

Lysosomal Storage Diseases

Molecular defects • cellular pathology • characteristic disorders

Inherited defects in lysosomal substrate processing lead to storage, impaired autophagy, and organ injury.

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning goals: From enzyme defect to phenotype

Explain primary lysosomal storage and secondary autophagy dysfunction.

Predict organ involvement from substrate distribution and cellular turnover.

Distinguish the major disorders by enzyme or transport defect, stored material, and morphology.

Relate disease mechanisms to clinical diagnosis and therapeutic strategies.

A lysosomal storage disorder is a failure of intracellular clearance

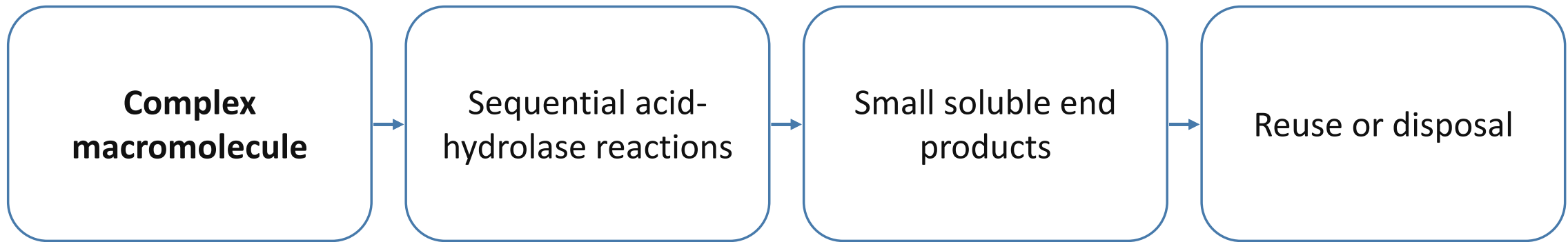
Lysosomes contain acid hydrolases that digest complex substrates.

Inherited defects may involve a hydrolase, an activator, transport or sorting machinery, or lysosomal integrity.

The undegraded metabolite progressively accumulates inside lysosomal compartments.

Organ dysfunction depends on the stored substrate and the affected cell population.

Normal lysosomal catabolism produces recyclable metabolites



Failure at any required step leaves incompletely degraded products in the lysosome.

Two routes deliver material to lysosomes

Heterophagy

Extracellular material enters by phagocytosis or endocytosis.

Phagosomes meet the lysosomal degradative system.

Especially relevant to phagocytic cells.

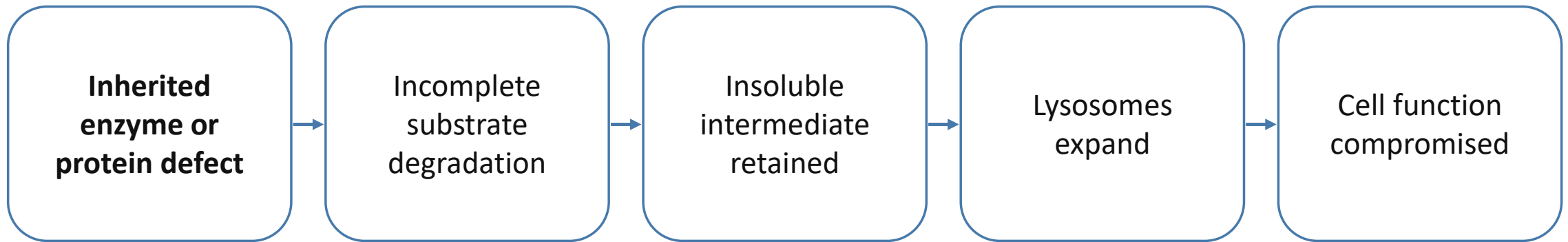
Autophagy

Intracellular proteins and organelles are enclosed by autophagic membranes.

Autophagic contents are delivered to lysosomes.

Critical for removing damaged mitochondria.

Primary storage begins at the blocked catabolic step



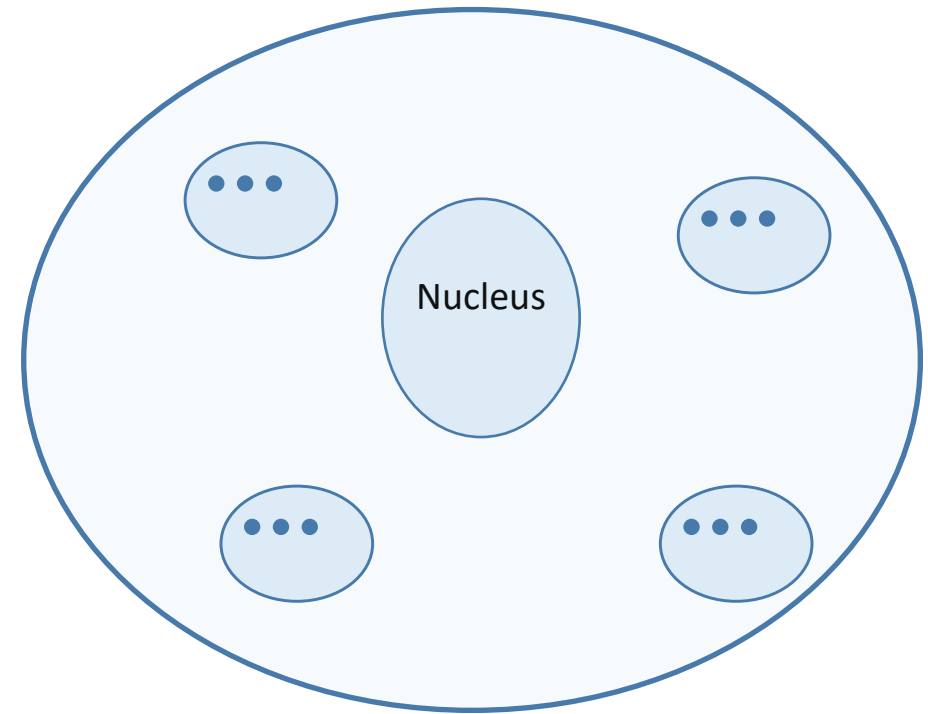
The stored product is the biochemical clue to the defective metabolic pathway.

Why swollen lysosomes disrupt cell physiology

Lysosomes become enlarged and increasingly numerous.

