Heinz

In Touch

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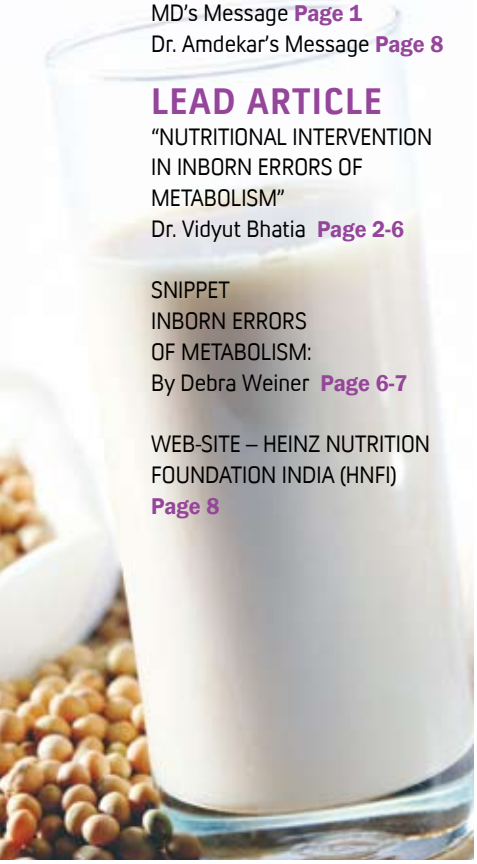
Contents



Inborn Errors of Metabolism

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CHAIRMAN & MANAGING DIRECTOR,
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In Touch is entering its fourteenth year of circulation and as designed, the newsletter has been offering its readers interesting articles of present day relevance, constantly. **In Touch** will continue to do so during the years to follow.

British physician, Archibald Garrod had published as early as 1923, a seminal text, based on his studies, 'Inborn Errors of Metabolism' (IEM). In the present day when an enormous number of diseases present themselves, where a wide range of systems get affected, the doctor might have to ponder whether it has any basis of a congenital metabolic disease. Commonly seen conditions like growth failure or failure to thrive (FTT) and weight loss, recurrent vomiting, diarrhoea, abdominal pain, or immunodeficiency disorders, it is believed are some of the potential manifestations of IEM. The incidence is, based on an article, 'Inborn Error of Metabolism – An Indian Perspective' which appeared in *International Journal of Human Genetics,* 2006 which focused on selected IEMs and highlighted those seen in the neonatal period, stated it as a total of 1.2 million out of 25 million births i.e. 4.8 per cent.

Dr. Vidyut Bhatia, Consultant Pediatric Gastroenterologist, Apollo Center for Advanced Pediatrics, New Delhi has dealt with this subject quite elaborately in this issue of **In Touch**. He has classified them under Inborn Errors of Carbohydrate Metabolism, Fat Metabolism and Amino Acid Metabolism. More importantly he has touched upon the diet recommendations, and apart from other things, medications to be avoided or controlled, while handling such patients.

In Touch is now available in a pdf format on our web-site **www.hnfi.org** for everyone to read.

"NUTRITIONAL INTERVENTION IN INBORN ERRORS OF METABOLISM"

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Individually all inborn errors of metabolism (IEM) are infrequent, but collectively they are numerous. Modern medicine has only just begun to understand this group of illnesses and they are now being diagnosed with increasing frequency. From a pathophysiological point of view, and depending upon the functions affected, the IEMs can be classified into three main groups.

GROUP I: This group includes those diseases in which the synthesis or catabolism of complex molecules is altered. These diseases have been classically defined as storage diseases. The symptoms are permanent, progressive and are not related to another disease process or food intake.

GROUP II: This group consists of diseases that provoke acute and progressive intoxication. In this group neurological symptoms predominate, followed by liver and muscle complications. Both the severity of the clinical symptoms and the age of onset depend upon the underlying genetic mutation and the percentage of residual enzymatic activity.

GROUP III: This group includes IEM where the symptoms are largely due to a deficiency in energy production or use. The clinical manifestations are compatible with generalized organ failure, liver involvement, hypotonia, growth failure and myopathy. These organs are the sites of major energy consumption. The clinical manifestations begin with a series of symptoms that include vomiting, fever, prolonged fasting and reduced oral intake. As a result the body uses alternative metabolic pathways that are not optimal. The child frequently presents various crises accompanied by these symptoms.

