ANNALS OF
INSTITUTE OF CHILD HEALTH CALCUTTA
(Affiliated to West Bengal University of Health Sciences)

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Government of India has taken the decision regarding polio immunization in India in conformity with the global polio endgame strategy as initiated by WHO. April 25, 2016 as the National Switch Date for switching from tOPV to bOPV all over the country. After the switch date, only bOPV will be used both in routine immunization (RI) as well as polio campaigns. Other important decisions are as below:

- Introduction of at least single dose of intramuscular (IM) IPV at 14 weeks or first contact afterwards in the RI along with 3rd dose of DTP in 6 states viz Bihar, Uttar Pradesh, Madhya Pradesh, Gujarat, Punjab and Assam
- Nationally coordinated switch from tOPV to bOPV all over the country on 25 April 2016 associated with cessation of use, withdrawal, destruction and validation of all available tOPV stocks from all over the country
- Introduction of fractional dose (0.1 ml) intradermal IPV (fIPV) at 6 and 14 weeks in Orissa, Andhra Pradesh, Telangana, Tamil Nadu, Kerala, Karnataka, Maharashtra and Puducherry from April, 2016.

The main objective of these initiatives is to enhance population immunity against type-2 poliovirus just prior to proposed switch from tOPV to bOPV (type 1 and 3) so that the risks associated with the complete removal of type-2 vaccine virus can be mitigated. These risks include future outbreaks of cVDPV type 2 emerged during or shortly after OPV type 2 withdrawal, importation of cVDPVs, or outbreak occurring due to break in bio-containment process in laboratories storing viruses. The decision to employ only a single dose of IPV is only an interim arrangement owing mainly to the limited supply and availability of IPV.

The recent recommendation of GPEI/GoI to use fractional dose IPV by ID route is based on the trial done in Bangladesh. In this study, ID-fIPV failed the non-inferiority test (i.e. with a non-inferiority margin of 10% in seroconversion) when compared with full dose IM-IPV for all serotypes for seroconversion and priming observed with 1 or 2 doses. The seroconversion at 18 weeks following two doses of fIPV at 6 and 14 weeks was 80.9% whereas the corresponding rate for IM-IPV was 91%. Further, the GoI intends to use standard BCG needle and syringe for intradermal administration of ID-fIPV whereas in the Bangladesh study, a microneedle based device, MicronJet 600 (MJ600) was used. A recent systematic review conducted on immunogenicity and effectiveness of 1 or 2 doses of IPV vaccine concludes that routine immunization with 2 full or fractional doses of IPV given after 10 weeks of age is likely to protect >80% of recipients against all types of polioviruses.

Dr Maya Mukhopadhyay
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Cytomegalovirus in Biliary Atresia – A Case Series

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Abstract: Cytomegalovirus (CMV) infection has been documented along with extra hepatic biliary atresia (EHBA) in children. However debate ranges on whether the association is causal or coincidental. We present a series of 4 cases who were admitted to our hospital over a period of 18 months. Two of them were treated with gancyclovir without any response. Two underwent surgical interventions without any appreciable benefits, One died and the fourth was lost to follow up.

Keywords: Neonatal cholestasis (NC), Extra hepatic biliary atresia (EHBA), Cytomegalovirus (CMV)

Introduction

Neonatal cholestasis (NC) has been documented in 19 – 33% of neonates affected with chronic liver disease and attending tertiary care hospitals in India. Out of these, almost one third has been attributed to biliary atresia. Cytomegalovirus (CMV) is a known agent to cause intra hepatic bile duct paucity and destruction. It has been suggested to cause extra hepatic biliary atresia (EHBA) in a few case series. We present a series of 4 cases who were admitted to our hospital over the course of last 18 months and were diagnosed to have EHBA along with CMV infection.

Case 1

3 months female baby was admitted with yellowish discolouration of eyes and urine since 3 weeks of age. She was having pale stool since 1 month of age. Investigations were suggestive of neonatal cholestasis (NC) [Table 1]. As she had CMV IgM and IgG reactive [Table 1], a CMV DNA PCR (polymerase chain reaction) was sent for assessing the viral load. Liver biopsy was suggestive of EHBA. Gancyclovir was started because of the high viral load and the child being symptomatic. However, even after 3 weeks as the jaundice was persisting, Kasai portoenterostomy was done. The child still continues to have conjugated hyperbilirubinemia with progressive enlargement of liver and spleen at 21 months of age.

Case 2

6 weeks male infant was admitted with yellowish discolouration of eyes and urine and occasional whitish stools since 3 weeks. On examination, he had hepatosplenomegaly. CMV DNA PCR was suggestive of infection and liver biopsy of EHBA [Table 1]. Liver transplant was advised but the parents could not do because of financial constraints. Kasai portoenterostomy was done within 2 weeks of diagnosis. At 8 months, child has conjugated jaundice with deranged liver enzymes and firm and enlarged liver and spleen.

Case 3:

7 months female baby was admitted with...
jaundice since 1 month of age and clay coloured stools. She had distended abdomen and enlarged and firm liver and spleen and ascites. HIDA (Hepatic technetium-99m-mebrofenin iminodiacetate scan) was suggestive of biliary atresia. Liver biopsy showed cirrhotic changes. CMV DNA PCR was significantly elevated [Table 1]. As the child presented late, with cirrhotic changes, operative intervention was not done. She was given supportive management and she died after 1 month.

**Case 4**

5 months female presented with jaundice and clay coloured stools since 2 weeks of age. She had enlarged liver and spleen. Liver biopsy was suggestive of EHBA and CMV DNA PCR was significantly elevated [Table 1]. Gancyclovir was administered for 2 weeks. However her jaundice persisted. She was eventually lost to follow up.

All 4 cases were diagnosed with EHBA with concomitant infection with CMV. Apart from jaundice with deranged liver function, none of the cases had abnormalities in hearing or vision. Head circumference was normal for age in all 4 babies.

**Discussion**

Viral infection has been proposed as a cause of EHBA. In 1 of the studies from Pakistan, patients with EHBA were searched for any evidence of infection with CMV, Ebstein Barr virus, Toxoplasma, Herpes, Hepatitis B and C. It concluded that CMV may play a role in the pathogenesis of EHBA. In another study from Brazil on 76 patients with NC, CMV IgM was positive in 28.5% of patients with extra hepatic cholestasis and 29.4% with intra...
hepatic cholestasis. They also found evidence of maternal infection being more common in extra hepatic cholestasis. All our 4 patients had CMV IgM positive along with significantly detectable copies of CMV DNA PCR. The liver enzymes, HIDA and liver biopsy was suggestive of EHBA.

Cases 1 and 2 underwent Kasai portoenterostomy without any improvement in follow up. Case 1 underwent the operation after 3 months and case 2 underwent early. A study from London found CMV IgM positive cases with biliary atresia as a distinct entity with late presentation and a poor response to Kasai operation. Except case 2 who presented early, all the other patients presented late. 2 patients underwent operation with poor response in follow up. Cases 1, 3 and 4 also had significant inflammation and fibrotic changes on liver biopsy as has been documented in this study.

Another study from China also reports a strong association between CMV and lower rate of jaundice disappearance following operation. They also found increased fibrosis as we found in our patients.

However a study from Canada, with CMV DNA analysis on bile duct biopsy specimens showed negative results ruling out any association of CMV involved in the pathogenesis of EHBA.

There is still no consensus on whether the association between CMV and EHBA is causal or co incidental. A study by Tarr et al have stated that infants with cholestasis with CMV infection should also be investigated for EHBA and monitored accordingly. Till data is available, CMV should be considered as an etiological agent for EHBA with poor prognosis even after operative intervention.

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In 1957, a solitary case of bone dysplasia with symmetric thickening of the shafts of long bones along with anemia was reported by Dr. S P Ghoshal in Indian Journal of Pediatrics. The patient was a 4 year old male child who presented with difficulty in walking, poor muscle mass, genu valgum and palpably thick long bones. The radiological features revealed generalised broadening of the long bones with extensive affection of the diaphyses and thickening of the cortices. The patient had moderate anemia with unexplained reticulocytosis but did not require blood transfusion. The disorder was designated as an unusual bone dysplasia though the clinical and radiological features were in favour of diaphyseal dysplasia with anaemia of undetermined cause.

The major form of diaphyseal dysplasia was reported separately by Camurati (1922) and Engelmann (1929). Though a probable case with similar clinical and radiological features was reported earlier by Cockayne in 1920, the diaphyseal dysplasia with its onset in childhood gained recognition as Camurati-Engelmann disease.

In 1961, Lennon et al described a case of Engelmann disease along with review of literature. The literature analysis revealed characteristic features of the disorder like generalized cortical thickening of long bones, severe bone pain, muscular hypoplasia, occurrence of the disease in several members of the same family, age of onset and progression to different long bones from its initial onset in femur or tibia. However the association of significant haematological abnormality especially anaemia was not described.

The 1973 publication by Hundley and Wilson on progressive diaphyseal dysplasia included a review of literature and report of seven cases in one family. They summarized the clinical and radiological features of 70 patients. Only 11 patients out of 35 who had haematological records, show low haemoglobin and only 2 of them were below the age of 5 years.

Neither of the two major reviews of the literature on diaphyseal dysplasia could document severe anaemia as a major clinical association in Englemann disease. None of these reports emphasized the existence of severe anaemia often requiring transfusion, as a major clinical feature of Englemann disease.

Since the 1957 case report, Dr S P Ghoshal and others physicians of Institute of Child Health, Kolkata became aware of the association of anaemia and diaphyseal dysplasia. As a result subsequent cases were identified in 1959, 1962 and 1971. All these children had significant anaemia, not responding to conventional treatments and
often required blood transfusion. Since a few publications on Englemann disease claimed some improvement of the radiological features after corticosteroid, a trial of this drug was given to all of these newly diagnosed patients of diaphyseal dysplasia with anaemia. Surprisingly there was significant improvement in haematological as well as radiological changes in all the patients. None of them required any transfusion after introduction of steroid.

In 1985, a 13 month old boy presented to ICH, Kolkata with severe pallor needing urgent transfusion, revealed thickening of diaphyseal cortices of long bones similar to the previous cases but more extensive and elaborate in nature. Steroid therapy produced almost complete haematological remission and a two year follow up showed significant radiological improvement as well.

In 1986, all the five patients who presented to Institute of Child Health, Kolkata between 1957 to 1985 with diaphyseal dysplasia and steroid responsive anaemia were analysed together to establish their common features and also to establish the essential difference between these cases and Camurati Engelmann disease. This research was published as an article by Dr. Ghoshal and his associates in Journal of Paediatrics in 1988, under the heading of “Diaphyseal Dysplasia Associated with Anaemia”.

