

Nutritional Diseases

Mechanisms, morphology and clinicopathologic consequences

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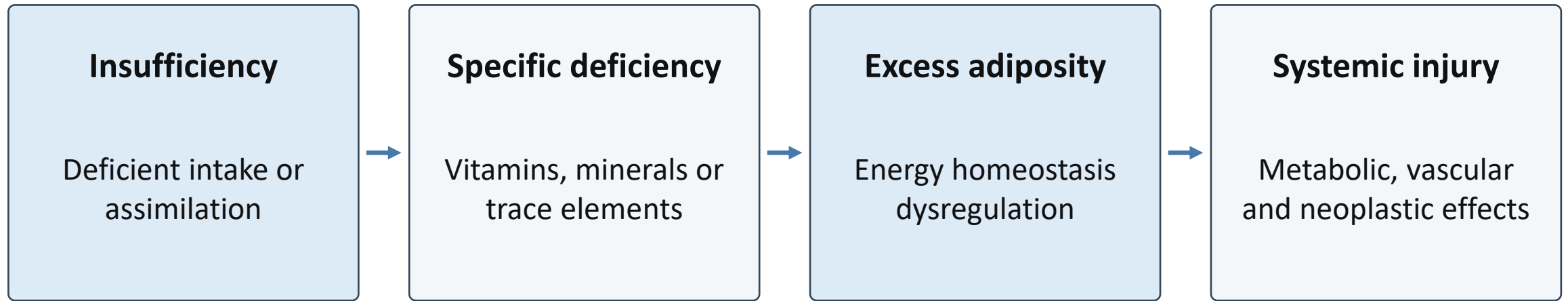
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Learning outcomes

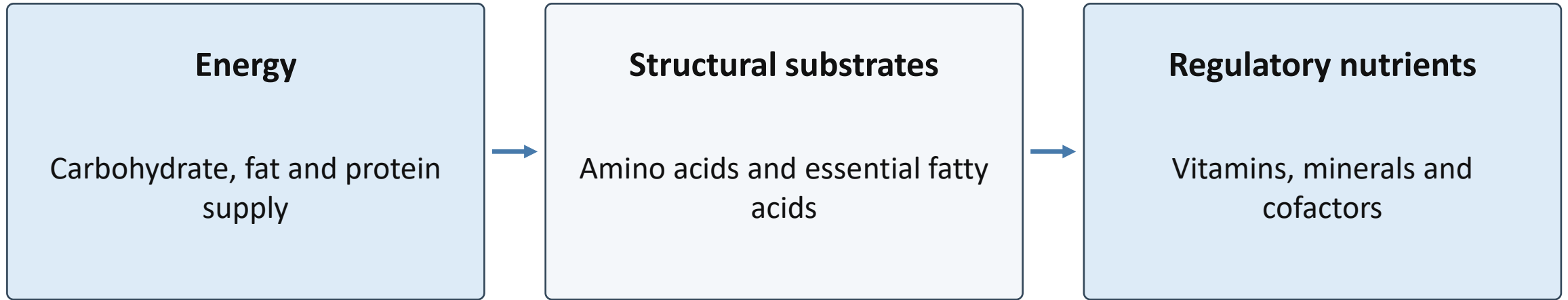
- Distinguish primary from secondary nutritional disorders and explain their pathogenesis.
- Recognize protein–energy malnutrition and its tissue manifestations.
- Link characteristic micronutrient deficits to their molecular functions.
- Explain how excess adiposity and dietary patterns contribute to systemic disease.

The nutritional disease spectrum



Undernutrition and overnutrition are both causes of structural and functional disease.

Three essential contributions of diet

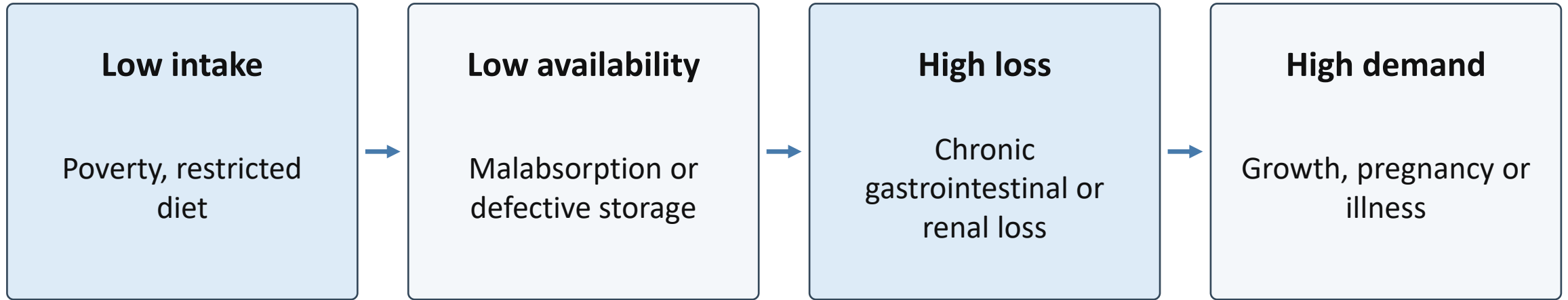


Defects at any level can compromise growth, tissue maintenance and repair.

Primary versus secondary malnutrition

Dimension	Primary	Secondary
Fundamental defect	Diet lacks required nutrients	Nutrients unavailable or inadequately utilized
Example	Food insecurity; Restricted intake	Malabsorption; Chronic illness
Physiologic problem	Insufficient supply	Impaired absorption, excess loss or increased need
Clinical implication	Restore adequate intake	Identify and address underlying disease

Mechanisms producing nutrient deficiency

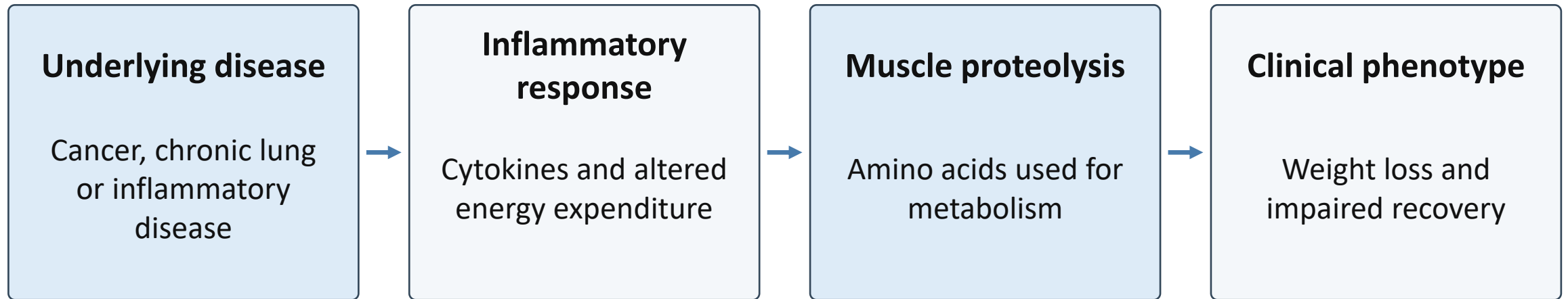


These pathways may coexist in the same patient.