From a nutritional point of view, the diseases in Groups II and III are amenable to dietary and nutritional intervention. The majority of conditions in group I do not have any dietary treatment, although it is being used in some cases. In the following passages, the general nutritional principles for a group of IEMs is discussed along with therapies for specific IEMs.

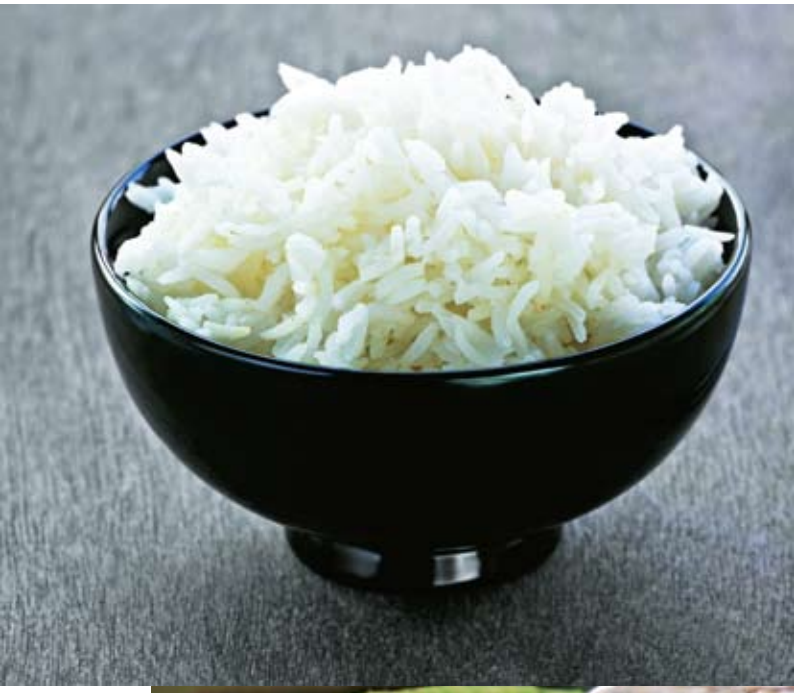
INBORN ERRORS OF CARBOHYDRATE METABOLISM

GLYCOGEN STORAGE DISEASES (GSD) are inherited metabolic disorders of glycogen metabolism. There are over 12 types and they are classified based on the enzyme deficiency and the affected tissue[2].

The principal treatment for this group of diseases is to maintain blood glucose levels at optimum levels, and most importantly, to prevent hypoglycemia[3]. The deficiency of the glucose-6 phosphatase activity causes GSD type I. Type 1 Infants usually require 8-9 mg/kg/min of glucose. During the day, it is advisable to feed every 2-3 hours. The same rate of feeding, every 2-3 hours, can be maintained at night (monitor blood sugar to advise frequency and use of formulas). Use of nasogastric feeding is cumbersome and requires motivated parents.

After four months of age, precooked starches (rice and

custard/sago) can be given in order to prolong gastric emptying. We generally reduce the frequency to intervals of three hours during the day and four hours during the night at an age of 6-12 months. The diet now should contain a composition of about 60-70 per cent carbohydrates, 10-15 per cent proteins and the rest, fats (20-30 per cent). Meals rich in complex carbohydrates



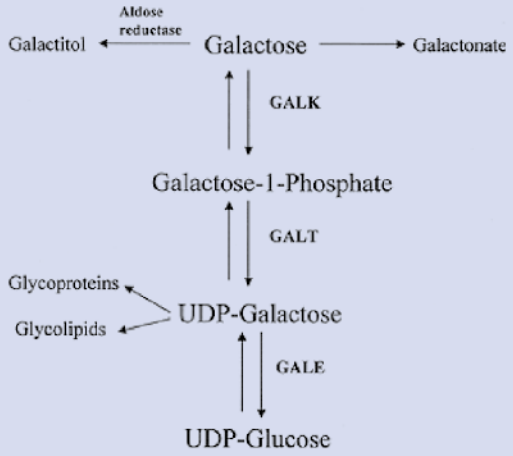
with slow or semi-slow absorption, such as rice, oats, *dal*, etc. are recommended. As this diet lacks micronutrients, vitamin and mineral supplements are added.

