Food and Metabolic Health: Managing Inborn Errors of Metabolism through Diet

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Abstract

Inborn Errors of Metabolism (IEM) encompass a wide range of genetic disorders that disrupt biochemical pathways essential for metabolic processes in both humans and animals. Inherited enzyme deficiencies that hinder the body's ability to metabolize carbohydrates, amino acids, lipids, and other vital nutrients were first recognized in the early 20th century. This chapter discusses the genetics, pathophysiology, and classification of IEMs, detailing all the affected metabolic pathways and inheritance patterns, primarily characterized as autosomal recessive, X-linked, and rarer forms. Clinically, the manifestations can appear from infancy to adulthood, necessitating early detection through neonatal screening and advanced diagnostic methods. Management strategies, including dietary modifications, enzyme replacement, gene therapy, and CRISPR technology, aim to address these conditions. However, IEMs continue to pose significant challenges due to limited resources, variability in disease expression, and low adherence to treatment regimens, especially in resource-constrained settings. Recent research breakthroughs indicate a promising future for personalized therapies, suggesting potential improvements in outcomes and transforming the prognosis for individuals affected by these lifelong disorders.

Keywords: Inborn Errors of Metabolism, Metabolic Disease, Genetic Disorders, Diagnosis, Management

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Introduction

Inherited metabolic diseases (or inborn errors of metabolism and IEMs), due to enzyme deficiency in a metabolic pathway, occur with an incidence of 1 in 800 to 1,000 live births (El-Hattab, 2015; Kruszka & Regier, 2019). Collectively rare, they present with neurological signs, have growth failure, or undergo a metabolic crisis, especially during the neonatal period (Ferreira & van Karnebeek, 2019). Figure 1 is showing the classification of metabolic disorders.

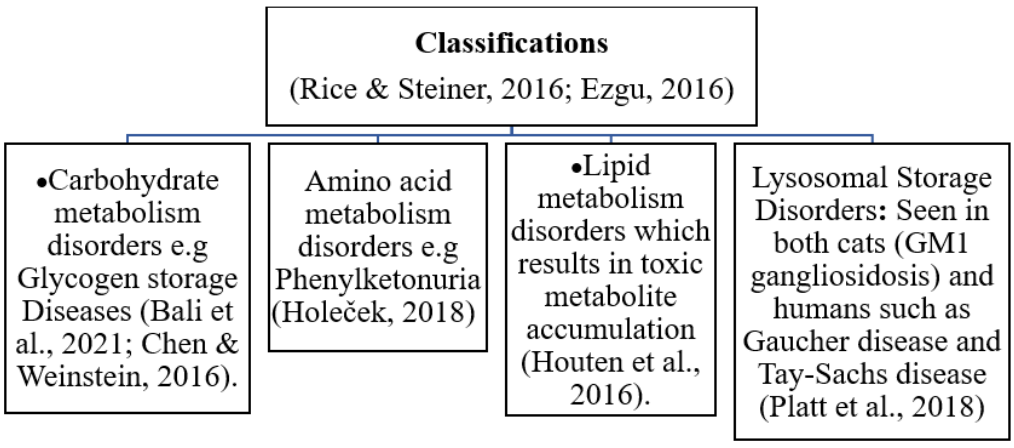

Fig. 1: Classification of Metabolic Disorders

Relevance to Veterinary and Human Medicine

In humans, newborn screening programs enable early detection and treatment of IEMs, improving outcomes. Early diagnosis of conditions like phenylketonuria (PKU) allows for dietary management that prevents intellectual disabilities (Kruszka & Regier, 2019; Jameson & Remmington, 2020). In animals, IEMs, especially in certain breeds, provide insights for translational research benefiting both veterinary and human medicine (Moura et al., 2022).

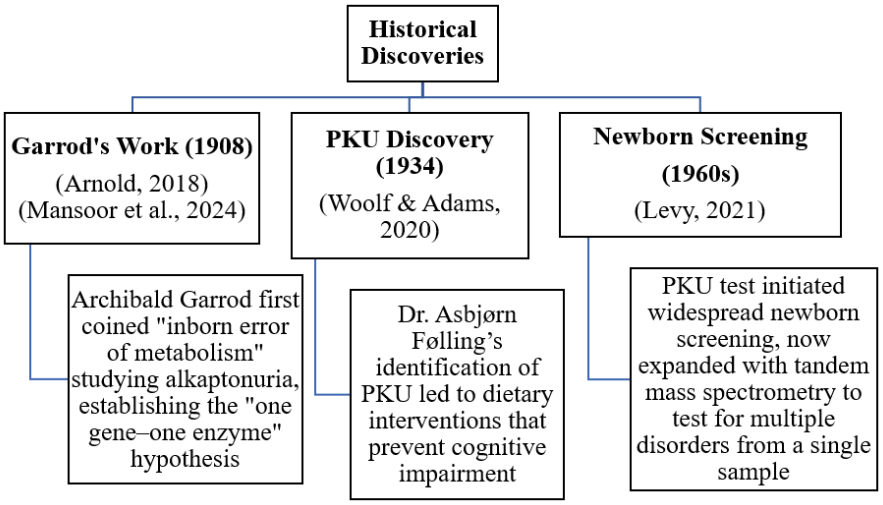

Fig. 2: Summary of Historical Discoveries

Genetic Basis and Pathophysiology of Inborn Errors of Metabolism (IEMs) Across Species

