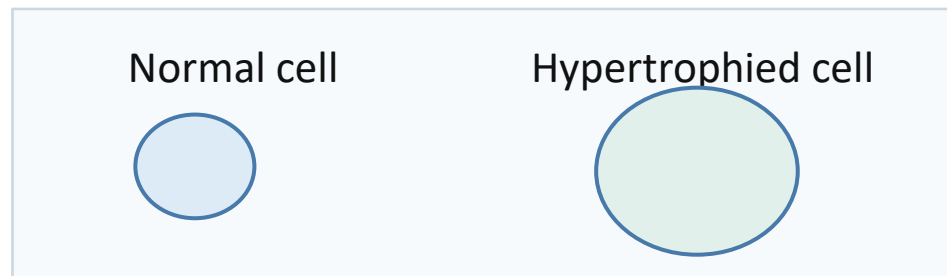


Hypertrophy

Cellular adaptation • functional demand • clinical consequences



Dr Abu Suraih Sakhri

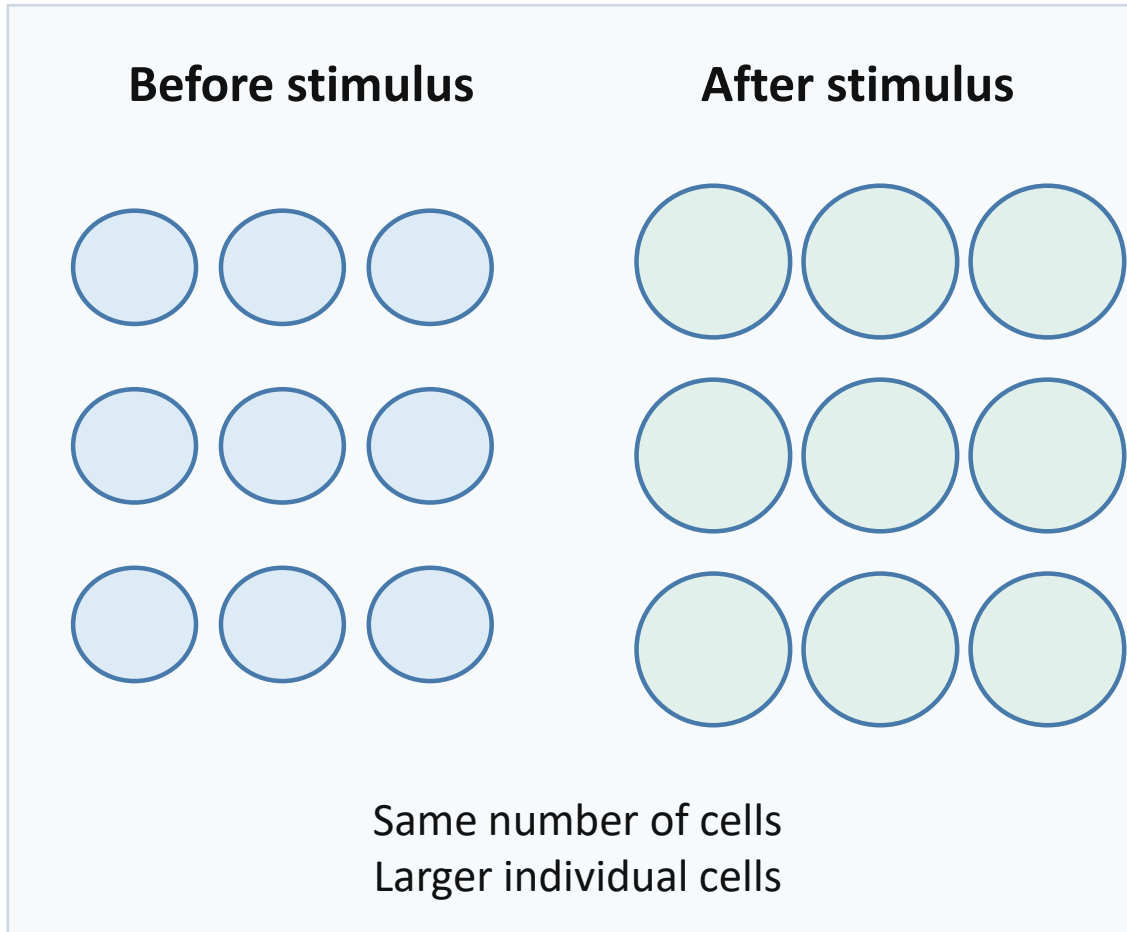
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Learning objectives

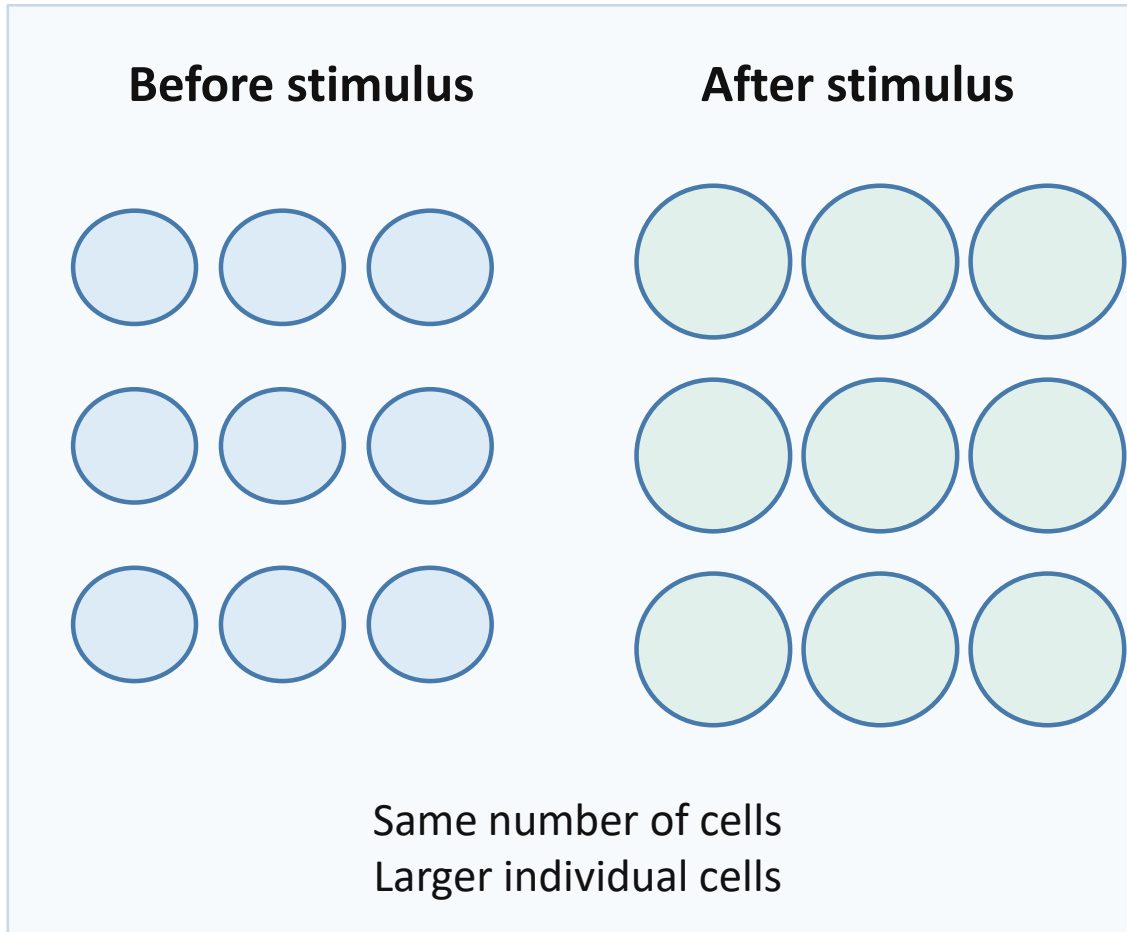
- Define hypertrophy and distinguish it from increased cell number.
- Relate workload and hormonal stimuli to increased cellular protein.
- Explain physiologic examples and maladaptive cardiac hypertrophy.
- Interpret core mechanisms and apply the concepts to short cases.

Adaptation changes cellular phenotype and function



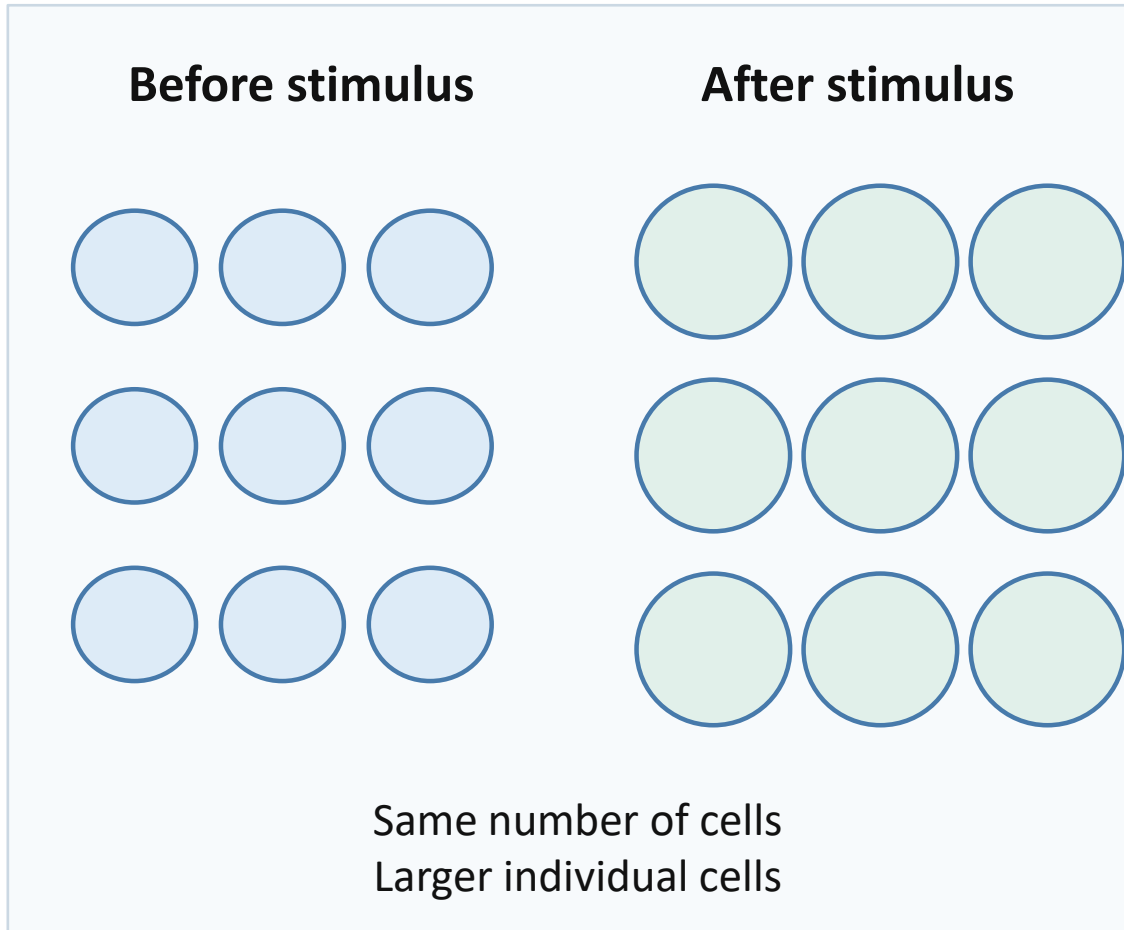
- Responses to environmental change can alter cell size, cell number, phenotype, metabolism, or function.
- Adaptations are potentially reversible while the precipitating conditions change.
- Hypertrophy represents the cell-size component of this response.

Hypertrophy is an increase in cell size



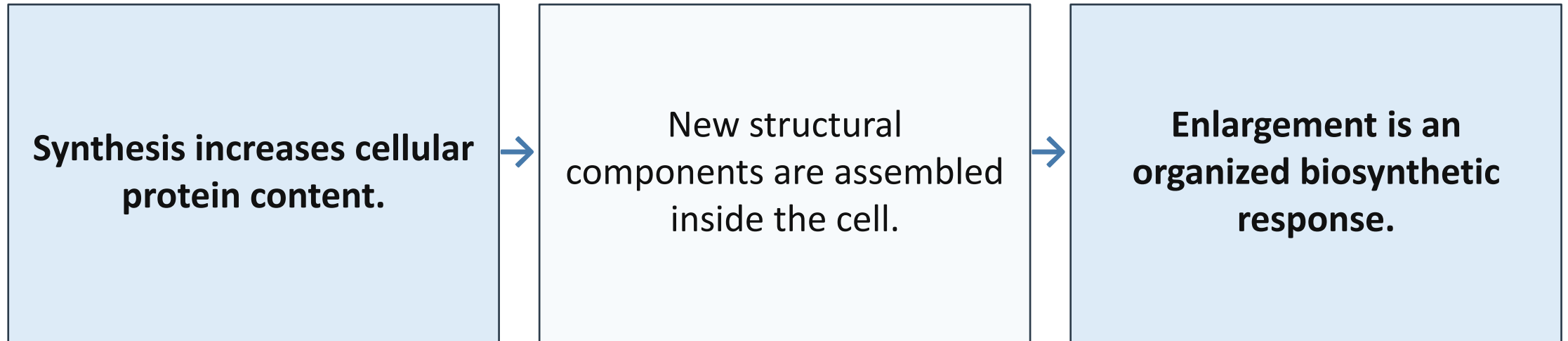
- Individual cells enlarge.
- The affected organ may consequently become larger.
- The defining change is cell size—not cell proliferation.

Enlargement does not require new cells

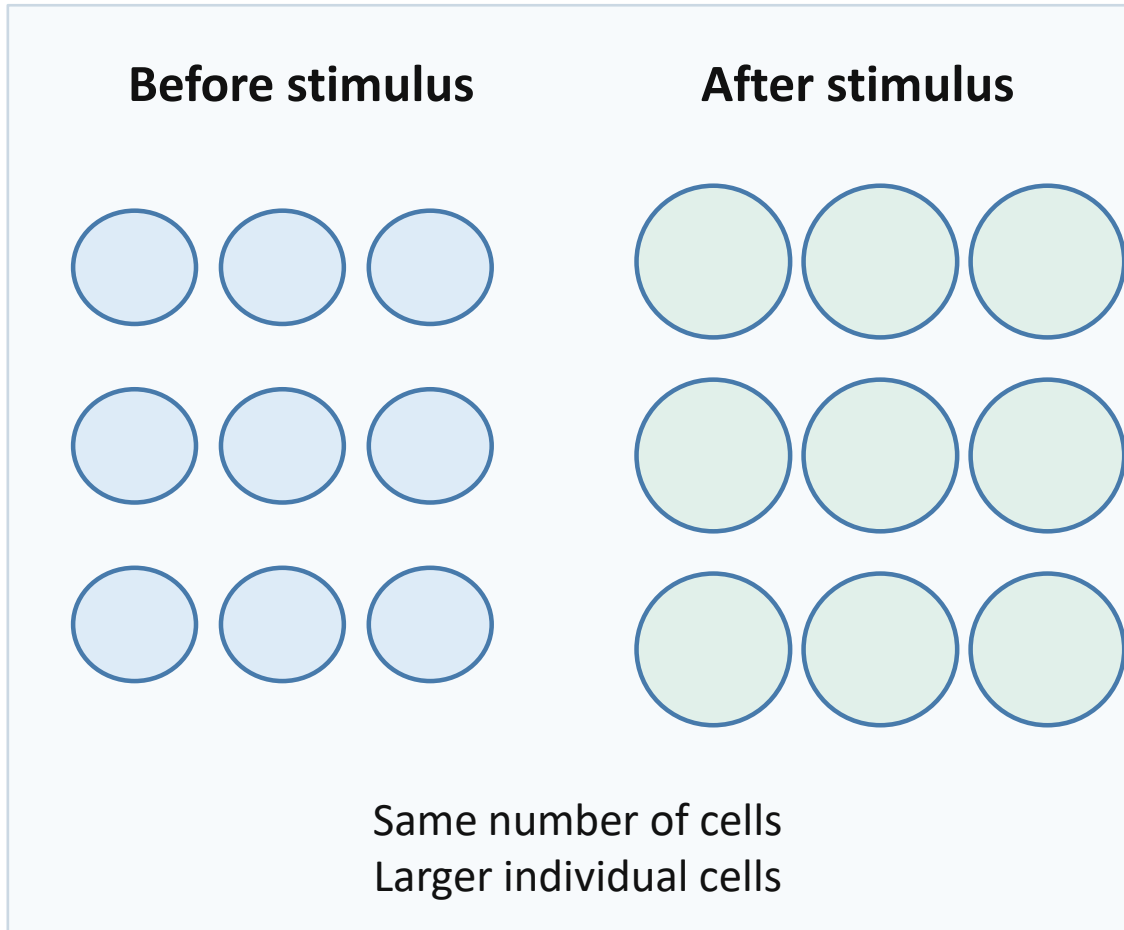


- A hypertrophied organ contains enlarged pre-existing cells.
- Cell number is not the defining contributor to hypertrophy.
- Determine whether a tissue has larger cells, more cells, or both.