Raw corn starch/custard (custard is a good substitute for cornstarch) can be introduced safely after two years of age, as it is not digested (infants lack pancreatic alpha amylase) well before this age (it contains a high concentration of branched glucose chains that are slowly hydrolyzed and released, allowing blood glucose levels to be maintained at normal levels for 6-8 hours; it's better than formula). It can be used as supplement to the oral feeds during the day with nocturnal enteral feeding or it can be given every 4-6 hours around-the-clock without nocturnal feedings provided metabolism and growth are under control. The dose of cornstarch can range between 1.5 and 2.5 g/kg every 4-6 hours during or after meals. It should be prepared in cold water at a concentration of 1:2

(weight: volume). Unheated milk or yogurt may also be used. It should not be mixed with sugars that are rapidly absorbed. Rice or wheat do not have the same desired results. Adolescents and adults require a nocturnal glucose infusion rate of less than 3-4 mg/kg/min. A meal rich in starch (1.5 g/kg cornstarch) at bedtime can provide adequate levels and can substitute nasogastric feeding once pubertal growth has occured. Some authors recommend restricting the intake of saturated fat and increasing polyunsaturated fats to control hyperlipidemia.

Glycogen storage disease type III results from deficient glycogen debrancher enzyme activity[4]. Deficiency in the enzyme results in an excessive accumulation of abnormal glycogen, which is harmful for hepatocytes. For type III a restriction on the intake of lactose or sucrose is not necessary as galactose and fructose can be normally converted to glucose. There is some debate surrounding the treatment of these patients[5]. Some people recommend treatment similar to that used in glycogenosis type I, but since the tendency for hypoglycemia is less severe, the treatment is normally less challenging (during the day frequent meals rich in carbohydrates that are slowly absorbed along with one nocturnal enteral feeding or supplements of raw cornstarch). For a young patient, the daily dietary intake should consist of 50-55 per cent carbohydrates, 25 per cent proteins and 20-25 per cent fats. Protein intake should not be restricted as the amino acids serve as a substrate for gluconeogenesis. It is thought that proteins play an important role in the treatment of myopathic forms of glycogenosis III.

FIGURE 1 GALACTOSE METABOLISM PATHWAY



GALACTOSEMIA: Individuals with this disorder have deficiencies in the enzymes required for the metabolism of the sugar galactose6. Galactose is converted into glucose by the action of three enzymes, known as the Leloir pathway (Figure 1). Accordingly, there are 3 known types of Galactosemia; type 1 (classic), 2 (galactokinase) and 3 (epimerase)[6].

The treatment of this disease requires the total elimination of lactose from the diet for life. Milk (including breast milk) and its derivatives is the main source of lactose, but it is also present in diverse medications, manufactured products and a wide variety of commercial products[7, 8].

For newborns, correct treatment includes the use of a formula

that is completely free of lactose, preferably based on soy products[9]. The real challenge is to maintain a galactose-free diet after the introduction of complementary foods. This is due to the current difficulty in obtaining information concerning the content of free or bound galactose in foods, as this is not routinely indicated on the packages of foodstuffs available. Lactose is commonly found in the composition of many medications. This is generally indicated on the packaging and, in the case of doubt, it is relatively easy to obtain information from the manufacturer.

It has been shown that in children on a galactose free diet that is not specifically supplemented, adequate intake of calcium is not assured. For this reason, after the age of three, oral Ca++ supplements must be included in the diet[9].

Hereditary fructose intolerance (HFI) or fructosemia is an IEM caused by a deficiency of liver enzyme aldolase B that metabolises fructose[10]. Dietary treatment of hereditary fructose intolerance includes exclusion of fructose, sucrose and sorbitol from the diet(10). This elimination diet must be strictly followed for life. Even small quantities of fructose can be harmful, causing abdominal pain, vomiting and possible failure to thrive[11]. Natural fructose is found in honey (20-40 per cent), fruits, fruit juices (20-40 per cent), vegetables (1-2 per cent) and other plant foods[12]. Storage of food products also affects the sugar content. For example, newly harvested potatoes have a higher content of fructose than stored potatoes (0.6 g/100 g versus 0.25 g/100 g, respectively). Fructose is frequently used as a sweetener in foods and medications (Corn syrup). Many products for diabetics are sweetened with fructose or sorbitol. Sucrose is found in the diet as sugar, syrups (including those used in medications), toffees, desserts, soft drinks and as a natural ingredient of fruits (1-12 per cent), fruit juices and many plants and vegetables (1-6 per cent). Sorbitol used as a sweetener in diet foods is another source of fructose. The total daily intake of fructose from all sources should be 1-2 g, derived from free fructose, sucrose and sorbitol. Glucose can be used as an alternative to sugar and can also constitute a useful source of energy.

