Free Sample

Foundations of Inherited Metabolic Disorders
A Workbook for Genetic Counselors Preparing for the ABGC Exam

This sample includes the table of contents, foreword, and a complete excerpt from Chapter 1 (questions and answer key), unedited from the full 267-page workbook.

Foundations of Inherited Metabolic Disorders: A Workbook for Genetic Counselors

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Table of contents

Foreword

Metabolic genetics has quite the reputation. Ask any genetic counseling student which topic they dread most, and metabolics will be near the top of the list. Too many pathways, too many enzyme names that are impossible to pronounce, too many labs that blur together. So what do you do? You can memorize buzzwords, pattern-match in practice questions, and hope the exam doesn't go too deep. Sometimes it works well enough to get by. But you walk away from metabolics without ever understanding the logic underneath.

This workbook exists because of a pattern we couldn't ignore. We have worked with hundreds of genetic counselors preparing for boards, and after reviewing the feedback from each exam cycle, the same gap kept coming up: metabolics. Students felt underprepared and intimidated, not because they hadn't studied, but because there was no framework for how these disorders actually connect to one another and to the underlying biochemistry. Excellent resources exist for learning about individual conditions. But the bigger picture -- the structure that makes all of it make sense -- was missing.

So we built it.

This workbook organizes metabolic disorders by what's actually happening: macronutrient metabolism and organelle (dys)function. The goal isn't just to tell you what to study. It's to change how you think about this group of conditions. By the time you finish, you should have a real foundation in the core metabolic disorders and the confidence to reason through them -- not just recall them as a list of unrelated facts.

How to use this workbook. Work through it in order, start to finish. The knowledge is cumulative, and each chapter builds on the last. Unlike traditional references that are meant to be consulted as needed, this workbook is meant to be completed cover to cover. We've included an appendix for quick lookups, but the real value comes from working through the material sequentially.

The fill-in-the-blank format is intentional. It forces active recall rather than passive consumption, which is how material actually sticks. Chapter 1 introduces a five-question framework called the "B-LIST" -- use it as your systematic approach to every metabolic disorder you encounter, both in this workbook and in practice.

For the disorders in Sections 2 through 4, the symptoms, lab findings, and treatments are all explained using a pathway-first approach. This is where you should spend the most time. Understand what the pathway does and what happens when it breaks. Most of the symptoms,

labs, and treatments will follow from that understanding. Take notes and add mnemonics in the margins to cement your understanding.

This workbook works for individual study and group review. It can also supplement an existing metabolics course, whether over a quarter (roughly one chapter per week for 12 weeks) or a full semester. A suggested pacing guide with a sample schedule is on the next page.

A note on scope. We focused on disorders that are highly testable on board exams, illustrate important treatment principles or exceptions, have established treatments, or appear on newborn screening panels. The metabolic disorders explicitly listed on the ABGC exam study guide (released Dec 2025) are all included here. This is not meant to be a comprehensive reference -- excellent resources already exist for that. Our goal is to help you build a foundation you can apply on exam day and extend over time.

I welcome your feedback. Email daniel@studyrare.com and let me know what worked and what could be improved. I'd love to hear from you.

Metabolic genetics clicked for me as a second-year resident, and ever since, I've wanted to give that experience back through teaching. I hope this workbook helps it click for you, too.

Wishing you all the best with your studies.

- Daniel, on behalf of the StudyRare team

Suggested pacing guide

FOR INSTRUCTORS

This workbook is designed to be completed in 15 sessions of approximately 30-40 minutes each. Three of the longer chapters (Ch. 4, 7, 9) are split into two sessions, and the shorter chapters (Ch. 10-11) are combined. We recommend working through the chapters in order. The knowledge is cumulative, and later chapters assume familiarity with concepts introduced earlier, particularly the B-LIST framework (Chapter 1), macronutrient and organelle categories (Chapter 2), and pathway logic (Chapter 3).