Poverty and environmental disruption

- Food insecurity may reflect limited access to protein, energy and micronutrient-rich foods.
- Crop failure, drought, displacement and conflict amplify nutritional vulnerability.
- Children, older adults and socially disadvantaged populations are particularly exposed.
- Deficiency patterns reflect both food quantity and dietary diversity.

Chronic disease promotes wasting



Nutritional support alone may not fully reverse inflammation-driven catabolism.

Excessive alcohol use and deficiency

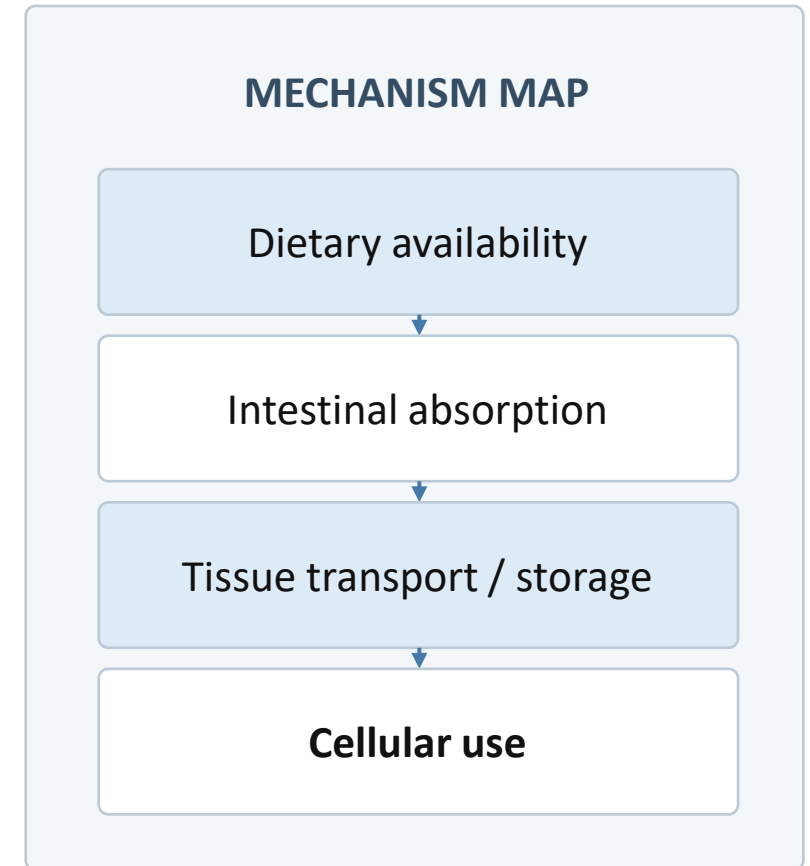
- Deficiency arises through poor diet, abnormal absorption, utilization and storage.
- Thiamine, pyridoxine, folate and vitamin A deficiencies are emphasized.
- Unrecognized thiamine depletion can lead to Wernicke encephalopathy and lasting neurologic injury.
- Clinical evaluation should assess specific deficits, not only caloric intake.

High-demand physiological states

- Infancy and adolescence require nutrients for rapid tissue growth.
- Pregnancy increases demands for selected nutrients and building blocks.
- Failure to adjust dietary intake may produce clinically important deficiencies.
- An apparently sufficient diet can become insufficient when needs change.

Impaired absorption, storage or utilization

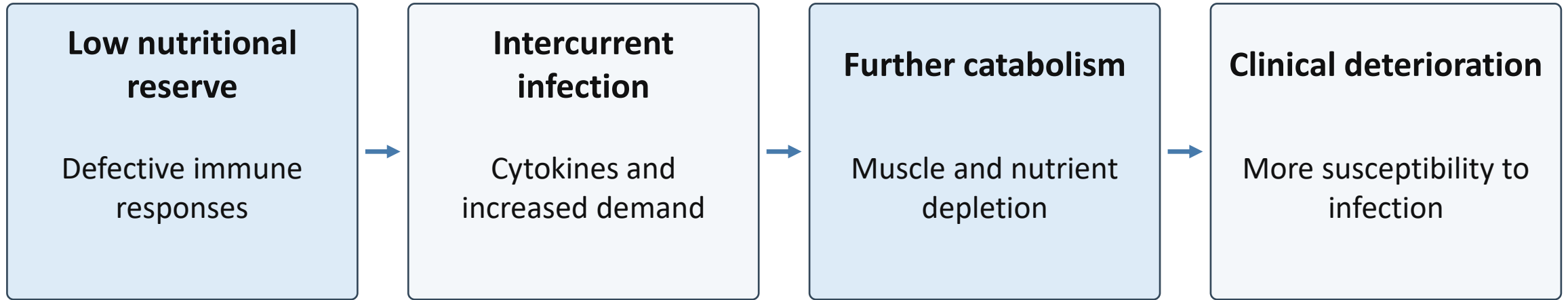
- Gastrointestinal disorders may prevent absorption despite adequate dietary supply.
- Certain genetic disorders or drug exposures interfere with nutrient use.
- Chronic protein losses can produce a kwashiorkor-like phenotype.



Common nutritional phenotypes

Phenotype	Dominant defect	Typical finding
Energy deficiency	Negative energy balance	Loss of fat and muscle
Protein-predominant deficit	Visceral protein depletion	Edema; Fatty liver
Micronutrient deficiency	Defective enzyme or tissue function	Specific organ syndromes
Obesity	Dysregulated adiposity	Metabolic and inflammatory injury

Why infection worsens malnutrition



Malnutrition and infection form a reinforcing pathogenic cycle.

Clinical assessment of undernutrition

- Anthropometric measures assess growth, body mass and tissue wasting.
- Subcutaneous fat stores and muscle bulk document somatic depletion.
- Edema may mask true weight loss, especially in kwashiorkor.
- Serum proteins require interpretation in the context of inflammation and disease.

Severe acute malnutrition: Textbook criteria

Criterion	Textbook threshold / observation
Mid-upper arm circumference	Less than 115 mm
Weight-for-height	More than 3 SD below reference median
Nutritional edema	Bilateral pitting edema of lower limbs

The source presents alternative criteria in young children; Not a substitute for a full clinical assessment.

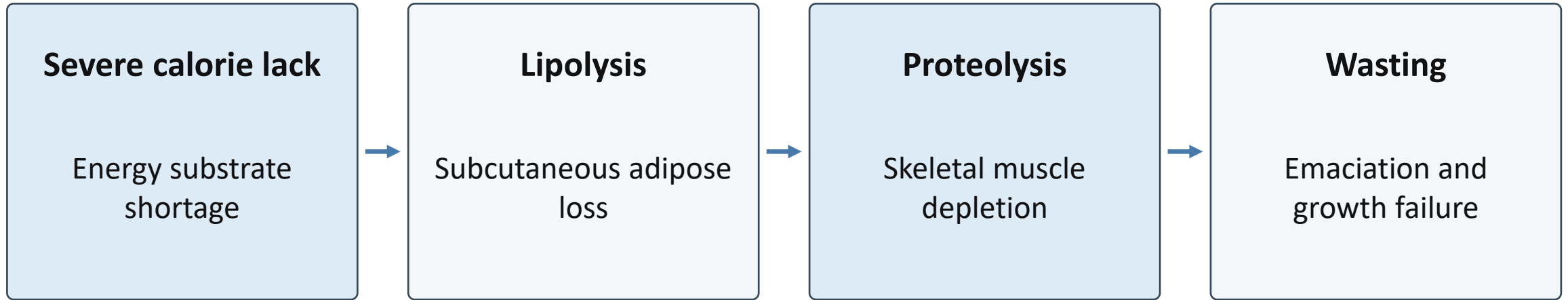
Wasting and stunting describe different patterns

- Wasting reflects reduced tissue mass relative to linear growth.
- Stunting reflects impaired longitudinal growth after sustained or early-life nutritional insult.
- Maternal and early childhood malnutrition may contribute to stunting.
- Acute and chronic nutritional disorders can occur together.