Even in 1957, when Dr. Ghoshal identified the very first child with bone dysplasia and anaemia, he surmised that this disorder might represent a hitherto undescribed condition in medical literature, clearly distinct from the classical form of diaphyseal dysplasia described by Englemann. The comprehensive 1988 report also ends with the suggestion that these cases represent a distinct group of patients. However more convincing evidence other than the radiological and haematological findings was lacking.

In 1989, Ozsoyulu reported a single child having similar disorder and parental consanguinity.

In 1993 in the European Journal of Pediatrics Gumruk et al. described two children, a brother and sister, born out of consanguineous marriage, with diaphyseal dysplasia, severe anaemia, leucopenia and thrombocytopenia. Radiologically both children had similar appearance of wide medullary cavities of the long bones with discrete cortical hyperostosis and hypocellular marrow. The presence of anaemia and other haematological abnormalities, absence of pain or muscular involvement also separated this disorder from Camurati-Engelmann disease. There was also a distinct possibility of autosomal recessive inheritance. Gurmuk suggested that these children probably represent a separate and new disorder.

Bagga and Choudhury reported a single case of diaphyseal dysplasia (corrected) with anaemia and thrombocytopenia in Indian Pediatrics in 1989 but did not mention Ghoshal’s cases.

Subsequently following Gurmuk’s publication, The Oxford Medical database entered Haematodiaphyseal dysplasia as a separate entity in the name of Dr. Ghoshal and was given a McKusik no. 231095, different from that of Camurati Engelmann disease. Even at this point confusion remained among...
many clinicians regarding the nature of the illness described by Dr. Ghoshal. In a report published as late as 2000\textsuperscript{10}, the author described Ghoshal diaphyseal dysplasia as a rare variety of Engelmann disease. The confusion was probably due to the fact that the genetics behind Ghoshal dysplasia was yet to be revealed, whereas that of Engelmann disease was well established.

Around the year 2000, the main distinction between GHDD and Camurati-Engelmaan disease (CED) were made on the basis of

(a) **Hematological features:** Whereas CED might have variable haematological abnormalities, GHDD persistently had a normochronic normocytic recurrent anaemia with or without hypocellular marrow and splenomegaly and the majority were transfusion dependant. The most important difference however was remarkable improvement in anaemia in GHDD following corticosteroid therapy and cessation of requirement of further blood transfusion.

(b) **Radiologically:** GHDD had a diaphyseal cortical sclerosis extending to the metaphysis of the tubular bones. There was no subperiosteal bone formation and the increase in the bone density was not always amorphous. There was usually no sclerosis of the cranial bones (fig 1 & 2).

(c) Apparent mode of inheritance: whereas Camurati Engelmaan disease was established to be an autosomal dominant disorder, GHDD was probably autosomal recessive in transmission.
In an elaborate review of sclerosing bone dysplasia Vanhoenacker (2000) expressed the opinion that distinction between different subgroups of sclerosing bone dysplasia as per the revised International Nomenclature and classification of Osteochondro dysplasias (1997), relies mainly on the morphological information provided by the radiologists. According to the International nomenclature GHDD was placed in the group of increased bone density with diaphyseal involvement, along with Camurati Engelmaan disease and other disorders.

A real breakthrough in GHDD came from Isidor B et al in 2007, who performed a genome wide search in two inbred families originating from Algeria and Tunisia. They could map the locus of the gene responsible for GHDD to chromosome 7q 33-34 in a 3.4 Mb interval between loci D7S2560 and AC 091742, which contained 37 genes.

In a subsequent study by Genevieve et al in 2008 in 2 similar families of GHDD of Tunisian and Pakistani origin, mutations of TBXASI gene, which encodes Thromboxane Synthetase (TXAS) were identified. TXAS is an enzyme of the arachidonic acid cascade, which produces thromboxane A2 (TXA2). Platelets from subjects with GHDD showed a specific deficit in arachidonic acid produced aggregation. They also found that TXAS and TXA2 modulated expression of TNFSF II and TNFRSF II B, which encodes RANKL (Receptor activator of nuclear factor Kappa-B ligand) and osteoprogenin, respectively in primary cultured osteoprogenin from patients of GHDD.

The molecular genetics of Camurati Engelmann disease which has an autosomal dominant mode of inheritance, was identified by Ghadami et al in 2000. They performed genomewide linkage analysis in unrelated Japanese family of 27 members, of which 16 were affected. They found the locus of responsible gene in 19q13.1 –q13.3. The responsible gene TGFBI (Transforming growth factor beta I), located at 19q 13 showed domain specific heterozygous mutation. A second form of the disease known as Camurati Engelmann disease type 2 was described in two unrelated girls by Nishimura et al in 2002. The morphological and radiological features remain similar to CED but no mutation of TGFBI mutation was detected.

In the last update on 04.09.2008 the OMIM database included this specific disorder under the title Ghosal Haematodiaphyseal Dysplasia with an alternate title of Ghosal Syndrome with a Phenotype MIM number 231095 and a Gene/Locus MIM number 274180.

In March 2015, Arora R et al published an article in skeletal radiology on Ghoshal haematodiaphyseal dysplasia – a concise review including an illustrative patient. They reviewed approximately 15 reported cases from literature though the number might have been a little more as many cases like that described by Bagga and Choudhury did not appear in the literature by the designation of Ghoshal haematodiaphyseal dysplasia. The most interesting fact about the case described by Arora was that it was a 21 year old lady who had severe and recurrent anaemia which was transfusion dependant but the cause remained undiagnosed. They concluded that...
such cases of Ghoshal Haematodysplasia may escape diagnosis because of unfamiliarity of the disease among the clinicians.

In the Journal of Pediatric Haematology – Oncology in May 2015 John RR et al described 3 cases of Ghosal Haematodiphyseal Dysplasia (GHDD) who presented with moderate to severe anaemia, splenomegaly, hypocellular marrow and increased reticulin. All the cases had significant improvement of anaemia with oral steroid and no longer needed blood transfusion. They therefore expressed the opinion “It should therefore be considered as a differential diagnosis of unusual anemia in early childhood, especially in children from the Middle East or the Indian subcontinent”.

It took nearly 50 yrs to understand different aspects of GHDD. From the 1st report in 1957 to the gene locus identification in 2007 only a few cases (less than 15) have been reported. The rare occurrence of this condition was probably responsible for such delay in the characterization of the disorder.

Conclusion

Ghoshal haematodiphyseal dysplasia is now recognized worldwide as a sclerosing diaphyseal dysplasia with a steroid responsive moderate to severe anaemia. Till date around 20 such cases have been reported in the literature. Most of the cases have been reported from The Asian subcontinent and the Middle East. Since it has an automosal recessive mode of inheritance, the occurrence is more in communities where parental consanguinity is common. Knowledge of GHDD is essential for hematologists who deal with resistant and unexplained anaemia (as pointed out by Arora et al John RR et al) and also for those who deal with hereditary bone diseases. Proper clinical surveillance of patients who might have escaped the diagnosis earlier appears to be of immense significance as the condition offers an easy and inexpensive cure.

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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.

Monday to Friday: 9.30 am to 3 pm, Saturday : 9.30-12.30 noon
Nosocomial infections (NI), are associated or related to health care, and represent a major public health problem in pediatric intensive care units (PICU) and neonatal (NICU) too, by causing high morbidity and mortality, a significant increase in hospital stay and generate increased health care costs (Centers for Disease Control and Prevention (CDC), 2010). Therefore, epidemiological surveillance and prevention must be considered fundamental objectives of quality and safety of pediatric and neonatal critical patient care.

In hospitalized adult patients the NI figures reach 5-10% according to data from the CDC (Yokoe, 2008). These figures are even higher in the pediatric intensive care patients and the prospective European study of UCIP reveals an incidence reaching 23.5% (Raymond, Aujard & the European Study Group, 2000). In the neonatal intensive care these figures are even higher if we take into account the higher risk newborn, the extreme low birth weight (ELBW <1000 grams), in who we find figures of incidence over 40%, both in Europe and USA. Being aware of their impact, monitoring and control of nosocomial infections should be a priority.

Through surveillance we obtain various indicators, the most interesting being those that relate the days of use of devices (urinary catheter, mechanical ventilation and intravascular devices) with the same associated infections (urinary tract infection, pneumonia and bacteremia). These indicators are also used by the NNIS (National Nosocomial Infections Surveillance System Report ((NNIS), 2003), which since 2005 is integrated into the NHSN (National Healthcare Safety Network, Edwards et al, 2007).

In addition to the NNIS, the NCID (National Center for Infectious Diseases, 2010; Edwards et al, 2007) and now the NHSN have represented over the years most important references in infectious diseases epidemiology and preventive fields.

The monitoring takes on new significance in the neonatal intensive care units. The patients seen in it, especially the lower gestational age and birth weight are always at high risk for nosocomial infection. This is due to their immaturity (minor immune function, impaired skin and gastrointestinal barriers) and their NICU longer stay days (major bacterial and fungal colonization, central venous catheters, parenteral nutrition and invasive manipulation).

The most common microorganisms found in Bacteremia are: Staphylococcus epidermidis, Enterobacter cloacae, Enterococcus faecalis, Pseudomonas aeruginosa, Coliforms and Candida parapsilosis.

The NI is certainly a problem in pediatric intensive care unit, although smaller than in the neonatal unit; and bacteraeemia was the
predominant, related to an excessive time use of intravascular devices (central venous catheters). Several comparative results helped to understand their impact on later to direct time and improvement strategies to reduce infectious morbidity:

"Guidelines for the Prevention of Infections Associated with Intravascular Devices in Pediatric and Neonatal Patients" (2005); and reinforcement of the "Hygiene Program Hands", Specific training courses for all the health personnel of neonatology and other pediatric areas can contribute to better results of NI indicators.

Currently, the program developed by the U.S. John Hopkins Hospital and recommendations established by the WHO, the Spanish Health Ministry,

Some Health care organisations (HCOs) are planning an ambitious strategic plan "Bacteremia zero" (Bacteremia zero 1st edition, 2009) which attempts to reduce the incidence of bacteremia intervention is based on two main critical points to reduce related bacteremia with central venous catheters: proper hand hygiene for all the care team, medical students, family and visitors, and the proper use of intravascular catheters.

As bacteremia, whether or not the use of intravascular devices, are the leading cause of nosocomial infection in many units, it should establish corrective measures to improve better indicator results. Bacteremia associated with central venous catheters is caused mainly by gram negatives, non-fermenters and coagulase-negative Staphylococci and others colonizing the skin around the insertion point of germs transmitted by the manipulation of the ICU staff. Moreover bacteremia is related to bacterial translocation from the intestinal reservoir. Thus both the care of central catheters, modification of bacterial colonization of the newborn and hygiene in the handling of this risk population has become primary goals in modern days.