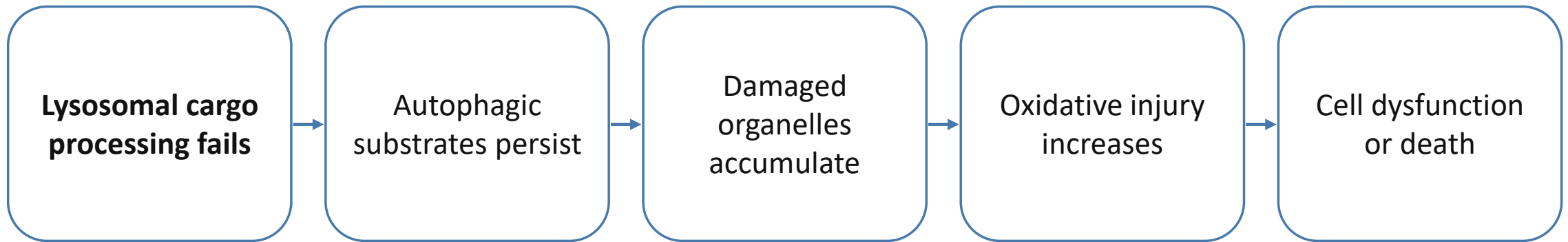
Undigested material displaces the functional cytoplasmic compartment.

The burden is not merely cosmetic: Storage interferes with normal cellular operations.



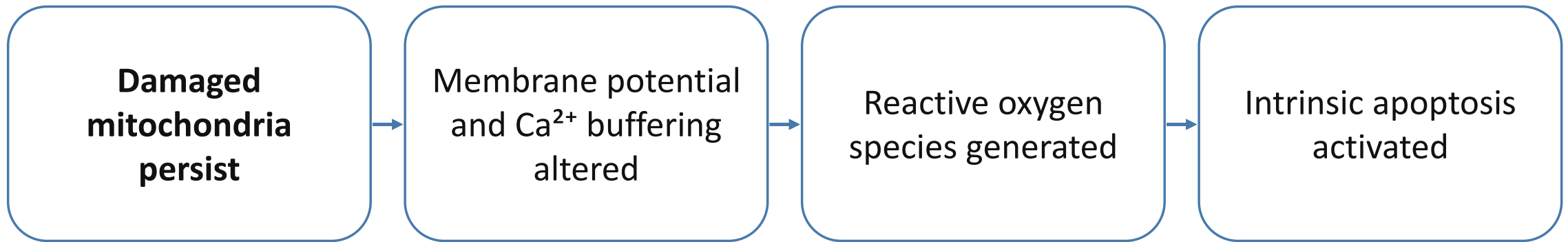
Schematic—not a histologic specimen

Defective autophagy creates a second pathogenic pathway



Primary substrate storage and secondary autophagic impairment are connected mechanisms.

Mitophagy failure links lysosomes to apoptosis



This provides a plausible mechanistic bridge to neurodegeneration.

Secondary accumulation includes aggregation-prone proteins

Autophagic turnover normally handles polyubiquitinated and aggregation-prone proteins.

Lysosomal dysfunction allows abnormal intracellular proteins to persist.

The Robbins discussion includes α -synuclein and huntingtin among implicated proteins.

This pathway helps explain links between lysosomal diseases and neurodegeneration.

Organ tropism reflects both substrate and cellular biology

Neurons and brain

Gangliosides are abundant in neural tissue.

Disorders of ganglioside catabolism prominently injure neurons.

Neurologic decline may dominate the clinical phenotype.

Macrophage-rich organs

Macrophages clear complex membrane-derived substrates.

Storage commonly enlarges liver, spleen, marrow, and lymphoid tissues.

Organomegaly and hematologic effects are frequent.

A common phenotype can arise from different storage products

Gangliosides: Predominantly neurologic manifestations in severe variants.

Sphingomyelin: Visceral phagocytes with variable CNS involvement.

Glucocerebroside: Macrophage-rich tissues, particularly marrow and spleen.

Glycosaminoglycans: Diffuse connective-tissue, cardiovascular, skeletal, and sometimes CNS disease.

Biochemical classification organizes the disorder family

Sphingolipidoses include GM1/GM2 gangliosidoses, Gaucher, Fabry, and Niemann–Pick A/B.

Sulfatidoses and leukodystrophies include metachromatic leukodystrophy and Krabbe disease.

Mucopolysaccharidoses result from defective glycosaminoglycan breakdown.

Mucolipidoses may involve defective lysosomal enzyme targeting.

Pompe disease is a lysosomal glycogen storage disorder.

Sphingolipid storage: Selected enzyme–substrate pairs

Disorder	Deficient factor	Accumulating substrate
Tay–Sachs	Hexosaminidase A (α subunit)	GM2 ganglioside
Sandhoff	Hexosaminidase A and B	GM2 ganglioside; Globoside
Gaucher	Glucocerebrosidase	Glucocerebroside
Niemann–Pick A/B	Acid sphingomyelinase	Sphingomyelin
Fabry	α -Galactosidase A	Ceramide trihexoside

Other lysosomal defects: Selected reference pairs

Disorder	Deficient factor	Major storage
GM1 gangliosidosis	β -Galactosidase	GM1 ganglioside
Metachromatic leukodystrophy	Arylsulfatase A	Sulfatide
Krabbe disease	Galactosylceramidase	Galactocerebroside
Pompe (GSD II)	Lysosomal acid α -glucosidase	Glycogen
Wolman disease	Lysosomal acid lipase	Cholesteryl esters; Triglycerides

MPS and mucopolipidosis: Different molecular failures

Entity	Primary defect	Accumulating substrate
MPS I (Hurler)	α -L-Iduronidase	Dermatan and heparan sulfate
MPS II (Hunter)	Iduronate-2-sulfatase	Dermatan and heparan sulfate
I-cell disease / ML II	Mannose-6-phosphate tagging defect	GAGs and glycolipids

Enzyme deficiency differs from mistargeting

Enzyme or activator deficiency

A specific catabolic reaction is slowed or blocked.

Examples: HEXA-related Tay–Sachs and GBA-related Gaucher.

Residual activity can modify disease severity.

