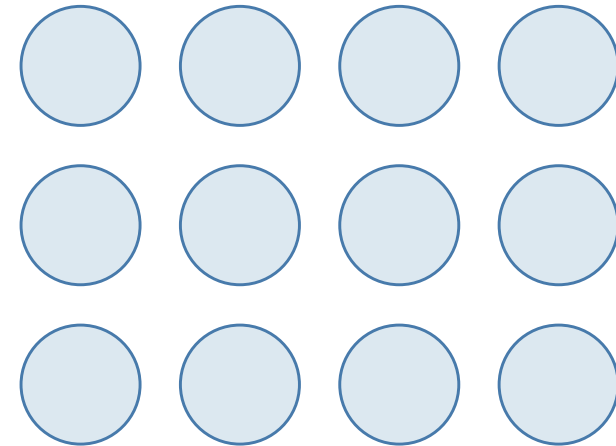


Schematic: Cell-size and cell-number effects

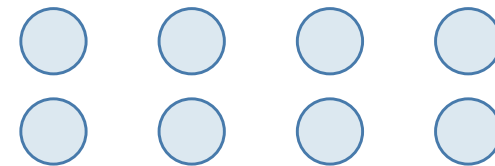
Atrophy is not hypoplasia

- Atrophy denotes reduction of a previously formed tissue or organ.
- Hypoplasia denotes incomplete development of tissue or organ mass.
- A history of normal prior development is essential when assigning the term atrophy.

Preserved cellular mass



Reduced tissue volume



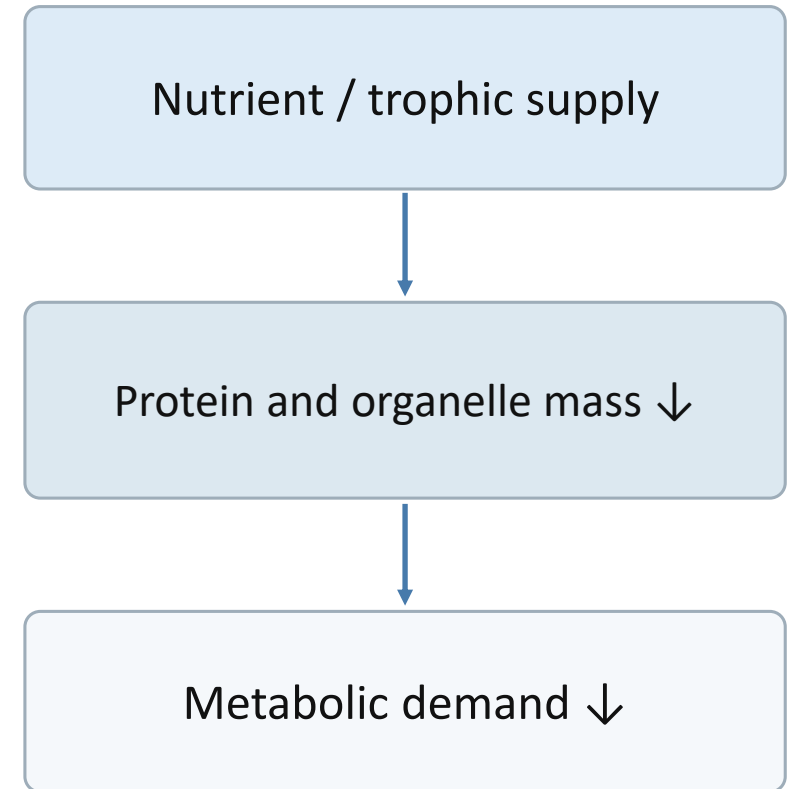
Schematic: Cell-size and cell-number effects

Atrophy is not hypertrophy or hyperplasia

Process	Primary cellular change	Effect on tissue mass
Atrophy	Cell size ↓; sometimes cell number ↓	Usually decreases
Hypertrophy	Cell size ↑	Increases
Hyperplasia	Cell number ↑	Increases

Atrophy is not synonymous with necrosis

- The early atrophic cell is smaller and may remain alive.
- Severe or persistent stress can subsequently induce irreversible injury and death.
- The presence of a small organ alone cannot establish whether necrosis occurred.

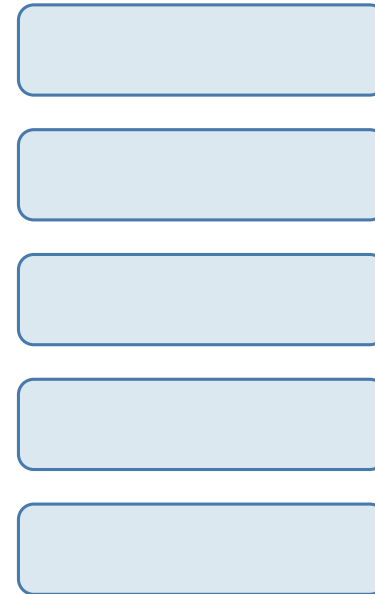


Adaptation can sustain viability despite loss of function

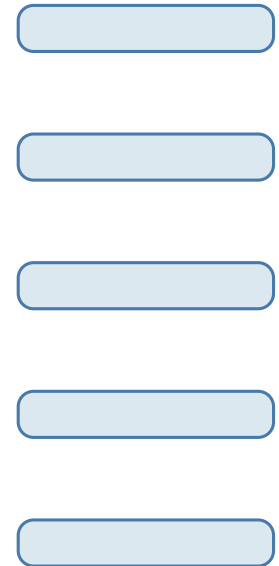
Reversibility has biologic limits

- Early disuse-related reduction in muscle cell size is described as reversible.
- Prolonged disuse can lead to muscle fiber loss through apoptosis.
- Reversal of the trigger need not restore cells already lost.