**Improve the management of central venous catheters**

There are several strategies that can be taken to reduce infections associated with intravascular devices, and usually is a set of them which we must take to achieve a reduction in nosocomial infection. Therefore needs to be an established protocol for good clinical practice guidelines, based on the best available evidence and adapted many times for adult medicine, with proven results even in neonatal units that have achieved lower the number of infections (Aly, 2005).

In this package includes not only those related to the act itself of catheter placement (choosing the right place, correct use of hand hygiene, barrier precautions such as gowns, caps, gloves and mask, a team of sufficient or proper disinfection of the skin) or maintenance (minimizing the number of entries, disinfect with alcohol keys to manipulate them, change dressings have become wet, dirty or rise, or every 7 days failure to fulfill the above, currently using chlorhexidine to clean the entry point), but should be reviewed with, the indications for placement, the criteria for withdrawal or catheter-related infection, of other indicator results.

**Hand hygiene**

The importance of hand hygiene is making
worldwide relevant and need the introduction of a specific hospital protocol for reduction of nosocomial infection (Capretti, 2008; Won, 2004). The hands of sanitary staff are the main reservoir and vehicle for transmission of pathogens among patients admitted in the NICU. The concept of hand hygiene is a broader concept than simply disinfecting hands, includes skin care, nails, and removing jewellery. This requires adequate use of alcohol solution (Boyce, 2002) or the hand washing with soapy water.

The creation of a multidisciplinary working group of infection control, which can involve Preventive Medicine of PICU and NICU, can facilitate the implementation of effective measures to control and prevention of nosocomial infection. Staff aware need to achieve a steady improvement among all the in-house indicator results, safety and quality obtained.

Further References:
1. CDC Protocol on NI, 2010

Immunization Clinic

Immunisation Clinic of the Institute of Child Health offers service of not only EPI Vaccine, but also of all newer vaccines at reasonable cost.

Thousands of children are benefitted by the service of this clinic.
Introduction

Part one of this publication discussed the global evolution of ethics in human research. The impact was felt in India too with the Indian Council of Medical Research (ICMR) formulating its own National guidelines in 1980. Now, researchers practicing or planning research studies involving human participants are bound to follow these guidelines as enumerated in the 2006 publication by ICMR Ethical Guidelines for Biomedical Research on Human Participants. For studies involving a new drug that is to be tested on human participants, additionally Schedule Y guidelines by the Central Drugs Standard Control Organization (CDSCO) need to be adhered to; these studies are termed as regulatory clinical trials. There are several international bioethics codes as well which are commonly referred to in biomedical research, namely, the Nuremberg Code; The Declaration of Helsinki; WHO – GCP (Good Clinical Practice); UNESCO’s Universal Declaration on Bioethics and Human Rights, 2005; CIOMS, 2004; Nuffield Council on Bioethics, 2003 ; and the ICH (International Conference on Harmonization) GCP, 1996 guidelines.

Part two is dedicated to the understanding of the broad statements of these guidelines, especially focusing on the ICMR ethical guidelines that need to be kept in mind when designing and executing biomedical research. Recently, ICMR floated the Draft National Ethics Guidelines for Biomedical Research involving children on its website, giving due importance to this vulnerable population on whom research should neither be exploited nor denied. The statements put forth in this draft shall be discussed with the general statements as outlined in the 2006 guidelines.

General Statements:

Research on human participants must ensure that:

1. Purpose of research is to increase knowledge and that there is betterment of all.
2. Conduct of research should ensure that well being and dignity of the participant is not compromised and that there is avoidance of all possible risks.
3. Evaluation of research should be conducted at all stages – design, experimentation and even declaration of results ensuring human safety at all levels.

Research proposals involving children should be justified, scientifically sound, conducted by experts, in a child-friendly environment. In general, drugs should be tested for safety and efficacy in adults before being tested in children.

General Principles

The core guiding values of health research are autonomy, justice, beneficence and non-maleficence on the pillars of which the 12 general principles are framed:

1. Essentiality: Research should be planned...
using human participants only when it is absolutely essential after due consideration of all possible alternatives and after the research proposal has been duly vetted and considered appropriate by an independent and responsible body of persons.

2. Voluntariness, informed consent and community agreement: Research participants should be fully apprised on the impact and risk of such research. They should retain the rights of abstaining irrespective of any legal or other obligation. When research entails treating any community or a group of persons, the principles of voluntariness and informed consent shall apply, mutatis mutandis, as a whole.

3. Non-exploitation: Research participants should be remunerated for their involvement. Irrespective of the social and economic condition or status, or literacy or educational levels, the participants should be fully aware of the merits and demerits of research that they have participated in and any physical/moral/psychological implications arising thereof. Participants should be selected in a manner such that the burdens and benefit of research are distributed without arbitrariness, discrimination or caprice. Each research should have a mechanism for compensation to cover all risks should any injury or death occur due to participation in research and to ensure that all remedial action (treatment, rehabilitation and after care) are taken if and when necessary.

4. Privacy and confidentiality: Identity and records of human participants should be kept confidential to prevent any kind of hardship, discrimination or stigmatization and should only be disclosed on scientific and legal grounds, only after a written consent from the participant is obtained.

5. Precaution and risk minimization: Care and caution should be taken at all stages of research to ensure that the research participants are put to minimum risk.

6. Professional competence: Research at all times should be conducted by competent and qualified persons who act with total integrity and impartiality and are morally and ethically driven to conduct research.

7. Accountability and transparency: Research should be conducted in a fair, honest, impartial and transparent manner. There should be full disclosure by researchers and of any conflict of interest that may exist. Full data and notes should be retained for a reasonable time for purposes of post-research monitoring, evaluation, scrutiny by legal and regulatory authorities.

8. Maximization of public interest and of distributive justice: The applicative use of the research outcome should benefit mankind in general and not to those who are socially well off, particularly to the participants themselves and the community from which they are drawn.

9. Institutional arrangements: All persons connected with research should ensure that institutional arrangements are made to comply with and conduct the research, to preserve and archive reports, materials and data and to ensure that subsequent use and application of research is made in a bonafide and transparent manner.

10. Public domain: The results and outcome of research should be brought to the
public domain so that it is made known through scientific publications subject to preserving the rights under law to the researchers and their co-workers.

11. Totality of responsibility: The professional and moral responsibility for the due observance of all principles, guidelines, and prescriptions laid down generally or as a result of research and experimentation devolves on all connected directly or indirectly with research including the researchers, those funding the research, the institution(s) where the research is being conducted, various persons, groups or undertakings who sponsor, use, or derive benefit from the research, market the product or prescribe its use.

12. Compliance: It is binding on all persons, conducting or connected with research using human participants to ensure that both the letter and spirit of these guidelines, as well as other norms, directions and guidelines which are applicable for that research are scrupulously observed and duly complied with.

Selection of Special Groups as Research Participants

Certain individuals or group of individuals are considered “vulnerable” because of reduced autonomy as research participants and thus having an increased likelihood of incurring additional and greater harm for example; children, students, prisoners, mentally challenged individuals and others. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence. They need to be specially protected during participation in research including detailed and documented informed consent process.

Children constitute a special group whose participation in research demands utmost attention with regards to formulating ethical guidelines, especially in developing countries when financial crunch and low levels of literacy in parents make the children more vulnerable. The 2006 guidelines have a small section on biomedical research on children; however the need to devote separate detailed guidelines on children and neonates was felt and the draft guidelines were formulated by ICMR.

The ethical issues in children are that children lack autonomy, i.e. they are intellectually and emotionally not mature to give consent for participation in research. Their parents or legally acceptable representative (LAR) can give consent on their behalf. Any research on children must consider the level of their physical, cognitive, emotional, and social development, with younger children requiring greater levels of protection. To minimize risks, research on animals and adults should precede research on children. These considerations uphold the spirit of the basic ethical principles of beneficence and non-maleficence. At the same time, research in children should be carried out to benefit them in the future; otherwise impedance to research in children goes against the spirit of justice. The benefits should be distributive; children from poor socio-economic background should not be exploited just because they are available and that their parents are not fully aware of their rights.

Risks

Risk or harm that may occur from participation in research needs to be carefully weighed against benefit received. Risk in
pediatric research may be specific such as fear and separation from parents. Risk may be may be physical (e.g., pain, disability, discomfort, or death), or psychological (e.g., fear, anxiety, or depression), or social (missing school etc). It should be emphasized that risk assessment should be considered for procedures that would be carried out over and above standard care which entail their own associated risks.

Benefit is a positive outcome which may be direct to the participant such as pain reduction, cure from disease etc. Indirect benefits may be developing new social relationships, learning more about the disease. Participants may perceive access to better care, free test analyses, be a ‘special patient’, as indirect benefits. Payment for participation should never be considered in the risk-benefit ratio.

Risks may be classified as minimal, low or high but again it depends on age of children being enrolled and also from child to child even for the same research procedure.

Minimal risk is defined as one which may be anticipated as harm or discomfort not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. This includes procedures such as questioning, observing, and measuring children, provided that procedures are carried out in a sensitive way, respecting the child's autonomy, and that consent has been given. Procedures with minimal risk include history taking, physical examination, chest X-ray, obtaining bodily fluids without invasive intervention, e.g., taking saliva or urine samples etc.

Low risk is defined as a slight increase in the potential for harms or discomfort beyond minimal risk (as defined in relation to the normal experiences of average, healthy, normal children). These include procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress; e.g., a blood test, oral sedation etc.

All research procedures which have a risk over and above the low risk are classified as high risk. These include procedures such as lumbar puncture, lung or liver biopsy, intravenous sedation for diagnostic procedures etc.

Some procedures such as exposure to chemotherapy or bone marrow aspiration may be relatively ‘routine’ for children suffering from leukemia, which otherwise are high risk procedures for normal healthy children. However, investigators should refrain from relative interpretation of minimal risk and should apply the same equitable protection to all participants. This nullifies chances of misinterpretation of categorizing studies as ‘minimal risk’ for those enrolling children who experience high risk in their daily lives because of their underlying socio-economic or medical conditions.

**Consent and Assent**

Before performing research on a human participant, consent of voluntary participation is absolutely necessary in respect of the individual’s autonomy. This is after the participant has been sufficiently informed about the research in a simple and easily understandable language that is clearly understood by the participant. The process is documented on the Informed Consent Form with Participant/ Patient Information Sheet. In the case of an individual who is not capable of giving informed consent such as a child, the consent of a legal guardian is permissible. Legally acceptable representative (LAR) means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to
participate in research or to undergo a diagnostic, therapeutic, or preventive procedure as per research protocol.