Cooked vegetables are recommended over raw because cooking results in the loss of free sugars. Sources of alternative carbohydrates to be included in the diet of these patients include glucose, lactose from milk and milk derivatives, and permitted starches[13].

It is important to supplement the diet with vitamins given that fruits are excluded from the diet. Sucrose, as well as fructose and sorbitol, are frequently used as excipients and coating for pills, as well as in syrups and suspensions for infants and children. Thus, the ingredients of all medications should be reviewed in detail before administrating the medication to the child. The introduction of any new food item must be closely controlled.

INBORN ERRORS OF FAT METABOLISM

Beta-oxidation of fats releases energy that is helpful in sustaining life during periods of fasting. Errors in the processing of fats (medium chain, long chain or very long chain) results in conditions that are life threatening. Treatment of these conditions is based on decreasing the dependency on this metabolic pathway. This is accomplished by avoiding fasting and controlling lipolysis by introducing a diet rich in slowly absorbed carbohydrates.

The diet should be characterized by frequent meals that contain starch and/or slowly absorbed carbohydrates to obtain a slow release of glucose and maintain the blood glucose at normal levels. In infants less than 6 months of age, nightly feedings are required to avoid periods of fasting longer than four hours. These can be gradually increased according to the individual tolerance of each patient and by monitoring blood glucose levels. Given that lipolysis increases as the period of fasting in prolonged, it is essential that a snack is taken during the night and that breakfast is not left out. The diet should be balanced to provide an intake of carbohydrates between 60-65 per cent, fats 30-35 per cent and proteins 10-20 per cent. Just as for glycogen storage disorders, at the age of two years, raw cornstarch can be introduced into the diet at a dose of 1-2 g/kg/day.

“The diet should be characterized by frequent meals that contain starch and/or slowly absorbed carbohydrates to obtain a slow release of glucose and maintain the blood glucose at normal levels”

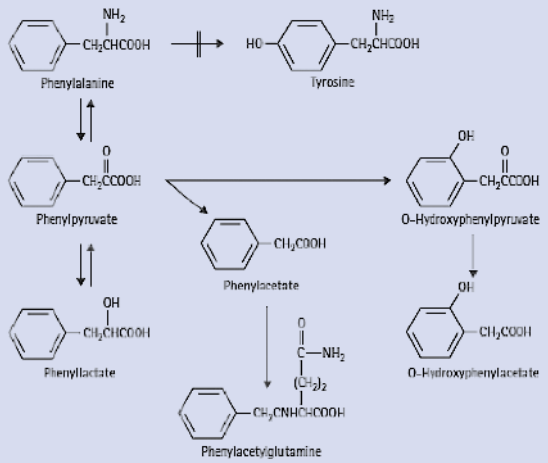
During situations of stress such as infections, fever or periods of prolonged physical exercise where there is a risk of hypoglycemia, an emergency regime should be introduced including frequent intake of fluids with high concentrations of sugar or glucose polymers. For cases of medium chain fatty acid disorders, foods rich in medium chain fatty acids, such as coconut and particularly coconut oil, and infant formulas rich in MCTs, must be avoided. In contrast, for long chain fatty acid disorders (LCFAD) when the intake of long chain fatty acids is limited to 40-60 per cent of the total fat intake, MCT oil should be incorporated into the diet in a proportion of 40- 60 per cent of the total fat intake (1-1.5 g/kg). MCT oils can be used for cooking in substitution of common oils or fats. They will provide an additional energy source, and improve the taste of the diet. However, they should always be introduced slowly into the patient’s diet.

Patients suffering from LCFA deficits are at risk of essential fatty acid (EFA) deficiency. It is necessary to monitor this. Although 1-2 per cent of the total fat intake is in the form of EFA, docosahexaenoic acid (DHA) levels may be low and may need to be supplemented in some cases.

