Editorial

Jaundice is one of the common medical conditions, particularly in preterm and breast-fed babies. It is categorized into hematologic, enzymatic/metabolic, infectious, and obstructive. Of these, obstructive jaundice, resulting from accumulation of conjugated bilirubin in the blood, is least common. This issue of Pediritz features a write-up, which discusses about the clinical features, pathology, pathophysiology, and complications of obstructive jaundice in infants, and biochemical/imaging tests and treatment options available for the same.

In this issue, we also feature an article that gives you an insight on pathophysiological basis of recurrent infections in children. Recurrent infections in children could occur due to internal factors such as immature immune defense system and defect in host defense mechanism and external factors such as microbial load and virulence of pathogenic microorganism. Septilin syrup and drops, phytopharmaceutical formulations of The Himalaya Drug Company, are indicated for the treatment and management of various infections, and to prevent their recurrence in children.

In addition to these, this issue also includes regular features such as “Difficult Case,” “Upcoming Events,” and “Picture Quiz.” We hope the articles in this issue are interesting and informative. For any suggestion/feedback/queries, write to us at pediritz@himalayahealthcare.com.

Happy reading!

– Editor
Obstructive Jaundice in Neonates

Jaundice is a common problem in neonates and occurs during the first week of life in approximately 60% of full term infants and up to 80% of preterm infants. However, obstructive jaundice, resulting from accumulation of conjugated bilirubin in the blood, is less common. Elevated levels of serum bilirubin (>2 mg/dL) causes jaundice and in neonates direct bilirubin of more than 10% of the total bilirubin is considered pathologic.

Clinical Features
Neonates with obstructive jaundice may have varying degrees of jaundice, and pass dark yellow colored urine and acholic stools. Other signs could manifest based on the underlying causes. It is very important to differentiate extrahepatic biliary atresia from neonatal hepatitis, and take prompt and early steps to prevent further liver damage in the neonate.

Pathophysiology
Unconjugated bilirubin undergoes conjugation in liver microsomes in the presence of the enzyme, uridine 5’-diphospho (UDP) glucuronyl transferase to form a more polar, lipid soluble, bilirubin glucuronide, which is the direct reacting bilirubin. Conjugated hyperbilirubinemia results from reduced secretion of conjugated bilirubin into bile or impaired flow of bile into intestine. Bile formation is sensitive to various hepatic insults including high levels of inflammatory cytokines, as in patients with septic shock. Although not neurotoxic, conjugated hyperbilirubinemia indicates severe liver and biliary disease or systemic illness. Jaundice that appears or persists beyond 2 weeks of age must raise a suspicion of obstructive jaundice and the conjugated bilirubin levels must be estimated.

The causes of obstructive jaundice may be intrahepatic or extrahepatic. Intrahepatic causes include hepatocyte and bile duct injury. Hepatocyte injury can occur due to viral infection, idiopathic neonatal hepatitis, familial cholestasis, and metabolic diseases such as galactosemia, α-1 antitrypsin deficiency, and cystic fibrosis. Bile duct injury may occur as a result of paucity of intrahepatic bile ducts and total parenteral nutrition (TPN). Extrahepatic causes include extrahepatic biliary duct atresia.

Pathology
The most common histopathological finding is the evidence of inflammation of liver cells or cells within the biliary tree. In conditions of intrahepatic injury, the hepatocytes get transformed into giant cells. If biliary tree is the primary site of insult, there is damage to the cells lining the biliary tract - cholangitis, which finally results in sclerosis and obliteration of the biliary tree.

In neonates, minor alterations in bile flow can result in severe disease manifestations. Neonatal hypoxia-ischemia can result in impaired secretion of bile, damage to biliary canaliculi, and alteration of bile ducts.