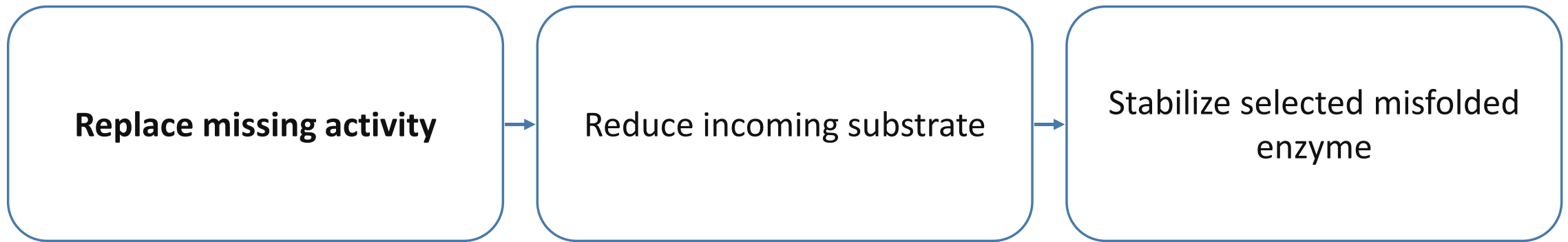
Sorting or transport defects

Cargo may not reach the correct compartment or leave it normally.

Mannose-6-phosphate tagging defects impair enzyme delivery.

NPC1/NPC2 affect late endosomal–lysosomal cholesterol egress.

Three treatment concepts address different steps



Treatment feasibility depends on tissue access and the molecular defect.

Enzyme replacement therapy restores a missing activity

An exogenous functional enzyme can supplement lysosomal degradation.

The target is the affected tissue and cell compartment.

The source identifies recombinant enzyme therapy as the mainstay for type I Gaucher disease.

The existence of an enzyme does not guarantee adequate CNS delivery.

Substrate reduction lowers the burden on residual enzyme

Therapy decreases synthesis of the material entering the defective pathway.

Reduced substrate production may allow residual catabolic capacity to cope.

Glucosylceramide synthesis is a cited therapeutic target in Gaucher disease.

This mechanism differs from supplying the missing enzyme.

Molecular chaperones can rescue some folding variants

A mutant enzyme may be unstable and degraded before reaching lysosomes.

A small molecule can stabilize a compatible mutant protein during folding.

In appropriate variants, restored trafficking may increase functional enzyme activity.

Fabry disease and investigational contexts for later-onset Tay–Sachs.

Tay–Sachs is a GM2 gangliosidosis

The critical deficiency involves the α subunit of β -hexosaminidase A.

Impaired GM2 ganglioside catabolism causes lysosomal neuronal accumulation.

Severe infantile disease is predominantly neurodegenerative.

It belongs to a group of biochemically related GM2 gangliosidoses.

GM2 degradation requires three different gene products

Gene	Encoded product	Related phenotype
HEXA	Hexosaminidase α subunit	Tay–Sachs
HEXB	Hexosaminidase β subunit	Sandhoff disease
GM2A	GM2 activator protein	GM2 activator deficiency

Hexosaminidase complexes explain GM2 variants

Hex A = $\alpha + \beta$



Hex B = $\beta + \beta$



GM2 substrate requires
proper Hex A plus activator

Similar storage phenotypes can have different underlying molecular lesions.

Tay–Sachs targets neurons and retinal ganglion cells

GM2 accumulates in neurons across the central and autonomic nervous systems.

Lysosomes swell and enlarge the neuronal cell body.

Progressive neuronal destruction is followed by microglial proliferation.

Swelling of ganglion cells surrounding the macula explains the ocular phenotype.

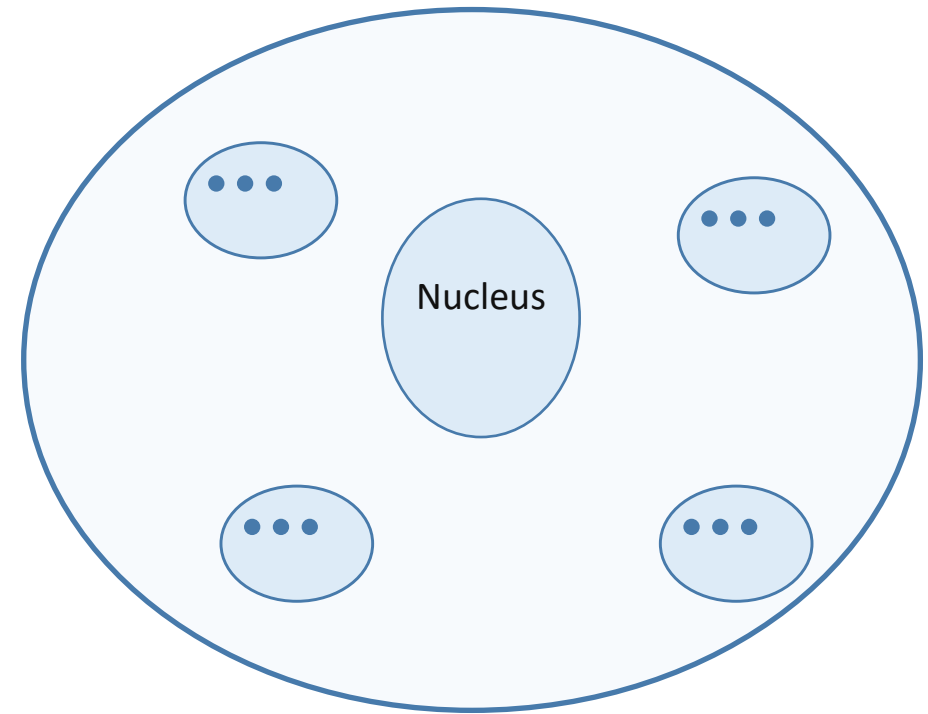
Microscopic Tay–Sachs: Ballooned, vacuolated neurons

Light microscopy: Large neurons with conspicuous cytoplasmic vacuoles.

The vacuoles correspond to distended storage lysosomes.