New intracellular structure drives enlargement



Cell-level change explains organ-level enlargement



- Greater size of each participating cell raises tissue mass.
- Tissue-level enlargement does not by itself identify the cellular mechanism.
- Morphologic interpretation must consider both size and number.

Division capacity shapes the adaptive response

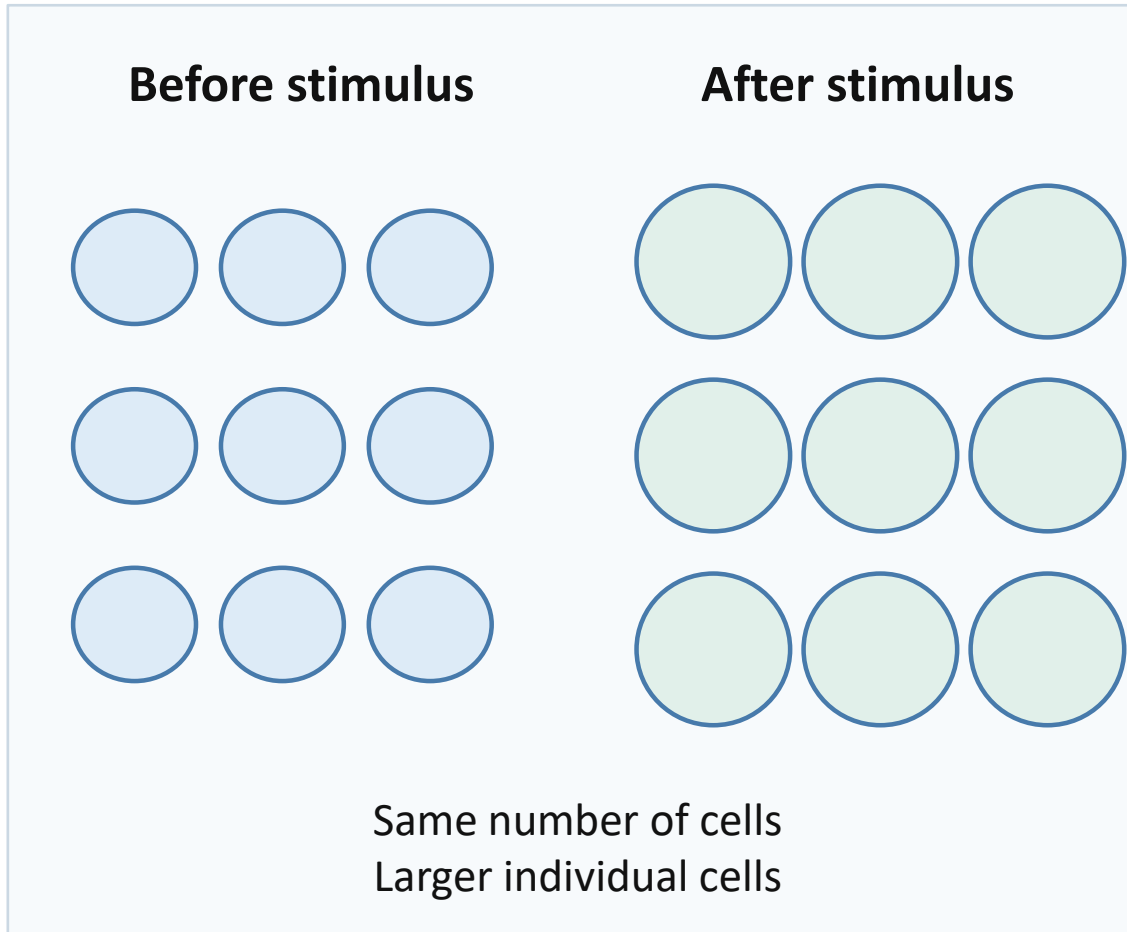
Dividing cells

Cells capable of proliferation can undergo hypertrophy and hyperplasia.

Cells with limited division

Cardiomyocytes enlarge mainly by hypertrophy because their division is limited.

Hypertrophy and hyperplasia may coexist



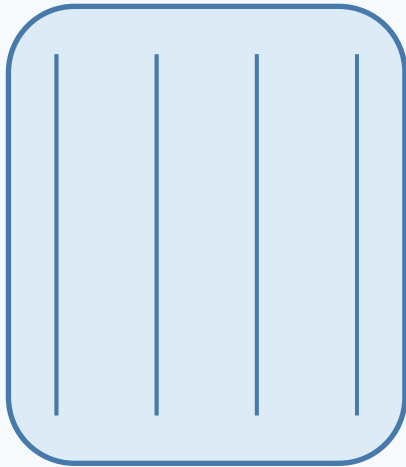
- More cells and larger cells can contribute simultaneously to organ enlargement.
- The contributions are biologically distinct despite a shared gross endpoint.
- Pregnancy-related organ growth can include both processes.

Hypertrophy is classified by context

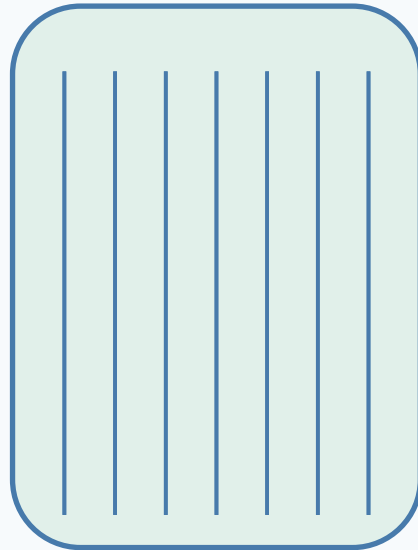
Category	Predominant context
Physiologic	Appropriate increased demand or hormonal stimulation
Pathologic	Disease-related persistent mechanical or trophic stress

Increased workload is a central stimulus

Normal muscle fiber



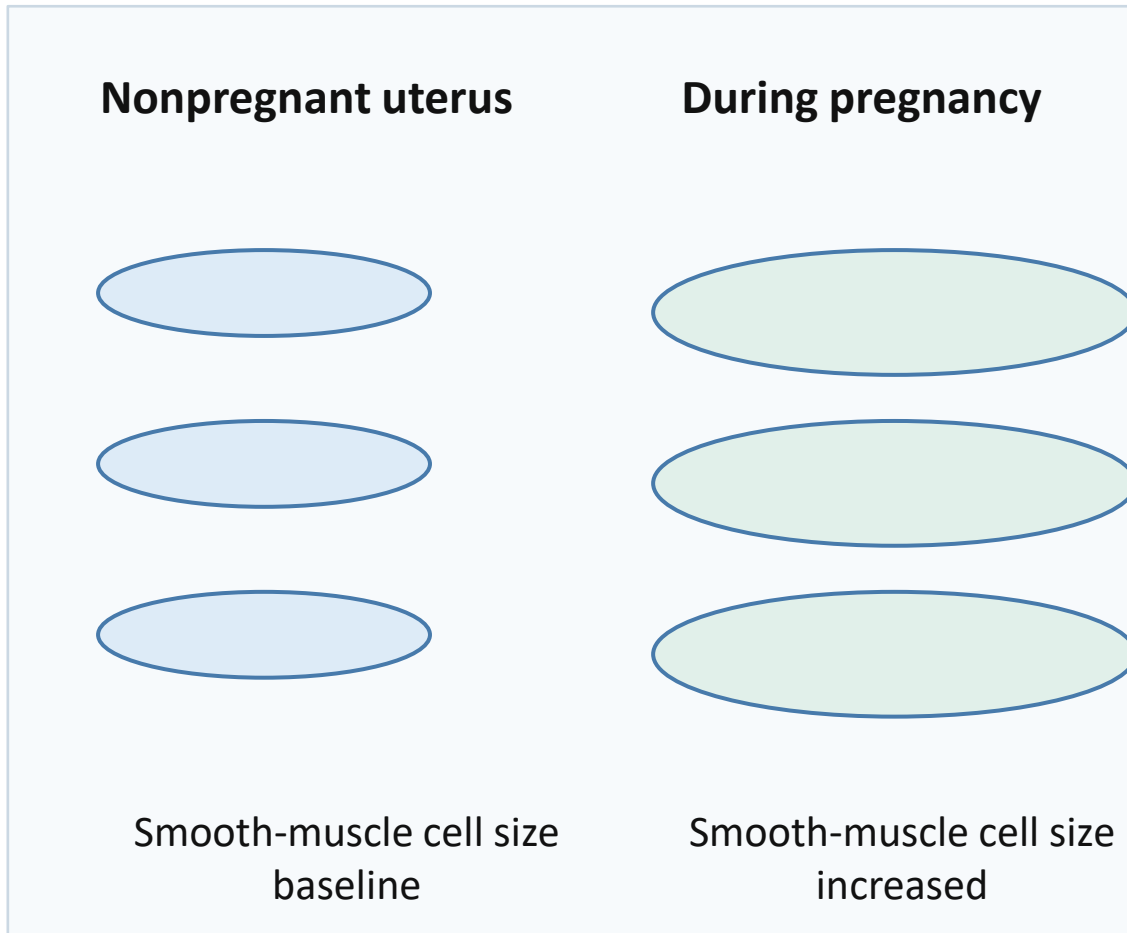
Hypertrophied muscle fiber



Schematic: Greater myofilament content per fiber

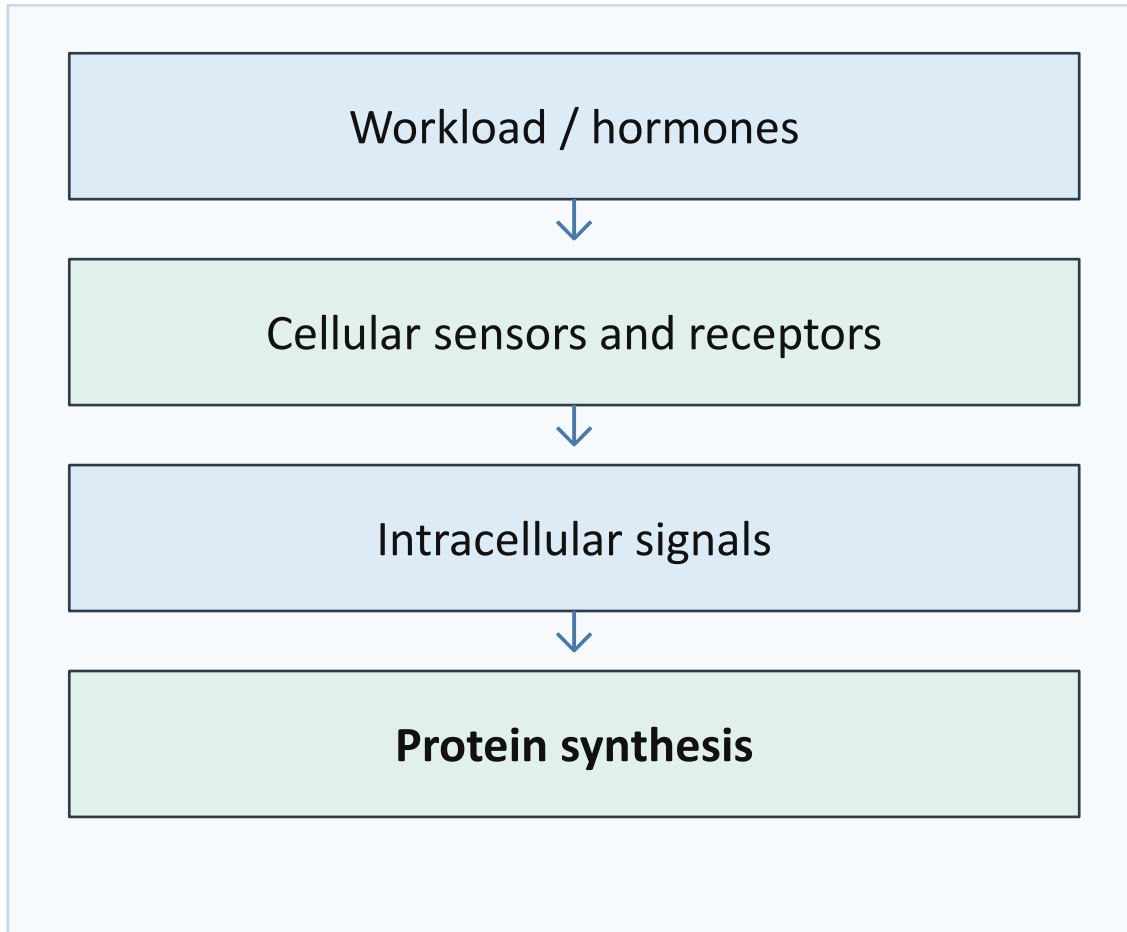
- Myocytes respond when greater work is required.
- Mechanical demand promotes the synthesis of cellular components.
- The adaptive result is increased contractile machinery.

Hormonal stimulation can enlarge cells



- Hormones act through cellular receptors and biosynthetic responses.
- The gravid uterus is the major Robbins example.
- Hormonal hypertrophy is not synonymous with pathologic growth.

Growth factors participate in hypertrophy



- Growth-factor signals can promote cellular protein synthesis.
- Hormonal, mechanical, and growth-factor inputs may converge.
- Specific intracellular pathways are illustrated in cardiac muscle.

Physiologic and pathologic do not mean different definitions

Physiologic hypertrophy

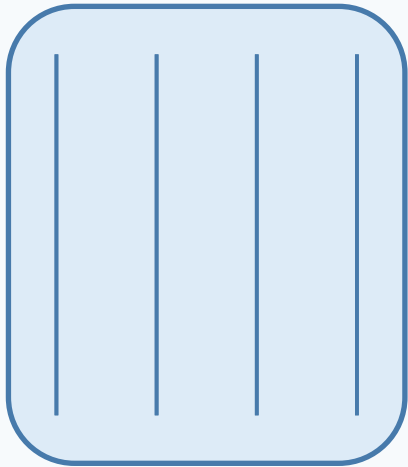
Appropriate workload or hormone signals increase structural cell mass.