Investigations
Laboratory investigations aid in diagnosing underlying pathology of cholestasis in neonates. Some of the common laboratory tests include:

- Complete blood cell (CBC) count to screen for hemolysis
- Serum aminotransferase (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) assay
- Fractionated bilirubin alkaline phosphatase (ALP) assay (elevated level of ALP is diagnostic of
obstructive pathology)  
- Gamma-glutamyl transpeptidase (GGTP) assay (helps in differentiating a hepatic source from other causes of jaundice)  
- Serum albumin and coagulation profile (indicates severity of hepatic dysfunction)  
- Serologic screen for hepatitis, including hepatitis C virus (HCV) antibody and hepatitis B surface antigen (HBsAg) or antihepatitis B core antibody (antiHbc Ab)  
- Thyroxine and thyroid stimulating hormone levels (helps to rule out associated endocrinopathy)  
- Sweat chloride test (to exclude cystic fibrosis)

Imaging tests  
- Ultrasonography (USG): USG of the abdomen, a noninvasive and safe procedure in neonates, is capable of revealing liver architecture and biliary tree. It also helps to diagnose choledochal cyst. However, sometimes bowel gas shadows make proper visualization of the biliary architecture difficult. In these cases, further investigations may be required.  
- Magnetic resonance imaging (MRI): Abdominal MRI provides detailed imaging of the biliary tree, without exposure of the neonate to ionizing radiation. It can also be used for guided biopsy of the liver and biliary tree.  
- Endoscopic retrograde cholangiopancreatography (ERCP): This test helps in the investigation that clinches the diagnosis in cases of obstructive lesions in the liver and biliary tree.

Liver biopsy  
Liver tissue obtained by biopsy will help in differentiation between neonatal hepatitis and cholestasis.

Complications  
Certain complications may arise in long standing cases. Some of them include growth failure, malnutrition, pruritus, progressive fibrosis and cirrhosis, portal hypertension, ascites, esophageal varices, and hypersplenism.

Genetic disorders associated with cholestasis include:  
- Alagille syndrome: This syndrome is commonly associated with biliary atresia. Characteristic facies include a broad forehead; deep set, widely spaced eyes; and long straight nose. Cardiovascular system abnormalities such as pulmonic stenosis, Fallot’s tetralogy, vertebral anomalies, and tubulointerstitial nephropathy may occur.  
- Zellweger syndrome or cerebrohepatorenal syndrome: It is a rare, autosomal recessive disorder. Associated features include abnormal head shape, unusual facies, severe generalized hypotonia, hepatomegaly, and renal cortical cysts. Zellweger syndrome is usually fatal and death occurs within 6 to 12 months.  
- Aagenaes syndrome: It causes intermittent cholestasis and is associated with lymphedema of the lower extremities.  
- Neonatal iron storage disease: This is an autosomal recessive disorder, which is rapidly progressive and associated with increased iron deposition in the liver, heart, endocrine glands, and reticuloendothelial system. Familial cases can occur but prognosis is poor.  
- Defective bile acid synthesis: Lack of normal bile acids results in accumulation of primitive hepatotoxic metabolites resulting in liver injury. Early diagnosis will enable replacement of the targeted bile acids which could reverse the damage.

Treatment  
Treatment of neonatal cholestasis depends on its underlying cause. It is important to differentiate between neonatal hepatitis and biliary atresia, as these are commonly found causes in neonates.

Medical management  
Medical management is empirical and is aimed at correction of deficiencies that result from bile acid abnormalities. Malnutrition is a common concern and needs replacement of medium chain triglycerides. Micronutrient deficiency of calcium, zinc, or phosphate requires supplementation. Fat soluble vitamins may be deficient and need to be replaced with daily

Himalaya Moisturizing Baby Soap
To Keep baby’s skin clean, soft, and moisturized...
recommended dietary allowance (RDA) doses. Water soluble vitamins need to be supplemented in doses of double the RDA requirements.

**Surgical management**

Early diagnosis of biliary atresia, before the occurrence of significant loss of biliary tree, will result in a better prognosis. The procedure of choice is Kasai’s procedure or hepatopancreaticoenterostomy. The transected porta hepatitis, which could have remnants of viable bile ductules, is anastomosed to the bowel. Bile drainage normally starts within first few months after surgery, in which case functions of the liver will be maintained. In case there is no bile drainage, it results in irreversible damage and cirrhosis of the liver. Hence, it is ideal to perform the procedure early, as Kasai procedure performed within 8 weeks of postnatal life ensures the best prognosis. In case there is no improvement following the surgical procedure, liver transplantation may be considered as a treatment option.