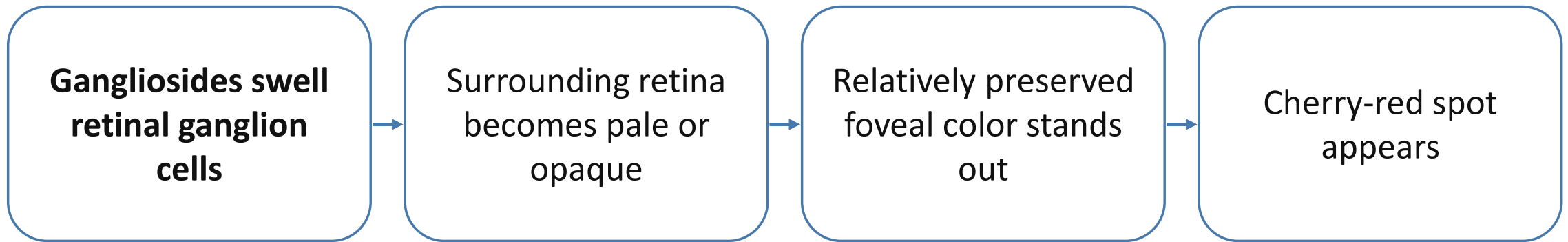
Electron microscopy: Concentric, whorled membrane inclusions.

Progressive neuronal loss underlies regression and disability.



Schematic of vacuolated neuron; No specimen image reproduced

A cherry-red macula is a contrast phenomenon



The sign is characteristic but not specific to Tay–Sachs disease.

The classic infantile course is relentlessly progressive

Affected infants typically appear normal at birth.

Neurologic impairment often starts around six months of age.

Motor and mental deterioration progress toward flaccidity and blindness.

The severe infantile form is fatal in early childhood description.

Tay–Sachs: Clinical sign versus molecular diagnosis

Clinical pattern

Progressive infantile neurologic regression.

Macular cherry-red spot may be present.

The retinal finding is not pathognomonic.

Confirmatory approach

Measure relevant lysosomal enzyme activities.

Identify a causative molecular variant when appropriate.

Enzyme assays and DNA analysis also inform carrier detection.

Why carrier screening is informative in Tay–Sachs

Tay–Sachs is inherited as an autosomal recessive disorder.

Carrier frequencies differ across populations and ancestry groups.

High historical carrier frequency among Ashkenazi Jewish individuals.

Biochemical screening and molecular testing address different questions and may complement each other.

GM2 disorders: Distinguish the affected molecular component

Tay–Sachs

HEXA-related deficient Hex A α subunit.

GM2 ganglioside accumulation.

Neuronal lysosomal distention and degeneration.

Sandhoff / activator variant

HEXB defects reduce both Hex A and Hex B.

GM2A defects prevent efficient substrate presentation.

Overlapping phenotypes require enzymatic or molecular discrimination.

Case application: An infant with neurologic regression

A previously well infant develops progressive developmental regression and visual impairment.

Examination reveals a cherry-red macular spot.

Explain the retinal appearance using ganglion-cell lipid storage.

Identify the specific hexosaminidase component that must be evaluated to establish Tay–Sachs.

Niemann–Pick types A and B are acid sphingomyelinase defects

Inherited acid sphingomyelinase deficiency blocks sphingomyelin catabolism.

Sphingomyelin derives from membranes and is distributed widely.

Lysosomal storage prominently affects the mononuclear phagocyte system.

Residual enzyme activity and phenotype distinguish severe and attenuated forms.

Niemann–Pick A versus B

Type A: Severe infantile

Marked visceral lipid accumulation.

Severe progressive neurologic damage.

Failure to thrive and early death in the classic presentation.

Type B: Visceral-predominant

Prominent organomegaly.

Little or no major CNS involvement pattern.

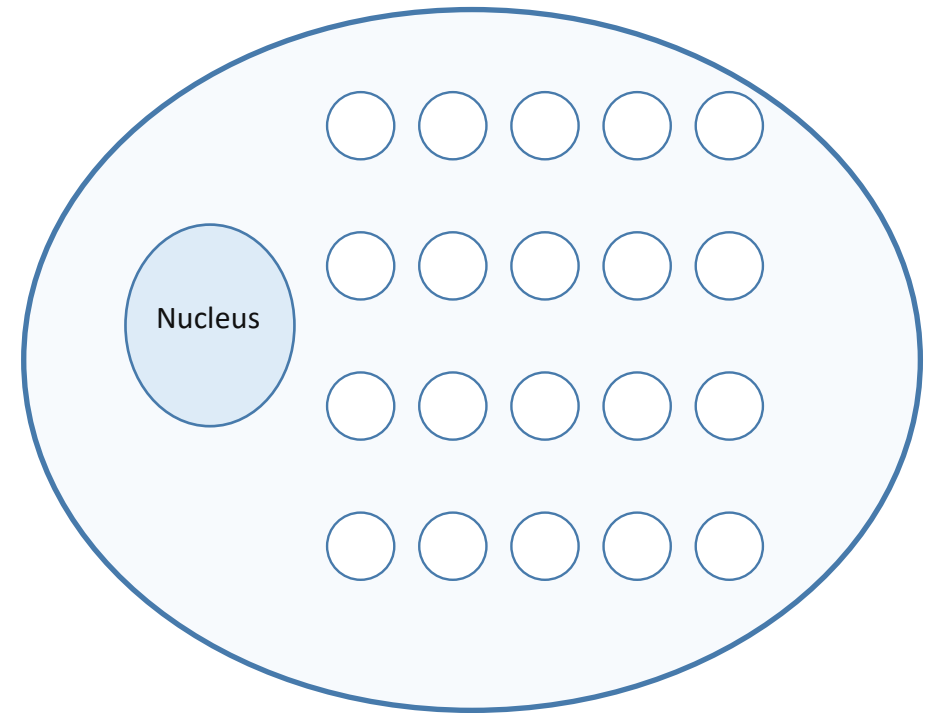
Survival frequently extends into adulthood.

Niemann–Pick macrophages have foamy cytoplasm

Macrophage lysosomes distended by stored sphingomyelin produce myriad small vacuoles.

The resulting cytoplasm appears foamy on routine morphology.

Electron microscopy may show concentric membranous “zebra” bodies.



Storage distributes across lymphoreticular organs

Foam cells occur in spleen, liver, lymph nodes, and bone marrow.

Tonsils, gastrointestinal tract, and pulmonary tissue may also contain affected phagocytes.

