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Polio Eradication - Now and Further

India introduced the oral polio vaccine in 1985 in the Universal Immunisation Programme. At that time over 200,000 cases of polio were reported annually which is as per estimates of the Indian Academy of Pediatrics. In 1995, the first national polio immunization campaign was held in India. Since then two national and multiple sub-national campaigns are rolled out every year for children up to 5 years of age.

In each national polio campaign about 2.3 million vaccinators, led by 155,000 supervisors, visit 209 million households to immunize 170 million children up to the age of 5 years. The magnitude of the program is unparalleled and perhaps the largest public health program in the world. Further, to immunize children on the move, transit vaccinators are positioned at bus stands, train stations, on trains, market places and important road intersections. Nearly 10 million children are immunized by the transit teams in each polio campaign, of them 100,000 on trains. Vaccination centres are also there along the international border of the country. Focusing on the migrant population, the people on the move in search of livelihood who miss polio immunization in view of their transient nature, the programme covers 70,000 brick kilns and 38,000 construction sites. Nearly 4.5 million children are immunized in the high-risk migrant settlements in each polio campaign.

Since the start of the polio campaigns in 1995, as many as 131 polio campaigns have been held in India till date, in which 12.1 billion doses of polio vaccines have been administered.

Many global health experts expected India to be the last country to eradicate polio because of its high birth rate, densely packed population and poor sanitation. But meticulous planning and sustained effort has helped India to be free of wild poliovirus cases over the last 3 years. Much of the country’s terrain was difficult to traverse and pockets of the population resisted vaccination.

In 2009, India took a gamble and switched to the bivalent OPV (P1 and P3) vaccine. The basis of this switchover is the fact that P2 hasn’t been seen anywhere in the world since 1999, and research studies found that babies who were given only OPV1 and OPV3 had higher antibody levels against those strains than babies who got trivalent vaccine. Based on this evidence, India started distributing a bivalent vaccine that excluded P2. It was the first country to scale up the research.
The coalition of global health leaders, including WHO, UNICEF, the US Centers for Disease Control and Prevention and private funders, gathered in 2013 to craft an updated global strategy to end polio under the banner of the Global Polio Eradication Initiative. They referenced India's success and included a goal to switch to the bivalent vaccine by 2016. The coalition's plan aims to end polio by 2018.

**Overcoming community resistance**

Widespread coverage is the most important issue for successful polio campaign. In Pakistan and Afghanistan, research suggests that despite the switch to the bivalent vaccine, low coverage due to social resistance and armed conflict have not declined as quickly as expected. In the last year alone, more than a dozen polio workers have been killed in Pakistan, where Taliban militants have declared polio vaccination campaigns a front for Western espionage.

Some Nigerian Muslim leaders have spoken out against polio vaccinations as well, claiming they cause infertility. Many parents in the populous African country don’t trust western immunization workers because of lingering anti-colonial sentiment.

All three countries are now piloting a program first developed in 2001 to address social resistance in India. Under the social mobilization effort, India hired more than 8,000 community members to go door to door to talk with parents about their vaccine reservations and attempt to resolve their concerns.

In the Indian state of Uttar Pradesh, for example, health leaders in 2007 observed that 70 percent of polio cases were Muslim children, so they organized a committee of religious scholars to speak to community members about the benefits of the vaccine. Within a year, the percentage had dropped to 37. Now, the Muslim scholars who helped to eradicate polio in India are volunteering their time in Pakistan.

**Devising a plan to reach every child**

While the effective bivalent vaccine and increased community cooperation have helped reduce polio, inoculating millions of children is still logistically complex.

India developed micro maps, breaking regions down by neighborhood, by street, by house. The goal was to make sure no child fell through the cracks. The government employed global positioning system and geographic information system technology to track mobile populations.

**End game**

Using OPV after WPV eradication is unethical and counterproductive. If continued then cVDPV will get the threshold in place of WPV. But at the same time it is not prudent to discontinue OPV suddenly. If OPV is discontinued, VAPP will no longer occur. But the immunity gap will increase under such circumstances. This will allow
pre-existing silent transmission of VDPV to expand rapidly and replace WPV that were eliminated. In actual sense the end game of polio eradication is the risk management of the aftermath of OPV use on WPV eradication.

It is to be noted that in the last decade about 1000 VDPV-2 cases have been detected in the world where as there has been no case of WPV-2. The majority were cVDPV and about 85% were due to Sabin type 2 virus. In order to halt dissemination of VDPV-2, it is imperative that Sabin type 2 has to be discontinued. Thus bOPV has to be used in place of tOPV globally in a synchronized manner. Again in order to pre-empt new VDPVs from emerging, type 2 immunity has to be augmented and sustained. This can be achieved by using IPV.

Thus the sequence of end game strategy is to introduce IPV and achieve high coverage, which can be done by routine national immunization and campaigns. Subsequently withdraw tOPV and use bOPV only. Once global eradication of WPV 1 and 3 are achieved, then bOPV also should be withdrawn. Thereafter only IPV will be used.

**IPV for the future**

A fourth generation IPV is in the process of preparation. It uses the Sabin virus strains instead of WPV. The main advantage is the safety at the manufacturing site. This will negate any possible leak of WPV from laboratory and leak of Sabin virus will be less serious and easy to stop. Sabin-IPV is licensed only in Japan.

**Further reading**


Secretory otitis media, otitis media with effusion (OME) or glue ear is a chronic inflammatory condition of middle ear. It is the most common cause of preventable conductive deafness among children. Young children between 3 and 7 years old are most commonly affected. Boys are more affected than girls.

OME is characterized by the presence of an effusion, glue-like fluid behind an intact tympanic membrane in the absence of signs and symptoms of acute inflammation. Histologically it is a chronic inflammatory condition, characterized by inflammation in the middle ear mucosa, overproduction of mucin which is more viscous with higher frictional adhesion and poorly transportable by cilia. Although there is no signs of inflammation, a bacterial pathogen is identified in the middle ear fluid in approximately one in three children with OME.

Young children are more prone to OME due to an anatomical predisposition. The eustachian tube is shorter, more flexible, and horizontal. Nasopharyngeal pathogens can easily enter the middle ear. As the eustachian tube matures by 7 years old; the incidence declines after this age. Reflux of gastroesophageal acid can also contribute to eustachian tube dysfunction and subsequent OM. Genetic factors influencing host immune response also play a role.

It has been seen that OME is more common in certain populations than the others. The risk is high in some cases such as age <5 years old, male sex, white ethnicity, low birth weight (<2.5 kg), premature birth (<37 weeks gestation). Other factors include pacifier use, lack of breastfeeding, day care attendance, number of siblings, lower socioeconomic groups, family history of ear infections, and prenatal/postnatal exposure to cigarette smoke. More recently, atopy and specific gene abnormalities have also been implicated as host risk factors for OM.

Over the last few years it has become recognized that bacterial biofilms are important in the etiology of OME. Chronic biofilm colonization of the adenoids may act as a reservoir for bacteria entering the middle ear cleft in OM. Children with OME exhibited lower levels of inducible NO-synthases (iNOS) than controls without middle ear disease. iNOS plays an important role in regulating the production of nitric oxide (NO) which is a key mediator in the local immune response of human airways. OME may occur as a consequence of AOM taking an extended period of time to resolve; e.g., weeks or months. Though OME is a disease without signs and symptoms of acute inflammation, bacteria has been isolated from the effusion. Stol K et al. showed that the occurrence of bacterial and viral pathogens in middle ear fluids did not significantly differ between patients suffering from recurrent AOM and
Chronic OME.

Chronic OM with effusion (persisting = 3 months) is 40–70% heritable. Several regions of linkage on chromosome 3p25, 10q22, 10q26, 17q12, and 19q13 have been identified by two genome-wide linkage scans, which appear to harbor susceptibility loci. In a study by Heilsinki Hafren L et al., showed a moderately strong and statistically significant genetic component for chronic otitis media with effusion. They concluded that the role of genetic factors in OME need to be explored.

OME may occur as a residual effect of AOM, or there may be no preceding history. There is no signs and symptoms of acute inflammation. The child presents with history of ear heaviness or mild pain. The fluid collected in the middle ear dampens the vibrations of the eardrum and ossicles made by the sound waves. The cochlea receives dampened vibrations and so the volume of the hearing is turned down. They have difficulty understanding people if the voice is low or in noisy background and become easily distracted and irritable. There may be problems with communication, learning and social skills which usually resolve once hearing is restored to normal. A study was done by Gouma P to investigate the behavioral trends of children with OME based on the Achenbach test by application of the Child Behavior Checklist questionnaire (CBCL). Patients suffering from OME had more anxiety/depression related disorders and attention disorders as compared with the control group.

Less common symptoms of glue ear include episodes of mild ear pain, irritability, sleep disturbances, tinnitus, clumsiness and poor balance. Otoscopy is vital in making the diagnosis, with sensitivity and specificity quoted at 90% and 80%, respectively. Pneumatic otoscopy gives more specific diagnosis. The clinical findings include abnormal color (eg, yellow/amber/blue), retracted tympanic membrane, and air-fluid levels. Audiogram (typically showing mild conductive hearing loss) and tympanogram (showing an immobile ear drum or negative middle ear pressure). Tympanometry has proved to be a valid method for diagnosis of the OME and it has a good clinical value as a predictor factor for the length of the appropriate treatment of the OME.

In most of the cases OME do not require treatment due to high rates of spontaneous resolution, but if it is bilateral and persistent for more than 3 months, the chances of natural resolution are much lower and treatment may be beneficial. The child should be observed for 3-months with serial audiometry. Then if hearing loss is still there and/or a child’s development is affected treatment should be started. Guidelines recommend either surgery with ventilation tubes (grommet) or hearing aids. Grommet insertion is associated with a number of risks, which include purulent otorrhea (10%–26%), myringosclerosis (39%–65%), retraction pockets (21%), and persistent tympanic membrane perforations (3%, although with longer-stay T-tubes, up to 24%). In addition, once tubes extrude and OME returns the child might need a second set of ventilation tubes. Adenoidectomy might be helpful if there is history of frequent or persistent upper respiratory tract infections. Yousaf M et al. suggested that all children with OME should be treated conservatively. It is cost effective and relieves symptoms in about 70% of patients. The ears with OME that fails to resolve or recur should
be managed with myringotomy and VT insertion or adenoidecotomy. On the other hand Hall AJ showed that early surgery for the child severely affected by OME may be associated with subtle benefits but the study size was very small to comment. Numerous other treatments for OME have been trialled, including antibiotics, antihistamines, and steroids, but are not currently recommended.