SUGGESTED 15-SESSION SCHEDULE

Session	Chapter	Topic	Sections	Est. Time
1	Chapter 1	Understanding inherited metabolic disorders	1.A - 1.F	30 min
2	Chapter 2	Cellular foundations of metabolism	2.A - 2.F	30 min
3	Chapter 3	Pathways and enzymes	3.A - 3.G	35 min
4	Chapter 4 (Part 1)	Urea cycle and aminoacidopathies	4.A - 4.H	35 min
5	Chapter 4 (Part 2)	Organic acidemias and management	4.I - 4.N	30 min
6	Chapter 5	Fatty acid metabolism	5.A - 5.J	40 min
7	Chapter 6	Carbohydrate metabolism	6.A - 6.H	35 min
8	Chapter 7 (Part 1)	Sphingolipidoses	7.A - 7.F	30 min
9	Chapter 7 (Part 2)	MPS, cystinosis, and LSD summary	7.G - 7.M	35 min
10	Chapter 8	Peroxisomal disorders	8.A - 8.F	30 min
11	Chapter 9 (Part 1)	Mitochondrial genetics and classic syndromes	9.A - 9.F	30 min
12	Chapter 9 (Part 2)	Deletions, maintenance, diagnosis, and management	9.G - 9.L	30 min
13	Chapters 10 + 11	CDG and metal/heme disorders	10.A - 11.D	35 min
14	Chapter 12	Nucleotide metabolism	12.A - 12.F	30 min
15	Appendices	Review and high-yield associations	Apdx. A - H	40 min

Each session corresponds to one class meeting. Students can complete the fill-in-the-blank sections independently before class, then use class time to review answers, discuss clinical connections, and work through pathways together. Alternatively, the workbook can be worked through live during class.

1.A. What are inherited metabolic disorders?

1.A.1. Inherited _____ disorders (IMD) are genetic conditions caused by defects in **metabolic pathways**, which are the set of chemical reactions that sustain life.

1.A.2. IMD are also known as inborn errors of _____ (IEM).

1.A.3. Most IMD can be organized into two main groups:

1. Disorders of _____ metabolism (processing nutrients from food)

2. _____ ("little organ") disorders (e.g. lysosome, peroxisome)

1.A.4. Energy metabolism disorders affect how the body breaks down the 3 main _____ in our diet: carbohydrates, fat, and protein.

1.A.5. Organelle disorders are caused by defects in how these specialized structures are built, or in the _____ that work inside them.

1.A.6. While many IMD present early in life (e.g., neonatal period), others can present in older children and even _____.

1.A.7. Diagnosing IMD relies on both _____ sequencing and biomarkers in blood and urine. Some biomarkers also help monitor disease progression and responses to treatment.

1.A.8. Some IMD can be detected before symptoms appear through newborn _____ (NBS) programs.

1.A.9. Many IMD on NBS are _____ with diet or medication, particularly the disorders of energy metabolism. This makes them different from most other genetic conditions, where treatment options are often limited to symptom management.

1.A. What are inherited metabolic disorders?

1.A.1. metabolic

1.A.2. metabolism

1.A.3.

1. energy
2. Organelle

1.A.4. macronutrients

1.A.5. enzymes

1.A.6. adults

1.A.7. genetic

1.A.8. screening

1.A.9. treatable

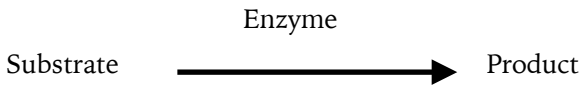
1.B. Mechanisms of disease

When learning about a new metabolic disorder, start with the mechanism of disease. The mechanism often connects directly to clinical symptoms, labs, and treatments.

1.B.1. The most common mechanism of disease in inherited metabolic disorders is _____ of enzyme function.

1.B.2. Loss of enzyme function causes two main problems:
1. The _____ accumulates (builds up), which can be toxic
2. The _____ becomes deficient (too little), which can be harmful

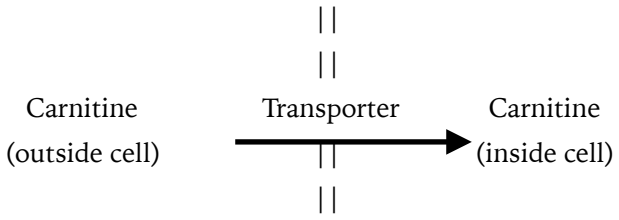
1.B.3. Draw an "X" over the arrow. Then, add an up arrow next to the word "substrate", and a down arrow next to the word "product."



1.B.4. A second mechanism of disease is impaired _____ of molecules. This means molecules cannot move to the right place in the cell.

1.B.5. For example, in carnitine transporter deficiency, _____ is unable to enter into cells.

1.B.6. Draw an "X" over the arrow. Then, add an up arrow next to the phrase "carnitine (outside cell)," and a down arrow next to the phrase "carnitine (inside cell)." Label the plasma membrane.