**Efficacy of Liv.52 in Viral Hepatitis**

The course of viral hepatitis in children is usually mild but can lead to posthepatic cirrhosis, chronic cholestasis, subacute necrosis, and hepatic failure. The chances of such complications are high in India, as malnutrition is rampant.

A study was conducted by Chawhan RN, et al (The Medicine and Surgery) on 130 children with viral hepatitis. The ages of these children ranged from 5 months to 12 years; the highest incidence was in the age group of 4 to 7 years and majority of them (65%) belonged to poor socioeconomic group. A detailed clinical history of these patients was recorded, and physical examination and routine laboratory investigations such as complete blood picture; urinalysis for bile salts, bile pigments, and urobilinogen; and liver function tests including serum bilirubin and serum transaminases analysis were done.

Majority of cases were treated with Liv.52 at a dose of 2 teaspoonfuls twice a day up to 2 years of age, 2 teaspoonfuls thrice a day from 2 to 10 years of age, and 2 tablets thrice a day to cases between 10 and 12 years. It was noted that jaundice lasted for <10 days prior to admission in 50% of cases and mortality rate was 3.8%. Complete biochemical recovery took 8 to 10 weeks in majority of the cases. No untoward side effects were observed even on prolonged administration of Liv.52, which makes it a safe and effective drug in the management of viral hepatitis in children.

**Facts About Liver**

- Every minute, human liver filters about 1.4 liters of blood. All blood runs through liver, which filters out different toxins, including chemicals, alcohol, and drugs.
- The Greeks considered the liver as the seat of inner emotions. They viewed it as the organ in closest contact with divinity.
- The liver is the main site of red blood cell production in the first trimester fetus but by the 32nd week of gestation, the bone marrow almost completely takes over this task.
Resistance to infection is dependent on several specific and nonspecific defense mechanisms. A defect in any of these may lead to recurrent infections. Any infection will depend on a combination of factors and most important among them are exposure to a microorganism; host defenses; microbial load; and virulence of the microorganism.

**Exposure to Infection**

Children with increased exposure to pathogens are subject to an increased frequency of infection. Thus, children of preschool age with siblings in school or children during the first year in day care or school are at greater risk of infection with viruses, especially *Hemophilus influenzae*.

**Defects in Host Defense Mechanisms**

**Anatomical defects**

Defects in the skin as in epidermolysis bullosa; stasis of secretions or increased secretion of mucus as in asthma and cystic fibrosis; stagnant urine due to anatomical blockages; blocked parotid duct; recurrent aspirations due to tracheoesophageal fistula; and reflux and repeated infections of abnormal lobes of lung are some of the factors that can lead to recurrent infections. Recurrent infection of the lower respiratory tract is the commonest among recurrent infections.

**Immunologic defects**

Defects in host immune defenses (discussed below) would result in vulnerability to opportunistic infections.

**Neutrophils**

Persistent neutropenia tends to present with relatively mild infections such as recurrent skin sepsis, oral ulceration, otitis media, and rarely deep-seated abscesses. In conditions such as chronic granulomatous disease, neutrophils are unable to generate superoxide anions required to kill phagocytosed organisms. These patients are susceptible to recurrent infections with catalase-positive organisms. They usually present with suppurative cervical lymphadenitis, lung abscesses, skin sepsis, hepatomegaly, and splenomegaly.

**Antibodies**

Normal antibody production depends upon differentiation of primitive stem cells into B-lymphocytes and plasma cells. Antibody is of particular importance in opsonizing encapsulated bacteria; thus antibody deficiency is typically associated with infection by these organisms. Isolated antibody deficiency syndromes may be present from birth in boys with X-linked hypogammaglobulinemia, or may develop in either sex during childhood. Affected children recover normally from viral infections with the exception of enteroviruses. Recurrent otitis media and recurrent pneumonia are the commonest presentations. Deep-seated infections such as meningitis or osteomyelitis caused by pyogenic organism are also common.