Mc Coul ED showed that children with otitis media with effusion and gastroesophageal reflux disease have improved quality of life following treatment with antireflux therapy. Control of gastroesophageal reflux may play a role in the management of otitis media and avoidance of tympanostomy.

**New development in management**

**Vaccine:**

Pneumococcal vaccine played an important role in reducing the incidence of otitis media. Despite promising results, concerns exist over the long-term benefit from vaccination. More research is needed.

**Biofilm and new drug delivery system:**

A therapeutic problem is the involvement of biofilms in OME. The biofilm causes persistent inflammation through a variety of mechanisms. The high rate of OME reoccurrence, (20%–25% after ventilation tube removal) This could also be explained by biofilm persistence because ventilation tubes remove the effusion but not always treat the underlying biofilm. The understanding the role of biofilm in the pathogenesis of OME opens up the potential for new treatment strategies based on biofilm eradication, including novel methods of delivering antibiotics to the site of infection.

Biofilm eradication typically requires 10–1,000 times higher antibiotic levels and the high levels of antibiotics is difficult to safely achieve systemically. Local drug administration can be tried. There are two strategies, transtympanic and intratympanic delivery. An alternative is delivery of drugs directly to the middle ear, which would allow a much greater amount of drug to reach the intended site of action. Potentially, the middle ear or the inner ear may be affected on hearing and/ or balance. Thus, comprehensive toxicity testing is warranted before clinical application.

A variety of different methods have been proposed, including drug delivery gels and antibiotic pellets. Antibiotic pellets can release antibiotics for up to 21 days and are able to eradicate biofilms in an in vitro model. Use of modified-release antibiotic formulations in the middle ear as a treatment for biofilms appears to be a potentially promising new therapy for otitis media with effusion.

**Prevention of glue ear**

Some measures to prevent glue ear:

1. Home should be smoke and dustfree.
2. Encourage breastfeeding and if bottle-feed, baby is to be hold upright while feeding.
3. The child should see a doctor if ears are painful or has greenish pus coming from the nose.
4. Hearing screening should be done preschool and school entry.

Glue ear is self limiting disease in most of the cases but it can cause serious speech and developmental delay. It should be treated properly and timely. In some cases we should be more careful, ie 1) sensorineural hearing loss independent of OME; 2) uncorrectable visual impairment; 3) Down’s syndrome or craniofacial anomalies; 4) cleft palate; 5) autism.
spectrum disorder or pervasive developmental disorder; 6) suspected or diagnosed speech and language delay; and 7) the developmental or other cognitive impairments.

References:


Allergies of the Gastrointestinal System

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Introduction

Allergy in the Gastrointestinal system is mainly caused by food. Its prevalence is higher in infants and children than that in the older age group.

Gastrointestinal allergy remains a challenge to the clinician because of its varying symptomatology and dearth of reliable diagnostic tests.

The varying symptomatology is due to variable pathophysiology.

Gastrointestinal allergies may be broadly grouped depending on the pathophysiology as follows.

a) IgE mediated reactions – Oral Allergy Syndrome (OAS) Gastrointestinal anaphylaxis.

b) Mixed IgE-cell mediated reactions – Eosinophilic esophagitis (EoE), Eosinophilic gastritis.

c) Cell mediated reactions – Food protein induced entero colitis syndrome, Food protein induced enteropathy, Food protein induced proctocolitis.

d) Uncertain mechanism – GI motility disorders¹.

IgE mediated reactions

Oral Allergy Syndrome (OAS):
This is an IgE mediated type I hypersensitivity. OAS occurs only in patients with established pollen allergy. It is a pollen-food-related syndrome with cross-sensitization between food allergens and aero allergens namely pollens.

Older children and adults are mainly affected. The condition is characterized by rapid onset of prurites, angioedema of the lips, tongue, palate and throat, usually confined to the oral cavity and rarely progressing beyond the mouth. Anaphylaxis is also rare. It is a short lived phenomenon².

Symptoms are caused by activation of local mast cells by fresh fruits and vegetables. Incidentally cooked fruits and vegetables fail to trigger the response.

Apple, banana, potato, carrots and melons usually cause OAS in individual hypersensitive to certain pollens³.

Gastrointestinal anaphylaxis:
Anaphylaxis is defined as a serious allergic reaction of rapid onset and may be fatal.

Anaphylaxis is a generalized reaction involving all the systems of the body, caused by sudden, massive release of active mediators from mast cell and basophils due to interaction between an allergen and the mast cell bound specific IgE.

Gastrointestinal anaphylaxis is usually a part of the generalized anaphylaxis reaction and is characterized by the rapid onset of the
following:

i) Itching of the lips, tongue and palate.
ii) Angio edema of the lips and pharynx.
iv) Vomiting and loose motions.

Associated with other signs like tachy cardia, arrhythmia, tachypnoea, severe hypotension, breathing distress, generalized urticaria and or angio edema.

The offending agents are same as anaphylaxis:

i) Food –
   Egg, shell fish
   Pea nut, Tree nuts
   Cow’s milk
   Some fruits and vegetable.
   [Food remain the most important cause of anaphylaxis outside hospital setting]
ii) Drugs –
   a) Antibiotics – Penicillin, cephalosporin and sulphonamides.
   b) Muscle relaxants – Suxamethonium, alcuronium, vecuronium etc.
iii) Insects – Insect venoms are important cause of anaphylaxis.
   Hymenoptera venom contains enzymes such as phospholipases and hyaluronidases and some proteins that can elicit IgE antibody responses.
iv) Latex : Is the most important cause of anaphylaxis in the hospital Setting.
v) Miscellaneous – Insulin, Horse derived antitoxin (which are used to neutralize venom in snake bites) are some of the causes of anaphylaxis.

One some occasions G.I anaphylaxis occurs localized only in the G.I.tract and is characterized by colicky abdominal pain, vomiting and loose motion.

**Mixed : IgE-cell mediated reactions**

**Eosinophilic esophagitis (EoE):**

This is a chronic isolated allergic disorder, characterized clinically by symptoms related to esophageal dysfunction and histologically by excessive infiltration of the esophageal epithelium with eosinophils. Typically the density of eosinophils in the oesophageal epithelium exceeds > 15/hpf. Other than eosinophils, mast cells are also found in large numbers in the esophageal epithelium in EoE.

Recent studies demonstrate that eosinophils are dependent on IL5 for their production in the bone marrow, accumulation in target tissues and subsequent activation. Once in the esophagus they produce growth factors and cytokines that promote survival of other inflammatory cells, like mast cell. Eosinophil produce IL9 which acts as an attractant for mast cell.

These mast cells produce growth factors such as transforming growth factor â1(TGFb1) which can cause both fibrosis and smooth muscle cell contraction.

However the factors that regulate mast cell accumulation in the esophageal epithelium is still not clear.

Usually the male gender is affected. Age of presentation is from 1-17 years, mean age of diagnosis being 7 years. The child presents with feeding problem, vomiting, chest or epigastric pain and dysphagia.

The patient usually has other atopic disorders and associated food allergies.

Except in EOE with GERD these symptoms
are refractory to anti reflux therapy. 
On endoscopy, the esophagus presents a granular ringed, furrowed or exudative appearances. Unlike GERD erosive esophagitis is not present.

Hystology of esophageal tissue reveals gross eosinophilia but it will be worth while to remember that only in about 30% of cases serum total IgE may be high.

**Eosinophilic Gastro enteritis (EG):**
It is a rare condition, the peak incidence being in the 3rd decade and like EOE is histologically characterized by eosinophilic infiltration of the mucosa of the stomach, small intestine and large intestine. Symptoms depend on the extent of involvement of the gut.
The most common symptoms are early satiety, abdominal pain, nausea, vomiting and diarrhoea. So irritable bowel syndrome remains an important differential diagnosis.

**Cell mediated reactions to food allergens:**
Most of the gastro intestinal food allergies are cell mediated hypersensitivities and are often the first form of allergy to affect infants and young children.

In these cases standard allergy tests like skin prick test and specific IgE estimations are of little diagnostic value. The cytokines TNF-α and and TGF-β1(transforming growth factor β1) appear to play an important role these reactions.

**Food protein induced enterocolitis syndrome:**
This condition usually presents in early infancy, manifested by irritability, diarrhoea, blood in stool, abdominal distension, vomiting leading to dehydration and often failure to thrive. Vomiting usually occurs 1-3 hours after feeding.

In young infants, the symptoms are generally provoked by cows milk or soya milk.

In older children - wheat, oats, rice, egg, peanut, nuts, chicken and fish causes similar symptoms.

**Food protein induced enteropathy :**
Often manifests in the first year of life. Clinical features comprises of diarrhoea which may be protracted, steatorrhoea, vomiting, malabsorption, abdominal distension, early satiety and failure to thrive, often occur.

Cow’s milk is the most common offender. However wheat, rice, soya, egg, chicken and fish may cause similar symptoms in older children.

Celiac disease is the most severe form of Food Protein induced enteropathy.

**Food protein in procto-colitis :**
Presents in the first few months of life. The typical presentation is blood streaked stools in an otherwise healthy infant. About 60% of these patients are breast fed and the rest are on cow’s milk feeds.

**Celiac Disease :**
The condition usually presents with chronic diarrhoea, steatorrhoea, flatulence and abdominal distension, malabsorption and failure to thrive.

Some patients may remain asymptomatic.

**The offending agents are wheat, rye, barley:**
Genetically susceptible individuals (HLA-DQ2 or DQ8) demonstrate cell-mediated response to transglutaminase (t-TG) deamidated gliadin which is present in wheat and some other cereals.
Histopathology of the small intestine characteristically shows loss of absorptive villi and hyperplasia of the crypts.

**Uncertain Mechanism:**

Patients present with impaired GI motility abnormalities like vomiting, GERD, cow’s milk allergy is often implicated.

**Conclusion**

Allergies of the gastrointestinal system are mainly caused by ingestent allergens namely food and some medication, with higher prevalence among infants and children.

The varying symptomatology of the gastrointestinal allergies still remain a challenge to the clinician due to the dirth of specific and reliable diagnostic tests.

The pathophysiology of gastro intestinal allergy is also variable. It can be classified as IgE mediated immediate hypersensitivity, Cell mediated hypersensitivity, Mixed IgE - cell mediated reactions and uncertain mechanism. Under the circumstances, a thorough clinical history and examination remains the corner stones of successful management of Gastro-intestinal allergies.


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**Allergy Department**

This unit has been serving the field of investigation, therapy and research in allergy for the past twenty five years. Comprehensive management of allergic disorders including detection of offending allergens, immunotherapy and computerised spirometry are done. This unit is recognised by the Directorate of Drugs Control, Govt. of WB as well as the Central Directorate of General Health Service (Drug Section) Govt. of India.