IEMs arise from genetic mutations affecting enzymes or transport proteins, leading to disruptions in metabolic pathways in both humans and animals. The inheritance of IEMs typically follows autosomal recessive, dominant, or X-linked patterns, often resulting from nucleotide changes or gene deletions. Summary of historical discoveries is shown in Figure 2.

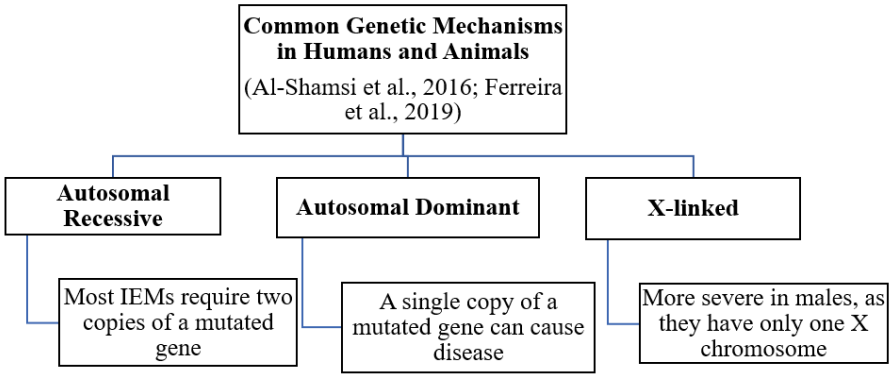

Fig. 3: Genetic Basis of IEMs

In both humans and animals, genetic mutations such as single-nucleotide changes, deletions, or duplications often disrupt enzyme function, leading to metabolic disorders. For instance, phenylketonuria (PKU) results from mutations in the **PAH** gene, affecting phenylalanine metabolism, demonstrating the cross-species impact of similar genetic defects (Blau, 2016; Hillert et al., 2020). Genetic Basis of IEMs is shown in Figure 3.

Comparative Genetics in Species:

- **Livestock:** Angus cattle are prone to alpha-mannosidosis (Allen, 2022).
- **Companion Animals:** Beagles and Siamese cats are affected by gangliosidosis and sphingomyelinosis, respectively (Lowell Ackerman DVM, 2015).

This knowledge of genetic mechanisms is critical for early diagnosis through newborn screening or genetic testing, aiding in effective management with dietary or therapeutic interventions.

Classification of Inborn Errors of Metabolism

In Humans Carbohydrate Metabolism Disorders

Disorders of Glucose Metabolism: Glycogen Storage Diseases (GSDs)

Glycogen Storage Diseases (GSDs) are inherited metabolic disorders characterized by abnormal glycogen accumulation due to enzyme deficiencies affecting glycogen synthesis or breakdown. Common types include GSD Type I, with subtypes Ia (Von Gierke's Disease, caused by

a deficiency of glucose-6-phosphatase α) and Ib (due to a defect in the glucose-6-phosphate transporter), and GSD Type II (Pompe Disease), resulting from a deficiency of acid α-glucosidase (GAA). Types of glycogen storage diseases are given in Table 1.

Table 1: Types of Glycogen Storage Diseases (Ellingwood & Cheng, 2018; Ross et al., 2020; Burton et al., 2020 ; Bali et al., 2021).