Two functional protein compartments

Compartment	Main representative	Depletion most apparent in
Somatic	Skeletal muscle proteins	Marasmus
Visceral	Proteins of liver and visceral organs	Kwashiorkor
Assessment correlate	Muscle circumference / serum proteins	Patterns differ by phenotype

Marasmus: Adaptive tissue catabolism

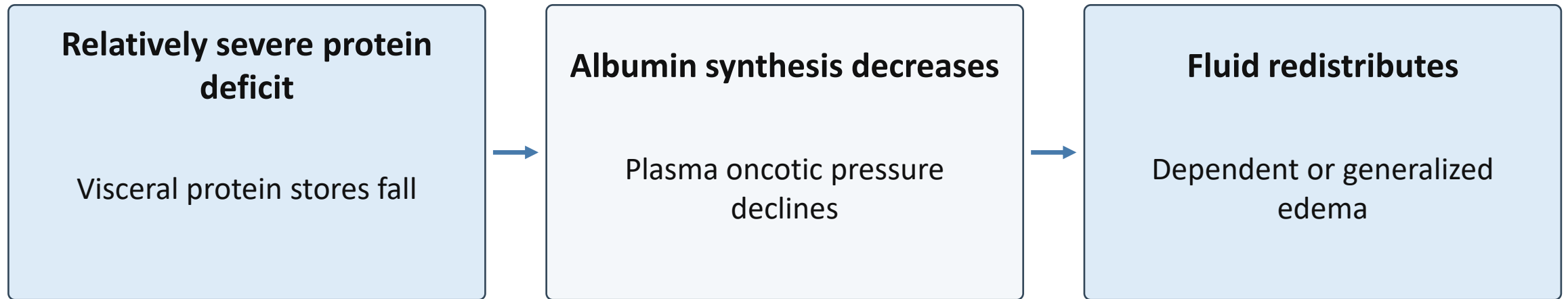


Visceral protein stores are relatively protected compared with somatic muscle.

Marasmus: Clinical morphology

- Marked loss of subcutaneous fat and skeletal muscle creates emaciated limbs.
- The head may appear disproportionately large relative to the wasted body.
- Growth failure, anemia and accompanying vitamin deficiencies are common.
- Defective cell-mediated immunity promotes secondary infections.

Kwashiorkor: Protein-predominant depletion

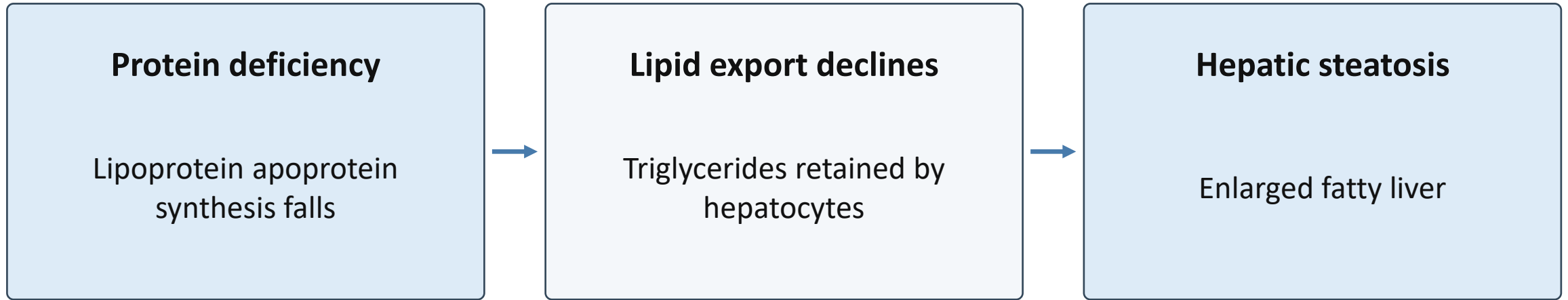


Edema can conceal loss of underlying lean tissue.

Kwashiorkor: Recognizable phenotype

- Peripheral or generalized edema and sometimes ascites.
- Patchy pigmentation, desquamation and hypopigmentation of skin (“flaky paint”).
- Pale or alternating hair bands, fragility and reduced scalp attachment.
- Apathy, anorexia and an enlarged fatty liver.

Why a fatty liver develops in kwashiorkor



Hepatic steatosis is a characteristic distinction from uncomplicated marasmus.

Intestinal injury in kwashiorkor

Crypt proliferative activity falls

Epithelial renewal slows



Villus / microvillus atrophy

Reduced absorptive surface



Disaccharidase deficiency

Transient milk intolerance

Potentially reversible mucosal changes with treatment.

Hematologic effects of severe malnutrition

- Bone marrow may become hypoplastic, particularly in the erythroid lineage.
- Anemia has multiple potential contributors: Protein, iron, folate and inflammation.
- Peripheral red cells may be microcytic, normocytic or macrocytic.
- Peripheral blood morphology reflects the dominant combination of deficiencies.

Immune and developmental consequences

- Thymic and lymphoid atrophy correlate with reduced immune competence.
- Infections increase demands and may accelerate nutritional deterioration.
- Growth faltering and developmental impairment may persist beyond acute illness.
- Severe early-life malnutrition can have neurologic consequences.

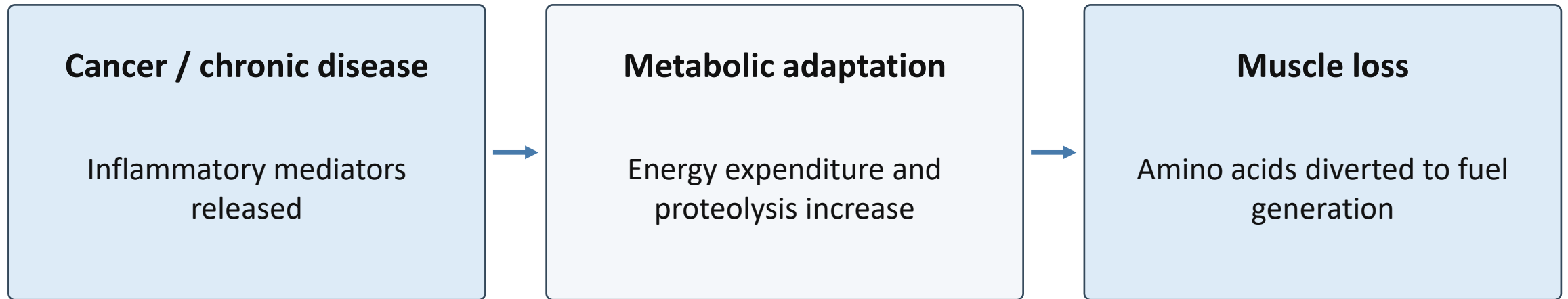
Marasmus versus kwashiorkor

Characteristic	Marasmus	Kwashiorkor
Predominant deficit	Severe energy lack	Protein deficit relatively greater
Somatic tissue	Marked muscle and fat loss	Relative preservation, often obscured
Visceral protein / albumin	Relatively preserved	Substantially depleted
Edema	Generally not characteristic	Characteristic
Liver	Usually not fatty	Fatty enlargement
Skin / hair	Less characteristic changes	Flaky-paint skin; Hair changes

Malnutrition in high-resource settings

- Chronic illness, advanced age and immobility confer substantial risk.
- Examine shoulders, upper limbs and thighs for loss of fat or muscle.
- Ankle or sacral edema can coexist with severe tissue depletion.
- Secondary malnutrition increases infection, wound-healing and postoperative risks.