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Nutritional Verses Non Nutritional Rickets

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Introduction

Nutritional deficiency continues to be an important cause of rickets in the underdeveloped and developing parts of the world. In the western hemisphere, predominantly non-nutritional forms of rickets and osteomalacia are now seen.

Normal bone growth and mineralization depends on the availability of adequate calcium and phosphate. Deficient mineralization at the growth plate leads to rickets. The mineralization defects can be classified as calcipenic rickets caused by calcium deficiency and phosphopenic rickets caused by phosphate deficiency 1,2.

Vitamin D is a prohormone which is involved in the metabolism of both, affecting calcium and phosphorous absorption from the gut. Until recently, it was generally accepted that nutritional rickets is caused by vitamin D deficiency alone and that dietary calcium deficiency might exacerbate the disease in the presence of vitamin D deficiency. Phosphorous deficiency in diet can rarely also cause nutritional rickets 3.

Pathogenesis of nutritional rickets has shifted among older children particularly in developing countries where dietary calcium deficiency plays a pivotal role. Though some studies have led to the realization that nutritional rickets may be caused by either vitamin D or calcium deficiency, but in the majority of situations variable combinations of both probably play a role 4.

It has been stated that rickets does not occur in malnourished children as it is a disease that manifests with abnormalities at the growth plates. However, this is not true, as the disease has been well described in severely malnourished infants5.

Abstract

Rickets is an important problem even in countries with adequate sun exposure. The causes of rickets are varied and include nutritional deficiency, especially poor dietary intake of vitamin D and calcium. Non-nutritional causes include hypophosphatemic rickets primarily due to renal phosphate losses and rickets due to renal tubular acidosis. In addition, some varieties are due to inherited defects in vitamin D metabolism and are called vitamin D dependent rickets.

In this review we are going to focus on the diagnostic dilemmas that we face while dealing with a child with rickets and its management after categorizing it into nutritional and non nutritional subtype.

Key words: Rickets, hypocalcemia, non nutritional, hypophosphatemia

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Etiopathogenesis of rickets

Rickets/osteomalacia is a disorder causing mineralization defect resulting in bone and skeletal fragility, although production of bone matrix proteins and their architecture is not impaired. Vitamin D deficiency, inability of activation of vitamin D in vivo or functional derangement in vitamin D receptor is involved in impaired actions of vitamin D. Common causes of hypophosphatemia are excessive actions of phophaturic fibroblast growth factor (FGF) 23 as in X linked hypophosphatemic rickets, or tubular dysfunctions such as in Fanconi’s.

Growth plate thickness is determined by chondrocyte proliferation and hypertrophy, vascular invasion, and conversion into primary bone spongiosa. Mineral deficiency prevents the normal process of bone mineral deposition. It occurs at the growth plate it is called rickets.

In calcium-deficient rickets, the primary defect results from lack of vitamin D or its effect. This results in decreased calcium absorption in the gut. This reduction in calcium absorption increases parathyroid hormone secretion, which acts to preserve blood calcium levels by 1) activating bone resorption, 2) decreasing renal calcium loss, 3) increasing renal phosphate loss, and 4) increasing vitamin D activation by upregulating the vitamin D 1-alpha-hydroxylase enzyme in the kidney as depicted in Fig. 1. The combination of decreased calcium and phosphate availability results in rickets.

In phosphate-deficient rickets, the primary defect is usually severe renal phosphate wasting. Decreased phosphate availability results in rickets. It has to be noted that often hypophosphatemia is a common denominator of both groups of rickets. In hypocalcemic rickets, phosphaturia leading to hypophosphatemia occurs due to secondary hyperparathyroidism. In phosphopenic rickets (hypophosphatemic rickets), phosphate deficiency is the primary defect that results most commonly from increased renal excretion of phosphate. It is associated with normal or slightly elevated serum parathyroid hormone (PTH). An approach to rickets has been elaborated in Table 1 and Fig 2. X linked hypophosphatemic rickets is the prototypic disorder of renal phosphate wasting, and the most common form of heritable rickets. Types of non nutritional rickets have been described in Table 2 and discussed in Table 3 and 4. Here we briefly outline them.

Nutritional rickets

Clinical findings:
The manifestations of rickets are initially seen at the distal forearm, knee, and costochondral junctions which are the sites of rapid bone growth.

Skeletal findings:
There is a delay in the closure of the fontanelles. There is parietal and frontal bossing, craniotabes (soft skull bones) with ping pong bones in infants, enlargement of the costochondral junction of ribs (the “rachitic rosary”) (Fig 3), harrison sulcus due to the muscular pull of the diaphragm on the lower ribs, widening of the wrist and bowing of the distal radius and ulna (Fig 4.), and progressive lateral bowing of the femur and tibia. Widening of ankle (double malleoli) can be seen. In toddlers, there is exaggeration of normal physiological bowing of the legs (genu varum) (Fig 5). Older children have either genu
valgum or windswept deformity of the lower limbs (genu varum on one side and valgum on the other). There may be kyphosis or scoliosis.

**Extra skeletal findings:**
The child may be asymptomatic or may present with pain, irritability, delay in motor milestones, and poor growth. In the first year of life hypocalcemic seizures are commonly seen. Along with that the children have visceroptosis, gait abnormalities (antalgic gait), dental abnormalities (hypoplasia of enamel), and are prone to frequent infections.

**Management**
Several therapeutic regimens have been attempted for deficiency of vitamin D. Short term administration of vitamin D2 or D3 2000 units daily or vitamin D2 50,000 units weekly has yielded equivalent outcomes in the treatment of hypovitaminosis D in young children. Stoss therapy is safe and can lead to hypercalcemia only at very high doses. Doses of 1,50,000 to 3,00,000 IU can be effective with less side effects. After the completion of treatment, vitamin D has to be continued at 800-1000 IU/day till serum alkaline phosphatase returns to normal, followed by RDA for age. The above has been described in Table 5.

Calcium supplementation: Should be given to all children even if they are not currently hypocalcemic as they are bound to be due to de mineralization going on. Dose recommended is 30-75mg/kg/day in 3 divided doses.

Once vitamin D supplements have been decreased to 400 IU/day with normal PTH and 25(OH)D, calcium supplementation is usually not necessary.

Calcitriol is not used for Stoss therapy, since it has a short half-life, does not build up vitamin D stores, and is expensive.

**Non nutritional rickets**

1. **Vitamin D resistant rickets:**
   (a) X linked dominant hypophosphatemic rickets - Unlike vitamin D deficiency, craniotabes and rachitic rosary are not common, and the first usual finding is frontal bossing which may appear as early as 6 months of age. As the child starts walking, progressive limb deformities become evident leading to disproportionate short stature with short limbs. Lower limbs are more affected leading to coxa vara, genu valgum, and genu varum. Dental abnormalities are common and may often be the presenting complaints. These abnormalities include abscessed noncarious teeth, enamel defects, and enlarged pulp chambers. It results from mutations of the phosphate-regulating gene on the X chromosome (PHEX gene) which impairs the inactivation of FGF-23 by a yet ill understood mechanism. FGF-23 results in renal wasting of phosphorus at the proximal tubule level results in hypophosphatemia. Elevated FGF-23 also results into normal or low calcitriol levels.

   (b) Autosomal dominant hypophosphatemic rickets (ADHR) – It has a variable age of onset. It has incomplete penetrance the defect being a mutated FGF23 leading to phosphaturia. Based on the age of presentation, there are two subgroups. One presents during childhood and mimics XLH. The other subgroup presents during adolescence or adulthood with bone pain, weakness, and pseudofractures, but no deformity.
A autosomal recessive hypophosphatemic rickets—

Autosomal recessive hypophosphatemic rickets (ARHR) type 1 occurs due to loss of function mutations in dentin matrix protein 1, a noncollagenous bone matrix protein expressed in osteoblasts and osteocytes. This protein has a role in osteocyte proliferation and in the downregulation of FGFR23. Another form of ARHR (ARHR 2) has been recently described. It occurs due to loss of function mutations in ectonucleotide pyrophosphatase / phosphodiesterase 1 (ENPP1). which is an essential physiologic inhibitor of calcification. Clinical manifestations, biochemical findings, and management of patients with ARHR are similar to those with XLH.

(d) Hereditary hypophosphatemic rickets with Hypercalciuria

The genetic defect is loss of function mutation in the gene that encodes NaPi2c (SLC34A3). Bone pain, muscle weakness, and pseudofractures are the common presenting complaints, while no dental abnormalities are reported. FGFR23 level is normal and 1,25(D3) levels are elevated for low phosphorus levels in contrast to X-linked hypophosphatemic rickets. These patients also exhibit hypercalciuria which predispose them to nephrolithiasis. The management of patients with HHRH differs from those with XLH since the former does not require calcitriol, which may worsen hypercalciuria and increases the predisposition for nephrocalcinosis. Supplementation with phosphate forms the mainstay of its treatment.

(e) Fanconi syndrome

This may manifest in the form of glycosuria, hypokalemia, proximal renal tubular acidosis, hyperuricosuria, and generalized aminoaciduria. It may be primary or secondary to conditions like cystinosis, Lowe's syndrome, drugs, Fanconi-Bickel syndrome.

2. Vitamin D dependent rickets:

Type I is secondary to a defect in the gene that codes for the production of renal 25(OH)3-1-alpha-hydroxylase. A normal physiologic dose of 1,25-dihydroxyvitamin D 3 is sufficient to maintain remission of rickets in this disorder.

Type II is a rare autosomal recessive disorder caused by mutations in the vitamin D receptor. The disorder is characterized by end organ hyporesponsiveness to vitamin D. Common presentation of the disorder is total body alopecia and onset of rickets during the second half of the first year of life. Patients may display progressive rachitic bone changes, hypocalcemia and secondary hyperparathyroidism. It is differentiated from vitamin D dependent rickets type I by virtue of response to physiological doses of exogenous vitamin D in the later. Type II does not respond to vitamin D treatment; elevated levels of circulating calcitriol differentiate this type from type I.

Target organ hyporesponsiveness can be overcome by higher doses of vitamin D or its analogues.

Miscellaneous

(a) Rickets of prematurity:

1. Premature infants are at risk of developing rickets (rickets of prematurity) from calcium and phosphorus deficiency and side effects of medications (e.g., loop diuretics, corticosteroids, anticonvulsants and antacids). Phenytoin may cause target organ resistance to calcitriol.