Visceral storage accounts for hepatosplenomegaly and generalized lymphadenopathy.

CNS injury is a major determinant of severity in the acute neuronopathic form.

Type A: Visceral disease plus neurodegeneration

The severe infantile form has profound loss of sphingomyelinase activity.

Hepatosplenomegaly often produces a protuberant abdomen.

Failure to thrive, systemic symptoms, and progressive psychomotor deterioration occur.

Death in the first few years of life.

Type B: Storage with relative neurologic sparing

Organomegaly remains a prominent manifestation.

Major CNS disease is generally absent in the classic type B pattern.

The clinical course is less severe than type A.

The distinction illustrates why substrate storage alone does not determine outcome.

Niemann–Pick A/B: Microscopy and confirmation

Morphologic evidence

Foamy vacuolated phagocytes in macrophage-rich tissues.

Engorged secondary lysosomes on ultrastructure.

Morphology indicates storage but is not an enzyme assay.

Defect confirmation

Measure acid sphingomyelinase activity in appropriate cells.

Molecular analysis characterizes the underlying genetic defect.

Assess phenotype rather than assigning subtype from foam cells alone.

Niemann–Pick type C is not a sphingomyelinase deficiency

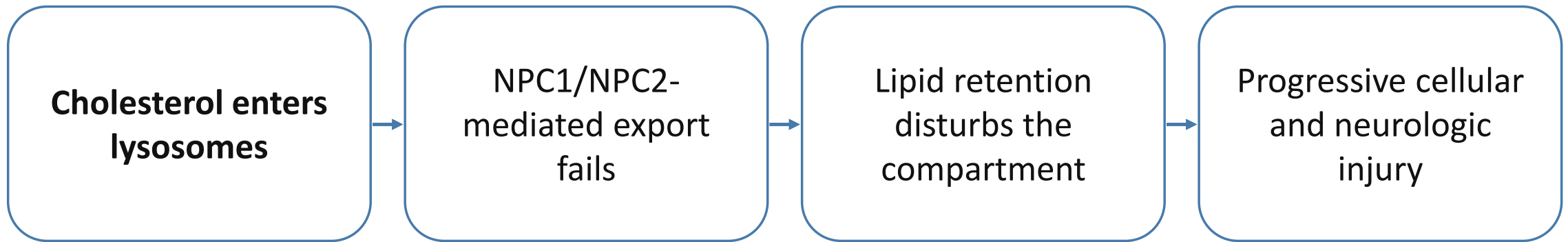
The primary lesion is a defect in late endosomal–lysosomal lipid transport.

NPC1 encodes a membrane protein; NPC2 encodes a soluble protein.

Both participate in export of free cholesterol from lysosomal compartments.

The accumulated material and mechanism differ from Niemann–Pick A/B.

NPC cholesterol trafficking failure



NPC illustrates a nonenzymatic lysosomal storage mechanism.

Niemann–Pick A/B versus type C: Do not conflate them

A/B: Enzyme deficiency

Acid sphingomyelinase pathway.

Storage of sphingomyelin.

Classic severe A and attenuated visceral B phenotypes.

C: Trafficking deficiency

NPC1 or NPC2 dysfunction.

Impaired cholesterol egress from lysosomes.

Phenotype often dominated by chronic neurologic dysfunction.

Niemann–Pick C shows broad clinical heterogeneity

Presentation ranges from severe fetal or neonatal involvement to chronic disease.

Neonatal hepatic dysfunction may precede later manifestations.

Chronic neurologic features include ataxia, dystonia, and dysarthria.

Vertical supranuclear gaze palsy is an especially helpful discriminating clinical feature.

Case application: Ataxia with vertical gaze palsy

A child has progressive ataxia, dysarthria, dystonia, and loss of acquired skills.

Examination finds vertical supranuclear gaze limitation.

Distinguish the likely cholesterol-transport defect from acid sphingomyelinase deficiency.

Explain why the Niemann–Pick name encompasses distinct mechanisms.

Gaucher disease is a defect of glucocerebroside turnover

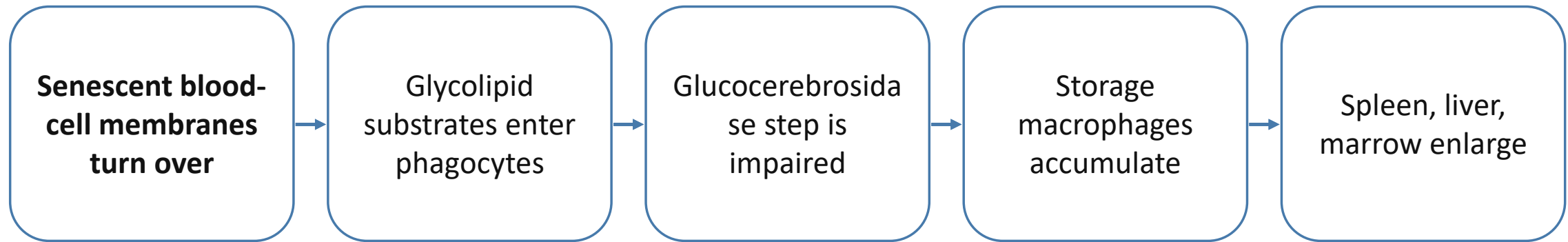
Autosomal recessive variants impair lysosomal glucocerebrosidase.

The enzyme normally removes glucose from glucocerebroside (glucosylceramide).

The undegraded glycolipid accumulates prominently in phagocytic cells.

The disease has visceral, skeletal, and—in neuronopathic variants—neurologic manifestations.

Macrophage exposure explains the burden in Gaucher disease



Cellular turnover and macrophage biology help explain tissue distribution.

Gaucher pathogenesis includes an inflammatory component

Activated storage macrophages release inflammatory mediators.

The source identifies IL-1, IL-6, and TNF as part of this response.

Cytokine-associated effects contribute to bone damage and systemic manifestations.

The clinicopathologic phenotype cannot be explained solely by the volume of stored lipid.

Gaucher phenotypes: Patterns of CNS involvement

Pattern	Characteristic distribution	Clinical emphasis
Type I	Visceral and skeletal; Classically no primary neuronopathic phenotype	Organomegaly, cytopenias, bone pain
Type II	Severe infantile neuronopathic plus visceral	Rapid CNS deterioration
Type III	Visceral disease with progressive neurologic features	Intermediate or chronic neuronopathic course

Type I Gaucher: Splenic, blood, and skeletal disease

Splenic enlargement may be massive.