Inflammation-associated adult malnutrition



Muscle wasting may continue despite apparently adequate protein intake.

Reduced intake versus cachexia

Feature	Predominantly reduced intake	Inflammation-related wasting
Principal driver	Substrate deprivation	Inflammatory, catabolic signaling
Muscle wasting	Energy adaptation	Often pronounced and persistent
Typical context	Dysphagia; Food insecurity	Advanced malignancy; Chronic disorders
Teaching implication	Correct intake and cause	Address illness-associated catabolism

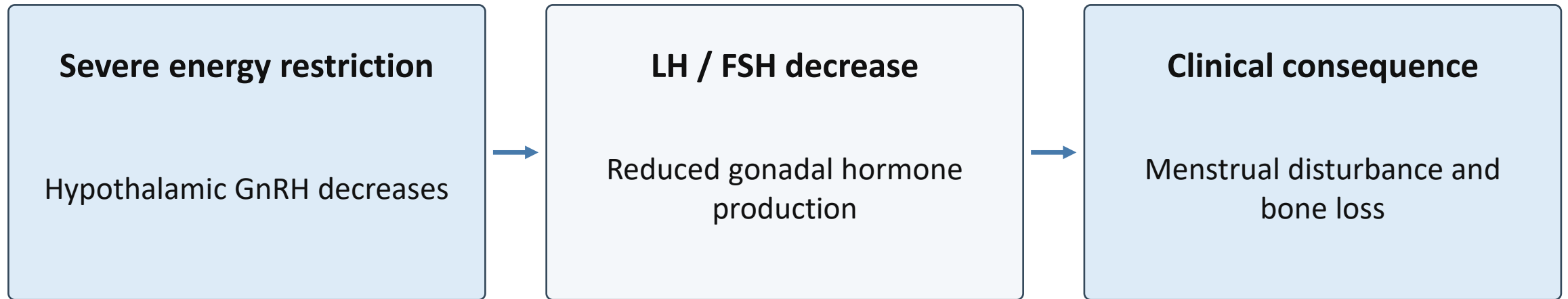
Eating disorders: Contrasting mechanisms

Disorder	Characteristic eating pattern	Key nutritional consequence
Anorexia nervosa	Severe restriction of intake	Marked weight loss and starvation effects
Bulimia nervosa	Binge episodes followed by purging	Fluid/electrolyte injury, often without severe low weight

Anorexia nervosa: Multisystem starvation

- Marked restrictive intake produces a severe malnutrition phenotype.
- Bradycardia, cold intolerance, constipation and dry skin reflect endocrine adaptation.
- Anemia, lymphopenia and hypoalbuminemia may occur.
- Electrolyte abnormalities can result in life-threatening arrhythmias.

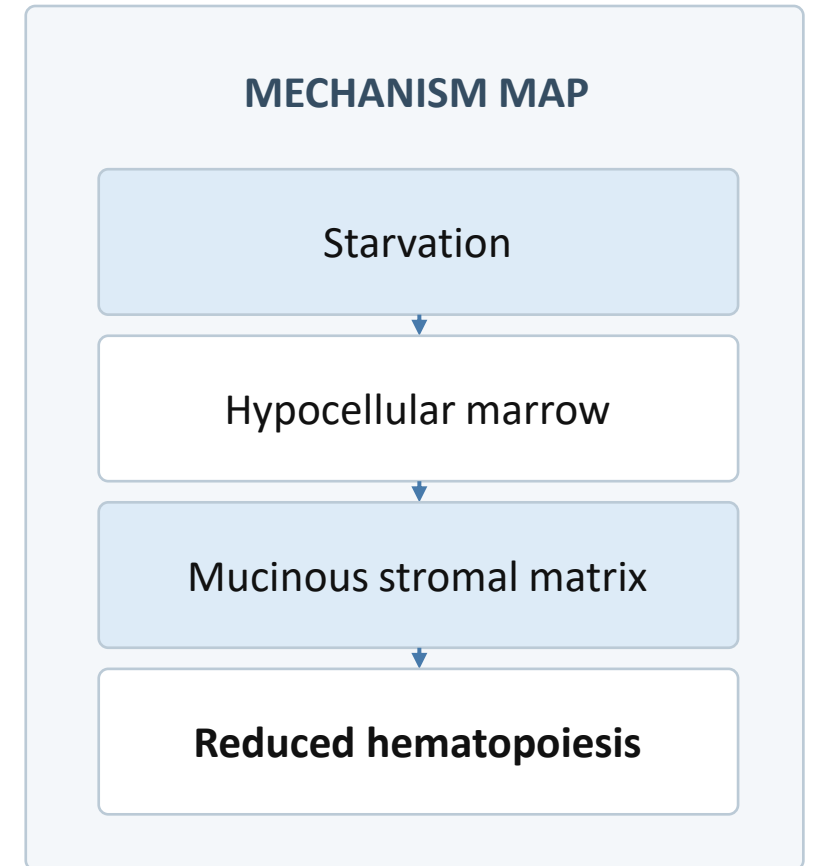
Hypothalamic–gonadal suppression in anorexia



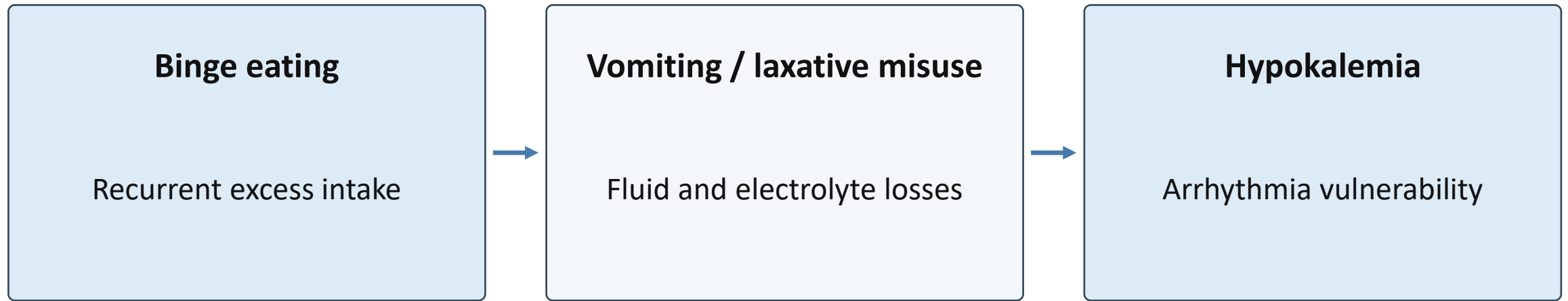
Low estrogen contributes to reduced bone mineral density.