Pathologic hypertrophy

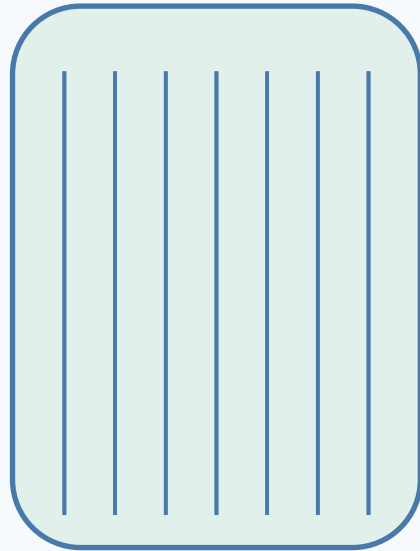
Abnormal persistent demand may progress from adaptation to injury.

Striated muscle is adapted by cell enlargement

Normal muscle fiber



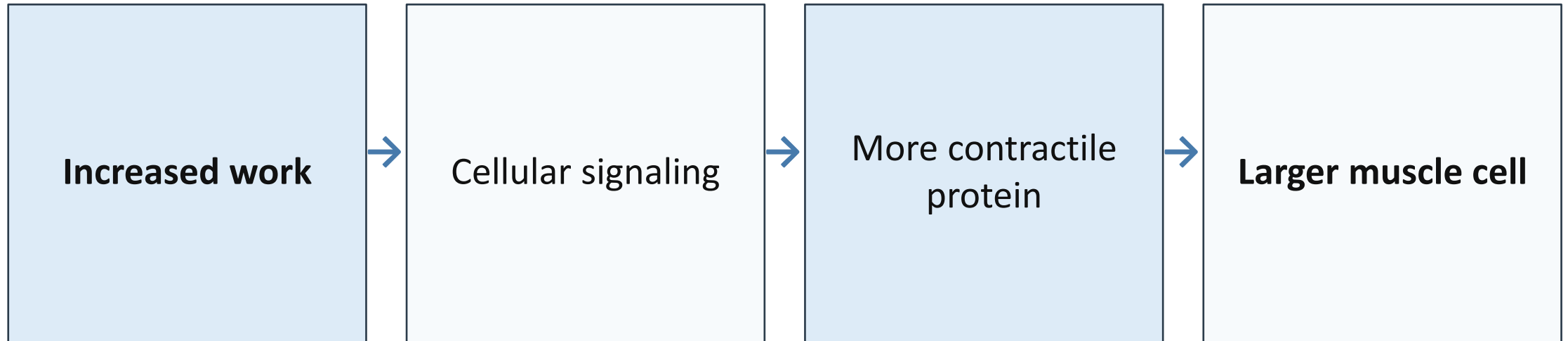
Hypertrophied muscle fiber



Schematic: Greater myofilament content per fiber

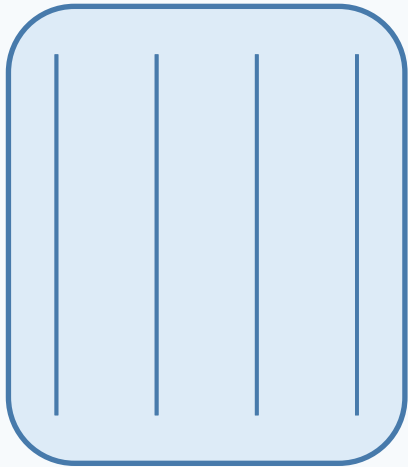
- Cardiac and skeletal muscle fibers have limited division potential.
- An increased workload is therefore met mainly by hypertrophy.
- Myofilament content increases within existing muscle cells.

Higher demand leads to more muscle proteins

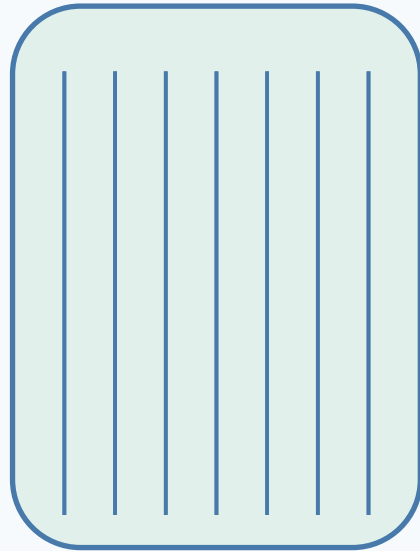


Myofilament accumulation is functionally relevant

Normal muscle fiber



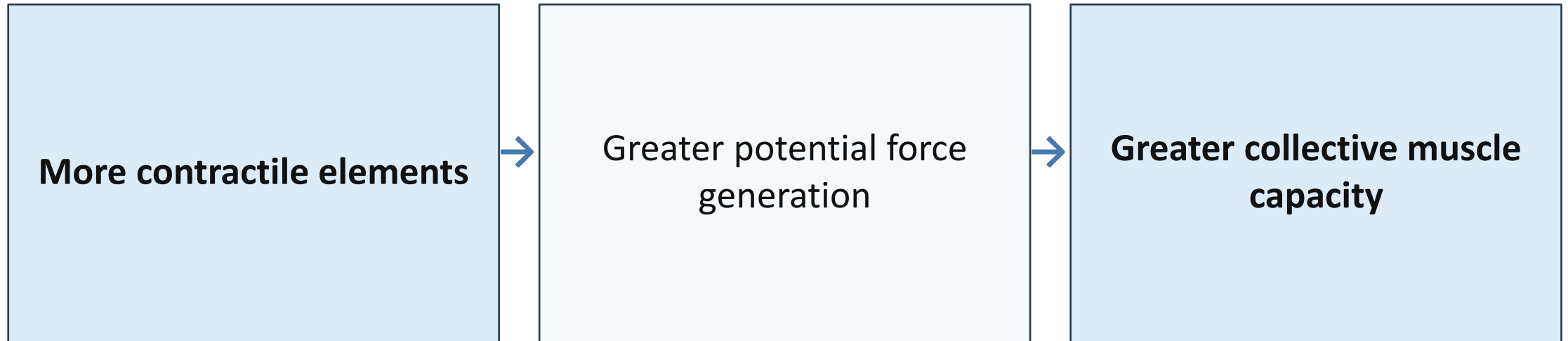
Hypertrophied muscle fiber



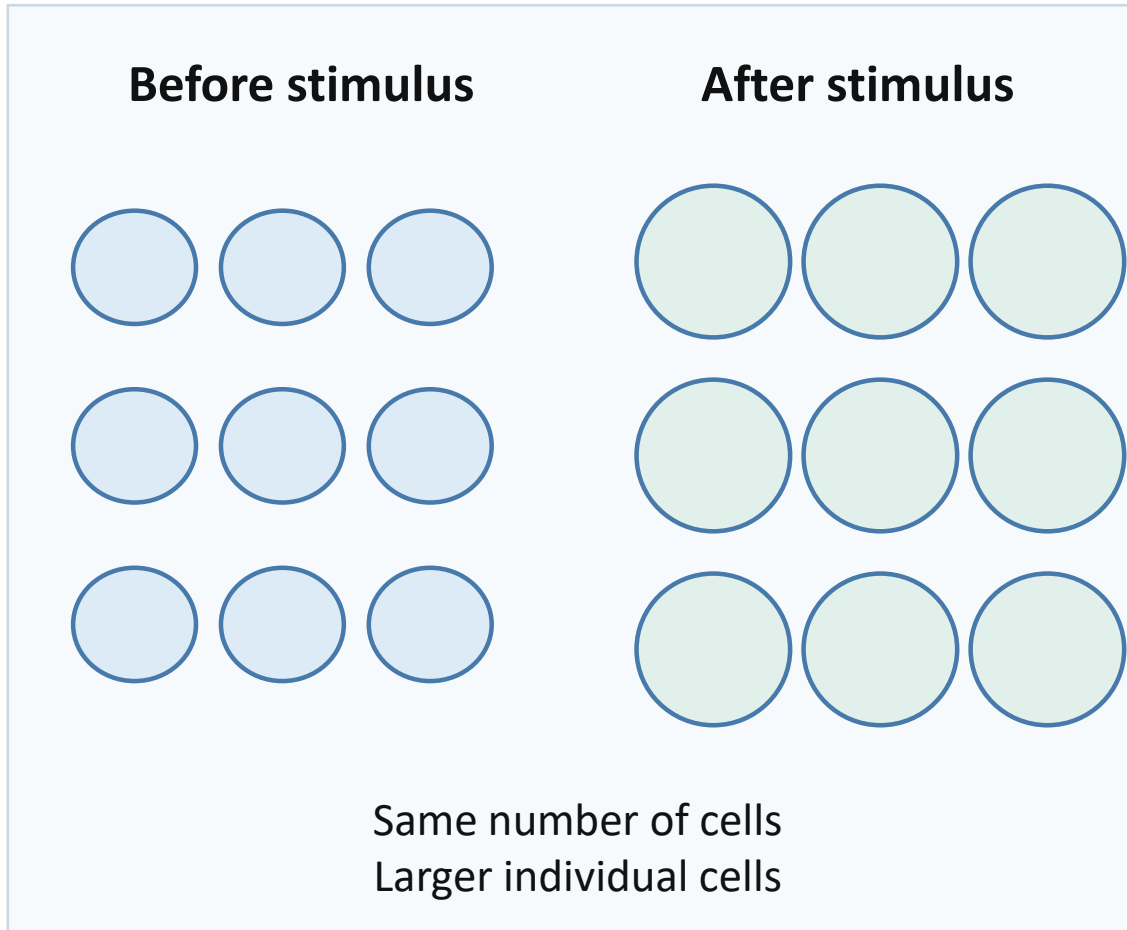
Schematic: Greater myofilament content per fiber

- Myofilaments provide the contractile apparatus.
- Additional myofilaments permit increased force generation.
- The tissue may initially achieve higher work capacity.

Hypertrophy enhances force per myocyte



The contractile apparatus—not water—is emphasized



- Hypertrophy to increased protein production.
- Its characteristic change is structural enlargement, not simple swelling.
- Link morphology to the stimulus and cellular composition.

Cardiac hypertrophy is a classic pathologic example

Increased load

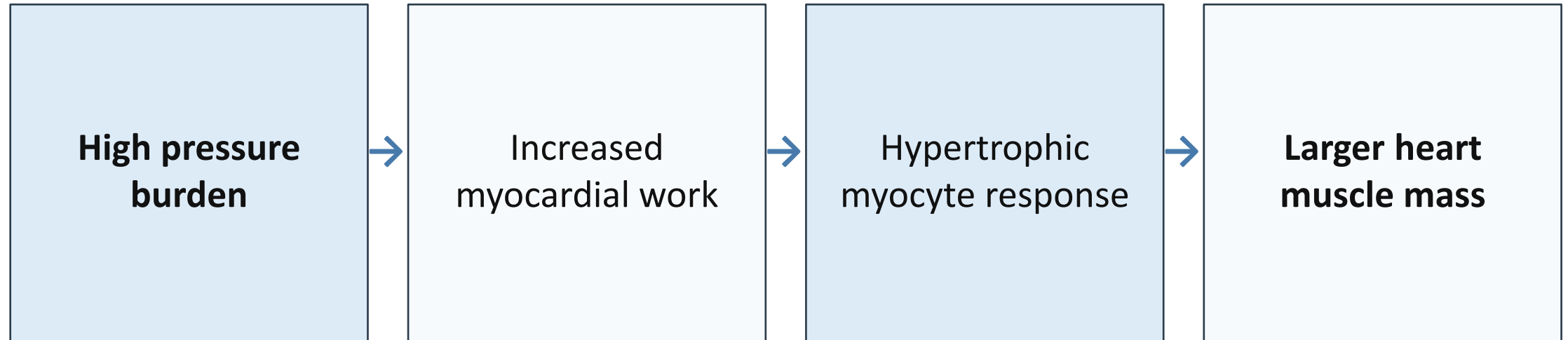
Adaptation More contractile machinery

Limit Persisting hemodynamic burden

Failure Loss of contractile elements

- Increased cardiac workload is a common initiating stimulus.
- Pressure overload is associated with enlarged myocardial cells.
- The process begins as adaptation but may progress to disease.

Systemic hypertension can impose pressure overload



Valvular disease can trigger the same response

Increased load

Adaptation More contractile machinery

Limit Persisting hemodynamic burden

Failure Loss of contractile elements

- Relevant valvular abnormalities may increase pressure load.
- Cardiac cells respond by increasing contractile protein synthesis.
- The initiating disease matters when interpreting hypertrophy.

Early cardiac enlargement can preserve performance

Increased load

Adaptation More contractile machinery

Limit Persisting hemodynamic burden

Failure Loss of contractile elements

- An increased number of myofilaments supports contractile force.
- The heart may initially meet an elevated workload.
- Compensation is useful but does not remove the original stress.

The compensatory response has a finite limit

Cell enlargement

Compensatory increase in work

Regressive change

Myofibrillar elements degrade

Cell injury

Possible myocyte death

- Persisting demand can outstrip increased muscle mass.
- Enlargement alone cannot indefinitely maintain function.
- The adaptive response may become maladaptive.

Loss of myofibrils marks regressive change

Cell enlargement

Compensatory increase in work

Regressive change

Myofibrillar elements degrade

Cell injury

Possible myocyte death

- Hypertrophied myocardial fibers can lose contractile elements.
- Myofibrillar degradation undermines previously increased capacity.
- The same tissue may exhibit adaptation and progressive injury.

Severe overload may progress to cell death

Cell enlargement

Compensatory increase in work

Regressive change

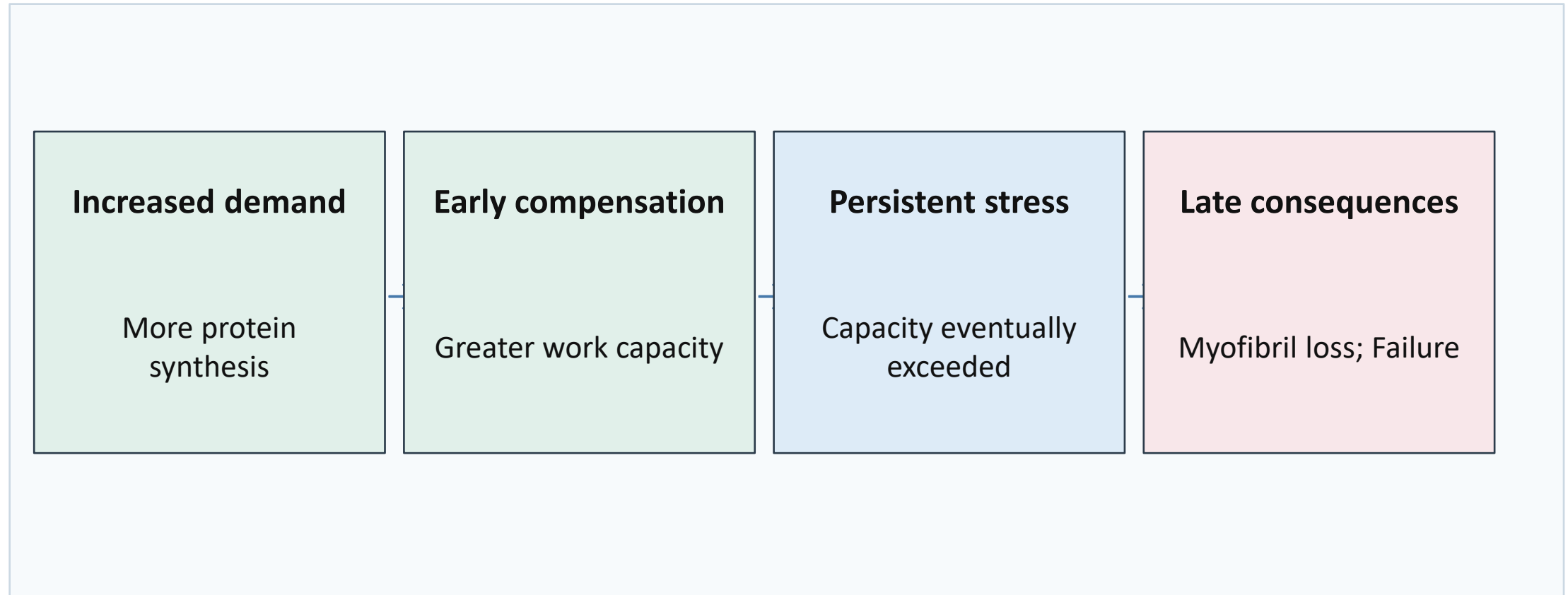
Myofibrillar elements degrade

Cell injury

Possible myocyte death

- When compensation fails, injury can become severe.
- Extreme cases may include myocyte death.
- Cardiac failure is a possible downstream result.