Hypersplenism causes thrombocytopenia and sometimes pancytopenia.

Bone marrow storage and bone damage cause pain and pathologic fractures.

Disease burden may be substantial even without the classic neuronopathic phenotype.

Why Gaucher disease damages bone

Storage macrophages accumulate extensively in the marrow.

Macrophage activation is associated with cytokine production.

Focal bone erosion, painful lesions, and pathologic fractures can result.

Bone manifestations integrate storage burden with inflammation.

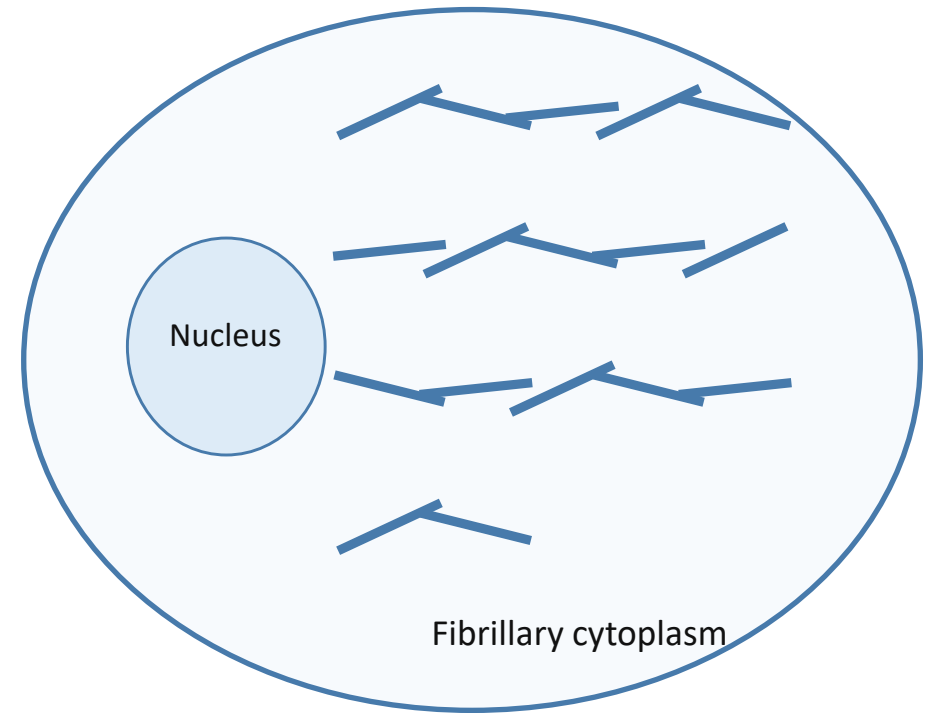
Gaucher cells: A distinctive fibrillary cytoplasm

Large storage macrophages possess abundant, often eosinophilic cytoplasm.

Rather than fine foaminess, their cytoplasm has a folded, “crumpled tissue paper” appearance.

The nucleus is often eccentrically placed.

PAS staining is strongly positive.



Conceptual macrophage only; Diagnostic recognition requires a genuine slide

Gaucher versus Niemann–Pick storage macrophages

Gaucher cell

Abundant fibrillary or wrinkled cytoplasm.

“Crumpled tissue paper” impression.

PAS positivity described.

Niemann–Pick foam cell

Numerous relatively uniform small vacuoles.

Foamy or bubbly cytoplasm.

Myelin-like concentric ultrastructural inclusions.

Gaucher deposits involve more than one reticuloendothelial site

Typical sites include spleen, liver, marrow, lymph nodes, and other lymphoid tissue.

Some patients also demonstrate pulmonary involvement.

The cellular distribution reflects clearance of aging hematopoietic-cell membranes.

Organ size and cytopenias are clinical surrogates for selected disease effects, not direct measures of enzyme activity.

Gaucher neuronopathic types are not simply type I plus storage

Type II is an acute infantile neurologic form with severe progressive disease.

Type III combines visceral manifestations with a slower progressive neurologic course.

Perivascular and macrophage-associated cerebral changes.

Clinical classification depends on neurologic pattern and disease trajectory.

GBA variants connect lysosomal dysfunction with Parkinson risk

GBA variation as an important inherited risk factor for Parkinson disease.

Lysosomal glucocerebrosidase dysfunction is linked to impaired clearance of α -synuclein.

Protein aggregation and defective autophagy provide mechanistic plausibility.

Genetic risk does not imply inevitable Parkinson disease in an individual with Gaucher disease.

Gaucher diagnosis relies on functional and genetic evidence

Markedly reduced glucocerebrosidase activity can be assayed in leukocytes or fibroblasts.

Pathologic macrophages suggest Gaucher disease but are not sufficient proof.

Molecular testing identifies pathogenic variants and can clarify familial risk.

Variant diversity means a limited targeted panel can miss some disease-causing alleles.

Gaucher treatment: Correct the biochemical deficit

Recombinant enzyme replacement is an established strategy for type I Gaucher disease in the text.

The treatment chiefly targets accessible systemic manifestations.

Substrate reduction aims to decrease glucosylceramide production.

CNS involvement creates additional therapeutic constraints.

Case application: Thrombocytopenia with bone pain

An adult has splenomegaly, thrombocytopenia, chronic bone pain, and a marrow storage-cell population.

Explain the link between macrophage lipid handling and marrow/spleen involvement.

Predict the expected cytoplasmic appearance of Gaucher cells.

Name the biochemical confirmation test rather than relying on morphology alone.