When the child’s LAR is illiterate and/or refuses thumb impression, verbal consent may be taken provided that the documentation is signed by an impartial witness. Audio-video recording of the process is mandatory in case of clinical trials.

Sometimes, it may be necessary to take a fresh consent or a re-consent during an on-going study such as the participant is now above 18 years of age or that the deviation of protocol has occurred. The investigator should familiarize himself/herself with the plausible conditions for re-consenting.

Waiver of consent is awarded by the ethics committee when the research involves not more than minimal risk or when the participant and the researcher do not come into contact such as retrospective data analysis or when it is necessitated in emergency situations. Such studies normally have protections in place for both privacy and confidentiality, and do not violate the rights of the participants.

Informed consent process should not be a mere formality but an interaction between the participant and the investigator wherein the participant is well informed about the research and can make a decisive independent choice to participate, without the fear of losing medical care and other benefits if he/she refuses. The participant should be assured of confidentiality of details, benefits of research, compensation for time spent, travel and other costs incurred, and compensation for trial related injury. This should not be a onetime process but an ongoing process through-out the study. The investigator should try and obliterate therapeutic misconception that purpose of biomedical research differs from the purpose of normal clinical care.

Children’s assent: Assent is defined as a child’s affirmative agreement to participate in research. Only if the child does not object, does not mean that he/she has given assent. The assent process should take into account the children’s level of understanding and their general independence and autonomy. Content of the assent process has to be in accordance with the developmental level and maturity of the child. Therefore, the same assent forms may not be uniformly applicable to all children in a particular age group. The draft recommends oral assent in children between 7 to 12 years of age, in the presence of parent/LAR. In children between 13 to 18 years of age, written assent must be obtained. If a child becomes 13 years old during the course of the study, then written assent must be obtained. In cases of verbal assent, the parent’s counter-signature must be obtained that the child’s verbal assent has been taken. Re-assent must be taken in all the same situations as re-consent. Waiver of assent may be afforded by the ethics committee in special situations.

Conclusion

Reading and understanding of the general principles along with the guidelines scripted in the 2006 publication by ICMR - Ethical Guidelines for Biomedical Research on Human Participants is a must for those involved in biomedical research involving human participation. The scope of ethical reviewing in children is expanding. ICMR has put forth its Draft National Ethics Guidelines for Biomedical Research involving children,
and a few important issues have been discussed above. Pediatricians and other clinical researchers who want to plan research involving children should be aware about the new recommendations for addressing the safety and ethical concerns especially for children as research participants.

**Suggested Readings:**

- Ethical Guidelines for Biomedical Research on Human Participants, ICMR, 2006
- Draft National Ethics Guidelines for Biomedical Research involving Children, last accessed 28.09.2015
- Guidelines for GCLP, ICMR, 2008

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**The Belmont Report**

Disclaimer: The above article is only an eye-opener to the various guidelines pertaining to bioethics and the reader is advised to read the referenced documents in entirety for complete understanding of such guidelines prior to its application in biomedical research. The article in no manner should be referenced as a substitute to guidelines already published. Most of these are freely available in the public domain.

Note: The Draft National Ethics Guidelines for Biomedical Research on Children is not applicable as of date, till the final version of the document is published by ICMR.

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**Quality Care At An Affordable Range**

Institute of Child Health

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Contact : Dr Taraknath Mukhopadhyay 9330962379
Mission Indradhanush is a flagship programme of Ministry of Health and Family Welfare (MOHFW), launched on 25th December 2014. It aims at improving full immunization coverage in the country from current 65% to more than 90% by the year 2020. The Mission Indradhanush, depicting seven colours of the rainbow, targets to immunize all children against seven vaccine preventable diseases namely Diphtheria, Pertussis, Tetanus, Childhood Tuberculosis, Polio, Hepatitis B and Measles. In addition to this, vaccines for JE (Japanese Encephalitis) and Hib (Haemophilus influenzae type B) are also being provided in selected states. Immunization is the key to protect children from life threatening conditions that are vaccine-preventable. As per MOHFW, immunization coverage in India has increased from 61% to 65% only, from 2009 to 2013. So, MOHFW has decided to intensify its efforts in immunization through this mission and aims at improving the full immunization coverage to all those children who are unvaccinated or are partially vaccinated. This initiative will eventually close immunity gaps and will strengthen immunization1.

The Government of India is committed to reduce child mortality and morbidity. Unfortunately, one-fifth of the world’s under-five mortality occurs in India, and a substantial number of these deaths are due to vaccine preventable diseases. Every year in India, 5 lakh children die due to vaccine-preventable diseases. Another 89 lakh children remain at risk, because they are either unimmunized or partially immunized. It is known that partially immunized and unimmunized children are most susceptible to childhood diseases and are at a much higher risk of dying as compared to fully immunized children. Immunization is one of the most cost-effective interventions to prevent the suffering that comes from avoidable sickness, disability and death. Vaccination as a public health intervention has proved to be one of the most successful examples of cost-effective prophylactic programme. The benefits of immunization are not restricted to improvements in health and life expectancy but also have social and economic impact at both community and national levels. It can help in preventing large-scale outbreaks of vaccine-preventable diseases as well as keeping the disease under control in an area, thus reducing the stress on an already burdened health system. Thus, full immunization is critical if we want to reduce child mortality and progress on socio-economic indicators2.

The Government of India launched the Universal Immunization Program (UIP) in 1985, one of the largest health programs of its kind in the world catering 27 million birth cohort annually. Despite being operational for
over 30 years, UIP has been able to fully immunize only 65% children in the first year of their life and the increase in coverage has stagnated in the past 5 years to an average of 1% every year. A coverage evaluation by WHO and UNICEF estimated that 87%, 73%, 70%, 74% of the children in India till the age of 24 months were vaccinated with Bacillus-Calmette-Guerin (BCG) vaccine, three doses of Oral Polio Vaccine (OPV) and Diphtheria-Pertussis-Tetanus (DPT) vaccine and a dose of Measles vaccine respectively. A 13% drop from BCG to Measles shows that a significant chunk of children in contact with service providers miss out on subsequent doses.

Objectives of Mission Indradhanush
Objective is to strengthen and invigorate the UIP program and achieve full immunization coverage at a rapid pace, so that all children under the age of two years and pregnant women are fully immunized with all available vaccines.

Special emphasis will be on the identified 201 high focus districts.

Areas under focus:
Key areas reached through this mission will be:
(a) Areas with vacant sub-centres; no auxiliary nurse midwife (ANM) posted for more than 3 months
(b) Villages/areas with three or more consecutive missed routine immunization (RI) sessions; ANM on long leave or other similar reasons.
(c) High risk areas (HRAs) identified by the polio eradication programme. These include populations living in areas such as Urban slums with migrants
Nomadic sites
Brick kilns
Construction sites
(d) Other migrant settlements (fisherman-villages, riverine areas with shifting populations (forested and tribal populations, hilly areas etc)
(e) Areas with low RI coverage, identified through measles outbreak, cases of diphtheria and neonatal tetanus in last two years.
(f) Small villages, hamlets, dhanis, purbas(field huts) etc., clubbed with another village for RI sessions and not having independent RI sessions.

Strategies:
Mission Indradhanush will be nationwide intensified RI drive for ensuring high coverage throughout the country and thus increase accessibility of all UIP vaccines to all the children of India under the age of 2yrs and pregnant women.

The government covered 201 high focus districts in the first phase of year 2015. These districts have nearly 50% of all unvaccinated or partially vaccinated children. Out of these 201 districts, 82 districts lie in just four states of India namely, UP, Bihar, Madhya Pradesh and Rajasthan. Nearly 25% of the unvaccinated or partially vaccinated children of India live in these 82 districts of 4 states. Furthermore, another 297 districts will be targeted in the second phase of year 2015.

The government has planned that this focused and systematic immunization drive will be through a “catch-up” campaign mode.
first phase of Mission Indradhanush four special vaccination campaigns has already been conducted between January and June 2015 with intensive planning and monitoring of these campaign and in each campaign there had been a total of four rounds. After the round, efforts are being made to include these sessions in regular RI plans, during fifth week of the month or by designating additional day(s) for RI. Each round started on Monday and lasted for 7 days(based on the need) The scheduled time of the activity is from 9 am to 4 pm. However, sessions should be planned according to the availability of the targeted population to maximize the benefits achieved .Although the targeted beneficiaries are children under the age of 2yrs and pregnant women, but children above 2yrs, seeking vaccination at any Indradhanush session will not be denied due vaccines

The Ministry will be technically supported by WHO, UNICEF, Rotary-International and other donor-partners. Mass media, interpersonal communication, and sturdy mechanisms of monitoring and evaluating the scheme are crucial components of Mission. 

High Focus Districts of West Bengal covered in 1st phase of Mission Indradhanush 5

<table>
<thead>
<tr>
<th>1) 24-Parganas (North)</th>
<th>2) 24-Parganas (South)</th>
<th>3) Bardhaman</th>
<th>4) Birbhum</th>
<th>5) Murshidabad</th>
<th>6) Uttar Dinajpur</th>
</tr>
</thead>
</table>

5 JE endemic districts. J-E vaccines already available under RI

* Other districts already identified as JE endemic districts where JE Campaign activity is planned/ongoing but not completed yet.