Cardiac hypertrophy: Adaptation-to-failure sequence



Sustained demand initiates growth. Early compensation raises work capacity. Later injury diminishes contractile capability.

Cardiac enlargement cannot be interpreted in isolation

Increased load

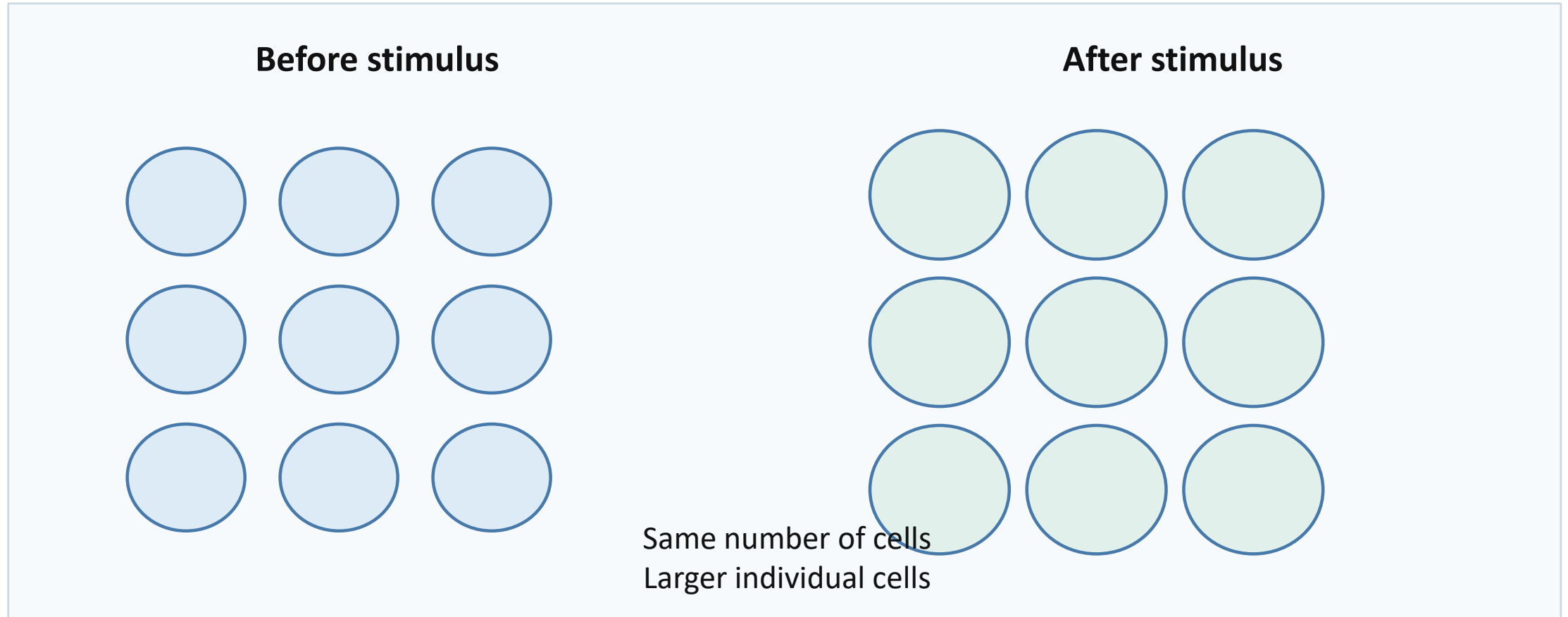
Adaptation More contractile machinery

Limit Persisting hemodynamic burden

Failure Loss of contractile elements

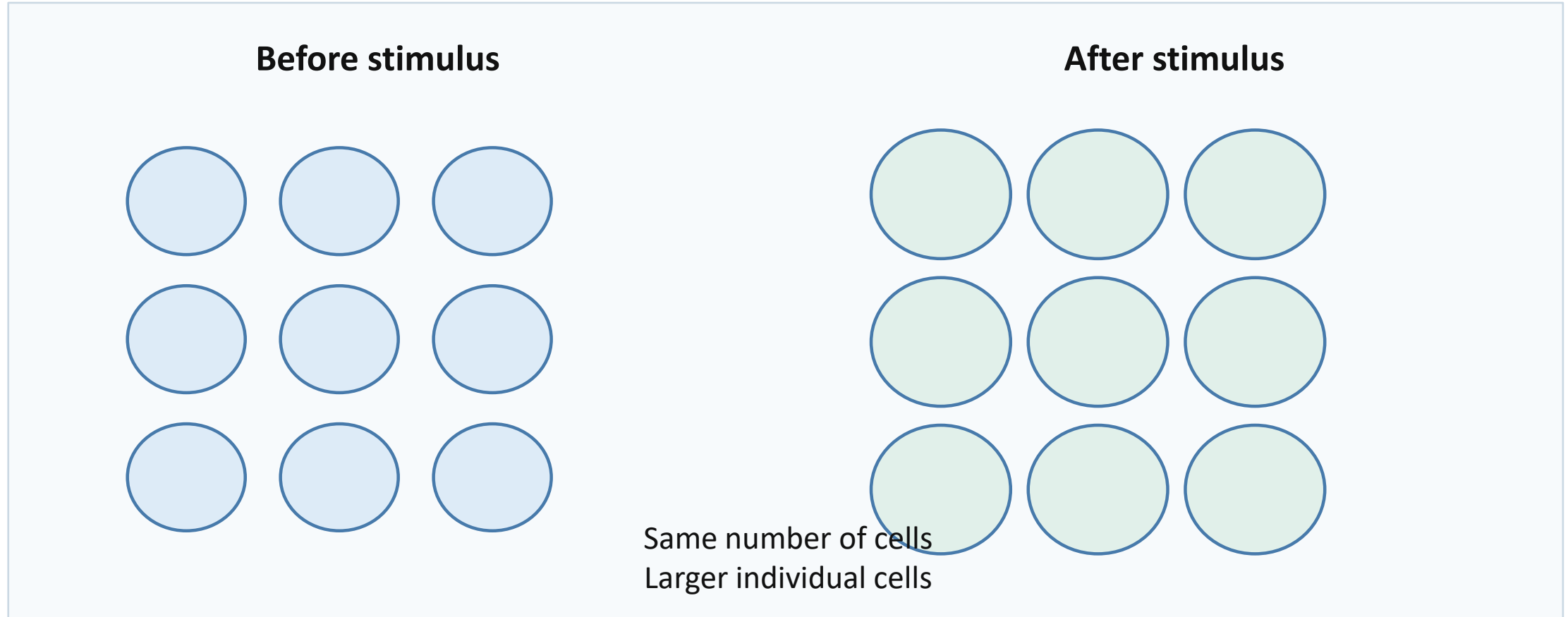
- Organ size reflects a response, not necessarily physiologic success.
- Identify the hemodynamic cause and functional status.
- Hypertrophy may coexist with late-stage cellular injury.

Cellular morphology: Larger contractile cells



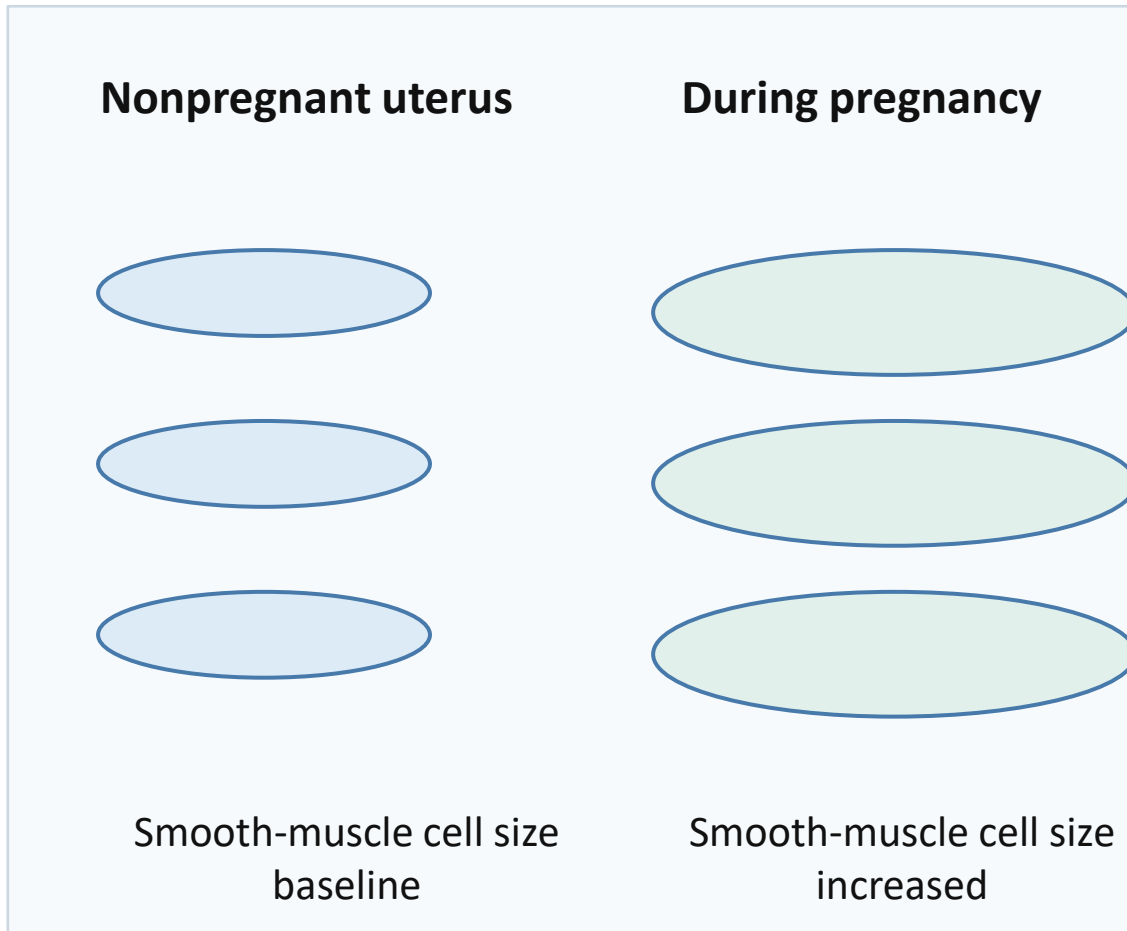
Myocardial myocytes become enlarged. • Additional protein and myofilaments account for increased volume.

A tissue-level schematic shows larger myocytes



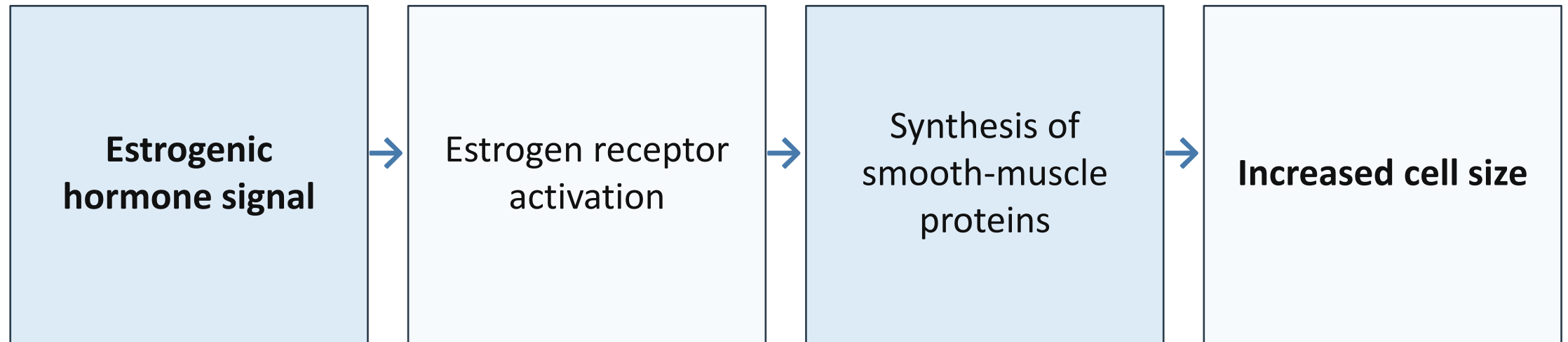
Compare like-for-like cellular outlines. • Preserve cell count in a hypertrophy-only depiction.

Pregnancy is a physiologic organ-enlargement example

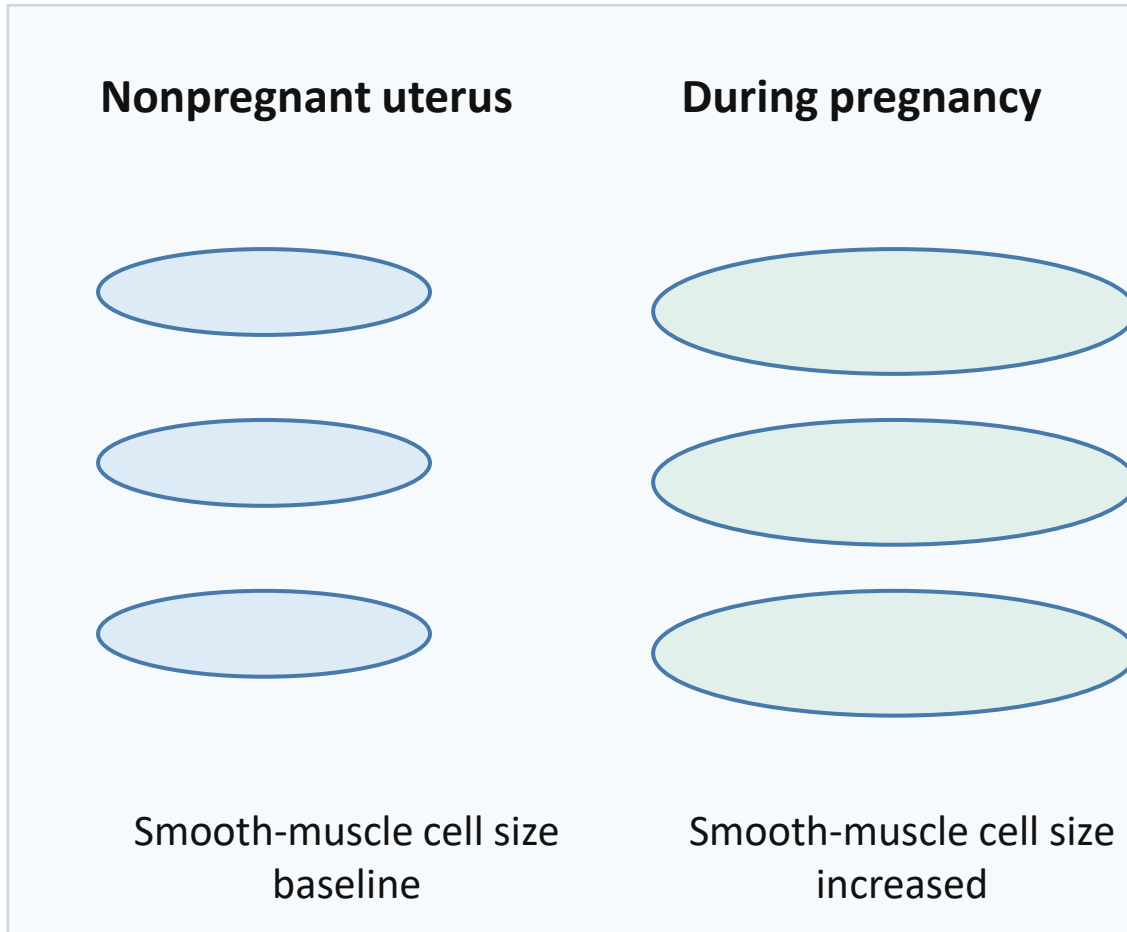


- The uterus enlarges markedly during pregnancy.
- Hypertrophy of uterine smooth-muscle cells is a major contributor.
- The relevant stimulus is endocrine rather than pathologic pressure.