**Immunoglobulins**

Isolated IgM deficiency, which is extremely rare may present with recurrent pyogenic infection such as bacterial meningitis. Secretory IgA which lines mucosal surfaces is important in preventing adherence of pathogens to the respiratory and gastrointestinal
Defective cell-mediated immunity may be indicated by lymphopenia (<1.5 x 10⁹ lymphocytes/L), but can be present despite a normal lymphocyte count. An acquired defect occurs in the acquired immune deficiency syndrome (AIDS) due to infection of helper T lymphocytes by a retrovirus, the human immunodeficiency virus (HIV).

Severe combined immunodeficiency (SCID) is a rare autosomal recessive condition, in which defects of both T and B lymphocyte functions result in susceptibility to overwhelming bacterial and viral infections. Children present with chronic diarrhea, usually with persistent excretion of rotavirus, failure to thrive, and severe sepsis in the first year of life. Thymic shadow in chest x-ray and tonsillar tissue are absent.

**Complement**

Complement may be activated via the classical pathway, wherein antigen-antibody complexes activate the components in the sequence C142356789, or via the alternate pathway when the activator acts on properdin and then complement in the order C356789. Complement is responsible for cell lysis, opsonization, and for generating chemotactic factors. Defects in components 3, 5, 6, 7, 8, or 9 will affect both pathways.

Defects in alternate pathway are associated with recurrent respiratory tract infections and recurrent diarrhea. Defects in classical pathway may present with recurrent pyogenic infections. In particular, absence in one of the terminal components leads to typical presentation of recurrent neisserial infections, either meningococcal or gonococcal.

Understanding the pathophysiological basis of recurrent infections and defects responsible for these infections will help in systematic investigation and management of rare and complex disorders.
Septilin in the Management of Persistent Low-grade Infections in Children

Certain factors such as malnutrition and poor environmental conditions are known to impair body's defense mechanism and make it susceptible to infection. Several herbal preparations are reputed to stimulate and improve body's immune and defense mechanisms to infection.

A placebo-controlled trial was conducted by Koti ST (Probe) to study the efficacy of Septilin in persistent low-grade infections in school children. A total of 225 children aged between 5 and 11 years, with persistent upper respiratory tract infection (URTI) and ear, nose, and throat (ENT) infections were considered for the study. Persistent low-grade infection was confirmed in 42 children during observation period of 1 month (Table 1). These children were divided into group A and group B of 21 children each. Group A was given Septilin at a dose of 1 tablespoon twice a day for 3 months and group B was given placebo.

Results of the study suggested that Septilin is a useful remedy in persistent URTI and ENT infections. Significant improvement was observed in patients belonging to group A with tonsillitis, pharyngitis, sinusitis, otitis media, and impacted wax. In the placebo group, no significant change was observed either symptomatically or clinically and the infection persisted.

| Table 1. Break-up of persistent URTI and ENT infections and therapy groups |
|---------------------------------|-----------------|-----------------|
|                                 | No. of cases    | Group A (Septilin) | Group B (Placebo) |
| Chronic tonsillitis             | 22              | 11              | 11              |
| Chronic pharyngitis             | 5               | 3               | 2               |
| Chronic laryngitis              | 2               | 1               | 1               |
| Chronic sinusitis               | 7               | 3               | 4               |
| Impacted wax leading to infections of the auditory canal | 3 | 2 | 1 | |
| Chronic suppurative otitis media (CSOM) | 3 | 1 | 2 | |
| Total                           | 42              | 21              | 21              |

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Difficult Case

A 14-year-old boy had visited an outpatient clinic for routine follow-up of a seizure disorder. He was accompanied by his brother and mother (who also visited the clinic to consult for pacemaker related problem). The patient seemed to be healthy and had no abnormalities on examination. He had a history of collapsing on several separate occasions at school (2 episodes occurred during assembly and the other 2 during physical activity) and is on anticonvulsant (carbamazepine) therapy since 4 years. No tonic-clonic movements or incontinence ever occurred, but he had appeared to be very pale for 1 to 2 minutes before recovery. Three more similar attacks occurred later. Two electroencephalograms (EEG) and a cerebral computed tomography scan were done which showed normal results.