Phase - 1 has completed with great success

Mission Indradhanush (Phase - 1) Final Coverage Report 5 Fig 1. (Figures in Numbers)

<table>
<thead>
<tr>
<th></th>
<th>Round 1</th>
<th>Round 2</th>
<th>Round 3</th>
<th>Round 4 (as on 18 Aug ‘15)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of sessions held</td>
<td>2,14,846</td>
<td>2,34,742</td>
<td>2,57,411</td>
<td>2,59,996</td>
<td>9,66,995</td>
</tr>
<tr>
<td>Total no. of Antigen administered</td>
<td>52,58,130</td>
<td>47,63,156</td>
<td>45,76,972</td>
<td>45,90,767</td>
<td>1,91,89,025</td>
</tr>
<tr>
<td>Total no. of pregnant women immunized</td>
<td>5,40,696</td>
<td>5,59,566</td>
<td>4,96,767</td>
<td>5,08,243</td>
<td>21,05,272</td>
</tr>
<tr>
<td>Total no. of pregnant women completely immunized</td>
<td>2,43,012</td>
<td>3,22,077</td>
<td>2,75,362</td>
<td>2,76,697</td>
<td>11,17,148</td>
</tr>
<tr>
<td>Total no. of children immunized</td>
<td>20,99,556</td>
<td>18,74,493</td>
<td>18,32,721</td>
<td>18,74,355</td>
<td>76,81,125</td>
</tr>
<tr>
<td>Total no. of children fully immunized</td>
<td>4,86,195</td>
<td>4,84,326</td>
<td>5,10,454</td>
<td>5,34,485</td>
<td>20,15,500</td>
</tr>
<tr>
<td>Total no. of Vit A doses administered</td>
<td>2,74,021</td>
<td>4,44,552</td>
<td>7,05,334</td>
<td>6,22,431</td>
<td>20,46,338</td>
</tr>
<tr>
<td>Total no. of ORS packets distributed</td>
<td>1,33,671</td>
<td>5,01,520</td>
<td>5,66,444</td>
<td>5,05,669</td>
<td>17,07,314</td>
</tr>
<tr>
<td>Total no. of Zinc tablets distributed</td>
<td>2,79,951</td>
<td>16,36,422</td>
<td>19,16,426</td>
<td>18,93,621</td>
<td>57,26,640</td>
</tr>
</tbody>
</table>

Phase 1 has completed with great success

Mission Indradhanush (Phase - 1) Final Coverage Report 5 Fig 1. (Figures in Numbers)
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:

PEDIATRIC NEPHROLOGIST TEAM
Dr. Sushmita Bannerjee, Dr. Rajiv Sinha, Dr. Shakil Akhtar, Dr Sudarsana Dey, Dr. Jayati Sengupta

References:
Hereditary Angioedema

Indrani Roy
HOD, Allergy Department, Institute of Child Health, Calcutta

Introduction
Hereditary angioedema (HAE) was first described by Sir William Osler in 1888, and ever since our knowledge about the disease is expanding.

Hereditary angioedema is characterised by repeated and transient attacks of subcutaneous and/or mucosal edema leading to angioedema of the extremeties, face, upper airways and the gastrointestinal tract. The condition is mostly seen in families and is transmitted as autosomal dominant trait. It is a debilitating disease which can be life threatening at times. Though about 10-20% of the world population suffer an attack of angioedema or urticaria at some point of time during their lifetime, the prevalence of HAE is estimated to be 1 in 100,000 and involves almost all races. Females are more prone than males. The reason for discussion about this rare disease entity is to emphasise the fact that prompt detection and treatment can significantly improve the outcome in life threatening situations, and can help to avoid unnecessary surgical procedures.

Pathophysiology

The basic defect in the affected individuals is the inability to synthesise normal levels of functional C1 inhibitor (C1-INH) of the complement system. Normally C1-esterase INH suppresses the action of proteases C1r and C1s, thereby inhibiting the cleavage of C2 and C4. C1-INH also suppresses MASP-2 (Mannose binding lecting Associated Serine Protease) of Lectine pathway and Factors Xla and XIIa of the Clotting system.

This is a normal control mechanism of the Complement system without which the unhindered consumption of complement components would cause severe damage to the host.

When C1-INH is absent or dysfunctional the uncontrolled C1 and Kallikrein activity lead to cleavage of C4 and C2 with release of bradykinine. Bradykinine produces vasodilation and localized nonpitting oedema or angioedema. Depending on the C1-INH status HAE is classified into 3 types.

(i) Type I HAE – Reduction in synthesis of C1-INH 80% of cases
(ii) Type II HAE-Synthesis of dysfunctional C1-INH 15% of cases
(iii) Type III HAE- With normal level of functional C1-INH. This has been described as recently as 2000 and studies point towards some correlation with estrogen levels of the patient.
Clinical features\textsuperscript{4,5}

The initial attacks are usually encountered between the age of 1yr and 5yrs. They become severe in late childhood and adolescence.

Females are more prone than males.

Usually the attacks are preceded by a history of trauma or invasive procedure like tooth extraction, rigorous exercise, menstrual periods, fever or emotional stress.

A strong family history is often present.

But TypeIII HAE may occur sporadically.

The attacks are typically recurrent and consists of “angioedema” or localized nonpruritic swelling involving all the layers of the skin or the walls of hollow viscera such as the respiratory system and the GI tract.

There is non pitting, non pruritic oedema of the skin with swelling of the lips, extremeties and genitalia.

Breathing distress and choking may occur due to involvement of the larynx .( laryngeal oedema)

Involvement of GI tract manifest as swelling of the tongue, abdominal pain of varying intensity, features of obstruction or nausea vomiting and diarrhoea.

Abdominal pain may present with acute onset leading to unnecessary surgical procedures or it may present as chronic recurring type.

It will be worthwhile to remember that bradykinine mediated angioedema of HAE is refractory to treatment with corticosteroids and antihistamines.

Drugs like ACE inhibitors worsens the disease process by inhibiting the degradation of bradykinine.

TypeIII HAE has some correlation with the hormone estrogen as it is seen mostly in females during menstrual periods. Intake of oral contraceptive pills appear to precipitate the condition.

Diagnosis

The striking clinical presentation of HAE should alert the physician.

There is no specific laboratory test for HAE.

C1-INH level is low in type I HAE but is normal type II and type III HAE.

C3 and C4 levels are low in both type I and type II HAE but normal in type III.

Treatment:

Treatment of HAE consists of the following

(i) Treatment of an acute attack.

(ii) Prophylaxis.

Treatment of acute attack

Infusion of CI-INH. In 2009 purified CI-INH, Berinert has been approved for treatment of acute attacks in a dose of 20 units/kg given IV\textsuperscript{8}.

Alternate agents recommended are Icatibant (selective competitive antagonist of Bradykinine B2 receptor) or Ecallantide (Kallikrine inhibitor) FDA approved the use of Ecallantide in adolosents 16yrs or older.

In rare cases Ecallantide can cause anaphylaxis\textsuperscript{4,9,10}.

As all the three above mentioned agents are not available in India yet. So our only reasonable choice remains infusion of fresh frozen plasma (FFP). FFP is useful in replacing
CI-INH levels. Very rarely the angioedema can worsen due to the complement factors present in FFP.

Prophylaxis

Human plasma derived, purified CIINH is approved for use in adolescents and older for prophylaxis. As the half life of this product is about 40 hrs, the approved regimen is 1000 U given twice a week. But this is not available in India.

Other options are attenuated androgens like Danazol and antifibrinlytes like Tranexamic acid.

But attenuated androgens should be used in children with caution for their side effects like premature closure of epiphyses, virilization on long term use.

Conclusion

Hereditary angioedema is a rare disorder, transmitted as autosomal dominant trait and characterized by repeated and transient attacks of angioedema often with serious consequences.

The basic defect is the inability to synthesize normal levels of functional C1 esterase inhibitors in affected individuals, leading to unhindered activity of bradykinine. Clinical feature characteristically consists of recurrent attacks of non-pitting, non-pruritic angioedema involving lips and, tongue and extremites, breathing distress and abdominal pain. Laryngeal oedema is the most dreaded manifestation. As this angioedema is caused by bradykinine it is refractory to antihistamines and corticosteroids.

Timely diagnosis and prompt management can avert life threatening consequences and unnecessary surgical procedures.

Plasma derived purified C1-INH is the main stay of the treatment.

Icabitant (selective competitive antagonist of bradykinine β2 receptor) and Ecallantide (Kallikrin inhibitor) are other two options.

As none of the three are available in India, Fresh Frozen Plasma (FFP) is the only reasonable choice.

Attenuated androgens like Danazol are recommended for prophylaxis. But these should be used with caution in children due to their serious side effects.

References:


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

**How long it is open?**

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

**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.

*Annals of ICH, Calcutta*
During the last few decades, there are lots of changes in the treatment protocol of thalassaemia. Treatment of thalassaemia becomes more scientific and specific now. Lifestyle like exercise, diet etc. are also an important part of the treatment. In general iron restricted diet is advised in case of thalassaemia; because increased iron absorption from the intestinal tract is characteristic of thalassaemia. The amount depends on the degree of erythropoiesis, the hemoglobin level and other potential in dependent factors. Drinking a glass of black tea with meals reduce iron absorption from food, particularly in thalassaemia intermedia. However, there is no evidence that iron-poor diets are useful in thalassaemia major. Almost every food contains more or less amount of iron. Milk is very poor source of iron and dairy product should be taken more, not only because it is low iron content but also it is rich source of calcium, which is very much important for thalassaemia patient. Iron intake of thalassaemia from any food not only depends on iron content of the food, but also its digestive factor and absorption factor. For this reason iron from animal source are more absorbed than plant source. If any food also contains phytate in addition to iron, it may hamper the absorption of iron (as in case of Thor), unlike the common belief green banana is not so rich source of iron. As a result, it is not rational, not scientific to impose too much restriction on diet of thalassaemia. It may even cause malnutrition of the patient.

Only food very rich in iron; such as liver, red meat, some health drinks or health vitamin cocktails should be avoided. Thalassaemia should never be given iron supplements.

Patients with thalassaemia do not have specific dietary requirements, unless they have special prescription. During growth a normal energy in take with normal fat and sugar content is recommended. During adolescence and adult life, a diet low in highly refined carbohydrate (sugar, soft drinks, and snacks) may be useful in preventing or delaying the onset of impaired glucose tolerance or diabetes.

In a nut-shell thalassaemia should not be too much anxious about the diet chart, restriction of diet etc. Only red meat, iron supplement, artificial food fortified with iron should be avoided. Milk or milk product should be taken in excess amount.
Complimentary Feeding - Some Facts

Arunaloke Bhattacharyya
Associate Professor, Institute of Child Health, Kolkata

Why complementary feeding is started at 6 months age?
If breast feeding is continued beyond 6 months age, there is a chance of nutrient deficiency from poor intake depicted in the following bar diagram (Fig-1).

From the development point of view, an infant starts to sit with support with proper head control and its oral phase of development allows it to open the mouth on the site of food and can accept the spoon with cushioned tongue and can swipe food with upper lip to keep it inside the mouth.

Weaning is accompanied by increase in circulatory hormones that influence intestinal maturation and brush border enzyme activity in preparation for adult type of food. Early weaning and exposure to antigens have been implicated in the development of food allergies and delayed small intestinal maturation. However, intestinal maturation is also impaired if weaning is delayed or if animals are weaned with milk-like food.

Infants need nutrients in higher densities than adults because they have to acquire that amount of nutrients from lesser total daily calories than adults.

Global statistics identify 6–18 months as the time when stunting and malnutrition sets in, exactly during complementary feeding period. This is the period of complementary feeding that has been recognised as a sensitive period of high risk for developing stunting, protein-energy malnutrition, iron-deficiency anaemia and rickets. Reversing stunting after the age of 2 years is highly difficult.