(b) Tumor induced osteomalacia or
oncogenous osteomalacia:
This is an acquired and paraneoplastic disorder caused due to humoral products known as phosphatonin produced by the tumors. The tumors are generally mesenchymal tumors of long bones, distal extremity, sinuses, nasopharynx, groin, etc. They are benign, slow growing, and predominantly of phosphaturic mesenchymal tumor of mixed connective tissue (PMTMCT) origin. They can present at any age with longstanding history of bone pains and muscular weakness.

(c) Rickets due to chronic kidney disease:
Can be due to the following causes and should be treated as given below:

1. Due to **aluminum toxicity** should be prevented in dialysis patients by maintaining aluminum concentration in dialysate fluid at <10 μg/L and by avoiding the use of aluminum-containing compounds.

2. Due to **vitamin D deficiency** should be treated accordingly.

Due to **hypophosphatemia** should be treated with neutral sodium phosphate salts. Concomitant active vitamin D therapy should be considered.

---

**Table 1. Causes of rickets**

<table>
<thead>
<tr>
<th>Vitamin D deficiency or resistance</th>
<th>Calcium deficiency</th>
<th>Phosphate deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary deficiency</td>
<td>Dietary calcium deficiency without concomitant vitamin D deficiency</td>
<td>Renal tubular loss: X linked</td>
</tr>
<tr>
<td>Lack of sunlight exposure</td>
<td></td>
<td>Hypophosphatemic rickets</td>
</tr>
<tr>
<td>Malabsorption</td>
<td></td>
<td>Fanconis syndrome</td>
</tr>
<tr>
<td>Failure of 25 hydroxylation of vitamin D: liver diseases drugs</td>
<td></td>
<td>Tumors: benign or malignant</td>
</tr>
<tr>
<td>Failure of 1 hydroxylation of vitamin D: Renal tubular damage Inherent deficiency of 1 alpha hydroxylase due to defects in the 1 alpha hydroxylase gene (vitamin D dependent rickets type I) End organ resistance to vitamin D (vitamin D dependent rickets type II).8</td>
<td></td>
<td>Inadequate intake</td>
</tr>
<tr>
<td>This disorder is usually due to mutations in the vitamin D receptor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hence if we exclude the dietary causes of rickets rest all can be categorized as non-nutritional causes of rickets.
Table 2: Biochemical findings in different types of rickets

<table>
<thead>
<tr>
<th>Type</th>
<th>Calcium</th>
<th>Phosphorus</th>
<th>Alkaline phosphatase</th>
<th>PTH</th>
<th>25 OHD</th>
<th>1,25 (OH)₂ D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D dependant rickets type I</td>
<td>↓</td>
<td>↓ or N</td>
<td>↑↑</td>
<td>↑</td>
<td>N</td>
<td>↓</td>
</tr>
<tr>
<td>Vitamin D dependant rickets type II</td>
<td>↓</td>
<td>↓ or N</td>
<td>↑↑</td>
<td>↑</td>
<td>N</td>
<td>↑↑</td>
</tr>
<tr>
<td>X-linked hypophosphatemic rickets</td>
<td>N</td>
<td>↓↓</td>
<td>↑</td>
<td>N or slightly ↑</td>
<td>N</td>
<td>N or ↓</td>
</tr>
<tr>
<td>Hereditary hypophosphatemic rickets with</td>
<td>N</td>
<td>↓ or ↓</td>
<td>↑</td>
<td>N or ↓</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>Nutritional phosphate deficiency</td>
<td>↑ or N</td>
<td>↓</td>
<td>↑ or ↑↑</td>
<td>↓ or N</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>↓ or N</td>
<td>↓ or N</td>
<td>↑ or ↑↑</td>
<td>↑</td>
<td>↓</td>
<td>↑ or N</td>
</tr>
</tbody>
</table>

Figure 1: Pathophysiology of Rickets
<table>
<thead>
<tr>
<th>Nutritional rickets Classification</th>
<th>Clinical features</th>
<th>Treatment</th>
<th>Non nutritional rickets Classification</th>
<th>Clinical Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D deficiency / Calcium deficiency/ Phosphorous Deficiency</td>
<td>Skeletal findings abnormal gait, failure to thrive, developmental delay, hypocalcemic seizures</td>
<td>Replace the deficient nutrient, vit D supplementation</td>
<td>Vit D dependent rickets Type 1</td>
<td>Younger than 2 yrs, hypocalcemic tetany, severe bony changes, seizures</td>
<td>Calcitriol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vit D dependent rickets Type 2</td>
<td>Younger than one year; severe bony changes, alopecia</td>
<td>Massive doses of calcitriol</td>
</tr>
<tr>
<td>Vit D resistant rickets</td>
<td>Dental abnormalities, short stature, bowing of legs</td>
<td>Oral phosphate and calcitriol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X linked dominant Hypophosphatemic rickets</td>
<td>Bone pain, muscular weakness</td>
<td>Oral phosphate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary hypophosphatemic rickets with hypercalciuria</td>
<td>Failure to thrive, glycosuria, aminoaciduria</td>
<td>Calcitriol, Vit D, Bicarbonate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Tubular Acidosis/ Fanconi syndrome</td>
<td>Bone pain, arthralgias, failure to thrive muscular weakness</td>
<td>Vit D and phosphate binding compound</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Fractures, bone pain, weakness</td>
<td>Treat underlying malignancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease/ Renal rickets</td>
<td>Osteopenia, fractures</td>
<td>Minimize iatrogenic causes, Dietary supplement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor induced/ Oncogenic rickets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rickets of prematurity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vitamin D deficiency rickets

25 OH Vitamin D

Low

Serum PTH levels

N/elevated

Low

Serum PO4 levels

VDD1 and 2

Hypophosphatemic rickets

Acidosis

TmPO4/GFR

Renal tubular acidosis, CKD

XLH rickets

Urine Calcium/creatinine ratio

elevated

HHH rickets

Figure 2: Approach to Rickets
Table 4: Steps to Approach Rickets

Step 1. X ray to confirm rickets
Step 2. Investigations to be sent in first sample: serum calcium, phosphorous, creatinine, alkaline phosphatase, serum 25 O H levels.
Step 3. Rule out nutritional rickets and chronic kidney disease.
Step 4. Investigations to be sent in second sample: Blood gas, Bicarbonate and serum PTH levels.

Table 5: Management guidelines of vitamin D deficiency rickets

<table>
<thead>
<tr>
<th>Group</th>
<th>Daily regimen</th>
<th>Weekly regimen</th>
<th>Stoss therapy (Oral or IM)</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mo old</td>
<td>1,000 IU</td>
<td>50,000 IU</td>
<td>-</td>
<td>400-1,000 IU</td>
</tr>
<tr>
<td>1-12 mo old</td>
<td>1,000-5,000 IU</td>
<td>50,000 IU</td>
<td>1 lakh - 6 lakh over 1-5 days (preferably 3 lakh)</td>
<td>400-1,000 IU</td>
</tr>
<tr>
<td>1-18 y old</td>
<td>5,000 IU</td>
<td>50,000 IU</td>
<td>3-6 lakh units over 1-5 days</td>
<td>600-1,000 IU</td>
</tr>
<tr>
<td>&gt;18 y old</td>
<td>6,000 IU</td>
<td>50,000 IU</td>
<td>3-6 lakh units over 1-5 days</td>
<td>1,500-2,000 IU</td>
</tr>
<tr>
<td>Obese, patients, patients with malabsorption syndrome, or on medications affecting Vitamin D</td>
<td>6,000-10,000 IU/ day</td>
<td>-</td>
<td>-</td>
<td>3,000-6,000 IU</td>
</tr>
</tbody>
</table>

Figure 3: Chest X ray showing rachitic rosary adjacent to the costochondral junction in a rachitic child.

Figure 4: Antero posterior X ray of hand showing widening, cupping, and fraying of the distal radius and ulna metaphyses with an associated increase in the thickness of the growth plate.
Figure 5: Characteristic demineralization of bones and bowing of legs

References:


NICU
with Radiant Warmer Beds, Monitors, Facility of Phototherapy, All Modern Gadgets, CPAP and Neonatal Ventilator

Institute of Child Health
11, Dr Biresh Guha Street, Kolkata 700 017
Phones: (033) 65000923, 9836057676
Imaging in Hydatid Disease

Dipankar Das
Associate Professor, Department of Radiology, Institute of Child Health, Kolkata

Introduction

Hydatid disease (human Echinococcosis) is a zoonotic infection caused by larval forms of the genus Echinococcus inhabiting the small intestine of carnivores.

There are many different species – common in human being are Echinococcus granulosus which causes cystic echinococcosis (Hydatid disease) and Echinococcus multilocularis which causes alveolar echinococcosis (alveolar hydatid disease), other rare types are Echinococcus vogeli which causes polycystic echinococcosis and Echinococcus oliganthrus. The commonest organ involved is liver (75%). Other organs involved are lungs, brain, muscles, bones, orbit etc.

Many hydatid cysts are asymptomatic and are diagnosed incidentally clinically or radiologically. Pulmonary hydatid cysts may present with cough, dyspnoea, chest pain, or haemoptysis. Hepatic echinococcosis who are symptomatic most often present with abdominal pain or a palpable mass in the right upper quadrant. Compression of a bile duct may mimic cholelithiasis, and biliary obstruction can result in jaundice. Other presentations are due to the involvement of bone (invasion of the medullary cavity with slow bone erosion producing pathologic fractures), the CNS (space-occupying lesions), the heart (conduction defects, pericarditis) and the pelvis (pelvic mass). Rupture of or episodic leakage from a hydatid cyst may produce fever, pruritus, urticaria, eosinophilia, or anaphylaxis.

Imaging Findings:

The lesions are usually rounded and cystic in appearance - either solitary or multiple conglomerated. Sonography is sensitive in detecting the cystic nature of the lesions, but not all organs can be imaged by this modality. CT scan is excellent for showing calcification in the lesions.

MRI can show the lesions in all organs. The cyst fluid is hyperintense with the wall being hypointense on T2W images.

Multilocular appearance and honey combing are often noted with multiple daughter cysts. The endocyst may detach from the pericyst causing “floating membranes” inside the cavity, a finding that is highly specific for hydatid disease. Complete detachment of the membranes inside the cyst has been referred to as the “water lily sign”.

Complications of hydatid cyst include

(i) Rupture - Secondary bacterial infection / Abscess formation causes Pain, anaphylactic reaction, peritonitis.