GSD Type	Enzyme Deficiency	Symptoms	Diagnosis	Treatment
GSD Type I (Von Gierke's Disease)	Glucose-6-phosphatase (G6PC) or glucose-6-phosphate transporter (SLC37A4)	- Hypoglycemia- Hepatomegaly- Growth retardation- Lactic acidosis	- Genetic testing for G6PC1/SLC37A4 mutations- Enzyme activity assays	- Frequent meals- Cornstarch supplementation- Low-fructose and low-galactose diet- Allopurinol and fibrates- Liver transplantation in severe cases
GSD Type II (Pompe Disease)	Acid α-glucosidase (GAA)	- Muscle weakness- Respiratory issues- Heart problems (infants)	- Enzyme activity assay for GAA- Genetic testing for GAA gene mutations	- Enzyme replacement therapy with recombinant human GAA (rhGAA)- Supportive therapies (physical therapy, respiratory support)
GSD Type III (Cori Disease)	Debranching enzyme (AGL)	- Muscle weakness- Hypoglycemia- Hepatomegaly- Cardiomyopathy	- Genetic testing for AGL mutations- Muscle biopsy to assess enzyme activity	- High-protein diet- Frequent meals- Management of hypoglycemia
GSD Type IV (Andersen Disease)	Branching enzyme (GBE1)	- Liver cirrhosis- Muscle weakness- Cardiac issues	- Genetic testing for GBE1 mutations- Liver biopsy for glycogen structure analysis	- Supportive care- Liver transplantation in severe cases
GSD Type V (McArdle Disease)	Muscle phosphorylase (PYGM)	- Exercise intolerance- Muscle cramps- Myoglobinuria	- Muscle biopsy to assess phosphorylase activity- Genetic testing for PYGM mutations	- Avoidance of strenuous exercise- High-carbohydrate diet
GSD Type VI (Hers Disease)	Liver phosphorylase (PYGL)	- Hepatomegaly- Growth retardation- Mild hypoglycemia	- Genetic testing for PYGL mutations- Liver biopsy for phosphorylase activity	- Frequent meals- Cornstarch supplementation

Galactose Metabolism Disorders (e.g., Galactosemia)

Galactose metabolism disorders, such as galactosemia, occur due to the body's inability to properly process galactose, a sugar commonly found in milk and dairy products. Galactosemia is categorized into four types based on the specific enzyme deficiencies involved in the Leloir pathway. Types of Galactosemia are given in Table 2.

Table 2: Types of Galactosemia (Conte et al., 2021)

Disorder	Enzyme Deficiency	Symptoms	Treatment
Galactosemia Type I	Galactose-1-phosphate uridyl transferase (GALT)	- Jaundice- Vomiting- Liver damage- Developmental delays- Cataracts	- Strict avoidance of galactose, especially dairy products- Lifelong dietary management
Galactosemia Type II	Galactokinase (GALK)	- Cataracts- Mild developmental delays- Liver involvement is less common	- Avoidance of galactose and dairy products- Monitoring for cataract development
Galactosemia Type III	UDP-galactose-4-epimerase (GALE)	- Similar to Type I but often milder- Possible developmental delays	- Dietary management may be necessary, depending on symptoms- Avoidance of galactose
Galactosemia Type IV	Galactose mutarotase (GALM)	- Rare and variable symptoms- Some patients may be asymptomatic	- Dietary restrictions may not be required for all patients- Monitor for any symptoms

Fructose Metabolism Disorders

Fructose metabolism disorders occur when the body cannot properly metabolize fructose, a sugar found in fruits and sweeteners. Types of fructose metabolism disorders are given in Table 3.

Table 3: Types of Fructose Metabolism Disorders (Tran, 2017 ; Steinmann & Santer, 2022)

Disorder	Enzyme Deficiency	Symptoms	Treatment
Essential Fructosuria	Fructokinase	- Generally asymptomatic- No significant health issues	- No treatment required
Hereditary Fructose Intolerance (HFI)	Aldolase B	- Abdominal pain- Nausea- Hypoglycemia- Shock-like reactions after fructose intake- Liver and kidney damage due to fructose-1-phosphate accumulation	- Strict avoidance of all fructose sources- Intravenous glucose for hypoglycemia- Supplementation with folate and vitamin C
Fructose-1,6-bisphosphatase Deficiency	Fructose-1,6-bisphosphatase	- Life-threatening hypoglycemic episodes- Coma- Symptoms triggered by illness, fasting, or high fructose intake	- Avoid catabolic triggers- Frequent feedings with slowly absorbed cornstarch- Correct hypoglycemia with oral or IV glucose- Restrict intake of fructose, sucrose, and sorbitol

Seen occasionally in dogs, leading to gastrointestinal distress upon ingestion of fructose.

Amino Acid Metabolism Disorders

Phenylketonuria

Phenylketonuria (PKU) is a genetic disorder caused by a deficiency in the enzyme phenylalanine hydroxylase, which is essential for breaking down the amino acid phenylalanine (Figure 4). Without a proper breakdown, phenylalanine accumulates, potentially causing neurological damage and other health issues. PKU is inherited in an autosomal recessive pattern, meaning a child must inherit the mutated gene from both parents to develop the condition. Symptoms include intellectual disability, behavioral issues, seizures, skin rashes, and a musty odor in breath, skin, or urine. PKU is usually identified through newborn screening, which checks blood for high phenylalanine levels. Treatment involves a strict, lifelong diet low in phenylalanine, avoiding high-protein foods, and using special formulas that supply nutrients without phenylalanine. With early diagnosis and strict diet management, individuals with PKU can lead healthy lives and develop normally, but consistent dietary adherence is essential to prevent cognitive and developmental problems (Strisciuglio & Concolino, 2014). Although more common in humans, it can occur in dogs and leads to neurological issues due to phenylalanine buildup (Chowdhury & Ghosh, 2024).

