HOLY FAMILY HOSPITAL NEW DELHI

NEWSLETTER

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DENGUE FEVER IN CHILDREN

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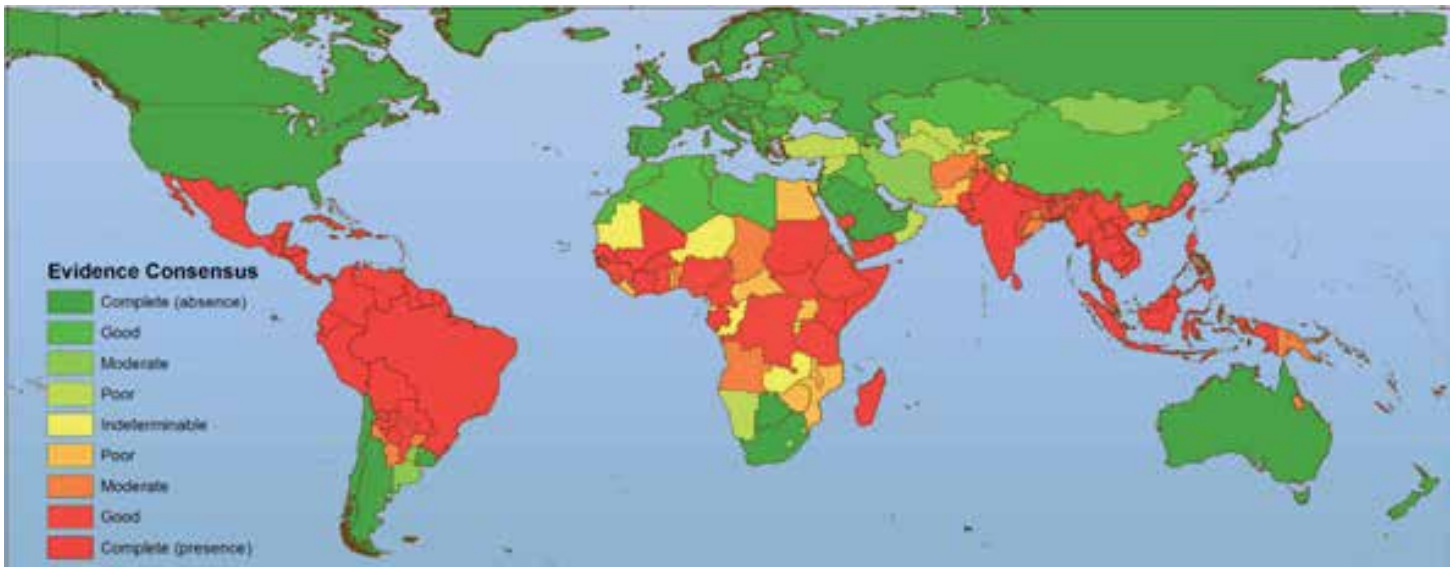
Dengue is a mosquito borne disease caused by a flavivirus, comprising of four serotypes (DENV1–4). Dengue has the greatest reach of all arthropod-borne viral infections, with an estimated 390 million infections a year. The vast majority of dengue cases (nearly 95 percent) are seen in children less than 15 years of age. The virus is transmitted by Aedes mosquitos, mainly Aedes aegypti. Aedes is a day-biting mosquito, that preferentially feeds on humans. Aedes mosquitos breed in containers and are closely associated with human dwellings, thus transmitting virus at higher rates in urban settings. Based on the current global evidence, virus transmission around the world is depicted in Figure 1. According to WHO estimates of dengue burden, 50 - 100 million infections seem to occur each year. However, other estimates suggest a burden as high as 390 million infections per year.



