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<b>INBORN ERRORS OF METABOLISM</b>
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## **EVALUATION AND MANAGEMENT OF A SICK INFANT WITH SUSPECTED INBORN ERROR OF METABOLISM**

**\*Ratnakumari TL**

**Abstract:** *Inborn Errors of Metabolism(IEM) are not very uncommon. They present as great mimics to common diseases of children with symptoms such as tachypnea, apnea, convulsions and dehydration. In the newborn they mimic sepsis with non specific symptoms and most often the presentation can be acute and catastrophic, referred to as 'metabolic distress'. Even though hundreds of IEM are described, making a diagnosis has been made simpler with advanced diagnostic tools like Tandem Mass Spectrometry (TMS) and genetic mutation studies which are currently available in India. With a 'staged evaluation' a diagnosis can be made and some of them can be treated effectively. This article is an attempt at giving a basic diagnostic approach for the management of a sick child, suspected to have IEM.*

**Keywords:** *IEM, Staged evaluation, Metabolic distress, Heritable disorder*

### **Points to Remember**

- *IEM are not uncommon*
- *Do suspect IEMs in all babies with unexplained deterioration of clinical condition and suspected sepsis when sepsis screen is negative.*
- *Start with a simple approach to hold on to a 'thread of logic' which will lead on to the diagnosis.*
- *Stabilization is the key to management.*
- *If a diagnosis is not made when the child is alive, do collect blood samples and freeze to send for subsequent analysis.*
- *An attempt to make a diagnosis gives the choice to the parents in subsequent pregnancies.*
- *We have a long way to go in effective treatment and in the current scenario genetic counseling to the parents is the crux.*

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## INBORN ERRORS OF METABOLISM

### **PRENATAL DIAGNOSIS AND NEWBORN SCREENING: RELEVANCE IN INDIA**

\* **Mamta Muranjan**

\*\* **Shruti Agarwal**

**Abstract:** *Inborn errors of metabolism (IEM) are progressive disorders characterized by high fatality and permanent disability in survivors. They are growing at an alarming rate in India. Evaluation and treatment of these disorders is expensive and not easily available. In a small proportion of patients who have access to therapy, the outcome may not be optimum due to late diagnosis and therapy. The option for many families affected by these disorders is prenatal diagnosis and newborn screening. Prenatal diagnosis for IEM is available with non-invasive modalities such as ultrasonography and biochemical, histopathological or molecular testing of fetal tissues obtained by invasive procedures and is fairly well established for lysosomal storage disorders with enzyme estimation. However in many cases, diagnosis in the index case is not established. In such situations newborn screening is often advised for high risk screening. Universal newborn screening is not yet practised except in some isolated regions. The options for universal newborn screening for IEM in India and the hurdles to be overcome are discussed.*

**Keywords:** *Inborn errors of metabolism, Chorion villus sampling, Amniocentesis, Ultrasonography, Fetal MRI, Tandem Mass Spectroscopy*

#### **Points to Remember**

- *Prenatal diagnosis for IEM should be offered to families for prevention of recurrence when the diagnosis is confirmed in an index case.*
- *Abnormalities such as fetal hydrops or visceromegaly detected by ultrasonography should prompt investigations for an IEM under appropriate circumstances.*
- *The appropriate option for prenatal diagnosis is chorion villus sampling or amniocentesis for estimation of enzyme activity or genotyping if the mutations have been tested in the index case. In other cases options such as substrate or metabolite profiling in the amniotic fluid supernatant may be appropriate.*
- *Newborn screening for IEM permits early diagnosis and treatment resulting in prevention of disabilities, especially neurodisability.*
- *Implementing universal newborn screening would lead to substantial gains in decreasing the infant mortality rates.*

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## INBORN ERRORS OF METABOLISM

### **SAMPLE COLLECTION, SUITABILITY AND INTERPRETATION IN SUSPECTED INBORN ERRORS OF METABOLISM**

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 \*\* **Minakshi Koch**  
 \*\* **Sabyasachi Ghosh**  
 \*\*\* **Shobha G**  
 \*\*\* **Suresh Kumar V**