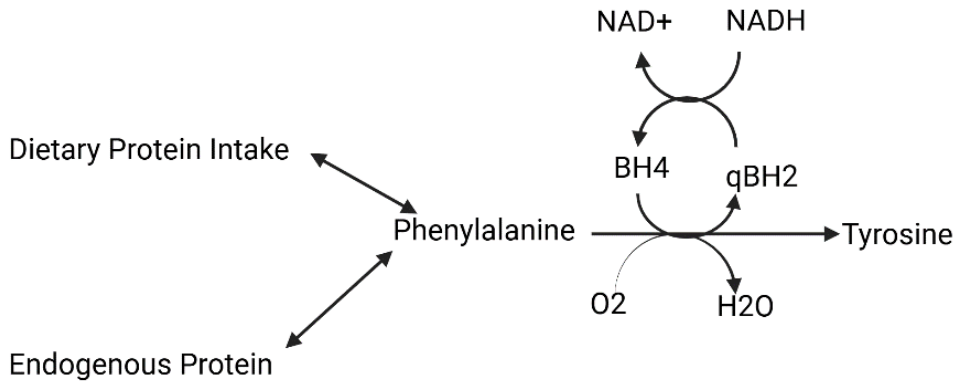

Fig. 4: Mechanism of Phenylketonuria

Maple Syrup Urine Disease

Maple syrup urine disease (MSUD) is a rare genetic disorder in which the body cannot properly break down certain amino acids—leucine, isoleucine, and valine—due to a deficiency in the branched-chain alpha-keto acid dehydrogenase complex. This leads to a buildup of these amino acids and their toxic byproducts in the blood, also affects certain breeds of dogs, resulting in symptoms such as poor feeding, vomiting, lethargy, and a distinctive sweet, maple syrup-like odor in urine and sweat. MSUD is inherited in an autosomal recessive manner, meaning both parents must pass on a copy of the mutated gene. MSUD can be detected early with newborn screening programs, enabling to begin immediate treatment. The management usually consists of two things: a low protein diet closely followed and special formulas to limit the intake of amino acids that are affected. People with MSUD can avoid severe neurological damage and live longer with early diagnosis and strict dietary control (Blackburn et al., 2017; Mengler et al., 2024).

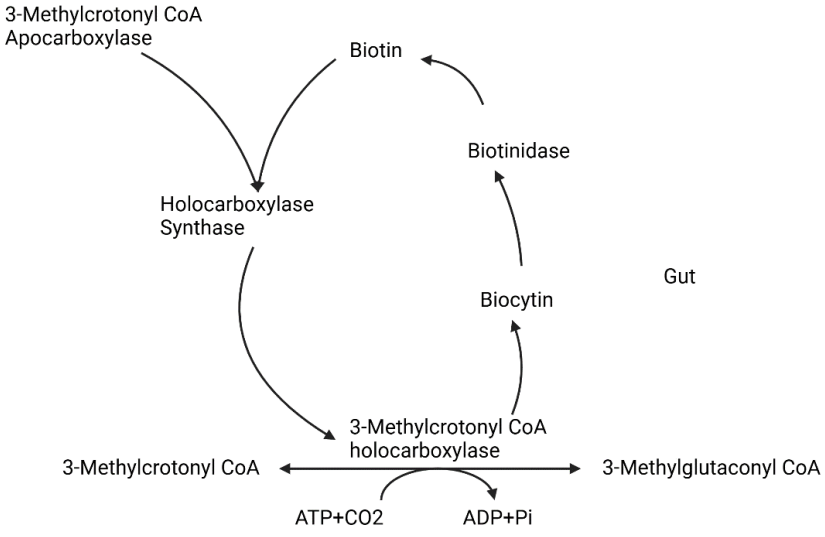

Fig. 5: Mechanism of Organic Acedemias Created in https://BioRender.com

Organic Acidemias

Organic acidemias are a group of rare inherited metabolic disorders, in which the breakdown of certain amino acids and fats is imbalanced due to enzyme deficiencies; resulting in increased concentration of toxic organic acids in the blood and urine (Figure 5). If these acids build up, it can cause problems ranging from poor feeding, vomiting, lethargy, low blood sugar, delays in development, and even life-threatening metabolic crises. methylmalonic acidemia (MMA), propionic acidemia (PA), and isovaleric acidemia (IVA) are common types, with different

enzyme deficiencies. Newborn screening usually detects organic acidemias and allows early diagnosis and intervention. Typically, treatment involves a protein restricted diet supplemented with specific amino acids, and sometimes medication that helps to remove the excess acids. Dietary and proper medical adherence are necessary for individuals with organic acidemias to live healthier lives, although the complications can be avoided with timely management (Villani et al., 2017; Ramsay et al., 2018).