If biliary tree is involved - Cholangitis, obstructive jaundice, pancreatitis.
Case 1. A 34 yrs old male presented with respiratory distress. On Chest X-Ray PA and Lat view show large rounded solitary lesion occupying upper and middle lobe of right lung. CT scan of chest show the lesion containing air and floating parasitic membrane in the dependant part (water lily sign) in the right lung.
Case 2. A 48 yrs old male presented with abdominal pain and vomiting.
Sagittal, Coronal and Axial T2W MR images show a rounded well-defined cystic lesion in the postero-superior part of the right lobe of liver with multiple daughter cysts of low fluid signal intensity than that of mother cyst.
Case 3. A 11 yrs old boy presented with hydatid disease of liver.
Axial and Coronal T2W and T1W MR images show well defined large rounded cyst in relation to the right lobe of liver with detachment of laminated membrane from the pericyst (water-lily appearance) with hydatid sand.
Case 4. A 6 yrs old girl presented with headache, nausea and vomiting.
Coronal, Axial T2W and FLAIR MR images show well-defined, smooth, thin-walled cyst in the left parietal region containing hydatid sand. No calcification is seen.
Case 5. A 17 yrs old boy presented with recurrent episodes of seizures.
Coronal and Axial T2W and T1W MR Images show multiple conglomerated hydatid cysts with pericystic edema in the right occipito-parietal and posterior temporal regions with mass effect. The lesions are compressing the posterior 3rd ventricle causing obstructive hydrocephalus.
Contrast enhancement is seen in the wall.
Case 6. A 59 yrs old lady presented with pain and swelling in the right gluteal region for last 6 months.

Coronal, axial and sagittal T1W and T2W MR images show a mixed signal intensity subcutaneous lobulated lesion with well-defined margin containing daughter cysts in the right gluteal region without any deeper invasions into the muscles and bones.
If bronchial tree involved- Hemoptysis, respiratory distress.

(i) **Infection** - abscess to full blown sepsis

(ii) **Allergic reaction** - Eosinophilia, urticaria, broncho spasm, Anaphylaxis.

(iii) **Pressure effect** - obstructive jaundice, Budd-Chiari Syndrome

(iv) **Organic Dysfunction** - Cholangitis, Biliary Cirrhosis

(v) **Spread** - Disseminated intraperitoneal hydatid disease

(vi) **Recurrence** - Iatrogenic puncture, Surgical inoculation.

**Treatment of hydatid disease**

Treatment of the hydatid disease depend on size, location and manifestation of the cysts and general condition of the patient.

**A. Medical treatment:**

3 major drugs are used - Mebendazole, Albendazole and Praziquantel. Albendazole is preferred drug and used for prolonged treatment.

**B. Surgical treatment:**

It may be radical, conservative or palliative depending upon the clinical situation.

Percutaneous aspiration, drainage under USG or CT guidance are also preferred technique now a days. The procedure involving Puncture, Aspiration, Injection of scolecoidal agents and Respiration (PAIR ) is popular as minimally Invasive treatment.

**Reference**


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**Department of Biochemistry & Pediatric Pulmonology**

Sweat Chloride Estimation is performed by PILOCARPINE IONTOPHORESIS (indigenous method developed by Prof. S K Kabra, AIIMS) on all weekdays between 11.00 am and 02.00 pm.

**Rates are:**

- Rs. 1000/-
- Rs. 500/- (For Govt Hospitals)
Pediatric Rheumatology – Pictorial Quiz

Priyankar Pal
Associate Professor, Institute of Child Health, Kolkata

Question 1
Identify this condition with these skin lesions.

Diagnosis?
1. Urticaria- angioedema
2. HSP
3. Urticarial vasculitis
4. C1 esterase deficiency

Question 2
1. A two and half months old boy presented with paucity of movements of right upper limb
2. No H/O fever, trauma, swelling of the affected limb

Investigations
1. Total leukocyte counts - normal
2. ESR-140mm
3. CRP-60mg/l
4. Blood culture-negative

x-ray showing-thickening of the scapular spine
MRI- diffuse thickening of the cortex, ill defined hyperintense marrow signals

Diagnosis?
1. Caffey's disease
2. Septic arthritis
3. Osteomyelitis of scapula
4. Scapular Trauma

Question 3

A 14 year old girl presented with deforming arthritis involving multiple small joints and soft tissue swellings.

She was Rheumatoid factor positive

What are the soft tissue swellings?
1. Subcutaneous nodules
2. Lipoma
3. Rheumatoid nodules
4. Sebaceous cysts

Question 4

1. 8 years girl presented with intermittent fever and weight loss for 1 month.
2. She was not keeping well since the last 3 months and complained of malaise and diffuse joint pains.
3. CBC on admission:
4. Hb 8.2 TC 4100 N 65 L 33 M2
5. Platelets- 1.3
6. ESR- 76
7. CRP – 6

Oral Cavity showed this lesion:

Diagnosis?
1. Systemic arthritis
2. Systemic vasculitis
3. SLE
4. Behcet’s disease
Question 5
SLE patient. Name this rash:

1. Malar rash
2. Annular rash
3. Vasculitic rash
4. Discoid rash

Question 6
Child with fever and following skin changes.

Diagnosis:
1. Systemic arthritis
2. Scarlet fever
3. Kawasaki disease
4. Rickettsial fever
**Question 7**

Diagnosis?
1. Slipped capital femoral epiphysis
2. Development dysplasia of hip
3. Osteoporosis
4. Perthes disease

**Question 8**

6 years old child presented with:
Fever for 20 days
Arthritis of left wrist
No organomegaly, lymphadenopathy, serositis
Hb 8.6 gm%, TC- 24300 N86 L12 M2
Platelets- 4.9
ESR- 96 CRP- 102
He had the following rash which appeared with fever

**Diagnosis?**
1. Systemic arthritis
2. SLE
3. Kawasaki disease
4. Rickettsial disease

**Question 9**

On D 24 of fever the above child developed seizures
Hb- 7.9 TC- 10400 N56 L40 M4
Platelets- 1.2
ESR- 34 CRP- 218
SG PT- 96. He had following skin rashes

What has happened to the child?
1. SLE
2. Systemic Arthritis
3. Macrophage Activation Syndrome
4. Systemic vasculitis
**Question 10**
A 4-year-old girl presented with insidious onset proximal muscle weakness and following skin changes.

**Question 11**
Kawasaki disease in recovery phase developed this nail changes. What are these?
1. Onycholysis
2. Onychomadesis
3. Leuconychia
4. Beau’s lines

**Question 12**
Presented with facial rash and progressive muscle weakness. Developed underlying complication.

Diagnosis?
1. SLE
2. Juvenile dermatomyositis
3. Post viral myositis
4. Myopathy
Question 13
Child presented with pain in shoulder and rashes.

Diagnosis?
1. Fracture
2. Osteosclerosis
3. Lipodystrophy
4. Calcinosis

Diagnosis?
1. Acute leukemia
2. Langerhans cell histiocytosis
3. Ewing’s sarcoma
4. Secondaries to skin and bones
**Question 14**

12-year-old boy had a peculiar dysmorphic appearance involving left side of the face.

1. Road traffic accident
2. Post burn scar
3. En coup de sabre- a localised form of scleroderma
4. Craniotomy scar

**Question 15**

1. This child of our clinic was diagnosed as oligo-articular JIA and some NSAID was prescribed.
2. He returned with vesiculo-bullous lesions which subsequently healed to form small hypo pigmented scars.

What is the most likely Diagnosis?

1. Bullous impetigo
2. Pseudoporphyreria induced by Ibuprofen
3. Pseudoporphyreria induced by Naproxen
4. Sulphasalazine induced drug rash

**Question 16**

5 years old girl with history of respiratory allergies presented with features of glomerulo nephritis.

1. Hb 8.9 TC 16900 N 81 L 12 E 6
2. ESR- 76
3. CRP- 82

Following is the Xray picture

1. Indirect immunofluorescence showed Anti-neutrophil cytoplasmic IgG antibodies (c-ANCA)
Diagnosis?
1. Wegener granulomatosis
2. Kawasaki Disease
3. Churg-Strauss Syndrome
4. Essential cryoglobulinemic vasculitis

**Question 17**
1. 13 years girl was diagnosed as oligo JIA one year back. Parents discontinued medicines 3 months back.
2. Presently she has been having fever for 3 weeks and a truncal macular rash and following mucosal changes.

**Question 18**
1. 6 years old female child presented with on and off arthritis involving multiple joints for 5 mo. Pain is worse at night, relieved by NSAIDS.
2. No organomegaly, lymphadenopathy. Tenderness around upper end of rt. Tibia.
3. CBC- Hb 8.2 TC- 2100 N16 L82 M1 E1
4. Platelets- 1.2 ESR- 108 CRP – 56 mg/dl. Xray of the hand showed:

An investigation that will clinch the most likely diagnosis:
1. ANA
2. Bone marrow aspiration cytology
3. PET – CT scan
4. Rheumatoid factor

**Question 19**

Diagnosis?
1. SLE
2. Systemic vasculitis
3. Herpes infection
4. Behcet’s disease
Presented with pain and stiffness in multiple joints. Inflammatory parameters normal. These are the X-rays.

Diagnosis?
1. Rickets
2. Juvenile idiopathic arthritis
3. Osteoporosis
4. Spondylo-metaphyseal dysplasia

Question 20

Infant presented with progressive anemia and pain in legs. X-ray shows

Diagnosis?
1. Acute leukemia
2. Hemato-diaphyseal dysplasia
3. Skeletal metastasis
4. Histiocytosis

Quiz Answers see Page No.49)
Certification of Polio Eradication In India - Envisioning Beyond

Rina Ghosh
Clinical Tutor, Department of Immunisation, Institute of Child Health, Kolkata

India along with 10 other countries of South East Asia Region is eligible for being declared as the 4th Polio free WHO region on 27 March 2014. WHO Regions are certified polio free and not individual country. From total of six WHO Regions, three are already been certified polio free. (American Region in Sept 1994, Western Pacific region in Oct 2000, European region in June 2002). The last case of polio myelitis caused by wild polio virus type 1 (WPV1) in the South East Asia region of WHO, was detected on 13 January 2011 from Howrah District of West Bengal. Wild Polio virus type 3 (WPV3) reported, had onset in District Pakur in Jharkhand. The last environmental isolate reported was from Delhi in July 2010\(^1\).\(^2\).

Globally the number of endemic countries have come down to 3 — Pakistan, Afghanistan and Nigeria. The global status of wild polio virus is shown in Table 1.

The achievement of zero polio status for more than 35 months by India is an outcome of continuous operational improvement, adoption of best strategies and use of appropriate vaccines through research.

Criteria For Certification\(^3\)-\(^5\)

Regional Certification Commission certifies a region as polio-free if it satisfies the following criteria.

1) There is no virologically confirmed indigenous case of poliomyelitis in human being in the region for three consecutive years.