Normal fibers



Atrophic fibers



Schematic — not a muscle biopsy

Clinical reasoning: Start with distribution and exposure

- Determine whether the wasting is localized, regional or generalized.
- Ask about immobilization, neurologic injury, arterial disease, nutrition and endocrine status.
- Identify an adjacent compressive mass when an isolated structure is affected.

Disuse

Denervation

Chronic ischemia

Malnutrition

Hormone loss

Pressure

Six cause groups

Teaching case: Immobilized limb

A patient undergoes prolonged cast immobilization after a fracture. The immobilized limb is visibly smaller after the cast is removed.

QUESTION

What initiating stimulus and early cellular change best explain this finding?

Interpretation: Disuse: Reduced mechanical workload; Skeletal muscle cells initially become smaller.

Teaching case: Localized weakness after nerve injury

After an injury to a peripheral nerve, weakness and visible wasting develop mainly in the muscles served by that nerve.

QUESTION

Which category of atrophy is suggested by the anatomic distribution?

Interpretation: Denervation atrophy: Loss of the nerve supply supporting normal muscle metabolism.

Teaching case: Chronic arterial compromise

A gradually worsening arterial lesion produces prolonged limitation of tissue blood flow; Tissue volume declines over time.

QUESTION

What distinguishes this process from acute ischemic cell death?

Interpretation: Chronic ischemic atrophy can initially lower cell mass and metabolic demand; Worsening supply may later cause irreversible injury.

Teaching case: Hormone withdrawal

Following loss of hormonal stimulation, a previously functional hormone-sensitive tissue develops a reduced epithelial or parenchymal mass.

QUESTION

Which trophic mechanism is implicated?

Interpretation: Loss of endocrine stimulation, with cellular shrinkage and sometimes apoptosis.

Teaching case: An enlarging benign mass

A slowly enlarging benign lesion is surrounded by a narrowed rim of otherwise non-neoplastic organ tissue.

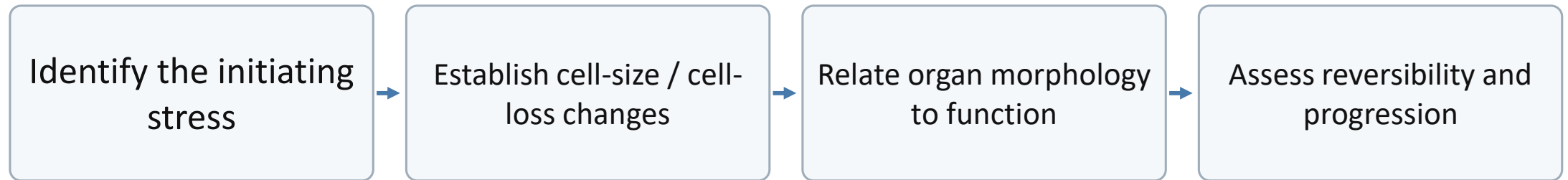
QUESTION

Why might normal tissue atrophy even though the mass is benign?

Interpretation: Sustained compression; Probable local ischemia from compromised microvascular supply.

Atrophy: Synthesis for interpretation

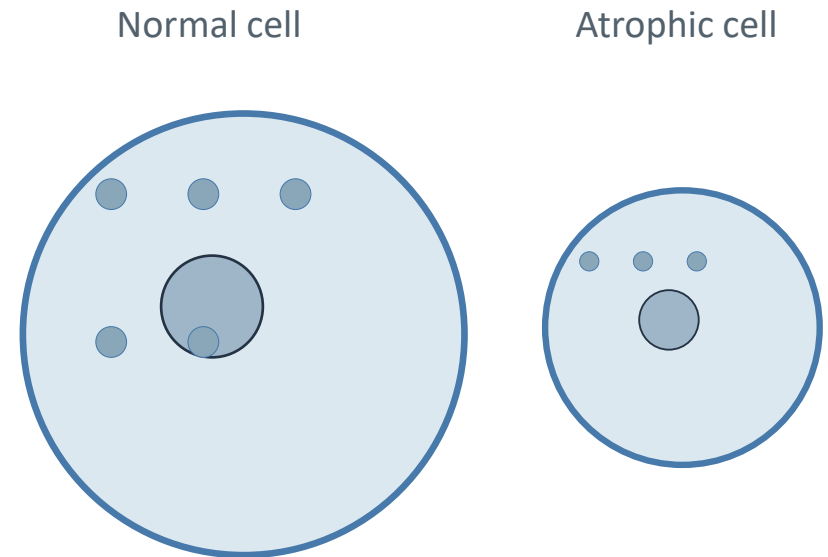
Trace the biologic sequence from the first disturbance to the tissue-level effect.



Interpret each arrow causally; The progression may be slowed or interrupted when the stress is relieved.

Essential conclusions

- Atrophy is a decrease in tissue mass caused by cellular shrinkage, often supplemented by cell loss.
- The six causes are disuse, denervation, ischemia, malnutrition, endocrine loss and pressure.
- Its shared cellular signature is lower anabolic activity, increased degradation and fewer organelles.
- Early adaptation may preserve life; Sustained stress can add irreversible injury and apoptosis.



Reduced cytoplasmic volume and organelles

Schematic — not histology

References and scope

Primary textbook

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026).

Chapter 2 — Cell Injury, Cell Death, and Adaptations.

Atrophy (pp. 54–55); Mechanisms of Atrophy (p. 55).

Slide schematics are editable conceptual drawings and do not represent authentic gross specimens, histology, or clinical imaging.