Clinical manifestations

Manifestations of Dengue fever are variable, ranging from an inapparent viral infection to life threatening plasma leakage and organ dysfunction. Three phases have been recognised in the clinical course of a dengue infection. The phases include febrile, critical and recovery phase. Patients in the febrile phase typically develop fever, headache with or without retro-orbital pain, myalgia, arthralgia, and a maculopapular to petechial rash. Although children usually suffer from high fever, they are generally less symptomatic than adults during this phase of the illness. Mild hemorrhagic manifestations like petechiae and mucosal membrane bleeding (e.g. nose and gums) may be seen. Febrile phase lasts for 3-7 days, after which most patients recover without complications. However, in a small proportion of patients, a systemic plasma leakage ensues around the time of defervescence. This phase, known as critical phase, is characterized by a progressive leukopenia along with thrombocytopenia, hemorrhagic manifestations, pleural effusion, ascites and hypoalbuminemia. Plasma leakage leads to hemoconcentration and shock which may lead to organ dysfunction and death. Capillary leakage and shock are more frequent and more severe in children than in adults while bleeding manifestations and organ involvement are more common in adults.

Children with profound and prolonged shock may also have clinically significant bleeding. The altered vascular

Diagnosis	Diagnostic Criteria	Management
Probable dengue	• Live in or travel to a dengue endemic area • Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test	• Outpatient management with daily monitoring • Oral rehydration solution • Acetaminophen for treatment of fever • Do not use non-steroidal anti inflammatory agents
Dengue without warning signs (Dengue fever)	• Laboratory-confirmed dengue • Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test	• Hospital admission of infants, consider outpatient management with daily monitoring in children > 1 year • Oral rehydration solution if tolerated • Closely monitor temperature pattern, fluid balance, urine output, warning signs, hematocrit, white blood cell and platelet counts
Dengue with warning signs (Dengue hemorrhagic fever)	• Laboratory-confirmed dengue • Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test • Any of the following warning signs: abdominal pain or tenderness, persistent emesis, volume overload (edema), mucosal bleeding, lethargy or restlessness, hepatomegaly, hemoconcentration	• Intravenous crystalloid solutions • Blood transfusions if necessary • Monitor hematocrit, vital signs, peripheral peripheral, urine output, blood glucose and other organ functions
Severe dengue (Dengue shock syndrome)	• Laboratory-confirmed dengue • One of the follOWing: shock, significant volume overload with respiratory distress, severe clinical bleeding, organ failure	• Intensive care treatment • Intravenous crystalloid or colloid solutions • Blood transfusion with fresh-packed red cells or fresh whole blood • Platelet concentrates in case of massive bleeding

permeability usually reverts back to normal after approximately 48 to 72 hours during the recovery phase. The patient starts feeling better and diuresis ensues. For ease of diagnosis and uniformity in management, WHO has divided dengue infection into severe and non severe dengue. (Figure 2)

Children infected with one dengue virus serotype (i.e. primary dengue virus infection) develop long-term protective immunity against re-infection with the same serotype. However, reinfection by a different serotype can occur and may lead to severe dengue. Hence, any one patient may be infected up to four times by heterologous virus serotypes. Infants born to mothers with established immunity against dengue are at high risk for severe dengue and may lead to hospitalization during primary infection in the first year of life.

Diagnosis

Diagnosis of dengue infection can be done by virus isolation, detection of viral antigens in peripheral blood or detection of host antibodies. Dengue virus is found in the blood and other body fluids in the first 5 days of illness. So, during the first 5 days virus isolation or detection of NS1 (non structural antigen - 1) antigen can be done. After day 5, virus/viral antigens disappear and humoral antibodies to dengue virus appear. So, after 5 days antibody against dengue (igM and IgG) can be detected using hemagglutination inhibition (HI), complement fixation, or any other assays.

A useful bedside clinical test for the diagnosis of Dengue infection is tourniquet test. In a tourniquet test, blood pressure cuff if inflated midway SBP and DBP and kept for 5 min. After 5 minutes, pressure is released and antecubital fossa is observed for petechial spots. 10 or more spots per square inch is considered a positive tourniquet test. It is an indicator of capillary fragility and help in distinguishing dengue fever from other illnesses.

Other laboratory manifestations include leucopenia, increased liver enzymes (SGOT often twice as increased as SGPT) and thrombocytopenia.

Management

No specific treatment for dengue is available. Clinical management of dengue includes close monitoring of blood parameters, fluid replacement therapy as required, and recognition of signs of severe disease. Temperature management should be done by paracetamol. Non-steroidal anti-inflammatory agents (NSAIDS) are contraindicated as they may aggravate or precipitate bleeding.