Anorexia: Bone marrow pathology

- Marrow hematopoietic cellularity decreases during severe starvation.
- An extracellular mucinous matrix may accumulate: Gelatinous transformation.
- The source describes this feature as highly characteristic of anorexia nervosa.



Bulimia: The medical consequences of purging



Repetitive vomiting may also produce aspiration and esophageal injury.

Anorexia and bulimia: Clinical distinctions

Finding	Anorexia nervosa	Bulimia nervosa
Body weight	Often severely reduced	May remain near expected range
Menstrual changes	Common suppression	Irregularity; Amenorrhea less common
Major mechanism	Starvation / endocrine adaptation	Recurrent purging injury
Potential emergency	Cardiac arrhythmia	Arrhythmia; Aspiration; Rupture

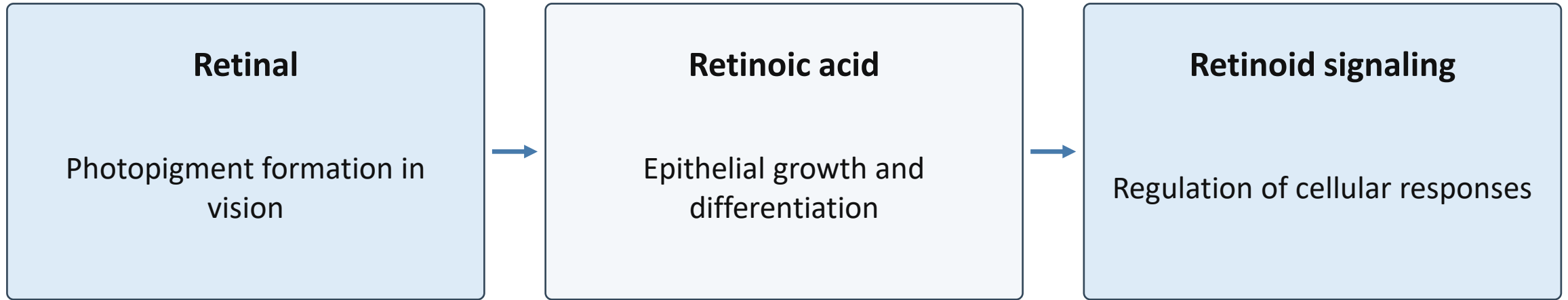
Vitamin deficiencies: Classification

- Thirteen vitamins are required for normal human physiology.
- Fat-soluble vitamins are A, D, E and K; Storage is generally more substantial.
- Water-soluble vitamins include B-group vitamins and ascorbic acid.
- Deficiencies may be dietary or secondary to abnormal absorption or metabolism.

Why solubility matters

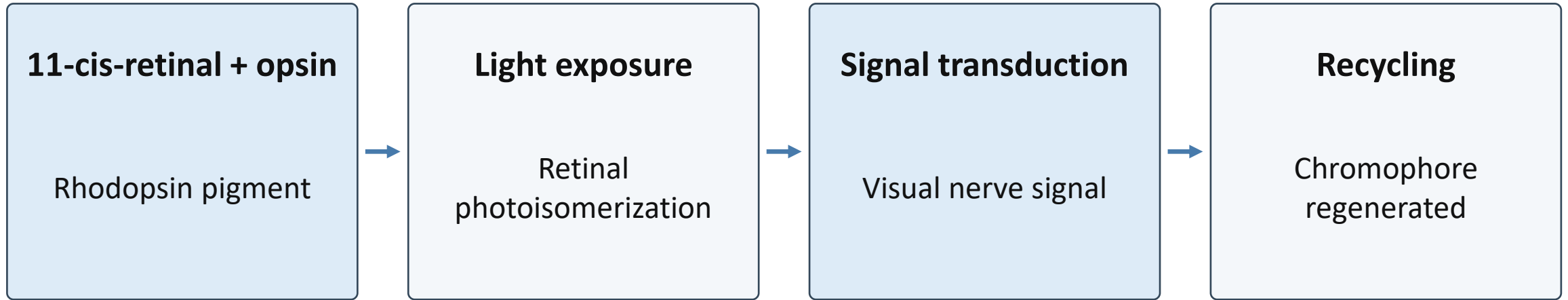
Property	Fat soluble	Water soluble
Members	A, D, E, K	B vitamins and C
Body storage	Often larger stores	Generally more limited stores
Malabsorption risk	Fat malabsorption particularly important	Variable by transport / disease
Example deficiency	Night blindness; Rickets	Beriberi; Scurvy

Vitamin A: Functions and target tissues



Vitamin A deficiency affects vision and the integrity of specialized epithelia.

Vitamin A in the visual cycle

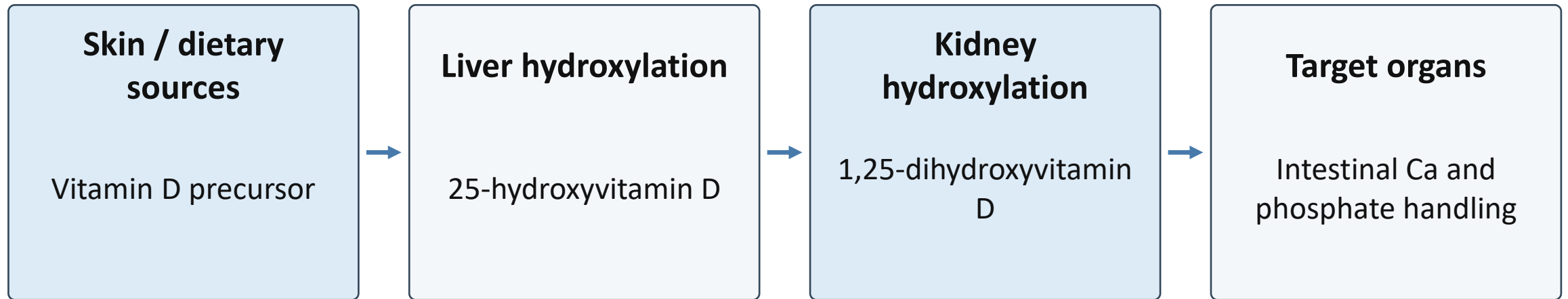


Insufficient vitamin A impairs dark adaptation and produces night blindness.

Vitamin A deficiency: Morphology and function

- Night blindness reflects impaired rhodopsin-dependent vision.
- Conjunctival and corneal dryness may progress to xerophthalmia and ocular injury.
- Abnormal epithelial differentiation predisposes to squamous metaplasia.
- Defective epithelial barriers and immune function increase infection risk.

Vitamin D: An endocrine nutrient



Vitamin D supports bone mineralization through calcium/phosphate homeostasis.

Vitamin D deficiency: The fundamental lesion

- Impaired mineral availability causes excess unmineralized osteoid.
- In children, mineralization failure disrupts the growth plate: Rickets.
- In adults, mineralization failure affects existing bone: Osteomalacia.
- Biochemical and skeletal findings must be interpreted together.