**Abstract:** *Inherited metabolic disorders are a heterogeneous group of genetic conditions mostly occurring in childhood. They are individually rare but collectively numerous, causing substantial morbidity and mortality. Screening for inherited metabolic disorders is therefore very important. The importance of screening for inborn errors of metabolism (IEM) introduces several decision points about specimen collection, processing, and storage for the investigator. The method of sampling is of greatest importance for precise results and hence for earlier and accurate diagnoses.*

**Keywords:** *Inborn errors of metabolism, Specimen collection, Processing, Interpretation.*

### **Points to Remember**

- *An appropriate sample according to the metabolite of interest is to be collected, processed and analysed as per standard protocol.*
- *While interpreting the result, factors influencing the result like whether sample has been collected during symptomatic or asymptomatic period, co morbid are conditions, etc. are to be considered.*

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**INBORN ERRORS OF METABOLISM**

## **INBORN ERRORS OF METABOLISM IN INFANCY AND CHILDHOOD PRESENTING WITH METABOLIC ACIDOSIS**

\* **Prasad C**

\*\* **Rupar CA**

**Abstract:** *Disturbances of acid-base homeostasis are not uncommon. These are important indicators of underlying disease in infants and children. Metabolic acidosis is one of the most common perturbations noted in acute pediatric emergencies. Frequent causes of metabolic acidosis include diabetic ketoacidosis, shock and tissue hypoxia, salicylate and ethanol poisoning. However, it is important to recognize that many inborn errors of metabolism (IEM) such as organic acidemias and primary lactic acidosis also present with a persistent metabolic acidosis. Calculation of the anion gap, presence or absence of hyperammonemia, hypoglycemia and ketosis are essential in the diagnosis of these patients. Early diagnosis and appropriate management is necessary to optimize the outcome. IEM have a genetic basis and appropriate genetic counseling needs to be provided to the families.*

**Key words:** *Organic acidemias, Lactic acidosis, Hypoglycemia, Ketosis.*

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### **Points to Remember**

- *Presence of metabolic acidosis particularly with high anion gap should alert the pediatrician to a possibility of inborn errors of metabolism.*
- *Inborn errors of metabolism can mimic common neonatal conditions such as sepsis and vice versa.*
- *Biochemical tests such as ammonia levels, presence or absence of ketones and lactate measurements can help with the diagnosis of inborn errors of metabolism.*
- *Prompt and early diagnosis is essential as many of these inborn errors of metabolism are treatable.*
- *Early treatment optimizes the neurocognitive development of the infant.*
- *Inborn errors of metabolism have a genetic basis in most instances so establishing a diagnosis will also help in genetic counselling and family screening.*

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**INBORN ERRORS OF METABOLISM****RECURRENT HYPOGLYCEMIA  
AND INBORN ERRORS OF  
METABOLISM**

\* **Madhulika Kabra**  
\*\* **Neerja Gupta**

**Abstract :** *Many of the inborn errors of metabolism, including urea cycle defects, organic acidemias, and certain disorders of amino acid metabolism, present in the young infant with symptoms of an acute or chronic metabolic encephalopathy. Typical symptoms include lethargy, poor feeding, apnea or tachypnea, recurrent vomiting, metabolic acidosis and/or hyperammonemia. Hypoglycemia may be the predominant finding in a number of inborn errors of metabolism, including glycogen storage disorders, defects in gluconeogenesis, and fatty acid oxidation defects.*

**Keywords :** *Hypoglycemia, Inborn errors of metabolism, Glycogen storage disorders, Fatty acid oxidation defects.*

**Points to Remember**

- *Diagnosis of IEM requires a high index of clinical suspicion.*
- *Presence of persistent vomiting, acidosis and seizures with normal sepsis screen points towards an IEM.*
- *The triad of hypoglycemia, marked hepatomegaly and lactic acidosis is characteristic of many gluconeogenesis defects.*
- *A stepwise correct choice of investigations can lead to a specific diagnosis and early management.*