Dengue fever without warning signs can be managed on outpatient basis except in case of infants who should be admitted as course can be very unpredictable in them. Older children need to be evaluated daily by health care workers for presence of warning signs. Home treatment includes paracetamol for fever, adequate oral hydration and bed rest.

Children with warning signs or severe dengue should be hospitalised. Hematocrit monitoring needs to be done at a frequency decided by the clinical condition of the patient. Ringer's lactate is the preferred fluid for management of dengue patients. Children with hemoconcentration need to be infused fluids at a higher rate initially and titrated with hematocrit monitoring. Children presenting with shock need to be given fluid bolus (RL or NS) and fluid titrated subsequently based on clinical response. Colloids (including dextran and starch contains fluids) and fresh frozen plasma can be given in case of inadequate response to crystalloids. A good response is improvement in hematocrits along with improved pulse pressure, urine output and peripheral perfusion. In case of worsening clinical condition and falling hematocrits, packed red cell transfusion is indicated.

Generalized body swelling, ascites and pleural effusion occurs creating fluid management difficult and tricky. Appropriate use of vasopressors, colloids and crystalloids is the cornerstone of dengue management. Mechanical ventilation may be considered in case of respiratory embarrassment due to massive effusion or refractory shock. Platelet concentrates can be given in case of bleeding manifestations. Studies have shown no role of routine use of prophylactic platelet transfusions. Corticosteroids are of no use in randomised trials.

Once the critical phase is over, capillary leak improves and third space fluid is reabsorbed along with diuresis. Hence, fluid administration needs to be reduced substantially or stopped once critical phase is over otherwise congestive heart failure may ensue. Diuretics may be useful at this stage.

Prevention

As of now, vector control is the only available approach for prevention and control of dengue. Reduction of vector breeding through municipal clean-up campaigns is the cornerstone. Discarded containers (tyres, plastics etc) need to be disposed of. Other approaches include use of insecticide sprays, full sleeves clothing, use of mosquito repellent ointments, mosquito nets etc are useful as well.

Vaccine development has suffered setback due to the existence of multiple viral serotypes and the association of prior dengue virus infection with an increased risk for more severe disease. A recent study published in NEJM performed reanalysis of previous studies and reported dengue serostatus by different methods. Previously dengue seropositive patients were protected by the vaccine (Dengvaxia) against future hospitalisation and severe dengue. However, those who were seronegative had increased risk of hospitalisation and death.

DENGUE FEVER

Dr. Supriya Bhushan
Consultant, Medicine

Dengue is the most rapidly spreading mosquito-borne viral disease of mankind.

Global scenario: 30-fold increase in global incidence over the last five decades .According to WHO, about 50–100 million new dengue infections are estimated to occur annually in more than 100 endemic countries, with a steady increase in the number of countries reporting the disease

National Scenario: Dengue virus was isolated in India for the first time in 1945. As breeding was more common in urban areas, the disease was observed to be mostly prevalent in urban areas .However, the trend is now changing due to socioeconomic and man-made ecological changes that have resulted in the invasion of mosquitoes into the rural areas. Every year, during the period July–November, an upsurge in the cases of dengue/DHF has been observed.

Dengue viruses, Genus Flavivirus. 4 serotypes- DENV-1, DENV-2, DENV-3 and DENV-4.

Vector : Aedes aegypti

Host Factor: People of all ages and both genders are at risk. Secondary dengue infection is a risk factor for DHF. Travel to dengue endemic areas . Intrinsic incubation period is 4 to 7 days (range 3–14 days). There are reports of dengue transmission through blood transfusion, organ transplantation, congenital dengue infections occurring in neonates born to mothers infected very late in pregnancy.

Immunopathogenesis:

Capillary leakage and shock

Coagulopathy in dengue

Causes of Bleeding in DF/DHF

Abnormal coagulogram

Thrombocytopenia & Platelet dysfunction

Prothombin complex deficiency secondary to Liver involvement

Endothelial injury

DIC and Prolonged aPTT

Decrease fibrinogen level

Causes of Thrombocytopenia

Destruction of platelet (antiplatelet antibodies)

DIC

Bone marrow suppression in early stage

Peripheral sequestration of Platelet

Clinical Manifestations: Dengue viral infected person may be asymptomatic or symptomatic and clinical manifestations vary from undifferentiated fever to florid hemorrhage and shock.