Rickets: Disturbed growth-plate sequence

Poor provisional calcification

Cartilage fails to mature normally



Disorganized metaphysis

Cartilage and osteoid persist



Weak bone

Expansion and deformity under load

Rachitic rosary, metaphyseal enlargement and skeletal bowing arise from weak mineralization.

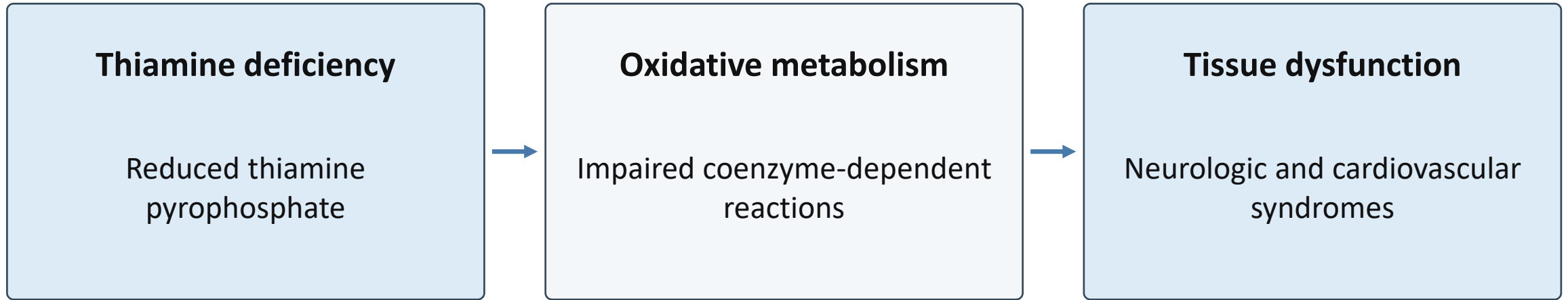
Rickets versus osteomalacia

Feature	Rickets	Osteomalacia
Patient context	Growing skeleton	Mature skeleton
Principal site	Growth plate and metaphysis	Newly deposited osteoid
Structural effect	Growth-plate disruption and deformity	Poorly mineralized bone; Fragility
Shared basis	Vitamin D–related mineralization failure	Vitamin D–related mineralization failure

Vitamins E and K: High-yield effects

Vitamin	Major physiologic role	Deficiency consequence
Vitamin E	Lipid-phase antioxidant	Neurologic dysfunction; Hemolytic anemia
Vitamin K	γ -carboxylation of clotting proteins	Bleeding tendency
Clinical context	Fat absorption matters	Fat absorption and gut availability matter

Thiamine (B1): Energy metabolism



Beriberi and Wernicke–Korsakoff syndrome are the characteristic associations.

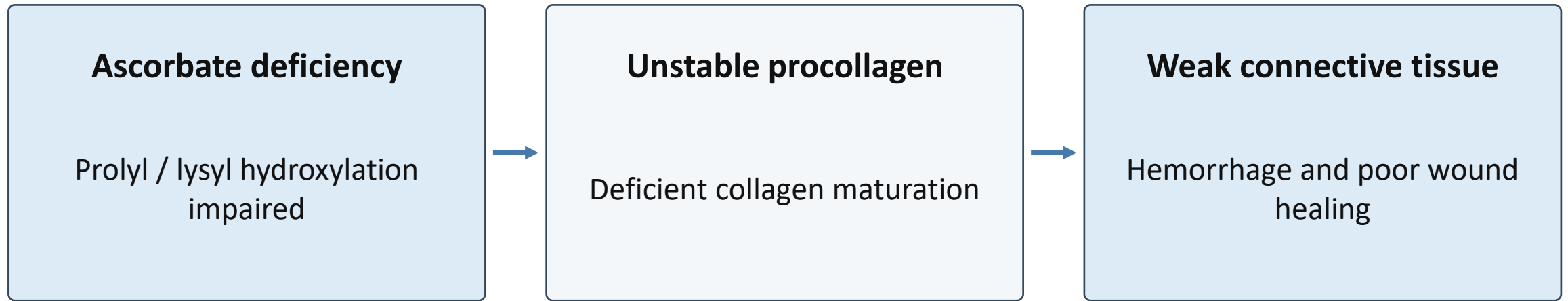
Niacin deficiency: Pellagra

- Niacin contributes to NAD and NADP-dependent oxidation–reduction reactions.
- Pellagra classically produces dermatitis, diarrhea and dementia.
- These organ systems are sensitive to altered intermediary metabolism.
- The constellation, not a single isolated sign, suggests the deficiency.

B6, B12 and folate: Contrasting syndromes

Nutrient	Biochemical role	Typical deficiency effect
Pyridoxine (B6)	Enzyme cofactor in intermediary reactions	Dermatitis; Glossitis; Neuropathy
Cobalamin (B12)	DNA synthesis / folate metabolism	Megaloblastic anemia; Spinal cord injury
Folate	One-carbon transfer for DNA synthesis	Megaloblastic anemia; Neural tube defects

Vitamin C: Why collagen loses strength



Scurvy is fundamentally a defect of stable collagen formation.

Scurvy: Morphology explains the symptoms

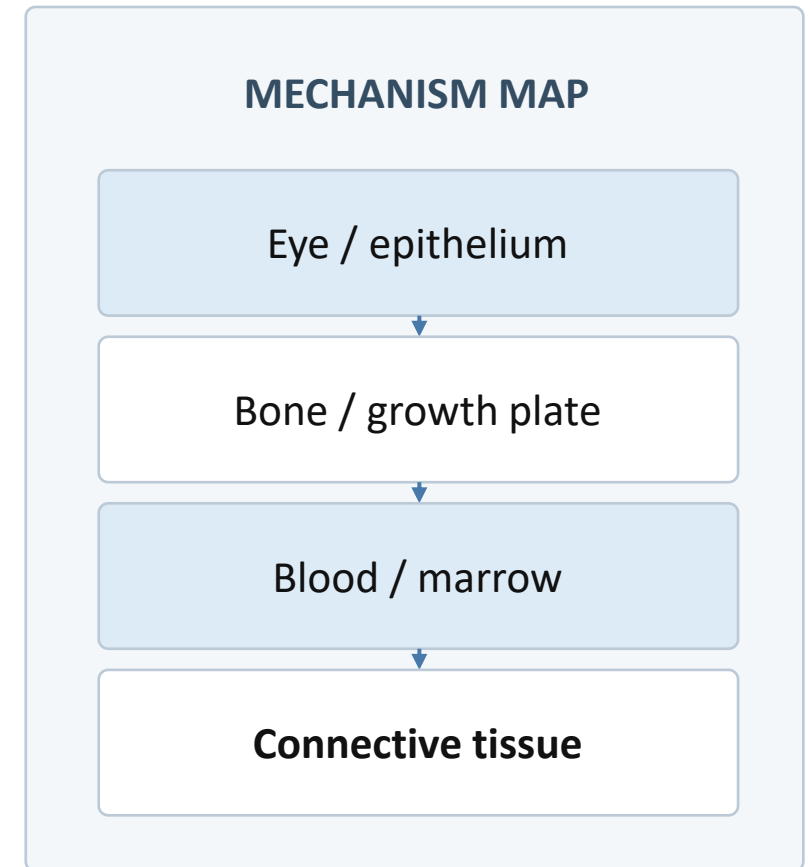
- Fragile connective tissue permits skin and mucosal hemorrhages.
- Gingival changes and poor wound healing reflect reduced collagen integrity.
- Defective osteoid matrix can produce bone abnormalities in growing children.
- Capillary fragility and connective-tissue weakness provide the unifying mechanism.