SPECIAL DIETS IN INBORN ERRORS OF AMINO ACID METABOLISM

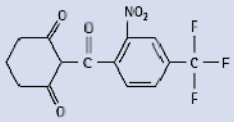
PHENYLKETONURIA: Phenylketonuria (PKU) is an autosomal, recessive, genetic disorder[14]. It is usually caused by a deficiency of the hepatic enzyme, phenylalanine hydroxylase. This is a mixed function oxidase which catalyses the hydroxylation of phenylalanine to tyrosine, the rate limiting step in phenylalanine catabolism (Figure 2). Deficiency of this enzyme leads to an accumulation of phenylalanine, resulting in hyperphenylalaninaemia and abnormalities in the metabolism of many compounds derived from aromatic amino acids. The enzyme deficiency varies from complete absence of detectable activity, up to a residual activity up to 25 per cent or more(14). The main treatment of PKU is a very limited intake of phenylalanine in diet, which is found in foods rich in protein. This diet has to be followed for life. Aspartame the sugar substitute is also to be avoided. The growth of the child has to be monitored. Special formulas are available that are meant for children with PKU that are low in phenylalanine and tyrosine. However, they are still not freely available in India. This provides all the remaining essential amino acids in appropriate proportions to the patient. A new drug called sapropterin (Kuvan) is available that increases the body's tolerance to phenylalanine. However, it is still experimental and not freely available[15, 16].

FIGURE 2 METABOLISM OF PHENYLALANINE.
The site of the defect in PKU is in phenylalanine hydroxylase. The compounds that accumulate as a consequence of the block are shown below.



TYROSINEMIA (See Figure 3): Elevated blood levels of the amino acid tyrosine characterize Tyrosinemia. Tyrosinemia is caused by the deficiency of one of the enzymes required for the multistep process that breaks down tyrosine[17]. If untreated, tyrosine and its byproducts build up in tissues and organs, which leads to serious medical problems. There are three types of tyrosinemia. Each has distinctive symptoms and is caused by the deficiency of a different enzyme. Type I tyrosinemia, the most severe form of this disorder, is caused by a shortage of the enzyme fumarylacetoacetate hydrolase. Dietary treatment of this disease includes a low intake of phenylalanine and tyrosine in order to maintain plasma tyrosine levels between 200-400 µmol/l (normal range 30-120 µmol/l) and phenylalanine between 30-70 µmol/l to minimize the formation of toxic metabolites. Proteins should be restricted with the intake of natural proteins between 0.5-1 g/kg/day, depending on the plasma levels of tyrosine and growth[18]. The remaining protein intake, in order to meet daily requirements, is in the form of protein supplements free of phenylalanine or tyrosine. In order to obtain an adequate energy intake and dietary variety, the same commercial products low in protein as those used in the phenylketonuria can be employed. Strict dietary treatment can prevent and repair renal tubular damage and improve growth, but does not prevent the progression of liver disease and the development of hepatocellular carcinoma.

FIGURE 3 NTBC, 2(2-NITRO-4 TRIFLUOROMETHYLBENZYOL)-1,3-CYCLOHEXANEDIONE.
NTBC (Nitisinone) is now being increasingly used for treatment of tyrosinemia type 1.



> "Strict dietary treatment can prevent and repair renal tubular damage and improve growth, but does not prevent the progression of liver disease and the development of hepatocellular carcinoma"

MAPLE SYRUP URINE DISEASE (MSUD) also called branched-chain ketoaciduria, is an autosomal recessive metabolic disorder affecting branched-chain amino acids. It is one type of organic acidemia. MSUD is caused by a deficiency of the branched-chain alpha-keto acid dehydrogenase complex (BCKDC), leading to a buildup of the branched-chain amino acids (leucine, isoleucine, and valine) and their toxic by-products in the blood and urine. In the acute phase of this disease, treatment must rapidly normalize BCAA levels, especially leucine, the most neurotoxic. This is followed by treatment that includes a diet to maintain adequate growth and development of the patient while avoiding a significant increase in BCAA levels18.

INDIVIDUAL ORGANIC ACIDURIAS (PROPIONIC ACIDEMIAS, ISOVALERIC ACIDEMIAS): General nutritional principals include to avoid de novo production of substrate and catabolism and to promote anabolism through increased nutritional intake of protein-free and energy dense products (glucose polymers with or without fats, plus electrolytes) for a maximum of 48 hours and preferentially by continuous enteral feeding (if not possible, by parenteral feeding). Proteins should then be introduced progressively beginning with a dose of 0.25-0.5 g/kg/day18.