Classification

Undifferentiated dengue fever (UDF)

Severe dengue fever

Dengue hemorrhagic fever

Dengue shock syndrome

Natural course of Dengue Fever:

Febrile phase- biphasic type, lasting 2-7 days with headache, flushing, pain in muscle/joint/bone and rash.

Critical phase (Leakage phase)- It begins after 3 to 4 days of onset of fever. Abnormal haemostasis and leakage of plasma leads to shock, bleeding, accumulation of fluid in pleural and abdominal cavity. The period of plasma leakage usually persists for 36-48 hrs.

Convalescent phase (Recovery phase) – It begins 6-7 days of fever and last for 2-3 days. Longer convalescence may be expected in some of the patients with severe shock, organ involvement and other complications which may require specific treatment.

Laboratory Diagnosis

ELISA-based NS1 antigen tests.

IgM-capture ELISA (MAC ELISA)

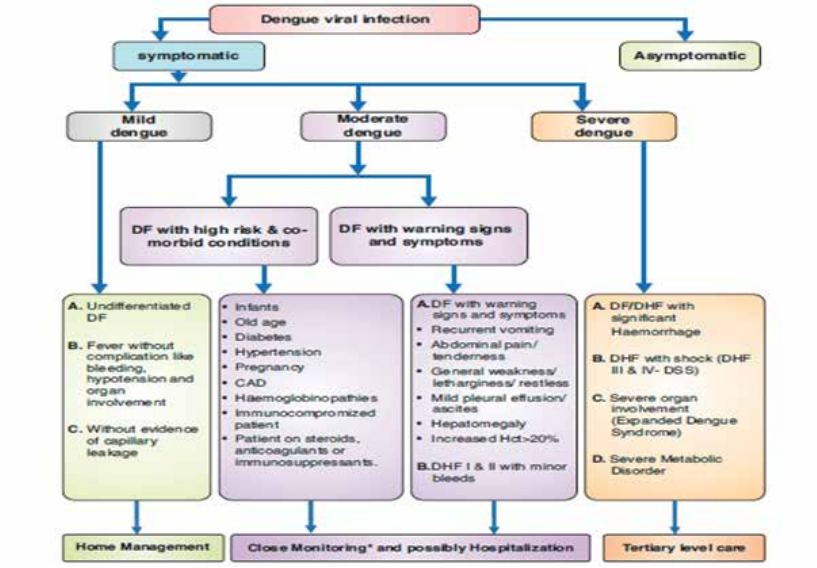
Isolation of dengue virus

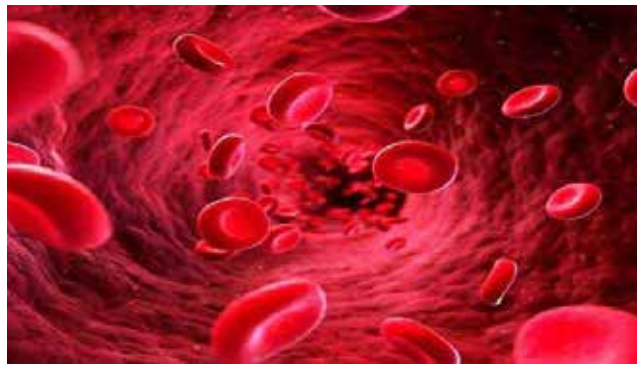
PCR

IgG-ELISA

Serological tests

Clinical Management





Indications for platelet transfusion:

Platelet count less than 10000/cu.mm in absence of bleeding manifestations (Prophylactic platelet transfusion). Hemorrhage with or without thrombocytopenia.

Complications of Dengue Fever:

System	Unusual or atypical manifestations
CNS involvement	Encephalopathy, encephalitis, febrile seizures, I/C bleed
G.I. involvement	Acute Hepatitis/fulminant hepatic failure, cholecystitis, cholangitis acute pancreatitis
Renal involvement	Acute renal failure, haemolytic uremic syndrome, acute tubular necrosis
Cardiac involvement	Cardiac arrhythmia, cardiomyopathy, myocarditis, pericardial effusion
Respiratory	Pulmonary oedema, ARDS, pulmonary haemorrhage. pleural effusion
Eye	Conjunctival bleed, macular haemorrhage, visual impairment, opticneurits

Criteria For Discharge: The admitted patients with no fever for atleast 24 hrs, normal BP, adequate urine output, no respiratory distress and persistent platelet count >50,000/cumm should be discharged from hospital.