2) All countries in the region must have certification standard surveillance to document the absence of wild poliovirus.

3) Absence of wild polio viruses from the communities as indicated by stool samples from normal children and where appropriate from waste water from high risk population.

4) All countries are required to complete

<p>| Table 1. Global status of wild polio virus (As of 12th February 2014) |
|-----------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Total cases</th>
<th>Year-to-date 2014</th>
<th>Year-to-date 2013</th>
<th>Total in 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Globally</td>
<td>11</td>
<td>2</td>
<td>400</td>
</tr>
<tr>
<td>- in endemic countries</td>
<td>11</td>
<td>2</td>
<td>160</td>
</tr>
<tr>
<td>- in non-endemic countries</td>
<td>0</td>
<td>0</td>
<td>240</td>
</tr>
</tbody>
</table>

Data in WHO as of 12 February 2013 for 2013 and 11 February 2014 for 2014 data.
and document Phase 1- laboratory containment i.e. list of laboratories that may possess polio infected or potentially polio infectious material, have been made.

5) Appropriate measures established to deal with importations of wild poliovirus.

The certification process includes field visits of National Certification Committee for Polio Eradication (NCCPE) members to review the quality of AFP surveillance, supplementary immunization campaigns and preparedness of the states to respond to any wild polio virus importation.

Risks to Maintain Polio Free Status in India

(1) Threat for reintroduction of polio in India

Potentially any area in the world with current WPV circulation constitutes a risk for India, but the most significant risks are from the remaining endemic countries which continue to have extensive transmission. From Nigeria and Pakistan virus is spreading to polio free countries in 2013. Pakistan and Afghanistan are in close proximity to India, and although Nigeria is distant, it has long history of exportation of wild polio virus. In fact polio can be imported to India from any part of the world where the virus is actively circulating. Recently wild polio virus was detected in Syria, Cameroon, Somalia, Kenya. Ethiopia. These countries were earlier detected as non endemic countries. Environmental samples positive for WPV which obtained in Israel, Egypt. This poses a very high risk of polio introduction in pockets with poor immunization in India. The historic reservoir areas of Western Uttar Pradesh and Bihar and areas with recent transmission of polio virus remain at higher risk of sustaining transmission, should wild polio virus be reintroduced. Migrant and mobile populations remain at significant risk of sustaining transmission and moving virus around the country should an importation occur.

(2) The development of Circulating Vaccine derived Poliovirus (cVDPV)

The rare situation of emergence of circulating VDPVs is also a risk for the programme in India. Although no cVDPVs were detected in India after 2010, but in 2011 a total of seven VDPVs were detected, out of which one was type3 while others were type 2. In 2012 one VDPV type2 was detected from West Bengal. In 2013 five cases were sought. There is no evidence that any of these viruses (from 2011-2013) are circulating. None of the detected viruses were related to each other or to VDPVs detected in 2009 or 2010.

Therefore experience from India and from other countries demonstrates that cVDPVs (particularly cVDPV type2) can develop if there are pockets of with very low immunity against polio virus type 2. The regular use of tOPV in national campaigns in the past 3yrs has reduced the risk of emergence of type2 cVDPV in India, but some level of risk remains.

(i) An extremely high level of vigilance is necessary in the coming months to ensure that any importation or circulation of polio viruses and VDPV are reliably rapidly detected. Environmental surveillance which is operational in
Mumbai, Delhi, Patna and Kolkata may be extended to Punjab and Gujarat as they have significant mobile migratory population.

(ii) All detected VDPVs should continue to be thoroughly investigated to determine any risk of circulation and appropriate action taken based on investigation findings.

Strategies To Ensure Maintenance of Polio Free Status in India Recommended by Indian Expert Advisory Group (IEAG)

(1) Maintaining immunity: Both supplementary immunization and enhanced routine immunization are needed to maintain high population immunity to minimize the consequences of any WPV importation, and to ensure that cVDPVs do not develop. Strengthening routine immunization by high levels of OPV coverage are essential to consolidate the gains and keep India polio free.

(2) OPV supplementary immunization activities (SIAs) schedules in 2014 & 2015: As per previous IEAG recommendation two NIDs with tOPV in all areas in first quarter (Jan Feb), and three SNIDs with bOPV ideally one in each of qr.2, (April), qr3(August), qr4(Nov) of 2014 and 2015, targeting all of U.P, Bihar, Delhi, and associated high risk areas of Haryana, Rajasthan, Uttarakhand, and migrant high risk areas in Maharashtra, Punjab, Gujarat, Jharkhand and West Bengal.

3) Annual seroprevalence surveys in select areas and population to provide information on immunity.

Measures to Mitigate Risk for Polio Reintroduction in India

A) Immunization of Travellers

(i) At Land Border Crossing

Immunization of travellers at land border crossing points from neighbouring countries is the most significant risk reduction strategy and should be continued until there is no longer an epidemiological risk. Round the clock cross border vaccination for travellers at international borders of India for all 365 days, has already been started from March 2013. Particular attention should continue to be paid to border populations to ensure that they are effectively covered by SIAs and routine immunization.

(ii) Immunisation for International travellers from India to Polio affected countries

Government of India has decided that travellers to or from the seven countries namely Afghanistan, Pakistan, Nigeria, Somalia, Kenya, Syria and Ethiopia should receive a dose of oral polio vaccine before travel and that this vaccination should be ideally undertaken at least 4 weeks before irrespective of their age and previous vaccination status at designated centres only.

B) Maintain Certificate Standard AFP Surveillance:

Minimum levels for Certification Standard are:

(i) Completeness of reporting – At least 80% of expected routine (weekly or monthly) AFP surveillance reports should be received on
time, including zero reports where no AFP cases are seen. The distribution of reporting sites should be representative of the geography and demography of the country.

(ii) Sensitivity of surveillance – At least one case of non-polio AFP should be detected annually per 100 000 population aged less than 15 years. In endemic regions, to ensure even higher sensitivity, this rate should be two per 100 000.

(iii) Completeness of case investigation – All AFP cases should have a full clinical and virological investigation with at least 80% of AFP cases having ‘adequate’ stool specimens collected. ‘Adequate’ stool specimens are two stool specimens of sufficient quantity (8 to 10 gm) for laboratory analysis, collected at least 24 hours apart, within 14 days after the onset of paralysis, and arriving in the laboratory by reverse cold chain and with proper documentation.

(iv) Completeness of follow-up – At least 80% of AFP cases should have a follow-up examination for residual paralysis at 60 days after the onset of paralysis.

(v) Laboratory performance – All AFP case specimens must be processed in a WHO-accredited laboratory within the Global Polio Laboratory Network (GPLN).

(c) Readiness to respond

The Emergency Preparedness and Response Plans (EPRPS) should be updated at a minimum annually; the update should include a full new risk analysis to inform risk mitigate measures. Simulations of the Emergency response Plans at National state levels should be conducted by the Union Government on an urgent basis.

As per previous IEAG recommendation the Union Government should ensure a rolling stock of 40 million bOPV and 10 million tOPV to enable wild polio virus or vaccine derived polio virus. Rapid SIA response reduces both the duration & of intensity of outbreaks. The IEAG reemphasized previous recommendations that any circulating polio virus detected, regardless of source, anywhere in the country, should be considered a public health emergency and responded to by multiple high quality mop-up vaccination campaigns. Each mop-up should cover about 2 to 5 million children. The first round should be conducted within 2 weeks following confirmation of a case. In non high risk areas mop-ups should consist of a minimum of 3 high quality rounds, using a short interval approach. In high risk areas: SNID rounds, in general, should be more than 3 rounds.

(d) Laboratory containment

After eradication the only source of wild poliovirus will be in the laboratories. Laboratory containment ensures that the virus is not reintroduced in the community through laboratories. Laboratory Containment has three phases:

Phase 1. Laboratory Survey and inventory
Phase 2. Global certification
Phase 3. Post-global certification

The national programme has already made on inventory of laboratories that retain such materials to ensure that certification requirements are met.

The parallel active search process has been fast-tracked to rapidly identify those laboratories most likely to be holding poliovirus and
already ensured their status is known; it must be ensured that the fast track process includes all Indian vaccine suppliers and their associated facilities, and any other relevant private sector facilities.

Given the complexity of Phase 1 of the containment process (the inventory process) the national programme should consider destroying or securing relevant stocks as the inventory is implemented (i.e. commence implementation of Phase2).

In South East Asia Region, India and Timor Lesle, these 2 countries have only recently completed the laboratory containment phase 1. The Government of India has formed a National Task Force for Laboratory Containment of Wild Polioviruses with Indian Council of Medical Research (ICMR) as nodal agency for this task.

(e) Post eradication policy and Preparing for the end game 4,5

I) tOPV to bOPV switch: The National immunization programme should now begin incorporation into its planning tOPV to bOPV (type I and 3 switch). Because at this juncture of zero polio status continued use of trivalent Oral Polio Vaccine (tOPV) in the polio eradication program poses the risk of paralysis from type2 circulating Vaccine Derived Polio Virus(cVDPV). The Sabin type 2 in the tOPV has been responsible for >90% of all cVDPV cases and about 40% cases of VAPP globally during the last few years. In order to mitigate this risk, it is important to discontinue tOPV and switch to bivalent OPV(bOPV) in both routine immunization and SIAs as a part of the global “polio end game” strategy potentially in 2016.

II) Introduction of IPV in routine immunization programme: However it will be critical to boost the population immunity against type2 polio virus prior to the tOPV-bOPV switch .The Global Scientific Advisory Group of Experts(SAGE) on immunization (2012) and the India Expert Advisory Group (IEAG) for polio eradication (2013) have recommended the introduction of Inactivated Poliovirus Vaccine(IPV) in the routine immunization program prior to this switch. Single Intramuscular dose of IPV at DPT3 contact in routine immunization is likely to be introduced in 2015 in advance of the global tOPV-bOPV switch.

III) Eventual cessation of use of bOPV at some point in the future.

Reference

1. Minutes of the 23rd meeting of the India Expert Advisory Group for Polio Eradication, July 2011
5. AFP ALERT. National Polio Surveillance Project, Jawaharlal Nehru Stadium, N.
**PEDIATRIC NEPHROLOGY DIVISION**  
**Institute of Child Health**

Well equipped PEDIATRIC NEPHROLOGY DIVISION including PEDIATRIC HEMODIALYSIS facility for the first time in Eastern India, at a very affordable cost, under the care of Pediatric Nephrology team in the state.

**Facilities available:**

(i) It is a 6 bedded fully Air Conditioned ward, including one Hemodialysis bed and one Peritoneal dialysis bed.