1.B.7. Less common mechanisms of disease include:
1. _____ of enzyme function (enzyme works too much)
2. _____ deficiency (helper molecules are missing)

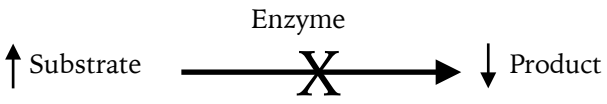
1.B. Mechanisms of disease

1.B.1. loss

1.B.2.

1. substrate
2. product

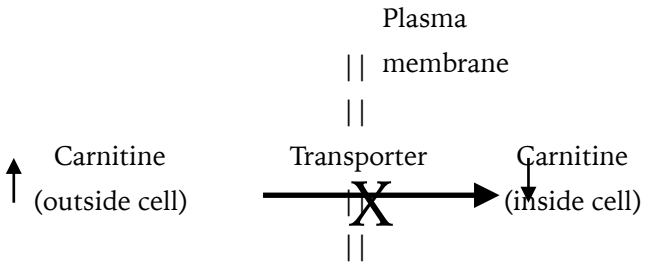
1.B.3.



1.B.4. transport

1.B.5. carnitine

1.B.6.



1.B.7.

1. Gain
2. Cofactor

1.C. Types of genetic variants and their effects

1.C.1. Both enzymes and transporters are proteins made of individual _____ acids (building blocks).

1.C.2. Loss of enzyme or transporter activity is linked to changes in the amino acid sequence, which itself is encoded by the RNA and _____ sequence.

1.C.3. Some DNA sequence variants cause *complete* loss of enzyme function, while others cause _____ loss of enzyme function (some enzyme activity remains).

1.C.4. Write the phrase "complete loss" or "partial loss" next to each type of DNA sequence variant, based on what the expected effect on the enzyme's function would be.

Frameshift (shifts the reading frame) _____
Nonsense (creates a stop codon) _____
Missense (changes 1 amino acid) _____

1.C.5. The amount of "residual" (left over) enzyme activity correlates with the _____ of disease.

1.C.6. Fill in the blanks below.

1. _____ loss of enzyme function causes severe, early-onset disease
2. Partial loss of enzyme function causes attenuated, _____-onset disease

1.C.7. The amount of enzyme activity that remains can be measured using an _____ activity assay.

1.C.8. Some people have reduced enzyme activity on laboratory testing but do NOT have clinical disease. This is called a _____ (false deficiency) and requires genetic testing to distinguish from true disease.

1.C. Types of genetic variants and their effects

1.C.1. Amino acids

1.C.2. DNA

1.C.3. partial

1.C.4.

Frameshift (shifts the reading frame)	complete loss
Nonsense (creates a stop codon)	complete loss
Missense (changes 1 amino acid)	partial loss

1.C.5. severity

1.C.6.

1. Complete
2. late

1.C.7. enzyme

1.C.8. Pseudodeficiency

1.D. Genotype-phenotype correlation in metabolic disorders

Genotype-phenotype correlation exists though is not absolute. Two individuals with the same exact variants may have different presentations due to modifier genes, environmental factors, and other influences.

1.D.1. Many metabolic disorders exhibit _____ expressivity, meaning that individuals with the same genetic variant can present with different symptoms (or the same symptoms with different severity).

1.D.2. The clinical presentation for most IMDs depends on the _____-_____ correlation, which describes the relationship between a patient's specific genetic variant and their resulting clinical symptoms.

1.D.3. Metabolic disorders are sometimes classified by their age of _____, which typically reflects the degree of residual enzyme activity.

1.D.4. _____-onset (severe) forms have very low or absent enzyme activity (typically <5%) and present with significant symptoms in the neonatal period or early infancy.

1.D.5. _____-onset (attenuated) forms have higher residual enzyme activity (typically 5-30%) and present in childhood, adolescence, or adulthood with milder, chronic symptoms.

1.D.6. Late-onset forms of metabolic disorders are often underdiagnosed or _____ because symptoms may be nonspecific and biochemical abnormalities may be absent between crises.

1.D.7. This pattern of variable expressivity based on residual _____ activity is seen across multiple metabolic disorder categories, including organic acidemias, urea cycle disorders, and lysosomal storage disorders.

1.D. Genotype-phenotype correlation in metabolic disorders

1.D.1. variable

1.D.2. genotype-phenotype

1.D.3. onset

1.D.4. Early (or Infantile/Neonatal)

1.D.5. Late (or Later)

1.D.6. misdiagnosed

1.D.7. enzyme