Evolution of complementary feeding
Evolutionarily speaking, human diets were not always deficient in micronutrients. In the pre-agricultural era, humans relied on hunting, fishing and gathering as a means to procure food. Based on economic subsistence data from 229 human hunter-gatherer societies, it was found that 45 to 65% of the energy intake was provided by animal source foods. Cereals and pulses were not a part of the pre-agricultural diet since they were difficult to process. Come agricultural revolution, the human diet notably changed to cereals grains such as rice, maize, wheat. Because of the poor quality of diet, deficiency of...
Micronutrients were also noticed. Using information from Bangladesh, Ethiopia, and Vietnam, it was suggested that unfortified local foods could theoretically meet the nutrient requirements only when iron rich animal liver is consumed everyday. However, this may not be feasible in all cases.

The figure (Fig 2) presents the unmet nutrient requirements of iron and zinc with various options of feeding in infants at the ages of 9–11 months. The graphs show comparison in iron and zinc intakes from breast milk, breast milk plus typical complementary feeding, breastfeeding in addition to diverse animal food-based diet and a hypothetical preagricultural diet along with breastfeeding.

As seen, bridging the gap for iron and zinc requirement is challenging in modern times. We cannot go back to preagricultural era and hence sustainable strategies for bridging the nutrient gaps need to be developed.

Where are we lacking to deliver proper concept of complementary feeding?

Importance of complementary feeding in child health is undeniable; however, it is often a neglected aspect in pediatric practice.

Substantial literature does exist on breastfeeding. However, comparatively little attention is given to the complementary feeding period, nature of foods provided and influence of complementary feeding on future health outcomes.

Recently a survey on complementary feeding practices was conducted among 151 pediatricians from North, South, East and West regions of India. Regular illnesses and immunization were the most common reasons for pediatric visits while only few of the visits were for nutrition problems/counselling. In addition, the survey showed that majority of the doctors (28-31%) spent only 4 to 5 minutes talking to mothers about complementary feeding.

Breastfeeding and child feeding seem to be natural acts; however they can also be learned behaviours. There are several barriers to initiate appropriate complementary feeding at the right time. Barriers at the caregiver’s/mother’s level can include lack of nutrition knowledge, poor hygiene, poverty and resultant high rate of infection, poor child feeding practices, cultural beliefs and taboos. Whereas, health...
care personnel may have limited knowledge and skills for counselling caregivers about appropriate complementary feeding. This may be because this aspect is inadequately covered in the basic training of HCPs.10

Is homemade food sufficient?

When the best case scenario of family food menus from low-income household were considered, they were shown to be of poor nutrient density.

Transition to “family foods” as the sole source of complementary foods may put the infant at risk of multiple micronutrient deficiencies.

Even “improved” complementary feeds may fall short of iron, zinc, and calcium. Grain- and legume-based diets may have limited bioavailable iron and zinc.

The net result: the complementary feed is deficient in nutrients such as iron, zinc, riboflavin, niacin, thiamine, folate, vitamin B-6, vitamin B-12, calcium, vitamin A, vitamin C, and vitamin E or iodine, selenium leading to poor nutritional status, if not properly made or complemented or fortified.11

Prevalence of iron deficiency anemia is much higher in children than among adult women and may be partly attributable to the high prevalence of hookworm among children. The National Family Health Survey found that children who are stunted, wasted, or underweight are much more likely than other children to suffer from moderate to severe anaemia. It was found that 7 out of every 10 children aged 6 to 59 months were found to be anaemic. Looking at the other micronutrient iodine, children require adequate amount of iodine in their diet to prevent iodine deficiency disorders. However, it was found that only half of children who are 6-59 months old live in households that use cooking salt containing an adequate level of iodine which is 15 parts per million of iodine.

Similarly, only one-quarter of children age 12-35 months were given any vitamin A supplements in the six months preceding the NFHS-3 survey. The Government of India recommends that children should be given vitamin A supplements every six months from age nine months to three years to avoid vitamin A deficiency (VAD)12.

Solution

The Ministry of Women and Child Development (Food & Nutrition Board) in 2004 established the Infant and Young child feeding guidelines in 2004 to formulate, endorse, adopt and disseminate these guidelines from an Indian perspective. The slide presents some of the key take away points mentioned by IAP. They are:

(i) Appropriately thick homogenous complementary foods made from locally available foods should be introduced at six completed months to all babies

(ii) Breastfeeding should be actively supported during this time

(iii) Each meal must be made energy dense by adding sugar/jaggery and ghee/butter/oil

(iv) Thick in consistency: Thick enough to stay on the spoon without running off, when the spoon is tilted

(v) Hygienic practices for food safety to be followed during all the involved steps viz. preparation, storage and feeding.
(vi) Practice responsive feeding.

(vii) Infant food should be a “balanced food” consisting of various (as diverse as possible) food groups / components in different combinations.

(viii) As the babies show interest in complementary feeds, the variety should be increased by adding new foods in the staple food one by one.

(ix) Iron-fortified foods, iodized salt, vitamin A enriched food etc. are to be encouraged

Reference:

1. WHO. http://apps.who.int/iris/bitstream/10665/44117/1/9789241597494_eng.pdf?ua=1&ua=1


3. Development of the Gastrointestinal Tract, Volume 1 By Ian R. Sanderson, W. Allan Walker, p-246


Antistreptolysin O (ASO) titre is a blood test to measure antibodies against streptolysin O, a substance produced by group A Streptococcus bacteria (GAS). In children, approximately 20% of pharyngitis cases are caused by GAS\(^1\). GAS are responsible for the great majority of infections and frequently colonize in the throat of an asymptomatic person. Among children, asymptomatic carriage rates of 15-20% have been noted in several studies. A rate of 13% was reported from India\(^2\).

GAS serology is used for the diagnosis of post-streptococcal diseases, such as acute rheumatic fever, scarlet fever, post streptococcal glomerulonephritis and erysipelas. An increase in the serum ASO titre is possible after an infection with GAS in any part of the body. Although the rising titre of ASO in streptococcal infection is widely accepted, it continues to be incompletely defined.

**Normal value** – The normal range of ASO titre depends on age, site, season and area. The upper limit of normal for streptococcal serology must be determined for individual populations because of differences in the epidemiology of GAS between populations. According to modified Jones criteria ASO titers more than 333 Todd units are generally considered elevated in children\(^3\). Most of the studies considered ASO titre more than 200U/ml as significant level. In a study from Chandigarh, this was found to be 239 IU in paediatric population\(^4\).

Rennebrg\(^5\) showed that the ASO titres in sera from children increased abruptly with increasing age, from a mean of 21 (CL 67) in infants of 3 years or less to 211 (CL 462) in children 7 to 8 years old. In children 9 to 12 years of age titres exhibited a plateau with mean values of 168-258\(^5\).

Gharagozolo et al\(^6\) reported that the same study population showed greater ASO levels during the winter season than in summer. There is an increase of the ASO titer one week after the infection with a maximal level in 3 weeks. The seroconversion more important than a high level of antibodies found alone. The antibodies titre decrease slowly and may persist longtime after the infection. A single ASO titre assay has some limitations, especially with regard to chronic nasopharyngeal group A beta hemolytic streptococcus carriage status\(^7\). These people have elevated, but not increasing antibody titers of a few weeks to many months. If these people develop a sore throat due to another etiology, a single positive culture and/or antibody determination would very likely show a false-positive association with GAS. In these cases the documented increase in titer is the most reliable indicator of streptococcal infection. Johnson et al\(^8\) also reported remarkably prolonged antibody “decay rate” following an acute immune response to GAS infection, even in the absence of positive cultures. A single elevated antibody titer may reflect antibody persistence.
from an infection that occurred months earlier. They concluded that evaluation of >1 antibody (eg, ASO and Anti DNaseB) will increase the probability of accurately diagnosing a true GAS infection. Blyth CC et al also had the same opinion. They advised to perform a combination of ASO and Anti DNaseB to achieve maximum sensitivity and specificity.

**Acute Rheumatic fever (ARF) and ASO**

ARF is one of the complications of streptococcal tonsillitis. Early and effective detection of streptococcal throat infection is important as rheumatic fever constitutes 25 to 40% of cardiovascular diseases in third world countries. Throat swabs culture is positive in 80% of acute streptococcal infections, but it might be negative in chronic tonsillitis. ASO titre test is the most widely used test. It is less costly with reasonable sensitivity.

Rheumatic fever and rheumatic fever reactivation is associated with raised ASO titre. High ASO titre is suggestive of recent streptococcal infection. On the other hand, Jawahar N et al did a study to evaluate the significance of several clinical and laboratory findings presented by a large number of pediatric patients who were suspected to have ARF by physicians. These suspecting reasons include elevated ASO titers and recurrent tonsillitis. They concluded that elevated ASO titer and normal ESR with arthralgia not reducing physical activity can exclude ARF.

**Post streptococcal glomerulonephritis (PSGN) and ASO**

The etiologic role of GAS in acute glomerulonephritis is well established. However, an acute nephritic syndrome clinically resembling that related to streptococcal infection may occur after many other bacterial, viral and parasitic infections. ASO titer is measured to rule out other causes. In a study in 1984 from Mumbai Shroff KJ et al showed that initially there is an elevation of ASO titres in both Post streptococcal (PSGN) or non streptococcal glomerulonephritis (NSGN) as compared to the normal population. But the elevated titres are significantly higher in the PSGN group than in the NSGN group (p < 0.05). C3 values are lower in both the group of patients of glomerulonephritis. However, at the onset of illness, the elevation of ASO titres and fall in the C3 levels are greater in the PSGN group as compared to the NSGN group (p < 0.01 and p < 0.001 respectively). Follow-up studies showed that there is a considerable fall in the number of patients having a raised titre. However, in the NSGN group the percentage of patients having raised ASO titres is more or less constant even after a follow up of 2 years.

At the onset of illness, 88% of patients in the PSGN group had significantly low values of C3 which returned to normal in most of the patients within 2 months; whereas in the NSGN, no such definite relationship of C3 levels to time interval could be found. It is important in our country where good nephrology care is not available in most of the centre.

High ASO titre can also be seen in different disease manifestations. Aran A et al showed there is high ASO titer in few children with recent onset of narcolepsy. In the children with psoriasis an increased ASO titer is related to the worsening of the psoriasis. Early treatment of streptococcal infections might be beneficial in childhood psoriasis. A statistically significant association is found between high anti-streptolysin-O titers and decreased number of exacerbations in those
children\textsuperscript{14}.