(ii) All modern facilities including Multipara monitors etc

(iii) Highly trained staffs round the clock.

(iv) Twice weekly Nephrology OPD clinic and daily inpatients visits by nephrologists team.

**Services Offered:**

1. Hemodialysis.
2. Peritoneal dialysis and CAPD initiation.
3. Kidney biopsy
4. Treatment of all types of Kidney problems in children including Nephrotic syndrome, Acute Nephritis. Acute kidney disease, chronic kidney disease, tubular disorders etc.

**PEDIATRIC NEPHROLOGIST TEAM**

Dr. Sushmita Bannerjee, Dr. Rajiv Sinha, Dr. Shakil Akhtar, Dr Sudarsana De Dr. Jayati Sengupta

**Quiz Answers (Contd from Page No. 43)**

1. HSP
2. Caffey’s disease
3. Rheumatoid nodules
4. SLE
5. Discoid rash
6. Kawasaki disease
7. Perthes disease
8. Systemic arthritis
9. Macrophage Activation Syndrome
10. Juvenile dermatomyositis
11. Beau’s lines
12. Calcinosis
13. Langerhans cell histiocytosis
14. En coup de sabre- a localised form of scleroderma
15. Pseudoporphyria induced by Naproxen
16. Wegener granulomatosis
17. Behcet’s disease
18. Bone marrow aspiration cytology
19. Spondylo-metaphyseal dysplasia
20. Hemato- diaphyseal dysplasia
The Cold Chain

Jaydeep Choudhury
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Vaccines are made of proteins, nucleic acids, lipids and carbohydrates. All the vaccines biodegrades over time and inappropriate storage outside the recommended temperature range may lead to irreversible damage to the potency and safety of vaccine. Vaccine potency once lost cannot be restored. The system of transporting, storing and distributing vaccines in a potent state at the recommended temperature from the point of manufacture to the point of use is the cold chain. The cold chain remains a highly vulnerable point for both National Immunization Programs and office practice. The importance of cold chain is more in tropical climates. There is no substitute to rigorous maintenance of cold chain.

The optimum temperature for refrigerated vaccines is between +2 and +8°C. Optimum temperature for frozen vaccines is -15°C or below. Protection from light is a necessary condition for some vaccines. Cold sensitive vaccines experience an immediate loss of potency following freezing. Vaccines exposed to temperature above the recommended temperature range experience some loss of potency with each episode of exposure. Repetitive exposure to high temperature results in cumulative loss of potency that is not reversible. Exposure to higher temperature may cause growth of harmful pathogen in the vaccine vial.

Components of a cold chain
(i) Personnel responsible for vaccine distribution.
(ii) Appropriate equipment to store and transport vaccines.
(iii) Appropriate transport facilities.
(iv) Maintenance of equipment.
(v) Monitoring.

Temperature and light sensitivity of vaccines
The correct temperature is the most important factor in maintaining the potency of vaccines. Unlike popular belief vaccines are also damaged by excessive cold in addition to heat.

Sensitivity of vaccines to heat
Each exposure to ambient temperature causes some degradation of the vaccine and subsequent exposures lead to cumulative impact. Vaccine potency cannot be restored after placing back at recommended temperatures. All vaccines are sensitive to heat but to different degrees. Live vaccines are more susceptible and in decreasing order of sensitivity include OPV, Measles, MMR, BCG, yellow fever, rotavirus and varicella vaccines.

Sensitivity of vaccines to freezing
Cold injury is more common than assumed.
Vaccines susceptible to damage by freezing include DTP, TT, DT, Td, TT, Hepatitis B, combination vaccines, Hepatitis A, human papilloma virus (HPV), pneumococcal conjugate vaccine (PCV), inactivated polio vaccine (IPV), pneumococcal polysaccharide vaccine (PPV 23), influenza vaccines, meningococcal vaccines, rotavirus vaccines, typhoid vaccines and Hib. Vaccines that can be frozen without harm include OPV (vial must not be frozen and thawed repeatedly), and lyophilized measles, MMR, BCG vaccines, and MMRV.

Sensitivity of vaccines to light
Lyophilized and reconstituted BCG, measles, MMR, varicella, rotavirus and HPV vaccines are particularly susceptible to light and need protection from strong light, sun light, ultraviolet and fluorescent neon lights.

**Vaccine Vial Monitors**
The Vaccine Vial Monitor (VVM) is a temperature sensitive colored label that provides an indication of the cumulative heat to which the vial has been exposed. VVMs consist of a temperature sensitive material, which changes color gradually on being exposed to heat. This change of color is irreversible. The VVM warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. It is used for temperature monitoring of OPV, which is the most thermo labile of all vaccines. The VVM is applied to the outside of a vaccine vial, and it applies only to that vial. It cannot be taken as a marker for the potency of the vaccine in other vials of the same lot or in the same storage facility.

The VVM consist of a dark outer circle and a lighter inner square. Interpretation of the color change of VVM is as follows:

1. Inner square is white, or lighter than outer circle: If the expiry date has not passed, vaccine can be used.
2. Inner square matches color of outer circle or is darker than outer circle: vaccine should be discarded, regardless of the expiry date.

**Cold chain equipment**
The cold chain involves two complementary aspects:

(i) Set chain represented by the walk-in cold rooms, deep freezers and refrigerators. These are used for bulk storage of vaccines at the manufacturer site, or at major distribution points.

(ii) Mobile chain represented by isothermic boxes and vaccine carriers.

**Domestic refrigerator**
The main compartment should have a temperature of 2 to 8 °C, and the freezer compartment should maintain a temperature of -5 to -15 °C. Ideally a double door refrigerator should be used. A voltage stabilizer is mandatory when voltage fluctuations are many and power cuts are frequent. A good well calibrated thermometer is a must.

The vaccines can be placed as follows:

(i) Freezer compartment: BCG, OPV, Measles, and MMR.

(ii) Top shelf: OPV, Measles and MMR.

(iii) Middle shelf: DTwP, DTaP, DT, TT, Tdap,
Combination vaccines, IPV, HPV, Typhoid, Hepatitis A, Hib, PCV, influenza, rotavirus vaccines.

(iv) Lower shelf: Hepatitis B and Varicella
(v) Crispator: Diluents
(vi) Baffle tray: should be kept empty. No vaccines should be stored in the door.

Cold box and Vaccine carriers
These are used for transport of vaccines. They should have frozen ice packs lining the sides, which should be conditioned before using. The vaccine packs should not be placed in direct contact with the icepacks but should have an intervening layer of plastic/bubble wrap/styroform peanuts. A thermometer should be placed in the cold box/vaccine carrier for recording temperatures. For keeping vaccines for longer durations the walls of the thermocol box should be 2 inches thick and has snugly fitting lid.

Vaccines should be transported only in cold boxes or vaccine carriers - vacuum flasks should never be used for this purpose. During shipment and transportation, temperature and time sensitive monitor marks are used to check the cold chain. Transport is the most vulnerable time for the cold injury to vaccines.

Further reading
Case of an Unusual Rash in a Newborn

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Case Presentation
A 2 day old female newborn was admitted to the neonatal intensive care unit with the complaint of erythematous rash all over the body sparing the face, with exfoliation of palms and soles (fig 1.) along with loose stools since one day. She was a healthy second born delivered at term through LUCS of a (27 years) old mother after an uncomplicated gestation period. Weight (2.56 kg), height (46 cm) head circumference (33.5 cm). No significant antenatal history was present. No family history of a child born with similar complaint.

Suspecting it to be a case of neonatal sepsis antibiotics were started and the required investigations were sent. Sepsis screen came out to be negative and BACTEC showed no growth after 5 days. In the following 3-4 days the skin lesions developed to become hyperpigmented and streak like along the lines of Blaschko. Distributed more so on extremities than on the abdomen and trunk while sparing the face, palms and soles. (fig 2, 3 and 4) Otherwise the baby’s cry/ reflex/ activity/ tone were good and she was accepting oral feeds.

Fig 1. Rash with Exfoliation of soles
Suspecting it to be a case of neonatal sepsis antibiotics were started and the required investigations were sent. Sepsis screen came out to be negative and BACTEC showed no growth after 5 days. In the following 3-4 days the skin lesions developed to become hyperpigmented and streak like along the lines of Blaschko. Distributed more so on extremities than on the abdomen and trunk while sparing the face, palms and soles. (fig 2, 3 and 4) Otherwise the baby’s cry/ reflex/ activity/ tone were good and she was accepting oral feeds.

Fig 2, 3. Showing hyperpigmentation of legs
liveborn children is approximately 33% unaffected females, 33% affected females, and 33% unaffected males.9

Clinical features:
No strict diagnostic criteria for incontinentia pigmenti (IP) exist. Establishing the diagnosis relies on detection of the characteristic clinical findings of the skin, teeth, hair, and nails. The clinical diagnosis of IP can be made if at least one of the major criteria is present. The presence of minor criteria supports the clinical diagnosis; the complete absence of minor criteria should raise doubt regarding the diagnosis.3

Family history consistent with X-linked inheritance or a history of multiple miscarriages also supports the diagnosis.

Major criteria (skin lesions that occur in stages from infancy to adulthood)
(i) Erythema followed by blisters (vesicles) anywhere on the body except the face, usually in a linear distribution. The blisters clear within weeks and may be replaced by a new crop. Erythema occurs in stage I (first weeks of life to age four months)
(ii) Hyperpigmented streaks and whorls that respect Blaschko’s lines, occurring mainly on the trunk and fading in adolescence; stage III (age four months to 16 years)
Pale, hairless, atrophic linear streaks or patches; stage IV (adolescence through adulthood)

Minor criteria
(i) Teeth - Hypodontia or anodontia (partial or complete absence of teeth), microdontia (small teeth), abnormally shaped teeth
(ii) **Hair** - Alopecia, woolly hair (lusterless, wiry, coarse)

(iii) **Nails** - Mild ridging or pitting; onychogryposis (hypertrophied, curved nails)

(iv) **Retina** - Peripheral neovascularization

**Discussing the above in detail with the differential diagnosis**

**Skin:**

Classically, skin lesions evolve through four stages: vesicobullous eruption, verrucous lesions, hyperpigmented and hypopigmentation macules.

**Stage I: Vesicobullous** - Typically occurs in the first 2 weeks of life with erythematous streaks, plaques, pustules or vesicles linearly distributed on the extremities, trunk and scalp. Eosinophilia occurs in 65% of cases in the first phase, reverting in 4–5 months of age. Differentials include: congenital herpes simplex, varicella, staphylococcal or streptococcal bullous impetigo, and (in severe cases) epidermolysis bullosa.