Mucopolysaccharidoses store glycosaminoglycans

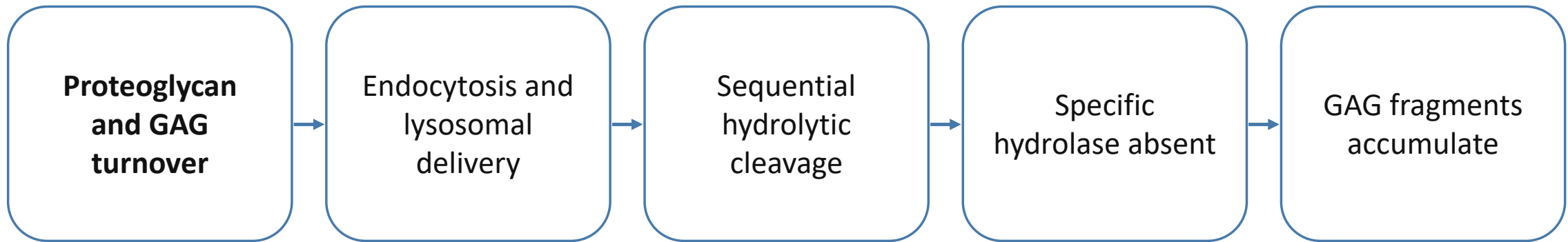
Glycosaminoglycans are long-chain carbohydrates within proteoglycans.

Normal turnover involves sequential lysosomal enzymes removing terminal residues.

Enzyme deficiency produces partially degraded glycosaminoglycan accumulation.

Abundant extracellular matrix distribution explains the broad organ phenotype.

MPS: Extracellular-matrix constituents become lysosomal cargo



Affected tissue reflects the normal distribution of glycosaminoglycans.

Glycosaminoglycans found in MPS storage

Dermatan sulfate and heparan sulfate are prominent in MPS I and MPS II.

Other MPS patterns may involve keratan sulfate or chondroitin sulfate.

The specific defective reaction determines the biochemical storage signature.

Urinary glycosaminoglycan excretion can support diagnostic evaluation.

MPS genetics: Most recessive, one major exception

Most mucopolysaccharidoses have autosomal recessive inheritance.

Hunter syndrome (MPS II) is X-linked recessive.

Different pathogenic variants in the same gene may confer different residual enzyme activity.

Clinical severity is therefore variable even within a biochemical category.

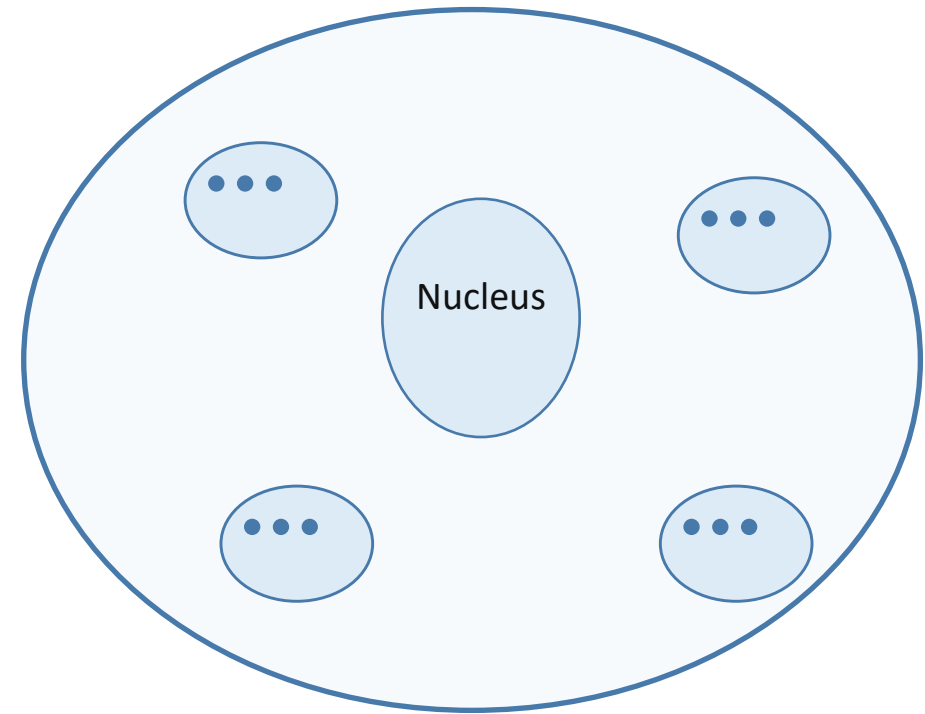
MPS pathology: Ballooned cells containing granular material

Affected macrophages, endothelium, smooth muscle, and fibroblasts become distended.

Light microscopy: Apparent clearing of cytoplasm in ballooned storage cells.

Electron microscopy: Swollen lysosomes with finely granular content.

A subset of MPS disorders also involves neurons.



Generic storage-cell schematic; Not a diagnostic specimen

MPS morphology is systemic rather than organ-restricted

Liver, spleen, marrow, lymph nodes, and vessels may contain storage cells.

Heart valves and coronary arterial walls may develop deposits.

Joints, skeleton, cornea, and sometimes brain are affected.

Cardiac and skeletal lesions follow from connective-tissue-rich distribution.

Clinical syndrome: Skeletal, facial, ocular, and neurologic changes

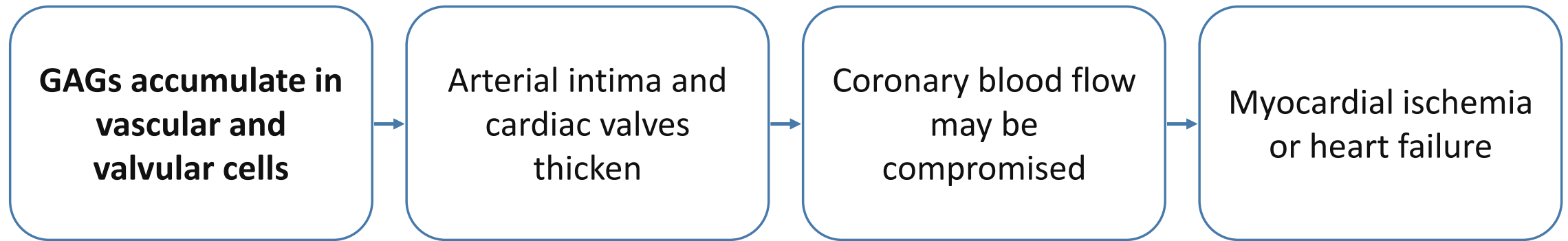
Coarse facial features and progressive skeletal deformities are typical.

Joint stiffness can restrict function.

Corneal clouding occurs in several MPS types, though not classically Hunter syndrome.

Intellectual impairment occurs in selected syndromes; The degree is variable.