Urea Cycle Disorders

These genetic metabolic disorders result from enzyme deficiencies that prevent the body from converting toxic ammonia into urea for excretion. When ammonia accumulates, it can lead to symptoms such as poor appetite, vomiting, lethargy, seizures, and, in severe cases, brain damage or coma. Summary of urea cycle disorders is given in Table 4.

Table 4: Summary of Urea Cycle Disorders

Disorder	Affected Enzyme	Clinical Features	Genetic Basis	Management Strategies
Carbamoyl Phosphate Synthetase 1 Deficiency (CPS1)	Carbamoyl phosphate synthetase 1	Hyperammonemia, poor appetite, vomiting, lethargy	Autosomal recessive	Low-protein diet; ammonia scavengers; intravenous fluids
Ornithine Transcarbamylase Deficiency (OTC)	Ornithine transcarbamylase	Most common UCD; hyperammonemia, seizures, lethargy	X-linked recessive	Low-protein diet; ammonia scavengers; emergency treatment for hyperammonemia
Argininosuccinate Synthetase Deficiency (Citrullinemia)	Argininosuccinate synthetase (ASS1)	Hyperammonemia, vomiting, lethargy, developmental delay	Autosomal recessive	Low-protein diet; arginine supplementation; ammonia scavengers
Argininosuccinate Lyase Deficiency (ASL)	Argininosuccinate lyase	Hyperammonemia, poor appetite, lethargy, seizures	Autosomal recessive	Low-protein diet; arginine supplementation; ammonia scavengers
Arginase Deficiency (ARG1)	Arginase	Progressive spasticity, developmental delay, seizures	Autosomal recessive	Low-protein diet; manage symptoms; ammonia scavengers
N-Acetylglutamate Synthetase Deficiency (NAGS)	N-acetylglutamate synthetase	Hyperammonemia, vomiting, lethargy, neurological symptoms	Autosomal recessive	Low-protein diet; N-carbamylglutamate supplementation; ammonia scavengers

UCDs are often detected through newborn screening, allowing for early intervention. Treatment involves a low-protein diet, medications to control ammonia, and amino acid supplements to manage symptoms. Fluids, dextrose, and intravenous lipid emulsion should be given to blunt the catabolic process Strict management is essential to prevent neurological damage and improve the quality of life for those affected (Summar & Mew, 2018; Matsumoto et al., 2019).

Lipid Metabolism Disorders

Disorders Involving Fatty Acid Oxidation

Fatty acid oxidation disorders (FAODs) are a group of genetic metabolic conditions where the body cannot properly break down fatty acids into energy, especially during fasting or periods of high energy demand. This process normally occurs in the mitochondria, using enzymes to convert fat into usable energy (Dixon et al., 2020). When specific enzymes are deficient, fatty acids accumulate, and energy production is impaired, leading to symptoms such as low blood sugar (hypoglycemia), lethargy, muscle weakness, liver dysfunction, and, in severe cases, heart problems or sudden death. Fatty acid oxidation disorders are given in Table 5.

Table 5: Fatty Acid Oxidation Disorders (Wajner & Amaral, 2016).

Disorder	Affected Enzyme	Fatty Acid Chain Length	Clinical Features	Genetic Basis	Management Strategies
Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	Medium-chain acyl-CoA dehydrogenase	Medium-chain (C6-C12)	Hypoglycemia, lethargy, vomiting, hepatomegaly	Autosomal recessive	High-carbohydrate, low-fat diet; avoid fasting; MCT oil
Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	Very long-chain acyl-CoA dehydrogenase	Very long-chain (C14-C20)	Hypoglycemia, cardiomyopathy, and muscle weakness	Autosomal recessive	Avoid fasting, high-carbohydrate diet; MCT oil; carnitine
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)	Long-chain 3-hydroxyacyl-CoA dehydrogenase	Long-chain (C12-C18)	Hypoglycemia, liver dysfunction, retinal disease	Autosomal recessive	High-carbohydrate, low-fat diet; MCT oil; carnitine
Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)	Short-chain acyl-CoA dehydrogenase	Short-chain (C4-C6)	Hypoglycemia, metabolic acidosis, lethargy	Autosomal recessive	High-carbohydrate diet; avoid fasting
Long-Chain Fatty Acid Oxidation Disorder (LCAD)	Long-chain acyl-CoA dehydrogenase	Long-chain (C12-C22)	Muscle weakness, hypoglycemia, cardiomyopathy	Autosomal recessive	High-carbohydrate diet; avoid fasting
3-Ketothiolase Deficiency	3-ketothiolase	Various	Hypoglycemia, metabolic acidosis, lethargy	Autosomal recessive	High-carbohydrate diet; avoidance of fasting

Lipoprotein Disorders

Lipoprotein disorders are a group of metabolic conditions characterized by abnormal levels or functions of lipoproteins, which are particles that transport fats (lipids) such as cholesterol and triglycerides in the bloodstream. These disorders can lead to elevated blood lipid levels, increasing the risk of cardiovascular diseases like atherosclerosis, heart attack, and stroke. Lipoprotein disorders can be genetic (primary) or influenced by lifestyle factors such as diet, obesity, and sedentary behavior (secondary). Summary of Lipoprotein Disorders is given in Table 6.