Estrogen signaling stimulates uterine hypertrophy

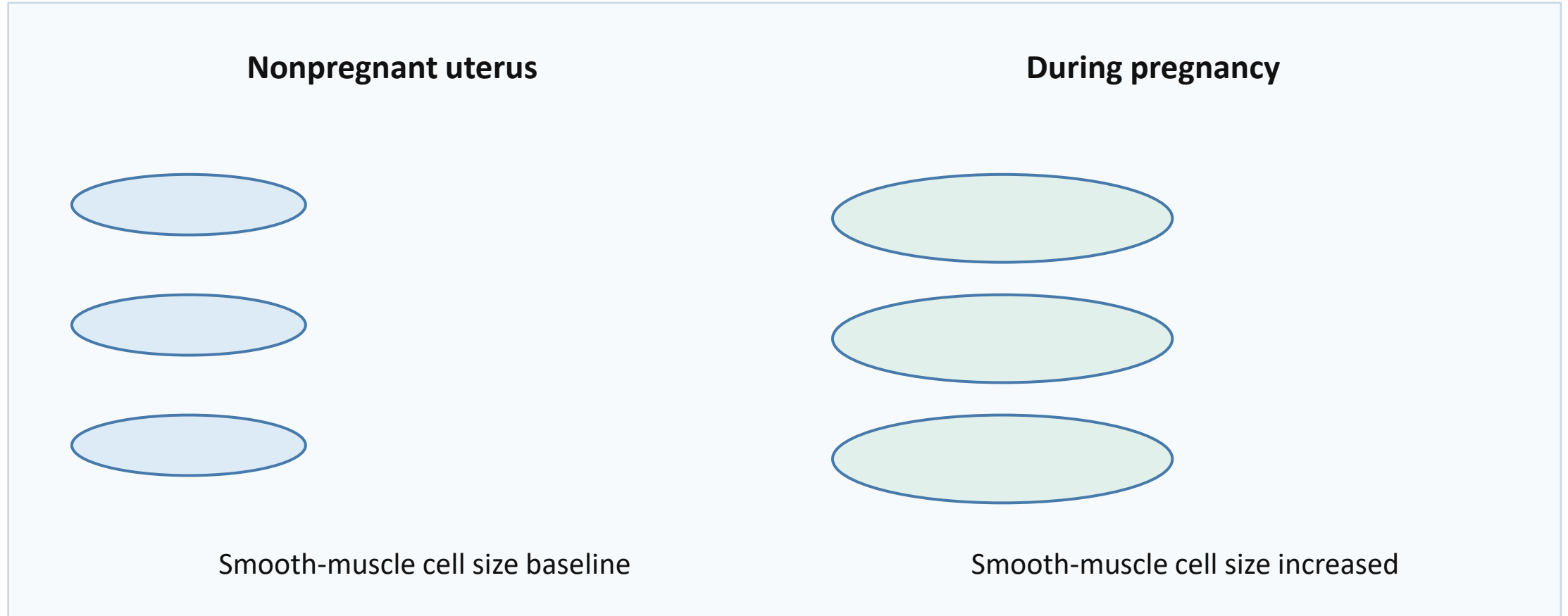


Uterine growth requires protein synthesis



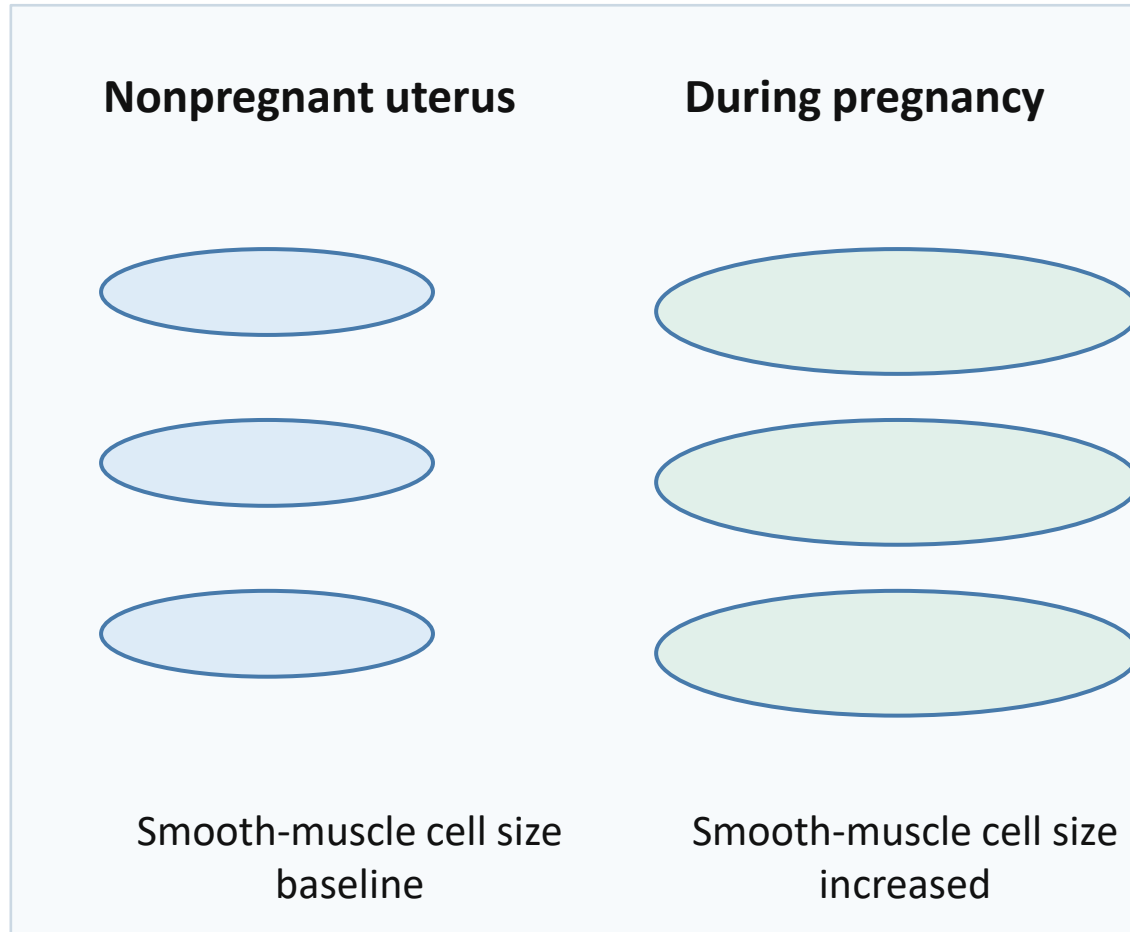
- Estrogen receptor signaling changes cellular protein production.
- New smooth-muscle proteins accumulate in the cells.
- The result is enlargement of pre-existing smooth-muscle fibers.

The gravid myocyte is larger than the baseline myocyte



Cells shift from small spindle-shaped forms to enlarged, plumper cells. • The comparative appearance is Fig. 2.25.

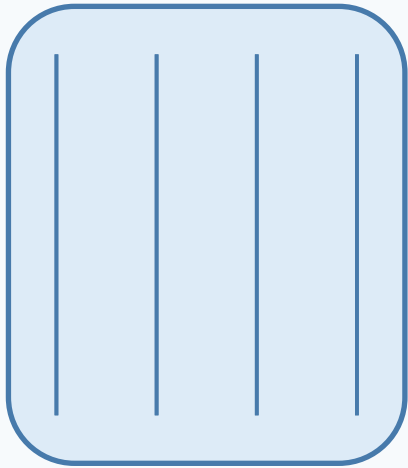
Hormone-driven hypertrophy has a clear causal chain



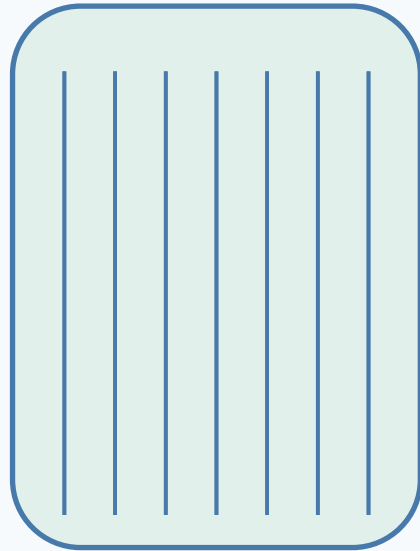
- Hormonal change is the stimulus.
- Receptor-dependent biosynthesis is the cellular mechanism.
- Smooth-muscle enlargement is the morphologic result.

Skeletal muscle responds to resistance loading

Normal muscle fiber



Hypertrophied muscle fiber

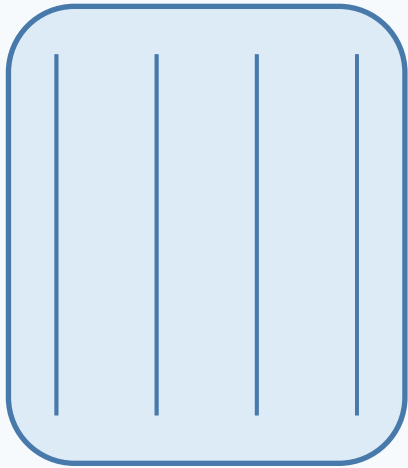


Schematic: Greater myofilament content per fiber

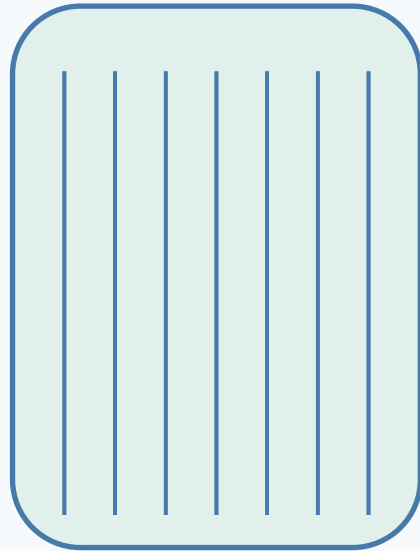
- Resistance exercise raises functional demand.
- Individual muscle fibers enlarge.
- The increase in muscle bulk primarily reflects fiber hypertrophy.

Muscle bulk and muscle fiber number are different

Normal muscle fiber



Hypertrophied muscle fiber



Schematic: Greater myofilament content per fiber

- Larger fiber cross-sectional size explains the classic training adaptation.
- Greater visible muscle mass does not itself prove fiber proliferation.
- This distinction parallels organ-level interpretation of hypertrophy.

Skeletal and cardiac hypertrophy share a cell response

Feature	Resistance-trained skeletal muscle	Pressure-overloaded heart
Stimulus	Increased exercise demand	Increased cardiac pressure workload
Cellular change	More myofilaments; Larger fibers	More myofilaments; Larger myocytes
Clinical frame	Physiologic adaptation	Can become pathologic

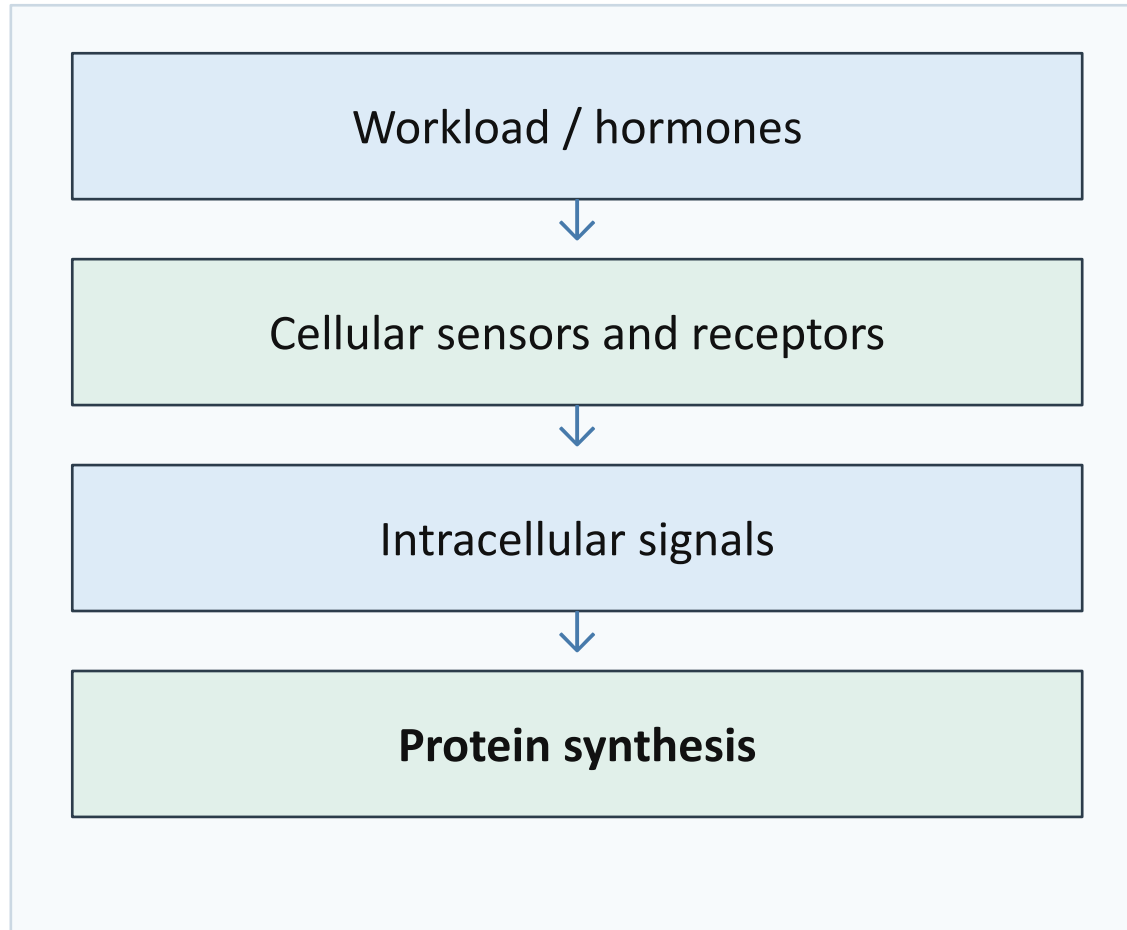
Uterine and skeletal examples differ by stimulus

Characteristic	Gravid uterine smooth muscle	Resistance-trained skeletal muscle
Major initiating stimulus	Estrogen signaling	Mechanical workload
Common response	Additional cellular protein	Additional contractile protein
Tissue-level outcome	Uterine enlargement	Skeletal muscle bulk

The same morphologic term spans several tissues

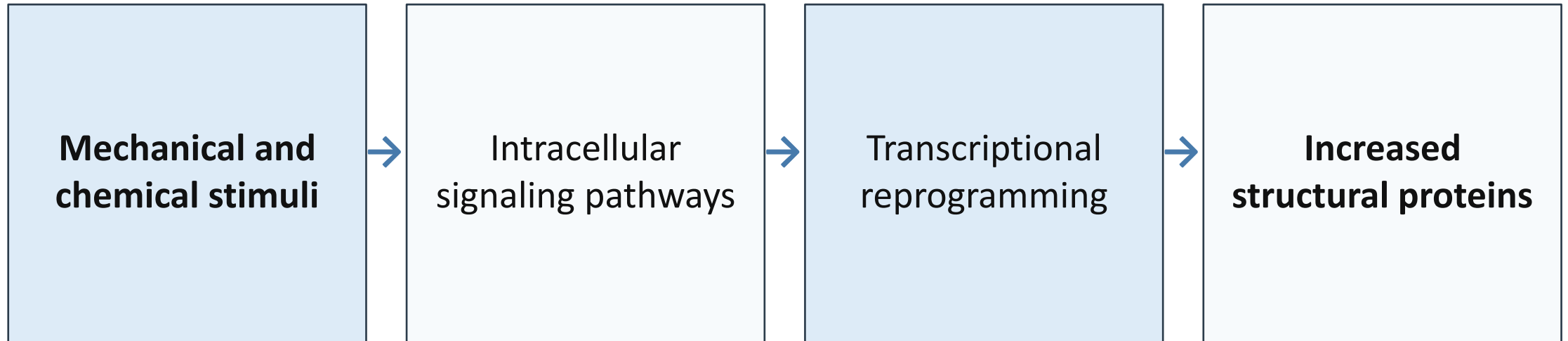
- Cardiac myocyte enlargement accompanies elevated workload.
- Skeletal fiber enlargement accompanies resistance exercise.
- Uterine smooth-muscle enlargement accompanies gestational hormone signals.