High ASO and tonsillectomy:

Tonsillectomy can cause reduction in ASO titre permanently in recurrent sore throat but only high serum ASO titre is neither reliable nor acceptable for tonsillectomy. FNAC of the tonsil core is a valid and a reliable test for the diagnosis of bacterial micro flora in recurrent tonsillitis. One should perform throat swab culture and FNAC along with ASO titre before doing tonsillectomy where no other indications are present. Identifying GAS in the tonsil by FNAC test and/or in the throat swab culture along with high serum ASO titre may be one of the ideal indications for tonsillectomy\textsuperscript{15}. In a study by Viswanathan N et al ASO titre estimation was done after 1 month, 3 months, 6 months and 1 yr. 22\% after 1 month, 62\% after 3 months; 78\% after 6 months and 88\% after 1 year became negative for ASO titre\textsuperscript{16}.

Falacy

Elevated ASO titres can be found in various clinical conditions other than the typical post-streptococcal associated diseases. In these cases it is not necessarily accompanied by positive culture and does not correlate with inflammatory parameters. GAS is a part of normal flora in the nasopharynx and the test must be repeated in case of high level in order to show the increase of the titre in a case of a true infection. It is not often feasible to obtain acute and convalescent sera, hence the use of a single cut off level. Only 20 \% cases of Rheumatic fever in early stage may present with normal ASO titre. Tuberculosis and liver disease may sometimes present with false positive ASO titre\textsuperscript{17}.

Key notes

(i) ASO titer measurement is important to diagnose recent streptococcal infection
(ii) Rising value is more important than single value.
(iii) Combination of ASO and Anti DNAse test will be more specific and sensitive.
(iv) We should be careful about false positive result.
(v) Only high ASO titer is not an indication of tonsillectomy.

Reference:

7. KaplanE, TopFJr, DuddingB, WannamakerL. Diagnosis of streptococcal pharyngitis: differ-


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**NICU**

34 bedded with Radiant Warmer, Monitors, Facility of Phototherapy, All Modern Gadgets, CPAP and Neonatal Ventilator in house ABG, portable USG and Portable X-ray, MRI and Neonatal EEG facilities are available

**Contact**

**Institute of Child Health**

11, Dr Biresh Guha Street, Kolkata 700 017

Phones : (033) 65000923, 9836057676
Acid base terminology

Acidemia is a pH below normal (<7.35) and alkalemia is a pH above normal (>7.45). An acidosis is a pathologic process that causes an increase in the hydrogen ion concentration. Alkalosis is a pathologic process that causes a decrease in the hydrogen ion concentration. Acidemia and alkalemia indicate the pH abnormality whereas acidosis and alkalosis indicate the pathologic process that is taking place.

We all know that the pH is inversely proportional to the number of (H+) in the blood. The normal pH range is 7.35-7.45. Multiple changes take place in acidotic or alkalotic state such as decreased force of cardiac contractions, decreased vascular response to catecholamines, diminished response to the effects and actions of certain medications in acidosis whereas An alkalotic state interferes with tissue oxygenation and normal neurological and muscular functioning. Significant changes in the blood pH above 7.8 or below 6.8 if remains uncorrected, will lead to death.

Primary acid-base disorder

There are 4 types like metabolic acidosis and alkalosis and respiratory acidosis and alkalosis. It is very important to have a good knowledge of compensatory mechanism that occurs in acidotic or alkalotic state. During a simple metabolic disorder, there is respiratory compensation. It happens quickly and is complete within 12-24 hr but it cannot overcompensate for or normalize the pH. Whereas during a primary respiratory process, there is metabolic compensation, mediated by the kidneys. Unlike respiratory compensation, which occurs rapidly, it takes 3-4 days for the kidneys to complete appropriate metabolic compensation.

Body buffer system

Buffers are substances that attenuate the change in pH that occurs when acids or bases are added to the body. As given the extremely low concentration of hydrogen ions in the body at physiologic pH, without buffers, a small amount of hydrogen ions could cause a dramatic decline in the pH. Buffers prevent the decrease in pH by binding the added hydrogen ions: The increase in hydrogen ion concentration drives this reaction to the right. Similarly, when base is added to the body, buffers prevent the pH from increasing by releasing hydrogen ions. The best buffers are weak acids and bases. This is because a buffer works best when it is 50% dissociated (half HA and half A-). The pH at which a buffer is 50% dissociated is its pK. The best physiologic buffers have a pK close to 7.40. The concentration of a buffer and its pK
determine the buffer’s effectiveness (buffering capacity). Bicarbonate buffer has a pK of 6.1 and non bicarbonate buffers like proteins - albumin and hemoglobin pK 6.5 Phosphate, pK 6.8 and bone play important role to prevent changes in body pH.

So to analyse an ABG report you have to be familiar with the normal values of different parameters, primary abnormality and compensatory changes. The following charts may be useful:

<table>
<thead>
<tr>
<th>Disorder</th>
<th>pH</th>
<th>pCO2</th>
<th>HCO3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Acidosis</td>
<td></td>
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<tr>
<td>Respiratory Alkalosis</td>
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<tr>
<td>Metabolic Acidosis</td>
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<tr>
<td>Metabolic Alkalosis</td>
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<table>
<thead>
<tr>
<th>Normal Values</th>
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<tbody>
<tr>
<td>pH</td>
</tr>
<tr>
<td>PaCO₂</td>
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<tr>
<td>PaO₂</td>
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<tr>
<td>SaO₂</td>
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<tr>
<td>HCO₃</td>
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<tr>
<td>% MetHb</td>
</tr>
<tr>
<td>%COHb</td>
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<tr>
<td>Base excess</td>
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</table>

<table>
<thead>
<tr>
<th>Primary Disorder</th>
<th>Compensatory Change</th>
<th>Expected Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Acidosis</td>
<td>Fall In HCO₃</td>
<td>?PaCO₂ = 1.2 × ?HCO₃</td>
</tr>
<tr>
<td>Fall In PaCO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td>Rise In PaCO₂</td>
<td>?PaCO₂ = 0.7 × ?HCO₃</td>
</tr>
<tr>
<td>Rise In HCO₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Acidosis</td>
<td>Rise In HCO₃</td>
<td>ACUTE ?HCO₃ = 0.1 × ?PaCO₂</td>
</tr>
<tr>
<td>Rise In PaCO₂</td>
<td></td>
<td>CHRONIC ?HCO₃ = 0.3 × ?PaCO₂</td>
</tr>
<tr>
<td>Respiratory Alkalosis</td>
<td>Fall In HCO₃</td>
<td>ACUTE ?HCO₃ = 0.2 × ?PaCO₂</td>
</tr>
<tr>
<td>Fall In PaCO₂</td>
<td></td>
<td>CHRONIC ?HCO₃ = 0.5 × ?PaCO₂</td>
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</tbody>
</table>
Case 1:
6 year old male child, weight loss for last 1 month with increased urinary output. Fever for 3 days, gradually deteriorating consciousness for 1 day. In ER GCS 6/15 tachypnea, dehydration: CBG 478. Diagnosis DKA. ABG reveals pH 7.1, pCO₂ 15, HCO₃- 4. Inference, Simple metabolic acidosis

CAUSES:
NORMAL ANION GAP
Causes of non ANION gap metabolic acidosis – DURHAM
Diarrhea, ileostomy, colostomy, enteric fistulas: Ureteral diversions or pancreatic fistulas: RTA type I or IV, early renal failure: Hyperalimentation, hydrochloric acid administration: Acetazolamide, Addison’s: Miscellaneous – post-hypocapnia, toulene, sevelamer, cholestyramine ingestion
Increased anion gap acidosis: Methanol, Uremia, DKA, Lactic acidosis, Rhabdomyolysis

Signs and symptoms of metabolic acidosis
CNS: Headache, confusion and restlessness progressing to lethargy, then stupor or coma.
CVS: Dysrhythmias
Kussmaul’s respirations
Warm, flushed skin as well as nausea and vomiting
Treatment: Volume replacement, vasopressors, bicarbonate therapy and treatment of cause.

Case 2
3 month old previously healthy male child came in ER with poor feeding and lethargy for 2 days and he has not passed urine for last 8 hours. On exam. C/R/A below average. CRT 5 sec, periphery cold, mottled. CBG 312 so the most probable Diagnosis is Septic shock. ABG pH 6.9, pCO₂ 38, HCO₃- 12 . Inference: Combined acute metabolic and respiratory acidosis

Causes of respiratory acidosis.
CNS DEPRESSION: Encephalitis, Head trauma, Hypoxic brain damage, Increased intracranial pressure, Medications (Narcotics, Barbiturates, Anaesthesia)
DISORDER OF NEUROMUSCULAR JUNCTION TO PERIPHERAL NERVES: Diaphragmatic paralysis, Spinal cord injury, Medications
RESPIRATORY MUSCLE WEAKNESS: Muscular dystrophy
PULMONARY DISEASE: Pneumonia, Pneumothorax, Asthma, Bronchiolitis
UPPER AIRWAY DISEASE: Aspiration, Laryngospasm, Angioedema

Signs and symptoms are very much non specific. Treatment of cause is indicated.

Case 3
6 yrs old male child with recurrent respiratory distress since around 3 years of age. O/E Height and weight below 3rd centile with presence of Clubbing and polycythemia. Diagnosis: chronic lung disease. ABG: pH 7.34, pCO₂ 65 HCO₃-34: Inference – Chronic respiratory acidosis with compensatory metabolic alkalosis

Metabolic alkalosis causes: CHLORIDE-RESPONSIVE ((URINARY CHLORIDE < 15mEq/L)
Gastric losses: Emesis, Nasogastric suction
Diuretics (loop or thiazide)
Chloride-losing diarrhea
Cystic fibrosis
Post-hypercapnia
Chloride Resistant (Urinary Chloride- >20mEq/L)
High blood pressure:
Adrenal adenoma or hyperplasia
Cushing syndrome
Liddle syndrome
Normal blood pressure:
Gitelman syndrome, Bartter syndrome
Patient should be treated for the cause in addition of volume replacement and stoppage of diuretic if possible.

Case 4

7 yr old male child came in ER with exertional dyspnea. Congested conjunctiva, muddy skin and clubbing and cyanosis .Loud, harsh systolic murmur along left sternal border
Diagnosis: Cyanotic heart disease :ABG pH 7.54 pCO2 34 HCO3- 15 :Inference: Chronic respiratory alkalosis with metabolic acidosis

Causes of respiratory alkalosis

Tissue Hypoxia Or Hypoxemia: Pneumonia, Pulmonary edema, Cyanotic heart disease, Congestive heart failure, Asthma
Lung Receptor Stimulation; Pneumonia, Pulmonary embolism, Hemothorax, Pneumothorax
Central nervous system disease: Subarachnoid hemorrhage, Encephalitis or meningitis, Trauma, Brain tumor, Stroke
Fever, Pain, Anxiety (panic attack)
Liver failure, Sepsis
Medications: Salicylate intoxication, Theophylline, Progesterone, Exogenous catecholamines, Caffeine

So to summarise we can gain valuable information from an ABG as to the patients physiologic condition . We must be systematic with our analysis, start with ABC’s as always and look for hypoxia (which we can usually treat quickly), then follow the four steps.and last but not the least we should never forget to look at the patient clinically.