Table 6: Summary of Lipoprotein Disorders (Varghese, 2014; Taghizadeh et al., 2019).

Disorder	Lipoprotein Type Affected	Lipid Abnormalities	Clinical Features	Genetic or Secondary	Management Strategies
Familial Hypercholesterolemia (FH)	Low-Density Lipoprotein (LDL)	Elevated LDL cholesterol	Early-onset atherosclerosis, xanthomas, and heart disease	Genetic (primary)	Statins, lifestyle modifications, Ezetimibe
Familial Combined Hyperlipidemia	Very Low-Density Lipoprotein (VLDL) and LDL	Elevated LDL and triglycerides	Premature cardiovascular disease, obesity, insulin resistance	Genetic (primary)	Statins, fibrates, lifestyle changes
Type III Hyperlipoproteinemia (Dysbetalipoproteinemia)	Intermediate-Density Lipoprotein (IDL)	Elevated IDL cholesterol and triglycerides	Xanthomas, premature coronary artery disease	Genetic (primary)	Dietary modifications, statins, fibrates
Lipoprotein Lipase Deficiency	Chylomicrons	Elevated triglycerides	Recurrent pancreatitis, abdominal pain, hepatosplenomegaly	Genetic (primary)	Low-fat diet, triglyceride-lowering medications
Hypertriglyceridemia	Chylomicrons	Extremely high triglycerides	Abdominal pain, pancreatitis, eruptive xanthomas	Genetic or Secondary	Very low-fat diet, fibrates, omega-3 fatty acids
Tangier Disease	High-Density Lipoprotein (HDL)	Low HDL cholesterol	Enlarged tonsils, peripheral neuropathy, corneal opacities	Genetic (primary)	HDL-raising therapies, supportive care
Familial Dysbetalipoproteinemia	IDL	Elevated cholesterol and triglycerides	Peripheral vascular disease, xanthomas	Genetic (primary)	Lifestyle changes, statins, fibrates
Apolipoprotein C-II Deficiency	Chylomicrons	Elevated triglycerides	Recurrent pancreatitis, hepatosplenomegaly	Genetic (primary)	Dietary fat restriction, triglyceride-lowering medications
Secondary Hyperlipidemia	Various	Elevated cholesterol and/or triglycerides	Related to underlying conditions (e.g., diabetes, hypothyroidism)	Secondary	Treat underlying conditions, lifestyle modifications, statins

Lysosomal Storage Diseases

Lysosomal storage diseases (LSDs) are inherited metabolic disorders caused by the deficiency of specific enzymes that lead to the accumulation of toxic substrates within lysosomes. This accumulation results in various clinical symptoms, including developmental delays, organ enlargement, skeletal abnormalities, and neurological impairments. Early diagnosis through enzyme assays and genetic testing is crucial for effective management, which may involve enzyme replacement therapy (ERT), substrate reduction therapy, and supportive care (Parenti et al., 2015; Ferreira & Gahl, 2017; Platt et al., 2018). Key types of lysosomal storage diseases are given in Table 7.

Table 7: Key Types of Lysosomal Storage Diseases

Disease	Enzyme Deficiency	Substrate Accumulation	Symptoms	Treatment Options
Gaucher Disease	Glucocerebrosidase (GBA)	Glucocerebroside	Anemia, hepatosplenomegaly, bone pain	ERT, substrate reduction therapy
Fabry Disease	Alpha-galactosidase A (GLA)	Ceramide trihexoside	Pain episodes, kidney dysfunction, and strokes	ERT, symptomatic management
Pompe Disease	Acid alpha-glucosidase (GAA)	Glycogen	Muscle weakness, cardiomyopathy	ERT, supportive therapies
Hurler Syndrome	Alpha-L-iduronidase (IDUA)	Dermatan sulfate, heparan sulfate	Developmental delays, corneal clouding	ERT, hematopoietic stem cell transplant
Hunter Syndrome	Iduronate-2-sulfatase (IDS)	Dermatan sulfate, heparan sulfate	Behavioral issues, joint stiffness	ERT, supportive care
Krabbe Disease	Galactocerebrosidase (GALC)	Galactolipids	Severe neurological decline, vision problems	HSCT