Mechanical sensors detect increased load

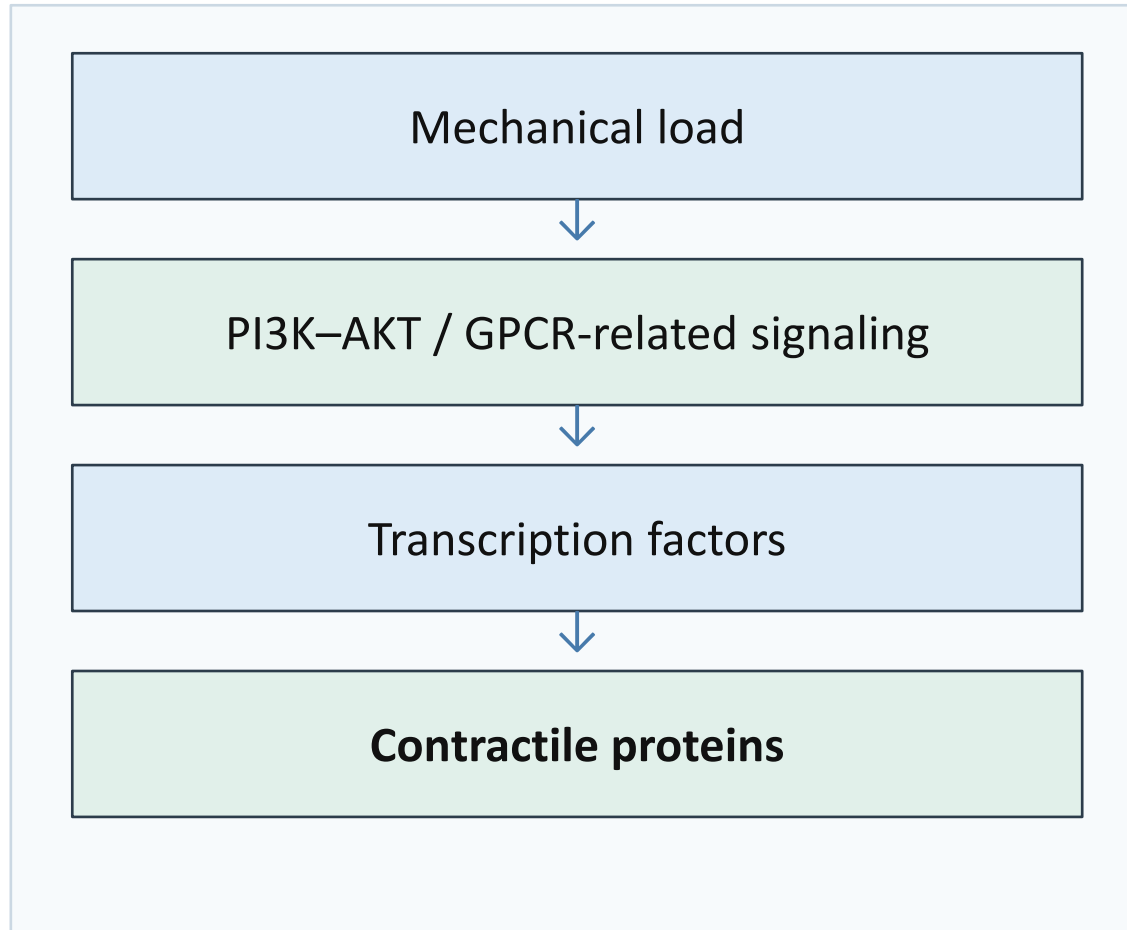


- Cellular sensors respond to mechanical stretch.
- The signal activates pathways that raise biosynthetic activity.
- Mechanosensing is a key part of the myocardial response.

Signaling connects extracellular load to protein synthesis

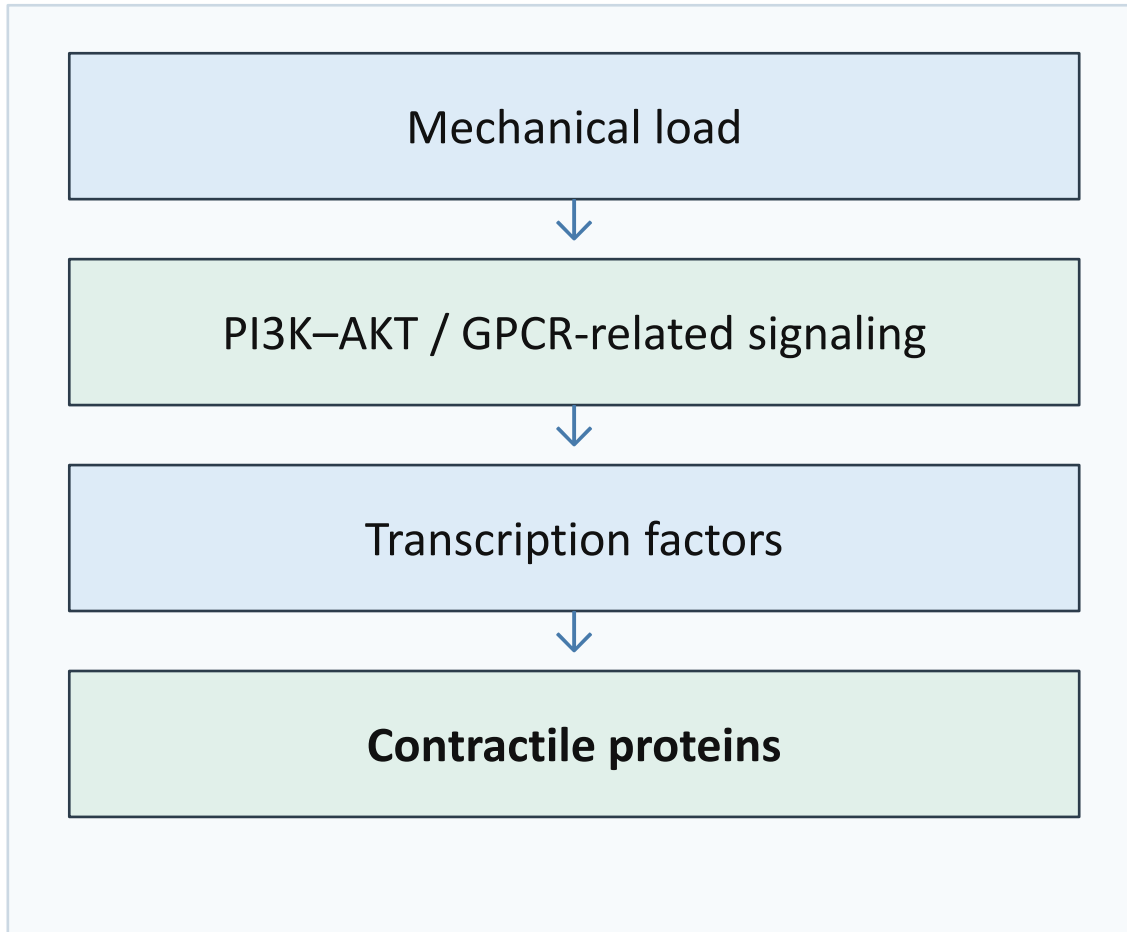


PI3K–AKT is linked to physiologic hypertrophy



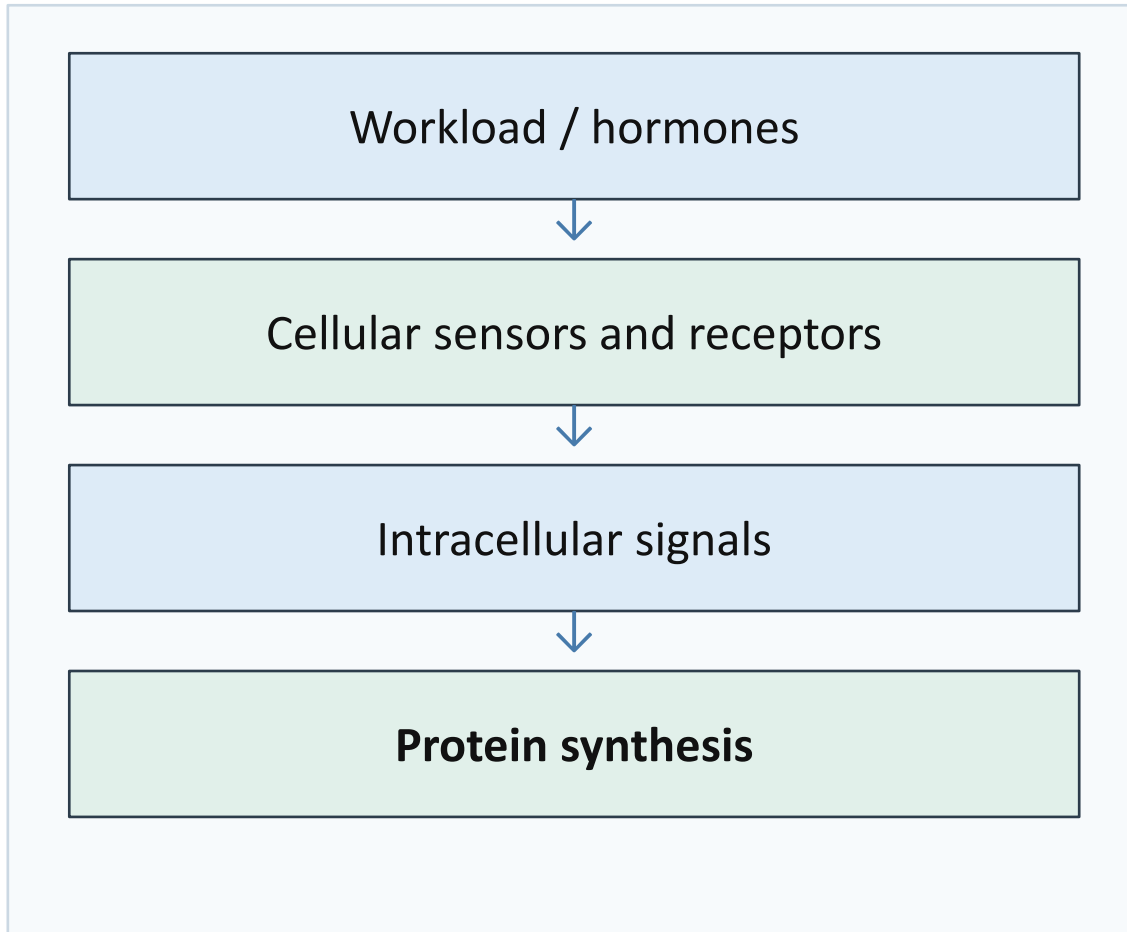
- Phosphoinositide 3-kinase and AKT participate in growth signaling.
- This pathway is particularly important in exercise-associated hypertrophy.
- Relative pathway dominance is a model, not an absolute separation.

GPCR pathways are prominent in pathologic contexts



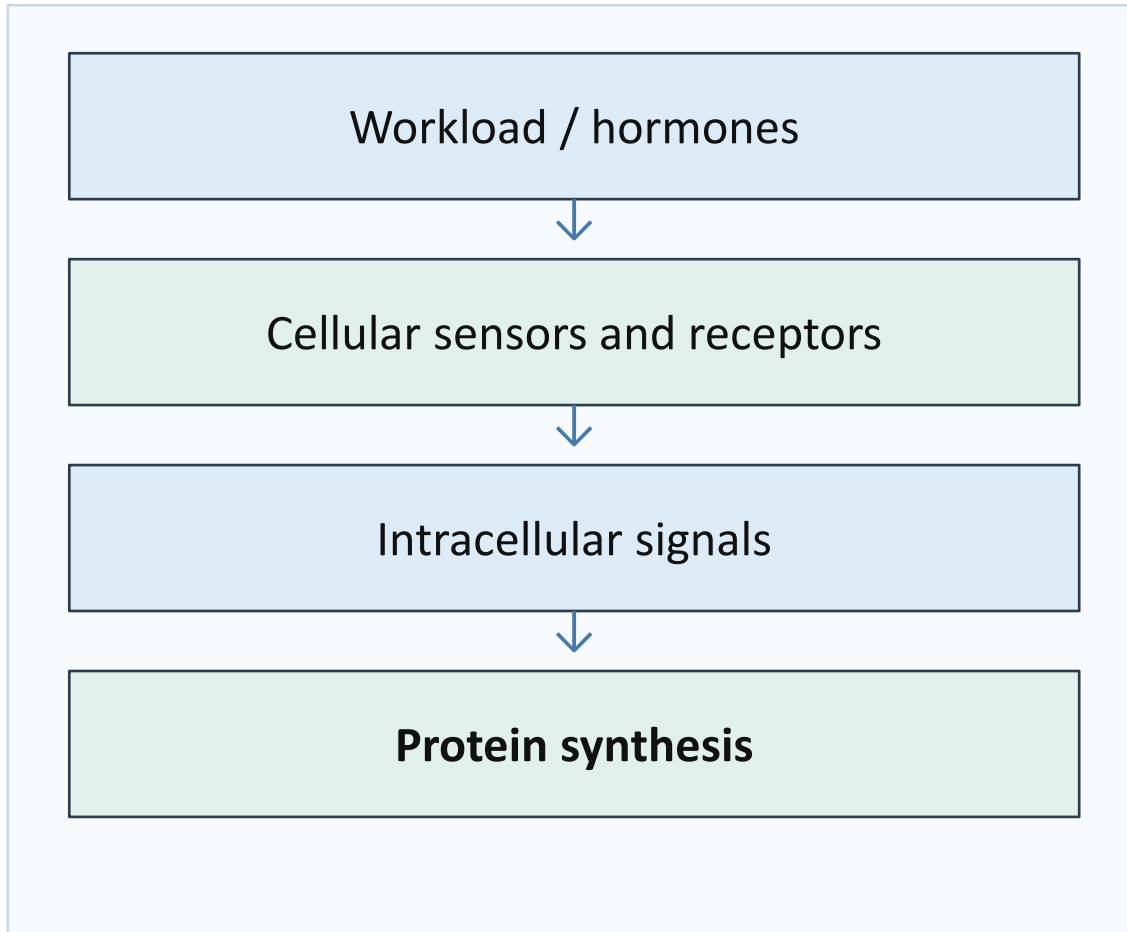
- G-protein–coupled receptor signaling integrates agonist stimulation.
- Vasoactive agents and growth factors can activate associated pathways.
- Greater proposed importance in pathologic hypertrophy.