UREA CYCLE DEFECTS:

The urea cycle involves a series of biochemical steps in which nitrogen, a waste product of protein metabolism, is removed from the blood and converted to urea. A urea cycle defect is a genetic disorder caused by a deficiency of one of the enzymes in the urea cycle, which is responsible for removing ammonia from the blood

stream[19]. Treatment for these disorders requires restriction of protein intake in order to reduce the need to excrete nitrogen. The protein tolerance depends on the degree of enzymatic deficit and the age of the child. The maximum protein tolerance should be determined (that which allows adequate growth without metabolic destabilization). After birth, the objective is to provide a protein intake of 1.5 g/kg/day beginning with quantities of 0.5-0.7 g/kg/day increased at the rate of no more than 10 per cent at a time gradually to avoid hyperammonemia[20]. The protein requirements of newborns change during the first months of life. After 6 months, the requirements per kilogram of bodyweight decrease. To confirm that adequate protein intake, clinical and biochemical parameters should be tested.

To conclude, while we wait for the possibility of gene therapy for these disorders, in most cases they are treated using dietary control. The interdisciplinary teams of pediatricians, geneticists and dietitians specialized in metabolism constitute the primary means of the diagnosis and treatment of these patients.

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SNIPPET

INBORN ERRORS OF METABOLISM

BY DEBRA WEINER IN MEDSCAPE REFERENCES

BACKGROUND

Inborn errors of metabolism (IEMs) individually are rare but collectively common. Its presentation is usually in the neonatal period or infancy but can occur at any time, even in adulthood. Diagnosis does not require extensive knowledge of biochemical pathways or individual metabolic diseases. An understanding of the major clinical manifestations of inborn errors of metabolism provides the basis for knowing when to consider the diagnosis. A high index of suspicion is most important in making the diagnosis.

For patients with suspected or known inborn errors of metabolism, successful emergency treatment depends on prompt institution of therapy aimed at metabolic stabilization. Asymptomatic neonates with newborn screening results positive for an inborn error of metabolism may require emergent evaluation including confirmatory testing, and as appropriate, initiation of disease-specific management.

PATHOPHYSIOLOGY

Single gene defects result in abnormalities in the synthesis or catabolism of proteins, carbohydrates, fats, or complex molecules. Most are due to a defect in an enzyme or transport protein, which results in a block in a metabolic pathway. Effects are due to toxic accumulations of substrates before the block, intermediates from alternative metabolic pathways, defects in energy production and use caused by a deficiency of products beyond the block, or a combination of these metabolic deviations. Nearly every metabolic disease has several forms that vary in age of onset, clinical severity, and, often, mode of inheritance.

Categories of inborn errors of metabolism, or IEMs, are as follows:

- Disorders that result in toxic accumulation
  - → Disorders of protein metabolism (eg. amino acidopathies, organic acidopathies, urea cycle defects)
  - → Disorders of carbohydrate intolerance
  - → Lysosomal storage disorders
- Disorders of energy production, utilization
  - → Fatty acid oxidation defects
  - → Disorders of carbohydrate utilization, production (ie, glycogen storage disorders, disorders of gluconeogenesis and glycogenolysis)
  - → Mitochondrial disorders
  - → Peroxisomal disorders

For more information, see eMedicine's articles in the Genetic and Metabolic Disease section of the eMedicine Pediatrics volume.

EPIDEMIOLOGY

Frequency

UNITED STATES

The incidence, collectively, is estimated to be approximately 1 in 4,000 live births. The frequencies for each individual inborn error of metabolism vary, but most are very rare. Of term infants who develop symptoms of sepsis without known risk factors, as many as 20 per cent may have an inborn error of metabolism.

INTERNATIONAL

The overall incidence and the frequency for individual diseases varies based on racial and ethnic composition of the population and on extent of screening programs.[1] Overall rates are in a range similar to that of the United States.

MORTALITY/MORBIDITY

Mortality can be very high for certain inborn errors of metabolism (IEMs), particularly those that present in neonates, but initial presentation of IEM even in adults may result in death. Prompt treatment of acute decompensation can be life-saving and is critical to optimizing outcome.

Inborn errors of metabolism (IEMs) can affect any organ system and usually affect multiple organ systems resulting in morbidity due to acute and/or chronic organ dysfunction.

Progression may be unrelenting with rapid life-threatening deterioration over hours, episodic with intermittent decompensations and asymptomatic intervals, or insidious with slow degeneration over decades.

RACE

The incidence within different racial and ethnic groups varies with predominance of certain inborn errors of metabolism (IEMs) within particular groups (eg, cystic fibrosis, 1 per 1,600 people of European descent; sickle cell anemia, 1 per 600 people of African descent; Tay-Sachs, 1 per 3,500 Ashkenazi Jews).