Trace-element deficiency: Organ consequences

Element	Main physiologic role	Deficiency-associated pathology
Iron	Hemoglobin and metalloenzymes	Microcytic hypochromic anemia
Iodine	Thyroid hormone synthesis	Goiter; Hypothyroidism
Zinc	Multiple enzyme functions	Periorificial dermatitis; Poor healing
Copper	Oxidases / connective tissue functions	Anemia; Neurologic abnormalities
Selenium	Glutathione peroxidase	Myopathy; Cardiomyopathy

Micronutrient deficiency: Diagnostic localization

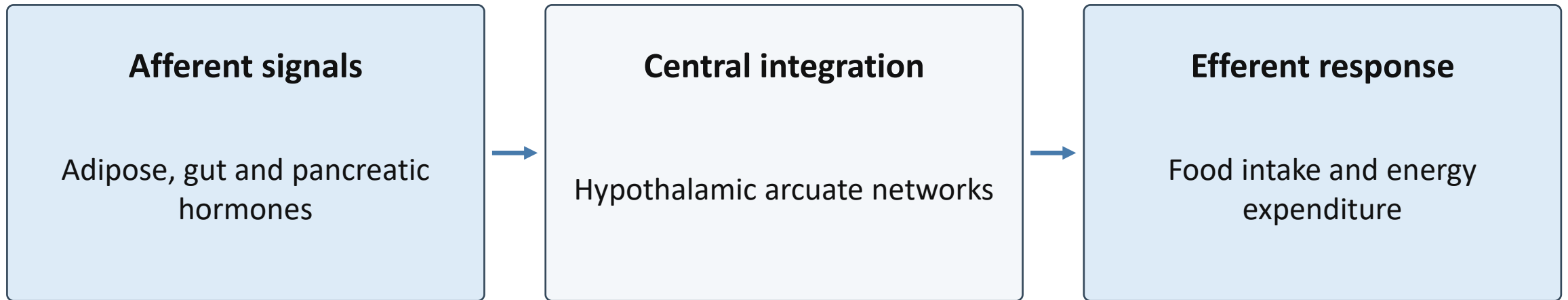
- Ocular and epithelial abnormalities suggest vitamin A depletion.
- Bone and growth-plate changes suggest mineralization deficits.
- Anemia morphology guides consideration of iron, B12 and folate deficits.
- Hemorrhage and poor wound healing suggest defects in vitamin C or vitamin K pathways.



Obesity is a disorder of energy homeostasis

- Body weight reflects long-term integration of nutrient intake and expenditure.
- Hypothalamic neuroendocrine networks respond to peripheral energy signals.
- Genetic, environmental and behavioral factors modulate these pathways.
- Central adiposity has prominent cardiometabolic consequences.

Three components of energy regulation



The system generates anorexigenic and orexigenic responses to energy state.

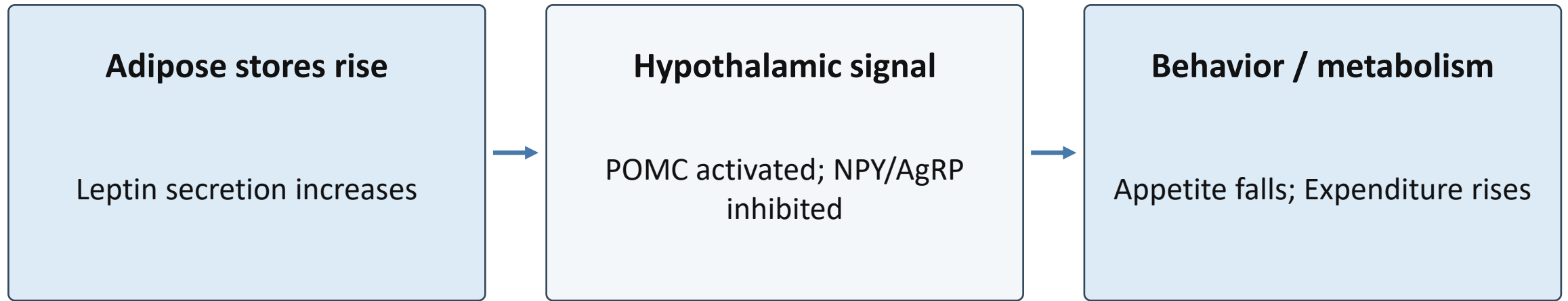
Peripheral appetite signals

Signal	Principal origin	Textbook action
Leptin	Adipocytes	Signals energy sufficiency; Reduces intake
Ghrelin	Stomach	Promotes hunger / food intake
PYY	Intestine	Postprandial satiety signaling
GLP-1 and GIP	Enteroendocrine cells	Meal-related gut signals
Insulin	Pancreatic β cells	Energy-status / anorexigenic signaling

Hypothalamic pathways: Opposite effects

Circuit	Mediators	Physiologic direction
Anorexigenic	POMC / CART → α -MSH → MC3/4R	Decreased food intake; Higher expenditure
Orexigenic	NPY / AgRP → Y1 / Y5	Increased intake; Lower expenditure
Integration	Leptin, insulin, ghrelin and gut peptides	Balances circuit activity

Leptin closes the energy-storage feedback loop



Reduced stores produce the opposite regulatory response.

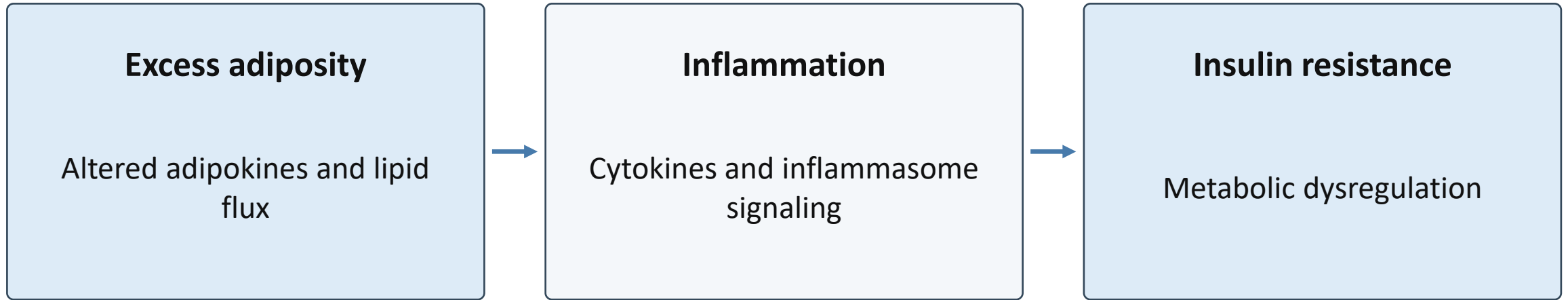
Obesity: Genetic signaling and resistance

- Rare disabling leptin or leptin-receptor variants can cause severe obesity.
- Loss-of-function variants affecting melanocortin signaling also contribute.
- Common obesity often features elevated leptin with diminished central response.
- A high leptin concentration does not imply effective leptin signaling.