**Stage II** - characterised by hyperkeratotic verrucous lesions on an erythematous base affects the distal extremities.

**Stage III: Hyperpigmentation** - The hallmark of IP, usually appears between 3 and 6 months of age, manifests during months or years and it is characterised by hyperpigmented lesions asymmetrically distributed along Blaschko’s lines. The presence of dermic melanin is a typical finding. Main differential being hypomelanosis of Ito, which can demonstrate the same “swirled” pigmentation pattern.

**Stage IV: Atretic** - The phase of hypopigmentation may start from childhood to adolescence, is permanent and consists of hairless, anhidrotic patches and streaks, with or without atrophy, on the flexor surface of the lower legs. The newborn may exhibit any of those stages, because the former can occur in uterus. Has to be differentiated from vitiligo.

**Central nervous system:**

It is the most affected system after the skin in about 10–40% of patients. Seizures are the most frequent neurologic complication and commonly arise in the first weeks of life and are associated with poorer prognosis. Other symptoms include motor and cognitive development delay, microcephaly, spasticity, ataxia, cerebral microangiopathy and haemorrhagic strokes.

**Eyes:**

In about 30% of patients, ocular disease may occur such as strabismus, microphthalmia, pigmentary retinal changes, retinal vessel anomalies with areas of ischaemia, retinal detachment, proliferative retinopathy, cataracts and optic nerve atrophy.

**Teeth:**

Abnormalities include hypodontia, microdontia, abnormally shaped teeth (e.g., conical teeth or accessory cusps), delayed eruption, or impaction. Enamel and tooth strength are normal.

**Nails:**

It can be dystrophic (i.e., lined, pitted, or brittle). These changes often resemble fungal infections of the nails. Dystrophic nails are most commonly associated with stage II.
Hair:
Alopecia may occur on the scalp and also on the trunk and extremities. Hair may also be lusterless, wiry, and coarse, often at the vertex in a “woolly-hair nevus.”
Skin lesions do not require specific treatment, although measures to prevent bacterial superinfection are necessary.

Testing Strategy:
To confirm/establish the diagnosis in a male or female
(i) To make a presumptive diagnosis, clinical evaluation including the history of skin abnormalities; detailed family history
(ii) To confirm the diagnosis, molecular genetic testing if not available then skin biopsy of an affected area for histologic examination.

Due to lack of molecular studies we could not confirm the diagnosis in this child but IP must be considered as a diagnosis in a newborn with vesicular skin lesions distributed linearly and after exclusion of infection.

Reference
1. Clinical acumen as good as CT scan!!!

Do we need to do routine repeat head computed tomography (RHCT) for traumatic brain injury (TBI)? In this retrospective study over 3 years of data were analyzed in a level 1 trauma care center. Indications for RHCT (routine vs. neurologic deterioration) and their findings (progression or improvement) were recorded. Neurosurgical intervention was defined as extraventricular drain placement, craniectomy, or craniotomy. Primary outcome was a change in management after RHCT. A total of 291 pediatric patients were identified; of which 191 patients received an RHCT. Routine RHCT did not lead to neurosurgical intervention in the mild and moderate TBI group. In patients who received RHCT due to neurologic decline (n = 7), radiographic progression was seen on 85% of the patients (n = 6), with subsequent neurosurgical interventions in three patients. Two of these patients had a Glasgow Coma Scale (GCS) score of less than 8 at admission. The study showed that the neurologic examination can be trusted and is reliable in mild to moderate pediatric blunt TBI and that RHCT be performed only when there are clinical indications.

2. Enforcing a bedtime routine for your children

Does a proper bed time schedule for children affects behavioral outcome? Data from 10,230 7-year-olds from the UK Millennium Cohort Study, with bedtime data were collected at 3, 5, and 7 years, and behavioral difficulties scores as rated by mothers and teachers were analyzed. Children with non regular bedtimes had more behavioral difficulties. There was an incremental worsening in behavioral scores as exposure through early childhood to not having regular bedtimes increased. For children who changed from regular to non regular bedtimes between ages 5 and 7 there was a statistically significant worsening in scores, ã = 0.42. Hence having regular bedtimes during early childhood is an important influence on children's behavior. This seems to be a clear area for life style advice / intervention by paediatricians which can have an important impact on children's behavior.
impact on health throughout life.

3. Again probiotics!!!


Is probiotic useful for excessive infant crying? In this systematic review and meta-analysis studies that randomized infants 3 months or younger to oral probiotics vs placebo or no or standard treatment with the outcome of infant crying, measured as the duration or number of episodes of infant crying/distress or diagnosis of “infant colic” were included. Out of the 12 trials (1825 infants) identified, 6 suggested probiotics reduced crying, and 6 did not. Among the management trials (n = 5), 3 concluded probiotics effectively treat colic in breastfed babies; 1 suggested possible effectiveness in formula-fed babies with colic, and 1 suggested ineffectiveness in breastfed babies with colic. Meta-analysis of 3 small trials of breastfed infants with colic found that Lactobacillus reuteri reduced crying time at 21 days (median difference, -65 minutes/d; 95% CI, -86 to -44). Out of 7 prevention trials, only 2 suggested possible benefits. Considerable variability in the study populations, study type, delivery mode/dose of probiotic supplementation, and outcomes precluded meta-analysis. The author's concluded that although L reuteri may be effective as treatment for crying in exclusively breastfed infants with colic, there is still insufficient evidence to support probiotic use to manage colic, especially in formula-fed infants, or to prevent infant crying.

4. At least one thing we cannot blame on lack of Vitamin D


Does Vitamin D supplementation reduce incidence of Flu? U.S. researchers while conducting a large blinded trial of vitamin D, and calcium supplementation for preventing large bowel adenomas did a sub-study to look at rates of upper respiratory tract infection among participants. Participants were healthy adults (age range, 45–75) whose initial vitamin D levels exceeded 12 ng/mL. During a period that spanned two winter “flu seasons,” 399 participants who were receiving daily vitamin D (1000 mg) and 360 participants who were receiving placebo reported identical rates of both serious and trivial upper respiratory infections. These results were unaffected by adjustment for receipt of supplemental calcium, receipt of flu vaccine, or body-mass index. Rates were similar during the first winter of the study, which overlapped the H1N1 flu pandemic (2009–2010), and during the subsequent one without pandemic influenza. Mean serum vitamin D levels did not differ among participants who did and did not report respiratory illnesses.

5. It happens even in San Fransisco!!!

Do we regularly check urine before diagnosing UTI and prescribing antibiotics for it? Urine testing in diagnosed cases of UTI were characterised in an ambulatory setting over a period of 5 years. Out of 28,678 children cases of UTI, urinalysis was performed in 76%, and urine culture in only 57%. 32% of children <2 years had no culture performed for an antibiotic-treated UTI episode. Urine culture use decreased during the study period from 60% to 54% (P < .001). As expected variation in urine culture use was observed with age (<2 years: odds ratio [OR] 1.0, 95% confidence interval [CI] 0.9-1.1; 2-5 years: OR 1.3, 95% CI 1.2-1.4; 6-12 years: OR 1.3, 95% CI 1.2-1.4, compared with 13-17 years); gender (boys: OR 0.8, 95% CI 0.8-0.9); and specialty (pediatrics: OR 2.6, 95% CI 2.5-2.8; emergency medicine, OR 1.2, 95% CI 1.1-1.3; urology: OR 0.5, 95% CI 0.4-0.6, compared with family INTERNAL medicine). The study concluded that in their ambulatory set up health care providers often did not obtain urine tests when prescribing antibiotics for outpatient pediatric UTI and recommended additional research to determine the implications of empirical antibiotic prescription for pediatric UTI without confirmatory urine testing.

6. Something cheaper and easier!!!


Can High Flow Nasal Cannulae Oxygen replace nasal CPAP? The use of high-flow nasal cannulae oxygen is becoming an increasingly popular alternative to nasal continuous positive airway pressure (CPAP) for non-invasive respiratory support of very preterm infants (gestational age, <32 weeks) after extubation. However, data on the efficacy or safety of such cannulae in this population are lacking. In this multicenter, randomized, noninferiority trial, 303 very preterm infants received treatment with either high-flow nasal cannulae (5 to 6 liters per minute) or nasal CPAP (7 cm of water) after extubation. The primary outcome was treatment failure within 7 days. The use of high-flow nasal cannulae was non-inferior to the use of nasal CPAP, with treatment failure occurring in 52 of 152 infants (34.2%) in the nasal-cannulae group and in 39 of 151 infants (25.8%) in the CPAP group (risk difference, 8.4 percentage points; 95% confidence interval, -1.9 to 18.7). Almost half the infants in whom treatment with high-flow nasal cannulae failed were successfully treated with CPAP without reintubation. The incidence of nasal trauma was significantly lower in the nasal-cannulae group than in the CPAP group (P=0.01), but there were no significant differences in rates of serious adverse events or other complications. Hence a trial of high flow nasal cannulae oxygen seems to be highly justified.

7. Not all syncope requires cardiac evaluation!!!


Is it possible to distinguish between cardiac and non cardiac syncope without
In this study 89 patients (4-18 years of age) with vasovagal syncope and 17 patients (4 months to 17 years of age) with proven cardiac syncope where compared in an attempt to identify any unique distinguishing features. The investigators found that among those with cardiac syncope, surrounding activity was present in 65% vs 18% (P < .001), family history of cardiac disease or sudden cardiac death was identified in 41% vs 25% (P = .2), abnormal findings on the physical examination supporting cardiac diagnosis were present in 29% vs 0% (P < .001), and abnormal findings on electrocardiograms were found in 76% vs 0%, respectively (P < .001). Screening for cardiac disease using any 1 of these 4 characteristics had a sensitivity of 100% and specificity of 60%. Hence they concluded that a screening rule that uses proper history, physical examination findings, and electrocardiogram should accurately separate patients requiring further evaluation for cardiac etiology from those with vasovagal syncope in whom cardiology referral is unnecessary.

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**MRI Department, Institute of Child Health, Calcutta**

**How long it is open?**

It is open from 9 a.m. to 7pm on weekdays. On Sunday, it is open from 9am to 1pm.

**What is the usual time required for MRI scan?**

About 30 minutes.

**How an appointment is made?**

It is usually done at the reception of MRI department by personal visit or by telephone. Telephone No.s (033)2289-3526 and (033)6526-6969.

**What preparation is needed for MRI?**

Usually no preparation is needed. For MRCP study 4-6 hours fasting is needed. For children, oral sedation is usually required. In some hyperactive, restless patients anesthesia is needed. We have fully equipped setup for anesthesia and extremely competent anesthetist for such patients. About 6 hours of fasting is needed prior to anesthesia.