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## INBORN ERRORS OF METABOLISM

### INBORN ERRORS OF METABOLISM PRESENTING AS HYPERAMMONEMIA IN NEONATES

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**Abstract:** Neonatal hyperammonemia is a medical emergency requiring prompt recognition and aggressive therapy. It is apparent that the clinical signs of hyperammonemia are non-specific and could be attributable to many serious illnesses of the neonate like sepsis, intraventricular hemorrhage, etc. Hyperammonemia can be primary or secondary. Urea cycle disorders and other inborn errors of metabolism though individually uncommon represent an important cause of hyperammonemia in neonates. Therapy is aimed towards minimizing endogenous production and removal of ammonia.

**Keywords:** Hyperammonemia, Neonates, Inborn errors of metabolism

### Points to Remember

- *Hyperammonemia incidence is under estimated in view of undiagnosed deaths.*
- *High index of suspicion in any acutely ill neonate especially if there is history of consanguinity and sibling death.*
- *Prompt diagnosis and early aggressive treatment may improve the neurological outcome in survivors.*
- *Neonatal diagnosis and general counseling should be offered to the couples.*
- *Hyperammonemia of newborn has a good prognosis if treated early and aggressively.*
- *Treatment modalities to remove ammonia from the circulation like PD, HD are necessary during acute episodes.*

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<b>INBORN ERRORS OF METABOLISM</b>
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## **FATTY ACID OXIDATION DISORDERS**

\* **Thangavelu S**

**Abstract:** *Fatty Acid Oxidation (FAO) disorder is an important group of inborn errors of metabolism. Clinical features develop during periods of fasting, because fatty acids are the major source of fuel. When diagnosed and treated early, they can be managed with simple dietary advice and can live a full life. If the physician is not aware of the features of FAO disorders, this may be mistaken as Reye syndrome or sadly parents may be blamed with the diagnosis of Munchausen Syndrome by Proxy. Any child with recurrent hypoglycaemia without ketones or with unexplained neuromuscular disorders or cardiomyopathy needs to be evaluated for FAO disorders.*

**Keywords :** *Fatty acid oxidation, SIDS, Hypoketotic hypoglycemia, Reye like syndrome, Cardiomyopathy.*

### **Points to Remember**

- *Fatty acid oxidation disorders are caused by deficiency of the transport protein or  $\beta$  oxidation enzyme system.*
- *Clinical presentation includes hypoketotic hypoglycemia, Reye like syndrome, involvement of skeletal and cardiac muscle.*
- *Rarely in mothers of affected fetus it can cause acute fatty liver of pregnancy.*
- *Management mainly involves avoiding fasting and providing frequent low fat and carbohydrate rich meals at bed time.*

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<b>GENERAL ARTICLE</b>
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## **MITOCHONDRIAL DNA AND DIABETES MELLITUS**

\* **Biswajit Mohanty**

\*\* **Balasubramanian J**

**Abstract:** *Diabetes mellitus affects approximately 5% of the general population with its prevalence varying between ethnic groups and geographic regions. The majority of cases are either type 1 or type 2 diabetes. Although these disorders share a common phenotype, fasting and postprandial hyperglycemia, their etiology is distinct. A growing body of evidence has demonstrated a link between mitochondrial functioning and type 2 diabetes. Certain mitochondrial DNA (mtDNA) mutations affect insulin secretion involving an attenuation of ADP/ATP levels leading to a re-setting of the glucose sensor in the pancreatic  $\beta$ -cell. Co-morbid conditions include impaired hearing, changes in pigmentation of the retina, gastrointestinal abnormalities, cardiomyopathy, and MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes).*

**Keywords:** *Type 2 Diabetes, Mitochondrial DNA, Comorbid Conditions.*

### **Points to Remember**

- *Type 2 diabetes mellitus may not be mere insulin insensitivity or release; it may be part of a global dysfunction of mitochondrial energy system.*
- *Mutation of mtDNA as a cause is to be considered in diabetes with hearing loss and maternal diabetes.*
- *Patients with mutation require insulin in due course.*
- *Metformin group of drugs are to be avoided as they lead to lactic acidosis.*