Neurodevelopmental Clinic

Neurodevelopment clinic is held every Friday from 12 noon. All types of developmental delay, cerebral palsy, speech delay, poor scholastic performance, autism, ADHD are dealt in this clinic.
Viral encephalitis is an important public health problem in our country and a significant cause of morbidity and mortality. Often it takes the form of an epidemic and affects both children and adults.

The neurotropic viruses gain access to the brain through different routes and accordingly involves characteristic areas of brain. The pattern of involvement and other imaging features help to suspect the causative agent which can be confirmed by serological analysis.

The common viruses that we come across in this country include Herpes simplex I & II, Varicella zoster, Japanese B, Influenza, EB virus etc.

MR imaging is extremely sensitive to show the area of affection as hyperintense (bright) on T2W and FLAIR images and hypointense (dark) on T1W images. The hemorrhagic lesions appear dark on GRE and SWI and bright on T1W images. Cortical and subcortical involvement are characteristic with relative sparing of white matter.

The lesions often show diffusion restriction on DWI earlier than other sequences. Variable enhancement and mass effect may be present.

**Herpes simplex encephalitis**
Bilateral but asymmetric involvement of temporal lobes, insula and cingulated gyrus.

Hemorrhagic components may be present with mass effect and contrast enhancement (Fig 1).

**Varicella zoster encephalitis**
Characteristic cerebellar involvement and vasculitis causing ischemia / infarction.

**Japanese B encephalitis**
Deep-seated structures of brain are involved like bilateral thalami, basal ganglia, substantia nigra, subcortical white matter. Other Toga viruses like West Nile virus, St. Louise Encephalitis, Equine encephalitis also share the same imaging abnormalities (Fig 2).

**Epstein-Barr encephalitis**
Deep gray matter nuclei including thalami and basal ganglia, white matter and splenium of corpus callosum (transient and reversible) involvement are common.

**Influenza- associated encephalopathy**
Symmetric lesions in bilateral thalami and hemispheric edema, involvement of white matter and splenium of corpus callosum are noted.

**HIV encephalopathy**
Diffuse white matter signal abnormalities and brain atrophy.

**Rabies encephalopathy**
Characteristic involvement of brain stem, thalami, hippocampi and spinal cord (Fig 3).
Chronic encephalitis

Subacute sclerosing panencephalitis:
Progressive encephalitis that occurs years after measles infection.
Imaging may be normal initially. Afterwards, bilateral asymmetrical white matter hyperintensities on T2W and FLAIR images. The fronto-temporal cortex and basal ganglia are also involved with features of brain atrophy.

Other entities include Progressive Multifocalleucoencephalopathy, Rasmussen encephalitis, Cruezfeld Jakob disease also present with characteristic imaging features.
For etiological diagnosis of viral encephalitis, detection of viral antibody in the blood and CSF is recommended. MRI plays a role for early diagnosis of encephalitis and predicting a probable causative agent.

References:

**Fig 1. Herpes Simplex Encephalitis**

The patient presented with fever and convulsion.
Axial and sagittal T2W images show confluent hyperintensities in bilateral perisylvian and temporal regions.
Axial T2W and FLAIR images show symmetrical hyperintensities involving the bilateral thalami, parieto-occipital cortex with dilated ventricles.

H/O Fever and drowsiness.

FLAIR axial and T2W Sagittal images show hyperintensities in bilateral basal ganglia, brain stem and cervical spinal cord.

H/O Dog bite and encephalopathy.

**Nivedita Challenged Center**

Since 1975 Child Guidance Clinic is probably the only specific institutional centre in Kolkata that runs a special school for challenged children and carries out regular academic, research and public awareness activities. It provides complete child psychiatric services through psychometry, pharmachotherapy, behaviour therapy, counseling, speech therapy etc, at inexpensive rates.
1. “Please be gentle they also feel pain”

Update on pain management in newborns: The updated AAP recommendations for Management of Procedural Pain in Neonates published in Jan 2016 reiterated the importance of objective assessment of pain, and judicious use of pain management tools. The prime recommendations include:

- Presence of validated neonatal pain assessment tools in all neonatal units.
- Non-pharmacological strategies (such as swaddling/facilitated tucking, non-nutritive sucking, breast feeding, massage, and skin-to-skin care) are recommended for short-term mild to moderately painful procedures such as heel lance and intravenous catheter insertion.
- Oral sucrose or glucose is safe and effective with mild to moderately painful procedures (e.g., immunizations) either alone or with non-nutritive sucking and swaddling.
- Pharmacologic treatments (e.g., opioids and benzodiazepines) are recommended for more painful procedures but after balancing benefits and side effects. Topical anesthetic agents (tetracaine gel and EMLA) decrease pain during venipuncture and insertion of venous and arterial lines.
- Evidence was found to be insufficient to recommend methadone, ketamine, or propofol, or routine use of opioids in mechanically ventilated infants.
- Pain management was recommended for circumcision and nonemergency intubation.

2. Keeping father happy also matters!!!

Father’s depression can also affect children’s cognitive function. The authors assessed the impacts of both prematurity and parental depressive symptoms on children’s early cognitive function. Data were assessed from the nationally representative Early Childhood Longitudinal Study, Birth Cohort (n = 5350). At 9 months, fathers of very preterm (<32 weeks gestation) and moderate/late preterm (32-37 weeks gestation) infants had higher depressive scores than fathers of term-born (=37 weeks gestation) infants (p value = .02).
In contrast preterm birth was not associated with maternal depressive symptoms. In multivariable analyses, preterm birth was associated with lower cognitive function at 24 months; which was unaffected by adjustment for parental depressive symptoms. Fathers' but not mothers' postnatal depressive symptoms predicted lower cognitive function in the fully adjusted model (β = -0.11, 95% confidence interval, -0.18 to -0.03). The study showed fathers of preterm infants have more postnatal depressive symptomology than fathers of term-born infants and this seems to affect the cognitive function of the babies also. It highlights the need for early identification and treatment of fathers of preterm infants with depressive symptoms.

3. “The warmth of mother care”

Another vindication for kangaroo care: In a meta-analysis and review of 124 studies, kangaroo care (early and continuous maternal skin-to-skin contact) was associated with a significant decrease in infant mortality and neonatal sepsis. It was shown to have a sustained beneficial effect on cognition, sleep, executive function, and maternal anxiety. In addition, it was also shown to improve breastfeeding, cardiorespiratory stability, and responses to procedural pain. Pooled analyses showed that compared to conventional care, kangaroo care was associated with a significant 36% decrease in mortality among low-birth-weight newborns. Kangaroo care was also associated with significant decreases in neonatal sepsis (47% lower), hypothermia, hypoglycemia, and hospital readmission. Other benefits were increased exclusive breastfeeding, lower mean respiratory rate, lower pain measures, and higher oxygen saturation, temperature, and head circumference growth. The review provides strong support for kangaroo care as a standard of care, especially for premature infants.

4. “Another boost for the hygiene hypothesis!!!”

Pets are good: In a cohort of roughly 276,000 Swedish children, 8.2% were exposed to dogs and 0.3% to farm animals (mostly cattle and sheep) during the first year of life. At age 6 years, 4.2% of the cohort had asthma. Adjusting for location, socioeconomic factors, and parental history of asthma, asthma at age 6 years was significantly inversely associated with exposure to dogs (odds ratio, 0.87) and farm animals (odds ratio, 0.48). Children exposed to farm animals during infancy had significantly lower risk at all preschool ages (adjusted hazard ratio, 0.69). Hence next when parents of infants ask about the pros and cons of having a dog, you can talk about a potential mild decrease in asthma risk.

5. “A double edged sword”

Inhaled budesonide for preventing BPD- still not crystal clear: In an industry-funded,
multinational, randomized, controlled trial, researchers evaluated outcomes with early administration (within 24 hours of birth) of inhaled budesonide (200 μg/puff) or inhaled placebo in 856 infants born at gestational ages of 23 weeks and 0 days to 27 weeks and 6 days. Infants were administered two puffs every 12 hours for 2 weeks followed by one puff every 12 hours until the study drug was stopped. Early budesonide therapy was associated with reduced BPD (27.8% of surviving infants compared with 38.0% in the placebo group, p = 0.004) but unfortunately there seems to be a higher trend for mortality (27.8% of surviving infants compared with 38.0% in the placebo group, p = 0.004). Hence the study leaves the decision to use budesonide therapy delicately balanced.

6. The pediatric obesity epidemic- “A ticking time bomb”


Cardio-metabolic risk factors are increased even in childhood obesity: Using data from the National Health and Nutrition Examination Survey from 1999 to 2012, researchers assessed the prevalence of cardio-metabolic risk factors according to obesity class in a cross-sectional sample of 8579 children and young adults (age range, 3–19 years) with body-mass index (BMI) > 85% of normal. The prevalence of abnormal levels of total cholesterol, HDL cholesterol, triglycerides, blood pressure, and glycated hemoglobin increased as the severity of obesity increased. In analyses adjusted for age, race/ethnicity, and sex, several abnormal risk factors were more prevalent in participants with higher class III obesity than in those with class I obesity (the reference) among males, but not females. In the same analyses, several abnormal risk factors were more prevalent in participants with mild class I obesity than in those who were overweight but not obese among both males and females. Hence risk for cardiovascular disease seemed to be present in obese children and young adults, especially severely obese males.

7. “Higher concentration does not mean higher efficacy”


No specific advantage of 3% saline vs normal saline in bronchiolitis. A prospective, randomized, double-blind, controlled trial was done with 227 infants younger than 12 months old admitted with a diagnosis of bronchiolitis. The aim was to investigate the effect of nebulized 3% hypertonic saline (HS) compared with nebulized normal saline 0.9% (NS) on length of stay (LOS) in infants hospitalized with bronchiolitis. Patient characteristics were similar in groups. The median LOS (interquartile range) of HS and NS groups was 2.1 (1.2-4.6) vs 2.1 days (1.2-3.8) P = .96. Seven-day readmission rate for HS and NS groups were 4.3% and 3.1%, respectively, P = .77. Clinical worsening events were similar between groups (9% vs 8%, P = .97). Treatment with nebulized 3% HS compared with NS had no difference in LOS or 7-day readmission rates.