Growth-factor mediators amplify the cellular response



- Examples named by Robbins include IGF-1, TGF- β , and fibroblast growth factor.
- These mediators can participate in growth-promoting feedback.
- They belong to the signaling network—not an independent cell-number increase.

Vasoactive agonists contribute to cardiac signaling



- Examples include α -adrenergic agonists, endothelin-1, and angiotensin II.
- Such mediators link physiological stress and receptor pathways.
- Multiple upstream inputs can converge on growth-related gene expression.

Transcription factors implement the growth program

GATA4 • NFAT • MEF2



Expression of contractile-protein genes



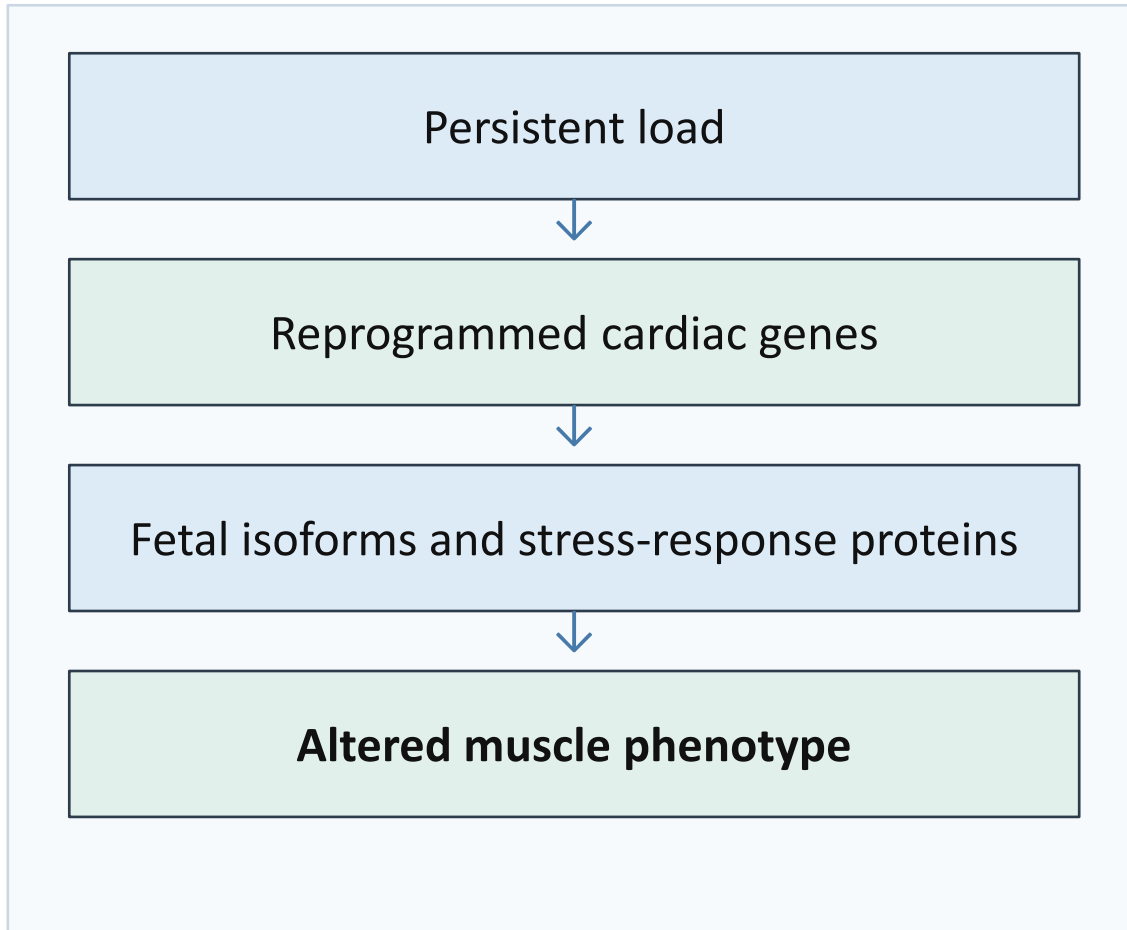
Increase in cellular protein



Myocyte enlargement

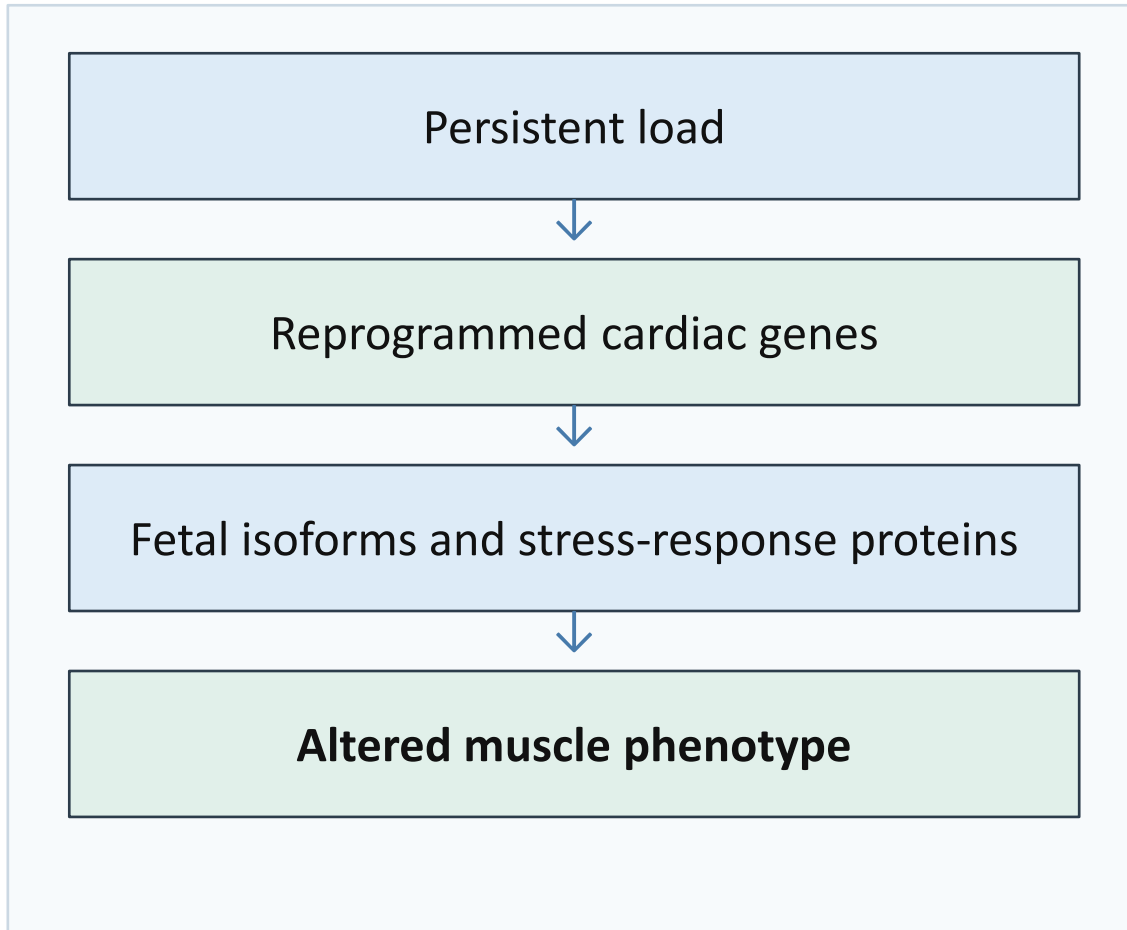
GATA4 NFAT MEF2 Contractile-protein gene expression

More gene expression produces more contractile proteins



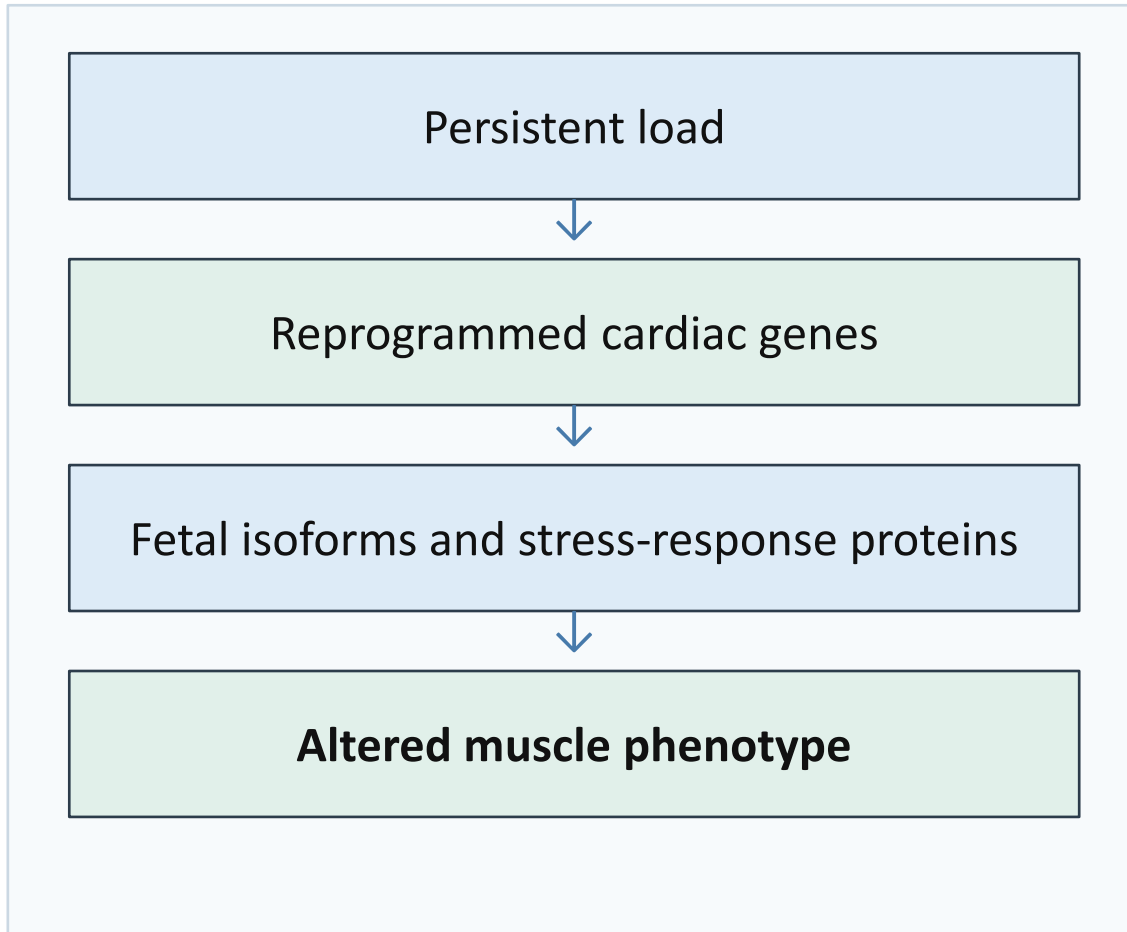
- Growth-related signaling activates selected transcription factors.
- Their targets include genes encoding contractile components.
- Additional protein yields greater structural cell mass.

Cardiac hypertrophy includes fetal gene re-expression



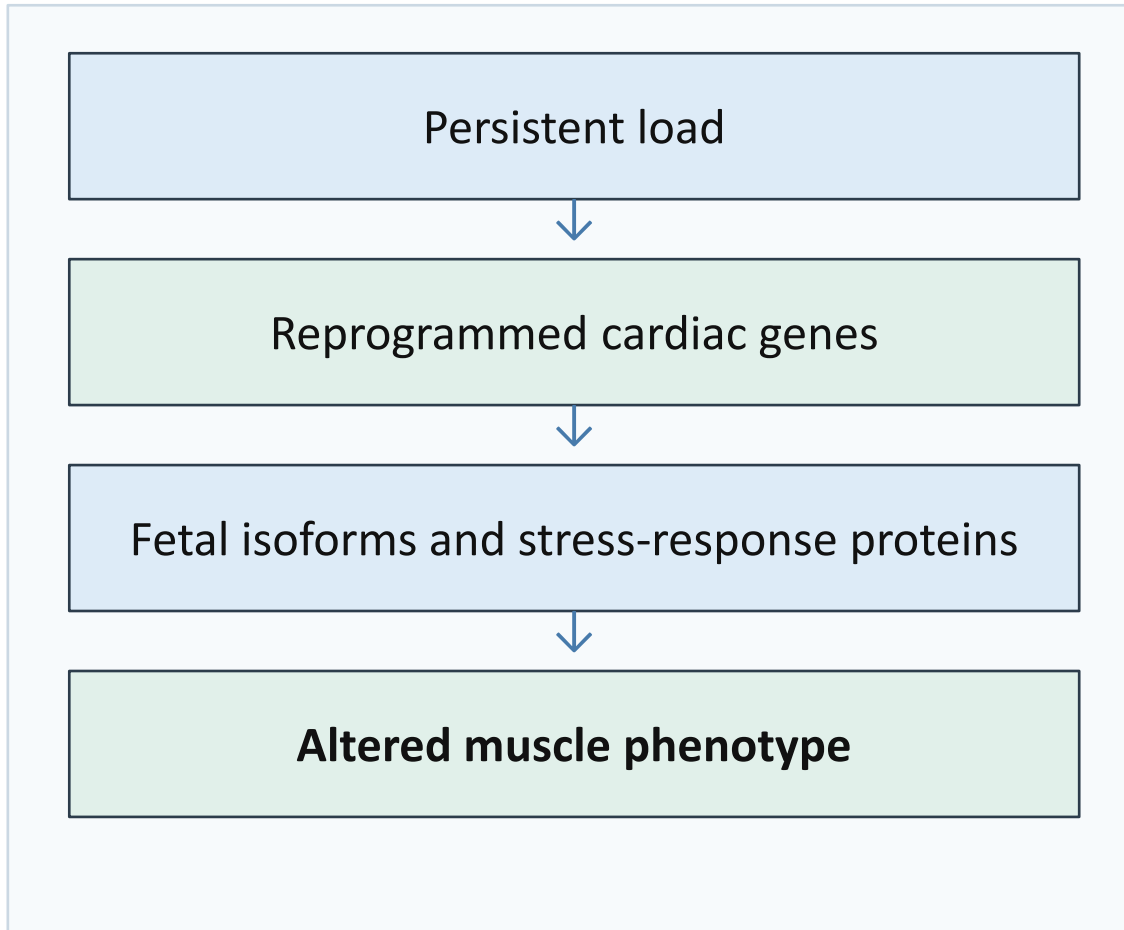
- Hypertrophic cardiac cells may shift their contractile-protein isoforms.
- Embryonic or fetal expression programs can reappear.
- Gene-expression changes accompany, but do not define, hypertrophy.