In Animals Specific Metabolic Diseases Affecting Livestock

Bovine Ketosis

Bovine ketosis is a metabolic disorder in dairy cows, typically occurring in the early lactation period when energy demands for milk

production exceed the cow's dietary energy intake. When this energy imbalance occurs, the cow uses up its fat reserves, and the products of fat metabolism accumulate in the blood, urine, and milk as ketone bodies, such as beta-hydroxybutyrate (Audor & Espinosa, 2018). Ketosis symptoms include loss of appetite, weight loss, reduced milk production, lethargy, and, in most cases, neurological signs. There are two types: High energy demands cause primary ketosis, and other illnesses that lower feed intake will result in secondary ketosis. Blood, urine, and, rarely, milk samples are tested for ketones to determine the diagnosis. Treatment consists of providing glucose precursors or intravenous glucose and modifying the diet to ensure adequate food energy intake. Preventive measures include proper nutrition and body condition management, in dry conditions (Audor & Espinosa, 2018).

Pregnancy Toxemia in Ewes

Pregnancy toxemia, also referred to as twin lamb disease, is a metabolic disorder of pregnant, multiple-lamb-bearing ewes that occurs in the last few weeks of pregnancy. In sheep, there exist times during this period when the ewe's intake is less than the fetal energy demand, resulting in a negative energy balance. An ewe trying to feed her lamb breaks down fat reserves in addition to her milk supply, and as a result, blood levels of ketones rise to such a degree as to cause symptoms such as loss of appetite, weakness, isolation from the flock or, in severe cases, neurological signs such as staggering or even coma. Poor nutrition, inadequate body condition, stress, and reduced feed availability are the risk factors. Treatment is by incorporating glucose or glucose precursors into the diet, along with increasing dietary energy intake. The focus of prevention is on supplying ewes with a balanced, high-energy diet, and monitoring ewe body condition to ensure that the diet doesn't lead to nutritional stress and prevent optimal lamb development (Ji et al., 2023).

Fat Cow Syndrome

Obesity in cattle is called fat cow syndrome and is characterized by excessive body fat in cattle, particularly dairy cows, which results from overfeeding, inadequate exercise, or untended management of the dry period. Such a syndrome can have profound effects on your health both before and after calving.

Fat cows are at a higher risk for metabolic disorders like ketosis, milk fever, and fatty liver disease. They might also find troubles at calving time, have lowered fertility, and lower milk production. It also bothers the normal physiological processes like hormone modulation and nutrient metabolism.

To prevent Fat Cow Syndrome, feed is given to meet energy needs, but not in excess calories; a balanced diet, free of overfeeding or failure to meet the energy needs. Regularly monitoring body condition scores (BCS) will make sure cows have the weight they should have. For healthy dairy cows, adjustments to feeding strategies are needed, including limiting energy-dense feeds and promoting regular exercise, to maintain body condition (Kunej et al., 2013).

Metabolic Diseases in Companion Animals

Feline Hyperlipidemia

Feline hyperlipidemia is a blood lipid abnormality of cats defined by increased blood triglycerides and cholesterol levels. The condition may be primary or secondary. Cats less commonly have primary hyperlipidemia, but some breeds, such as Siamese cats, may be predisposed to elevated lipid levels by their genetics. Secondary hyperlipidemia is more common and is typically secondary to comorbidities such as diabetes mellitus, hyperthyroidism, and hepatic lipidosis (especially in overweight cats). Severe cases can present with such signs as lethargy, vomiting, weight loss, or jaundice and symptoms can range from being asymptomatic to it.

The diagnosis of feline hyperlipidemia is made by blood tests to measure the amount of lipids in the blood and test the overall health of the cat (Li et al., 2024). Treatment normally involves treatment for any underlying condition that would contribute to the lipid elevation, including dietary management, which may include a low-fat or specific diet for lipid control. Aggressive nutritional support may be necessary in hepatic lipidosis cases. Cats with hyperlipidemia must be treated by prompt treatment of their underlying health problems, together with regular veterinary check-ups to ensure the wellbeing of these cats (Miceli et al., 2022; Li et al., 2024).

Canine Hyperlipidemia

Hyperlipidemia in dogs describes the presence in the blood of dogs of blood levels which are higher than normal. Unchecked, hyperlipidemia may result in a host of medical problems. As with felines, canine hyperlipidemia can be primary or secondary. The most common breeds to have this form of hyperlipidemia are breeds including Miniature Schnauzers, and Dachshunds, which have primary hereditary hyperlipidemia, sometimes due to high levels of triglycerides and cholesterol. As noted, secondary hyperlipidemia occurs more frequently and is frequently seen due to diabetes mellitus, hypothyroidism, pancreatitis, and liver disease. While many dogs with hyperlipidemia are asymptomatic, some may have signs associated with one or more underlying health issues, including vomiting, diarrhea, lethargy, and abdominal pain.