The patient’s family history revealed significant information that out of 9 children in the family, 3 children (patient’s siblings) were diagnosed as epileptic, of whom 2 died in their teens during attacks, one on a football field. The patient’s query was whether he would need to continue the therapy.

Questions
1) Does the patient need anticonvulsant therapy?
2) Should he be investigated further?

Answer

Further investigations are necessary to take a decision regarding continuation of the therapy.

Discussion

There are many questionable points in the patient’s history. In such cases one must be cautious and try to emphasize on 2 factors in the management of a seizure disorder: 1) Indication of anticonvulsants when there is no clear evidence of a seizure disorder; 2) Avoidance of anticonvulsants when there is no clear etiology of a seizure disorder. Patient’s history is crucial in such cases and do emphasize on 2 factors in the clinical approach. The patient’s diagnosis of epilepsy is not clear and other possibilities should be considered. The episodes described more closely resemble syncope attacks than episodes described more closely resemble syncopal attacks. Familial occurrence of epilepsy is not unusual either. There is a family history of epilepsy and the patient appears to be very unusual. There are many questionable points in the patient’s history.

Upcoming Events

Event: 4th International Workshop on HIV Pediatrics
Date: July 20 to 21, 2012
Venue: Washington DC, USA

Event: Pediatrics Review
Date: August 25 to September 1, 2012
Venue: Seattle, Washington, USA

Event: International Congress on Pediatric Airway
Date: September 8 to 9, 2012
Venue: Chennai, Tamil Nadu, India

Event: 2nd International Conference on Pediatrics & Gynecology
Date: September 24 to 26, 2012
Venue: Hyderabad, Andhra Pradesh, India

Event: 23rd Congress of the Asian Association of Pediatric Surgeons
Date: October 8 to 10, 2012
Venue: Seoul, Korea (South)

Event: Pediatrics
Date: October 12 to 22, 2012
Venue: Amsterdam, Norway
Murphy’s Laws at Work

A pat on the back is only a few centimeters from a kick in the pants.

Don’t be irreplaceable, if you can’t be replaced, you can’t be promoted.

Never ask two questions in a business letter. The reply will discuss the one you are least interested in, and say nothing about the other.

You are always doing something marginal when the boss drops by your desk.

There is never enough time to do it right the first time, but there is always enough time to do it over.

Machines that have broken down will work perfectly when the repairman arrives.

... 

A serious drunk walked into a bar and, after staring for some time at the only woman seated at the bar, walked over to her and kissed her. She jumped up and slapped him silly. He immediately apologized and explained, “I’m sorry. I thought you were my wife. You look exactly like her.”

“Why you worthless, insufferable, wretched, no good drunk!” she screamed.

“Funny,” he muttered, “You even sound exactly like her.”

... 

Son: I can’t go to school today.
Father: Why not?
Son: I don’t feel well.
Father: Where don’t you feel well?
Son: In school!

... 

Funny warning signs placed on all alcohol bottles to tip off drinkers about the possible peril of drinking a pint or two of any alcoholic beverage.

1. Consumption of alcohol may cause you to wake up with a breath that could knock a buzzard off a wreaking dead animal that is one hundred yards away.

2. Consumption of alcohol is a major factor in dancing like an idiot.

3. Consumption of alcohol may cause you to tell the same boring story over and over again until your friends want to assault you.

4. Consumption of alcohol may cause you to thay shings like thish.

5. Consumption of alcohol may cause you to tell the boss what you really think of him.

... 

Teacher: Why were you late?
Student: Sorry, teacher, I overslept.
Teacher: You mean you need to sleep at home too!

...
Skin Diseases in Newborns

A newborn baby can manifest skin conditions in various forms. These conditions could be considered as variations from the normal rather than as an abnormality. The salient features of some of the common skin conditions are described below.