Cardiovascular MPS injury can become life-limiting



Structural cardiac involvement is a major clinicopathologic concern.

Hurler syndrome (MPS I): Severe α -L-iduronidase deficiency

The deficient enzyme is α -L-iduronidase.

Dermatan and heparan sulfate accumulate.

Clinical manifestations include hepatosplenomegaly, coarse facies, skeletal deformity, and corneal clouding.

The classic severe phenotype features early progressive multisystem disease and cardiovascular complications.

Hunter syndrome (MPS II) differs in three key respects

Deficient enzyme: Iduronate-2-sulfatase.

Inheritance: X-linked recessive, unlike most other MPS disorders.

Corneal clouding is classically absent comparison.

A generally milder course than severe Hurler syndrome.

Hurler versus Hunter: A high-yield differential

Characteristic	Hurler — MPS I	Hunter — MPS II
Enzyme	α -L-Iduronidase	Iduronate-2-sulfatase
Inheritance	Autosomal recessive	X-linked recessive
Major storage	Dermatan/heparan sulfate	Dermatan/heparan sulfate
Corneal clouding	Typical	Classically absent
Clinical course	Severe in classic Hurler form	Often less severe than classic Hurler

Case application: Coarse facies and corneal clouding

A child develops growth failure, joint stiffness, hepatosplenomegaly, and corneal clouding.

Explain why glycosaminoglycan storage affects these diverse tissues.

Identify the biochemical defect in classic Hurler syndrome.

State which inheritance pattern and ocular finding favor Hunter syndrome instead.

Pompe disease is a lysosomal glycogenosis

Acid α -glucosidase normally digests glycogen inside lysosomes.

Deficiency prevents degradation of the lysosomal glycogen pool.

The disease is distinct from cytosolic enzyme defects causing other glycogenoses.

Prominent cardiomegaly in the classic severe presentation.

Glycogen turnover has separate lysosomal and cytosolic routes

Lysosomal route

Acid α -glucosidase breaks down lysosomal glycogen.

Pompe disease blocks this compartment.

A prominent cardiac storage phenotype can result.

Cytosolic route

Phosphorylases and debranching enzymes catabolize cytosolic glycogen.

Defects in this system lead to other hepatic or myopathic glycogenoses.

Different pathways predict different clinical syndromes.

Why Pompe belongs here but not all glycogenoses do

Pompe is defined by a lysosomal hydrolase deficiency.

Most glycogen storage diseases involve nonlysosomal glycogen synthesis or degradation enzymes.

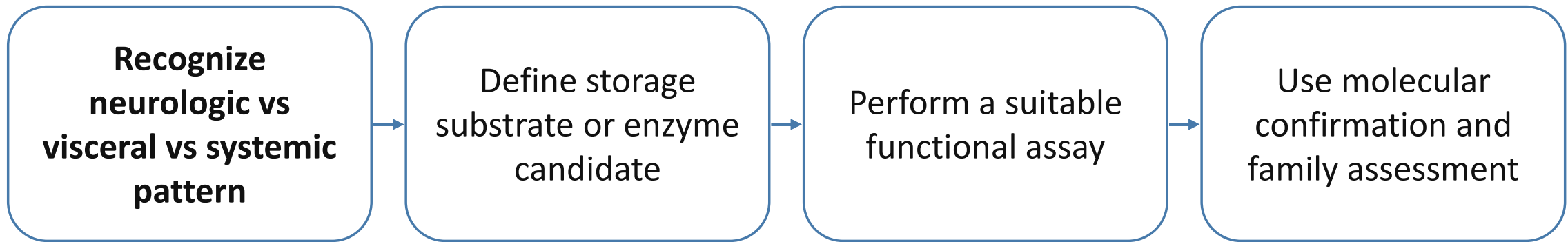
The functional cellular compartment is essential when classifying a metabolic disorder.

This lecture addresses Pompe as a boundary example, not as a complete glycogenosis review.

Diagnostic recognition: The decisive discriminator

Presentation	Consider	Molecular or biochemical discriminator
Infantile neuroregression + cherry-red spot	GM2 gangliosidosis	Hex A / HEXA pathway
Foam cells + visceral organomegaly	Niemann–Pick A/B	Acid sphingomyelinase
Vertical gaze palsy + ataxia	Niemann–Pick C	NPC1/NPC2 cholesterol trafficking
Splenomegaly + bone lesions	Gaucher	Glucocerebrosidase
Coarse facies + corneal clouding	MPS I (Hurler)	α -L-Iduronidase

A disciplined diagnostic approach starts with the phenotype



Morphology generates hypotheses; Functional and genomic evidence help test them.

Why morphologic recognition alone is insufficient

Vacuolated neurons are not unique to one lysosomal disorder.

Cherry-red spots occur in more than one storage condition.

Foam cells indicate lipid-rich lysosomes but do not identify the exact enzyme defect.

Definitive categorization relies on targeted biochemical and/or molecular analysis.

Mechanism should guide a therapy discussion

A hydrolase defect may be amenable to enzyme replacement in reachable tissues.

Residual function may be leveraged through substrate reduction.

Certain folding mutants can respond to molecular chaperones.

Transport defects and severe CNS pathology require different considerations.

Integrative challenge: Predict organ involvement

Storage dominated by neural glycolipids

Predict neuroregression, altered neuronal morphology, and possible retinal involvement.

Explain why gangliosidoses can present before conspicuous visceral disease.

Storage in macrophages and connective tissue

Predict splenic/liver enlargement and marrow pathology.

For GAG accumulation, additionally expect skeletal, valvular, corneal, and vascular lesions.

Summary: Five mechanistic anchors

Enzyme or transport failure → primary lysosomal substrate storage.

Defective autophagy and mitophagy amplify cell injury.

Biochemical substrate and tissue distribution determine organ tropism.

Morphologic patterns guide but rarely establish the specific diagnosis.

Therapeutic strategies target enzyme activity, substrate availability, or mutant-protein stability.

Primary reading and source boundaries

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026). Chapter 5: Genes and Human Diseases, “Lysosomal Storage Diseases.”

Teaching content is grounded in the supplied topic extract and adjoining Robbins material on lysosomal glycogen degradation.

Concept diagrams are original editable PowerPoint schematics; no source histology figures were reproduced.

The chapter PDF was not available for independent page-image or original figure verification.