Myosin heavy-chain isoforms illustrate the switch



- A shift from α - to β -myosin heavy-chain isoforms.
- β -myosin heavy chain supports slower, energetically economical contraction.
- The example illustrates functional consequences of altered gene expression.

Atrial natriuretic factor is a stress-response product



- Cardiac hypertrophy can increase atrial natriuretic factor gene expression.
- This peptide contributes to renal salt excretion.
- The resulting fall in volume and pressure tends to reduce hemodynamic load.

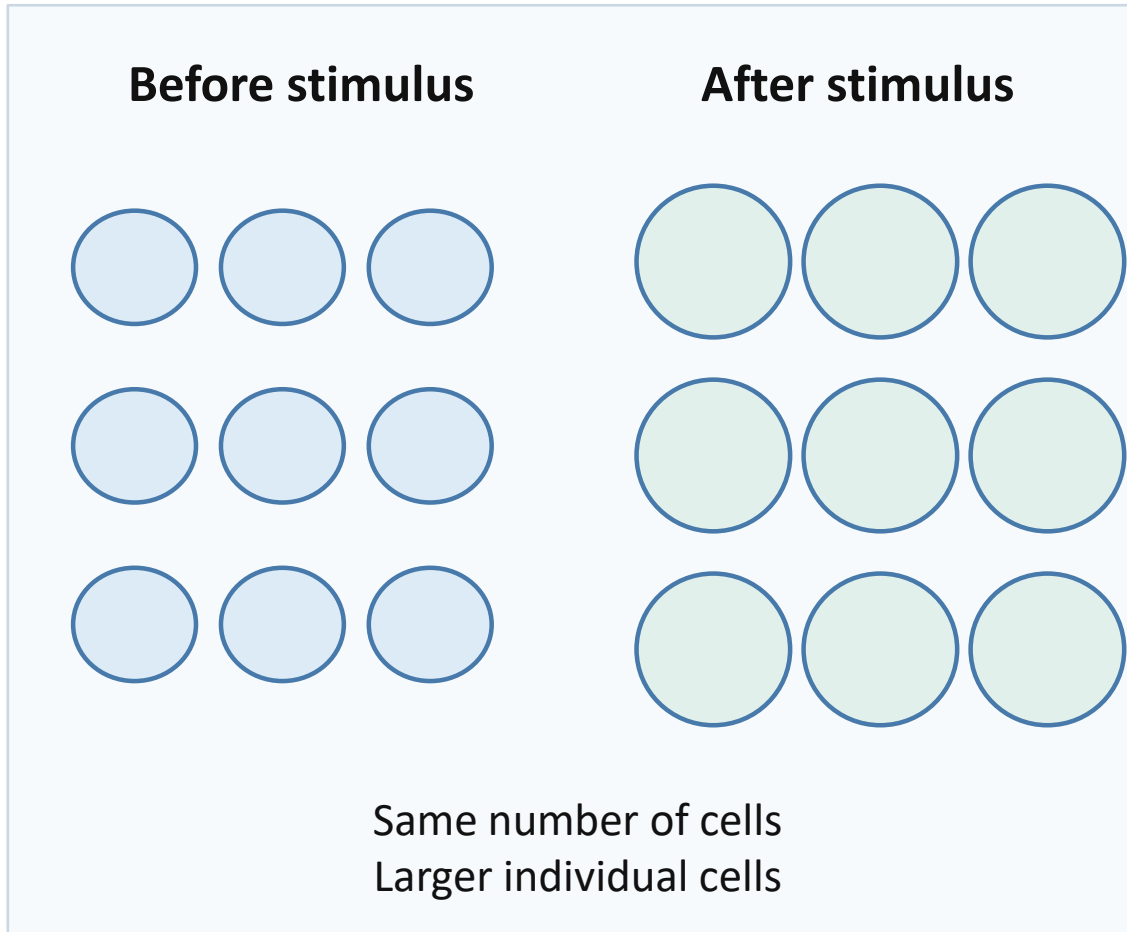
Signaling pathways are overlapping, not exclusive

Mechanistic theme	Physiologic example	Pathologic example
Illustrative upstream input	Exercise-related stretch	Vasoactive/receptor stimuli
Textbook emphasis	PI3K–AKT signaling	GPCR-associated signaling
Shared endpoint	Increased cellular protein	Increased cellular protein

Hypertrophy and hyperplasia: The diagnostic distinction

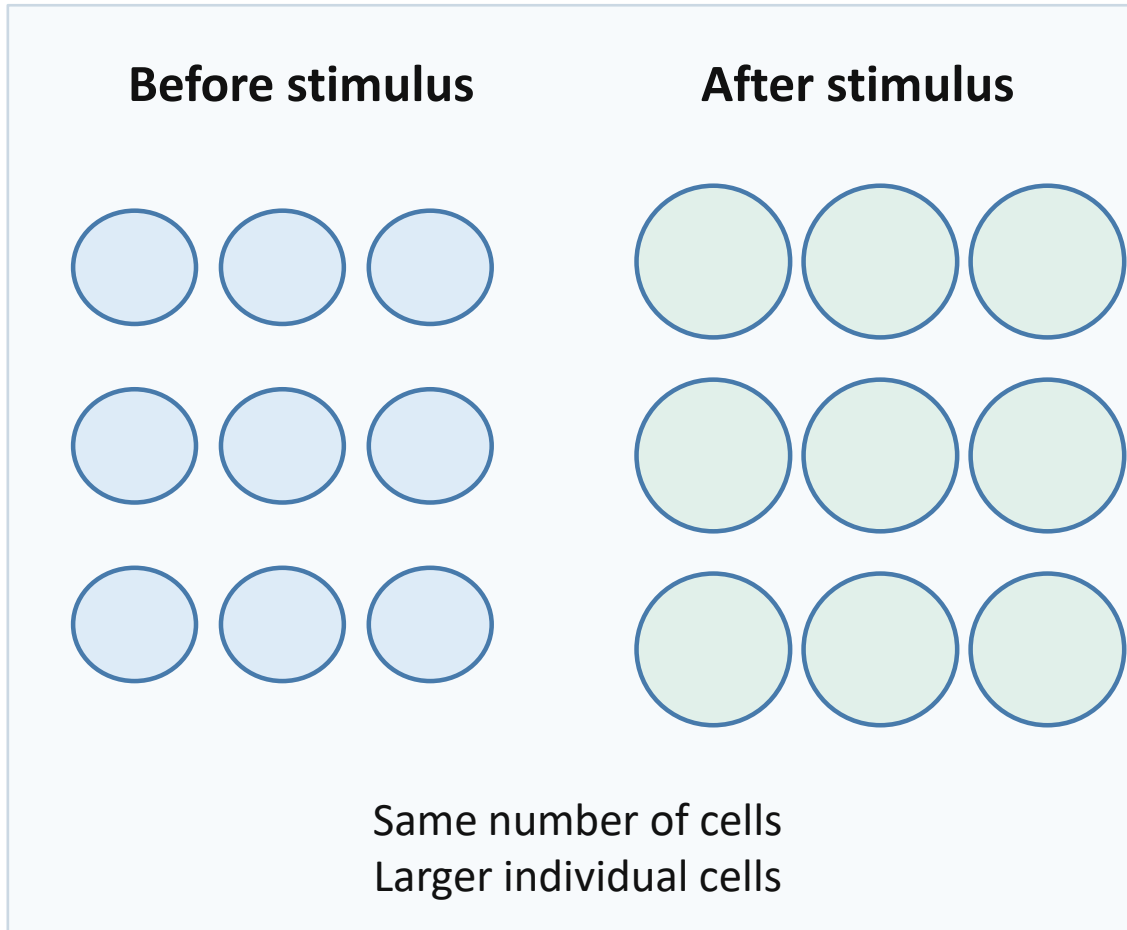
Feature	Hypertrophy	Hyperplasia
Defining cellular change	Increased cell size	Increased cell number
Pre-existing cells	Enlarge	Proliferate
May coexist?	Yes	Yes

Cell proliferative capacity limits hyperplasia



- Hyperplasia requires cells capable of division.
- Striated-muscle hypertrophy is prominent because proliferative reserve is limited.
- Do not equate every large organ with hyperplasia.

Mixed growth must be assessed as mixed growth



- Some organs enlarge through both increased cell size and number.
- The contribution of each process varies by tissue and stimulus.
- Descriptions should explicitly distinguish these components.

Case: Cardiac pressure overload

A patient with long-standing systemic hypertension is found to have an enlarged heart.

Reason through the stimulus, cell population, and expected adaptation.

- Which adaptation is expected in myocardial cells?
- Why might this initially preserve function?
- What cellular changes may eventually precede cardiac failure?

Cardiac case: Mechanism-based resolution

Increased load

Adaptation More contractile machinery

Limit Persisting hemodynamic burden

Failure Loss of contractile elements

- The persistent pressure burden increases myocardial workload.
- Myocytes synthesize additional contractile proteins and enlarge.
- Progressive myofibril loss and injury can limit contractility.

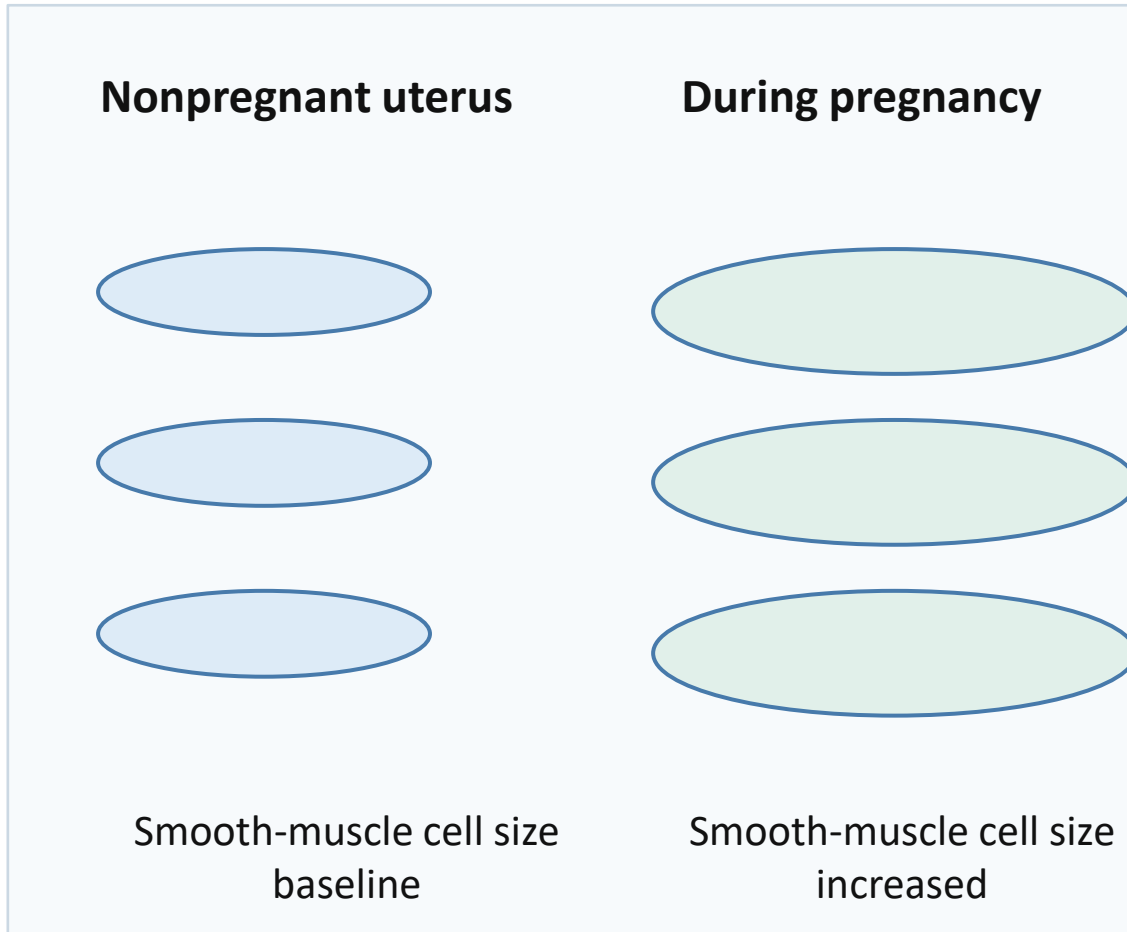
Case: Pregnancy-related uterine growth

An otherwise healthy pregnant patient has marked uterine enlargement.

Reason through the stimulus, cell population, and expected adaptation.

- Which smooth-muscle cellular adaptation contributes to the change?
- What endocrine signal is emphasized?
- Is this example classified as physiologic or pathologic?

Uterine case: Mechanism-based resolution



- Uterine smooth-muscle cells enlarge substantially.
- Estrogen receptor signaling promotes cellular protein synthesis.
- The growth illustrates physiologic hormone-associated hypertrophy.

Case: Resistance training

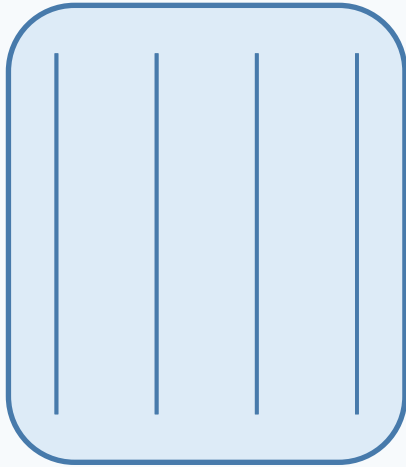
After a prolonged period of resistance training, skeletal muscle bulk increases.

Reason through the stimulus, cell population, and expected adaptation.

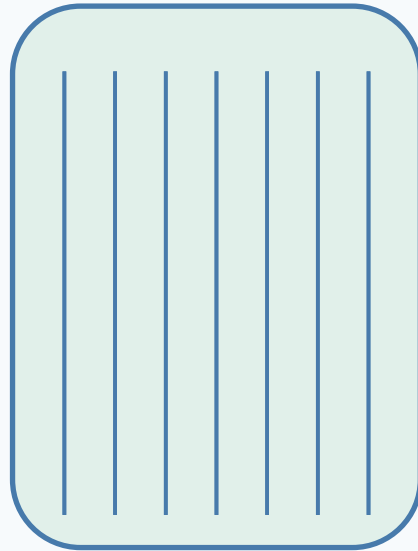
- What happens to individual muscle fibers?
- What structural content explains greater contractile capacity?
- How does this differ from cellular proliferation?

Skeletal case: Mechanism-based resolution

Normal muscle fiber



Hypertrophied muscle fiber



Schematic: Greater myofilament content per fiber

- Greater workload stimulates new contractile protein production.
- Individual fibers enlarge through additional myofilaments.
- The primary described adaptation is hypertrophy, not hyperplasia.

Integrate stimulus, cellular response, and outcome

Setting	Stimulus	Cell response	Outcome
Heart	Pressure overload	Myocyte hypertrophy	Initial compensation; Potential failure
Uterus	Estrogen signaling	Smooth-muscle hypertrophy	Physiologic organ growth
Skeletal muscle	Resistance demand	Fiber hypertrophy	Greater muscle bulk

Essential principles of hypertrophy

- Cell enlargement reflects additional intracellular structural components.
- Workload, hormones, and growth factors are important initiating inputs.
- Physiologic growth and maladaptive growth share protein synthesis.
- The cardiac response may eventually become injurious.

References and source limitations

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026). Chapter 2: Cell Injury, Cell Death, and Adaptations, pp. 52–53.
- Primary sections: Hypertrophy; Mechanisms of Hypertrophy. Comparison context: Hyperplasia.
- Conceptual drawings are original native PowerPoint schematics; no simulated histopathology is shown.
- Original chapter PDF and licensed tissue images were not available for direct figure verification.