SEX

- The mode of inheritance determines the male-to-female ratio of affected individuals.
- Many inborn errors of metabolism (IEMs) have multiple forms that differ in their mode of inheritance.
- The male-to-female ratio is 1:1 for autosomal dominant and autosomal recessive transmission. It is also 1:1 for X-linked dominant if transmission is from mother to child.

AGE

Age for presentation of clinical symptoms varies for individual inborn errors of metabolism (IEM) and variant forms within the IEM. The timing of presentation depends on significant accumulation of toxic metabolites or on the deficiency of substrate.

- The onset and severity may be exacerbated by environmental factors such as diet and intercurrent illness.
- Disorders of protein or carbohydrate intolerance and disorders of energy production tend to present in the neonatal period or early infancy and tend to be unrelenting and rapidly progressive. Less severe variants of these diseases usually present later in infancy or childhood and tend to be episodic.
- Fatty acid oxidation defects, glycogen storage, and lysosomal storage disorders tend to present in infancy or childhood. Disorders manifested by subtle neurologic or psychiatric features often go undiagnosed until adulthood.

FROM: HTTP://EMEDICINE.MEDSCAPE.COM/ARTICLE/804757-OVERVIEW#SHOWALL

Courtesy: Dr. J. S. Pai

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DIET MODIFICATION – THERAPEUTIC APPROACH TO INBORN ERRORS OF METABOLISM

Inborn errors of metabolism are being increasingly recognized in childhood. They are progressive disorders with high mortality and morbidity with permanent sequalae. Many of them present acutely with involvement of brain, liver or muscles. Early diagnosis is imperative and suitable modification of diet is the only present form of treatment for most of these disorders. If employed in time, outcome is favorable though diet restrictions need to be followed for life. Gene therapy is a future hope. In this issue of **In Touch**, Dr. Vidyut Bhatia – Pediatric Gastroenterologist has discussed role of nutritional intervention in these disorders. It is most important because, much before future therapeutic options become available, simple diet modification will help to maintain quality of life in these patients.

WEBSITE – HEINZ NUTRITION FOUNDATION INDIA (HNFI)

Today various universities in USA are bending backwards to offer vast new learning opportunities for students around the world. These are free online courses from different universities referred as MOOCs (massively open online courses). Heinz Nutrition Foundation India is pleased to announce that it is doing its might in the field of nutrition by launching its website whose main purpose is "To advance the knowledge and practice of Nutrition with the goal of ensuring the nutritional well-being of the emerging generation" and in pursuit of offering free nutritional counselling for the needy.

The website can be accessed at **www.hnfi.org.** It provides users an introduction to the foundation and its members, details of the initiatives taken up and various publications issued by the foundation.

The website is available for anyone to access all the articles published by 'The Foundation' in the last thirteen years in the newsletter called **In Touch**. All the issues since inception are on the website in a pdf format. If anyone is interested in receiving the article immediately on publication through email, might do so by providing the email ID to the managing editor of **In Touch**.

The consultant nutritionists who manage "Free Nutrition Counselling and Consultation Clinics" would be contributing articles in the print media. These articles will be available on the website and can be accessed by any reader.

Heinz Nutrition Foundation India selectively funds nutrition research by institutions and there are plans to make available some of the research findings for public access in future.

Heinz Nutrition Foundation India selectively funds nutrition research by institutions and some of the research findings will be made available for public access. Going ahead we plan to make the proceedings of the symposia available on the web-site.

Heinz Nutrition Foundation India would be conducting scientific symposia on pressing nutritional problems where eminent and leading specialists in that area would be presenting papers. The proceedings of the symposia can be accessed from the web-site.

Lastly, Heinz Nutrition Foundation India is one who has pioneered personal free consultation centers called NutriLife Clinics in Chennai and Bengaluru. Leading Nutritionists will be providing free counselling on personal nutritional problems at the clinic on prior appointments. Their numbers and details can be had from the web-site. These nutritionists are also available to answer queries on the email.

Correspondence is welcome. Please write to: Heinz Nutrition Foundation India, D-Shiv Sagar Estate, 7th floor, Dr. Annie Besant road, Worli, Mumbai 400 018. Tel.: (022) 40085555 Fax: (022) 40085551 E-mail: p.jagannivas@in.hjheinz.com Website: www.hnfi.org

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