Gut hormones help regulate meal timing

- Ghrelin rises around hunger states and activates orexigenic hypothalamic pathways.
- PYY and incretin peptides participate in postprandial signaling.
- GLP-1 and GIP connect nutrient sensing to pancreatic and central regulation.
- Meal-to-meal signals operate within the long-term adiposity feedback system.

Adipose tissue as an inflammatory organ



Adipose tissue is biologically active, not merely an energy-storage depot.

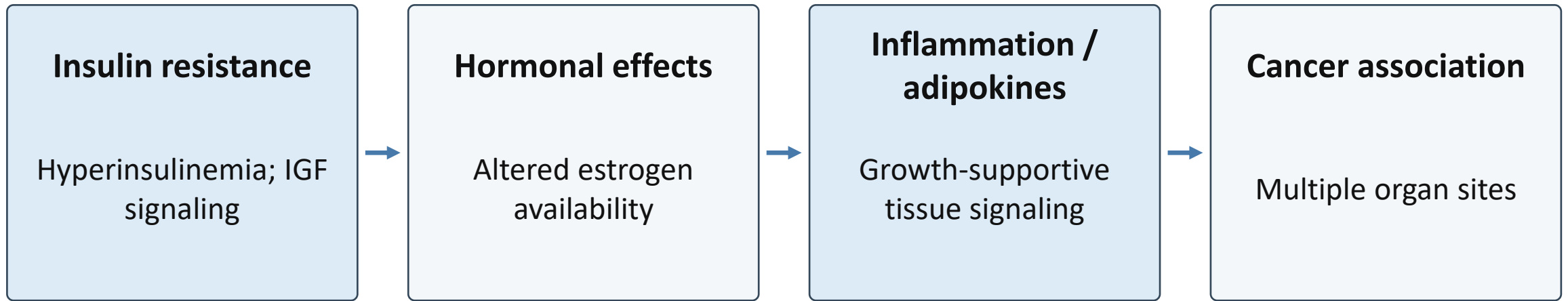
Obesity: Cardiometabolic consequences

Process	Associated complication	Pathophysiologic link
Insulin resistance	Type 2 diabetes mellitus	Impaired glucose regulation
Dyslipidemia	Atherosclerotic disease	Triglycerides ↑; HDL often ↓
Blood-pressure dysregulation	Hypertension	Neurohumoral and vascular effects
Visceral adiposity	Metabolic syndrome	Combined inflammation and risk factors

Obesity: Organ-system manifestations

System	Representative consequence
Liver	Steatotic liver disease; Possible fibrosis
Gallbladder	Cholesterol-rich gallstones
Respiratory	Obstructive sleep apnea; Hypoventilation
Musculoskeletal	Degenerative joint disease
Cardiovascular	Increased atherosclerotic burden

Mechanistic links between obesity and cancer



Several plausible mechanisms; A single mechanism is not established.

Diet and carcinogenesis: Evidence boundaries

- Dietary compounds may contain carcinogens or influence endogenous carcinogen formation.
- Associations have been described between dietary patterns and organ-specific malignancies.
- Mechanistic and epidemiologic evidence has important inconsistencies.
- Robbins does not establish a single diet that reliably causes or prevents cancer.

Dietary fats and atherogenesis

Fat composition

Saturated versus
polyunsaturated fractions



Lipid response

Serum cholesterol may change



Vascular context

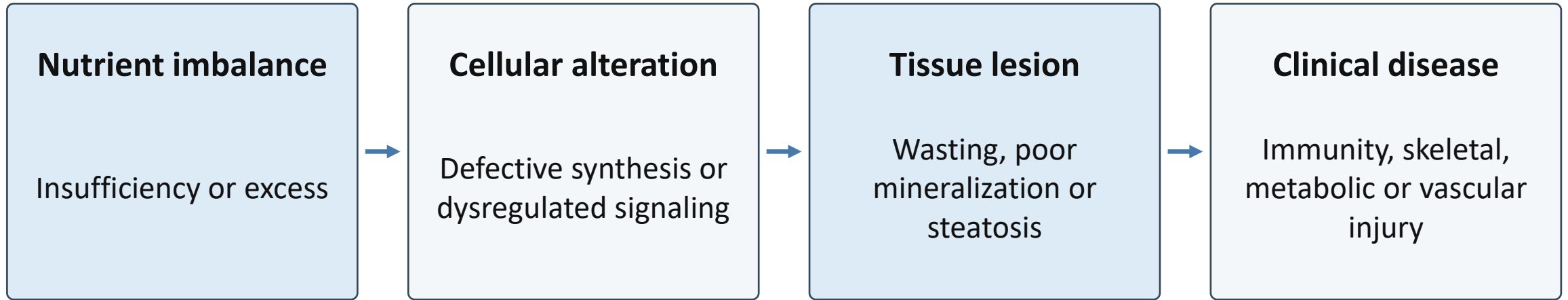
Atherogenic lipoproteins drive
plaque risk

Separate changes in intermediate lipid markers from demonstrated clinical-event benefits.

Diet composition beyond calorie count

- Sodium restriction can reduce blood pressure.
- Dietary fiber increases stool bulk and alters transit.
- Metabolic and cardiovascular consequences depend on diet composition as well as energy intake.
- Specific supplement claims require evidence from clinical outcomes, not mechanistic plausibility alone.

Clinicopathologic synthesis



Start from the affected biochemical function, then explain the observed morphology.

Application: An edematous malnourished child

CLINICAL PRESENTATION

A young child has restricted dietary diversity, generalized edema, pigmentary skin changes and hepatomegaly.

Which protein compartment is preferentially depleted—and why is the liver enlarged?

CLINICOPATHOLOGIC INTERPRETATION

Kwashiorkor pattern: Visceral protein depletion lowers albumin; Deficient lipoprotein synthesis favors hepatic triglyceride retention.

Application: Obesity and systemic risk

CLINICAL PRESENTATION

An adult with central adiposity has hypertension, hypertriglyceridemia and impaired glucose regulation.

What shared disease process links these findings?

CLINICOPATHOLOGIC INTERPRETATION

Metabolic syndrome links insulin resistance, dyslipidemia, hypertension and chronic low-grade inflammatory signaling.

Five clinicopathologic principles

- Determine whether nutrient supply, absorption, storage, demand or regulation is abnormal.
- Distinguish somatic muscle loss from visceral protein depletion.
- Relate specific vitamin and mineral functions to affected tissues.
- Treat adiposity as an endocrine and inflammatory condition.
- Avoid attributing systemic disease to diet without considering evidence quality.

Selected source

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

Chapter 9: Environmental and Nutritional Diseases, pp. 394–410.

Primary lecture scope: Nutritional Diseases and the contiguous sections on dietary insufficiency, severe acute malnutrition, vitamin deficiencies, obesity and diet-associated systemic disease.

Slides are original educational syntheses; diagrams are native PowerPoint schematics, not clinical specimens.