**Mongolian Spots**
Mongolian spots are benign pigmented birthmarks typically seen in Africans, Asians, Hispanics, and Native Americans. It is due to melanocytes that are trapped deep within the layers of the skin. The spots are bluish green in color and are typically seen in lumbosacral area and buttocks. Most lesions fade by 2 years, and completely disappear by 7 to 13 years. They rarely persist for life. These spots must be documented in order to avoid misdiagnosis of abuse.

**Erythema Toxicum Neonatorum**
Erythema toxicum neonatorum (ETN) is one of the most common skin lesions often seen in full-term infants. They begin as erythematous macules or papules. Pustules may also develop later, surrounded by erythema.

The lesions usually appear on face, trunk, arms, and legs but spare palms and soles. There is no internal organ involvement. ETN occurs in 30% to 70% of newborns. It is seen usually at 24 hours to 2 weeks of age, and then the lesions fade away. ETN may recur in the first few weeks of life and usually does not require any active management as it resolves spontaneously.

**Milia**
Milia are benign skin lesions noted in newborn babies. They are superficial inclusion cysts that occur due to retention of keratin and are seen in 40% to 50% of newborns. Milia appear as whitish papules (1 mm–2 mm in size) most often on the face (including forehead, cheeks, nose, and chin), upper trunk, extremities, and penis. They might sometimes appear on oral mucosa in which case they are called Epstein’s pearls. No active management is required as they resolve spontaneously in the first few months.

**Miliaria (Miliaria Crystallina and Miliaria Rubra)**
Miliaria is a benign condition in which sweat accumulates in vesicles below the stratum corneum layer of the skin due to partial obstruction of eccrine glands. The vesicles are 1 mm to 2 mm in size and are seen on the head, neck, and trunk without any surrounding erythema. The vesicles rupture, desquamate, and resolve within a few days. These lesions are referred to as miliaria crystallina.

Sometimes sweat infiltrates deeper below the epidermis, with inflammation and sweat duct obstruction. In such cases, there may be pruritic erythematous papules and vesicles. This is termed as miliaria rubra. Management would include avoidance of over dressing and exposure to cooler environment.

**Neonatal Acne**
Acne is seen in about 20% of neonates when maternal androgenic hormones stimulate sebaceous glands. Lesions appear over the forehead, nose, and cheeks. Acne resolves without scarring when the maternal
hormone level wanes after 3 to 4 months. As there is spontaneous resolution, no treatment is required. Soaps with low pH can be used.

Harlequin Color Change

This is a normal newborn skin color change in response to change of position with dependent erythema. It happens in 10% of newborns within first few weeks of life due to an immature hypothalamus with inconsistent regulation of peripheral vessels. When a baby is lying down facing to a side, the dependent side turns deep red and the opposite side pale. This condition resolves spontaneously and no intervention is required.

Cradle Cap

Cradle cap, also called seborrheic dermatitis, is an inflammatory skin condition in which whitish to yellowish scales or flakes occur on skin, especially scalp. It occurs due to excessive oily secretions from sebaceous glands on the scalp. This condition can sometimes be complicated by fungal infection, especially malassezia.

Seborrheic dermatitis is not contagious, nor is it due to poor hygiene. It may persist for the first 2 to 3 years of life and may or may not cause itching. The best way to deal with seborrheic dermatitis is to gently massage the baby's scalp with or without oil, and wash with a mild shampoo suitable for babies. Brushing the scalp with a wide toothed soft brush may help to get rid of the scales.

Common Rashes in Neonates

Dermatological diseases in neonates are commonly benign and self-limiting, but they may also herald underlying systemic disease and can be life-threatening. Functionally, neonatal skin is predisposed to greater heat and fluid loss as well as drug and toxin absorption. Structurally, its immaturity often results in understated, atypical, and ambiguous skin symptoms and signs. Common morphologies of neonatal skin diseases include pustules; vesicles and bullae; dry, red, and scaly skin; and, less commonly, ecchymoses and crusts. Although many common dermatoses are transient reactions to hormonal and environmental factors such as heat and trauma, infection by bacteria, viruses, and fungi can cause both morbidity and mortality. Neoplastic, genetic, metabolic, and nutritional diseases are less common but important to diagnose. Clinical and laboratory findings can be limited and clinicopathological correlation is critical.

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