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<b>GENERAL ARTICLE</b>
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**APPROACH TO ANASARCA**\* **Maiya PP**\*\* **Sharanabasavesh M**

**Abstract:** *Generalized edema otherwise known as anasarca, is a common presentation of various conditions. Common causes include renal, cardiovascular, nutritional and hepatic diseases. Majority of children presenting with anasarca may have diagnosis referable to any of the systems mentioned. Occasionally in a child with anasarca there may be difficulty in diagnosis for which a systematic approach will help. The approach should include carefully taken history, clinical examination and basic investigations. An occasional child may require extensive investigation for the diagnosis.*

**Keywords:** *Anasarca, Edema, Hypoalbuminemia, Child.*

**Points to Remember**

- *Edema more in the morning and subsiding by evening is suggestive of renal edema.*
- *Ascites to start with, followed by edema may suggest a possibility of hepatic failure.*
- *Nutritional history combined with anthropometry, vitamin and mineral deficiency signs, points to the diagnosis of nutrition deficiency states like kwashiorkor.*
- *Edema in the dependent part associated with tachypnoea and abnormal findings in the heart suggest the diagnosis of cardiovascular conditions for anasarca.*

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<b>DRUG PROFILE</b>
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**MACROLIDES IN CHILDREN**\* **Jeesson C Unni**

**Abstract:** *Macrolides are useful and safe antibiotics for pediatric infections, especially if the child is allergic to penicillin and/or cephalosporin. They can be used to treat streptococcal pharyngitis, other respiratory tract infections, community-acquired pneumonia and cutaneous infections.*

**Keywords:** *Macrolides, Erythromycin, Azithromycin, Clarithromycin, Antibacterial spectrum, Indications, Dosage, Pharmacokinetics, Drug interactions, Adverse effects.*

**Points to Remember**

- *Macrolides are the safest group of antimicrobial drugs available.*
- *Erythromycin is a good alternative to penicillin in penicillin allergy in mild to moderate infections by susceptible organisms. Also useful in treating atypical pneumonia and neonatal C.trachomatis conjunctivitis. It eradicates B. pertussis from the nasopharynx (reduces period of infectivity but does not alter course of disease). GI side effects is a drawback.*
- *Clarithromycin is used in eradication regimens for H. pylori. Cost and palatability are drawbacks.*
- *Azithromycin is highly concentrated in tissues allowing short course therapy with once daily dosing.*
- *Newer macrolides are preferred to erythromycin in otitis media, sinusitis and non bacteremic pneumonia due to better H. influenza and M catarrhalis cover and atypical mycobacteria infections.*

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## DERMATOLOGY

**DRUG ERUPTIONS –  
AN OVERVIEW****\*Anandan V**

**Abstract:** *Adverse drug reaction is a common problem in clinical practice posing high degree of confusion in diagnosis and management. It may lead to fatal results if there is a delay in the initiation of the appropriate management. A proper knowledge about the various morphological patterns of drug eruptions and proper management will reduce the morbidity and mortality.*

**Keywords:** *Adverse drug reaction, AGEP, SJS, TEN.*

**Points to Remember**

- *Early diagnosis and management is rewarding.*
- *Steroids are life saving, especially in TEN.*
- *Supportive measures are a must.*

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<b>CASE STUDY</b>
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## **INCONTINENTIA PIGMENTI WITH MACROCEPHALY**

\* **Gopal Subramoniam**

\*\* **Prabhu Thanga Marthandan**

**Abstract :** *Incontinentia pigmenti (IP) is an X linked dominant disorder of skin which is often associated with ocular, dental and central nervous system abnormalities. Though life expectancy is normal, quality of life is dependent on the associated abnormalities.*

**Keywords :** *Incontinentia pigmenti.*

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