Diagnosis of canine hyperlipidemia includes blood testing of blood lipids to determine the levels at play and identify underlying conditions causing the disorder. Treatment often involves dietary changes such as diets low in fat and proper weight control, and any medical problems that may be helping make the problem worse. In some cases, medications like fibrates or omega-3 fatty acids can be prescribed to help regulate lipid levels. Canine hyperlipidemia can be managed well with regular veterinary care and monitoring, which will help to keep your pet healthy long-term and minimize the chances of complications. Signs are common, such as vomiting, diarrhea, abdominal pain, and potential complications, such as pancreatitis caused by severe hyperlipidemia (Villm, 2021; Carroll, 2022).

In aggregate, these investigators believe that IEM is a heterogeneous group of disorders, based on different species sharing a common underlying mechanism for enzyme deficiency and metabolic disruption. Knowing these classifications helps diagnose and care for affected individuals.

Challenges in Treating Inborn Errors of Metabolism (IEMs)

Humans

Treatment of inborn errors of metabolism (IEMs) in human beings is beset by multiple problems, which can complicate management. Variability in treatment response among individuals is another problem that is affected by genetic factors, patient age, and comorbidities. This variability complicates the development of standardized treatment protocols based on which personalized measures should be implemented (Vockley et al., 2019). In addition, there are long-term care challenges that families often face, such as strict dietary restrictions and psychological stress accompanying the management of chronic conditions. It is well known that parents of children with IEMs feel emotionally overwhelmed and lifestyle adjustments can seriously impair family dynamics and future planning (Summar & Mew, 2018 ; Mussap et al., 2018).

Animals

IEM treatment is particularly challenging in veterinary medicine. The economic consequences are particularly well perceived in livestock, where the cost of managing genetic disorders can erase farmers' profits. The scarcity of resources allocated to rare diseases limits treatment options even further since many practitioners have no specialized knowledge, nor access to specialized diagnostic tools used to tackle IEMs that are lesser known. There are also ethical considerations, including companion animals, where treatment decisions may involve considering the quality of life versus the financial expense on pet owners (Das, 2013).

Research Advances in Inborn Errors of Metabolism

Comparative Research between Animals and Humans

Understanding IEMs across different species is only possible using comparative research. The pathophysiology of many metabolic disorders has been studied in animal models. The problem is that findings in animal studies don't translate to human conditions. However, recent advances in induced pluripotent stem cell (iPSC) technology have arisen, enabling researchers to generate human cellular models closer to actual known disease states in IEMs. The progress becomes possible so that more relevant studies and potential therapeutic developments are made (Escribá et al., 2021).

Genetic Editing Technologies and Their Application across Species

Genetic editing technologies, such as CRISPR-Cas9, have now made the emergence possible for treating IEMs in veterinary and human medicine. These very innovative technologies allow genomic targeted changes to genes linked to metabolic disorders, which might cure these disorders, or at least significantly change how the patient is dealt with medically. These approaches are being researched to determine safety and efficacy in different species, Initial studies on such approaches are proving promising (Busch et al., 2022 ; Brinegar et al., 2017).

Emerging Therapies in Both Veterinary and Human Medicine

Based on a wealth of experience with enzyme replacement therapies and gene therapies, therapies for these metabolic deficiencies are becoming increasingly available, with both emerging therapies targeting defects at a molecular level. The development of drugs that target specific disrupted metabolic pathways in IEMs has advanced significantly in humans and has improved patient outcomes (Alfadhel et al., 2013; Collaud, 2021). Though treatment options in veterinary medicine are limited compared to human medicine, interest in adapting known therapeutic strategies is also rising for the treatment of metabolic disorders in companion animals (Lagler, 2019; Escribá et al., 2021). Finally, the treatment of IEMs in all species still presents some challenges but should be ameliorated through continued research and technological advancement, and thus improved outcomes can be expected both in human and animal patients. Effective treatment of these complex disorders will continue to depend on continued collaboration between the veterinary and medical research communities.

Conclusion

Inborn Errors of Metabolism (IEM) are a critically important area of medical and scientific research because they have dramatic implications for the health and welfare of both humans and animals. These pathologies are often inherited early on and can disrupt metabolic pathways, resulting in grave health problems. Early diagnosis by neonatal screening and using advanced molecular diagnostic techniques is key to preventing the effects of these disorders and to better patient outcomes. Genetics and biotechnology advances, including gene therapy and CRISPR, are changing personalized medicine by offering more personalized treatments, specifically, based on what each person needs. These advancements, however, are not enough, as there is genetic variability related to these disorders, significant disparity between healthcare resources, and treatment adherence problems. These obstacles need continuing research, increasing access to healthcare, and new therapeutic strategies. As efforts continue, the possibility of therapeutic approaches that improve such quality of life and long-term outcomes in people with IEM increases.

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