Dengue Vaccine: Currently, WHO has licensed the Sanofi vaccine called Dengvaxia for use in endemic countries but not yet prequalified its use which requires an NRA of record in the manufacturing country.In India, DSV4 Vaccine developed by ICGEB (International Center for Genetic Engineering and Biotechnology) in collaboration with Sun Pharma offers protection against all 4 strains of Dengue but is still to undergo human trials.

DENGUE IN PREGNANCY- PROTOCOLS IN MANAGEMENT

Dr. Ratna N. Rao
Sr.Consultant (OB/GYN)

Introduction

Dengue fever is a mosquito borne viral disease affecting humans,caused by any of the four sero types of Flaxivirus(RNA) and transmitted by the Aedes mosquito especially A.egypti.

The health effects of Dengue in pregnancy are not well understood and studies on this issue have produced variable results, reasons being of small cohorts being studied.

WHO in their revised guidelines in 2009 have reclassified Dengue cases as either with or without "warning signs" in all affected cohorts and irrespective of Pregnancy. Dengue without warning signs present as an acute febrile illness with at least two of the following features: nausea, vomiting, rash, aches and pains, leucopenia and a positive "tourniquet test" .

Warning signs are classified as abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing haematocrit, with decreasing platelets:(at least one must be observed.

Severe Dengue is associated with severe bleeding, plasma leakage, or organ failure.

Clinical manifestations, treatments and outcome follow a similar pattern in pregnancy

Misdiagnosis and delayed diagnosis in the pregnant population do result in case fatalities (which can be reduced from 20% to less than 1%) which need early diagnosis and management.

Overlapping clinical conditions and deranged laboratory features common with HELLP, pulmonary embolism, abnormal bleeding conditions etc can impact fetal and maternal outcome.

Impact of Dengue on Pregnancy

1. Adverse pregnancy outcomes like preterm labor, low birth weight, and CSD are still uncertain, however risk of vertical transmission is well established
2. Dengue in First Trimester. Insufficient data on embryopathy
3. Parturition: severe bleeding complicates delivery and various surgical procedures during the 'critical phase' which is a period of marked thrombocytopenia with or without plasma leak. However this does not warrant pregnancy termination.

Principals of Management

1)Close monitoring
2) Supportive treatment
3) Management of 3rd space leaks.
4) Control of haemmorragic complications

Management in Pregnancy (FOGSI Protocol 2014)

Baseline CBC on D1/2P (WBC is N /lower ....do supportive RX of DF and repeat

CBC after 24hrs and compare for fall of Platelets/rise of PCV by10%

Admission Criteria

As per CDC criteria. Pregnancy falls under Group B class for management.Admission indicated for close surveillance.

Dengue fever without warning signs:

Monitor 4hrly vitals

Ensure 4-6hrly urinary output (minimum 100cc/4hrs)

Intake/Output Chart

Daily CBC & other investigations

Paracetamol 500-650 mg 6hrly. Don't exceed 4gm in 24hrs

Encourage oral intake (2.5 lit /day)

Alert for "warning"symptoms

Any signs of capillary leak can progress to severe Dengue, start I/V fluid therapy.

DF with warning signs

Monitor vitals

Cathetrize for urine output (5 ml/kg/hr)

Intense fluid resuscitation. Normal saline bolus 5-10ml/ kg /hr followed by 3-5 ml/kg/hr

Avoid IOL or planned surgery

DF with shock

ICU management

Fluid management/fluid bolus 10 cc/kg over 15 min, optimize fluid to clinical response

CBC/LFT/PCV/SE/BS

Convalescence

Increasing WBC and Platelet

Watch for fluid overload

Discharge

Afebrile for 24hrs with normal hemodynamic and lab parameters

Challenges in Management

Vomiting is a warning sign

Failure to recognize plasma leak early leads to de compensated shock and multi organ failure

Inevitably delivery in the critical phase

Bleeding should be anticipated and monitored

Blood and blood products should be cross matched and saved in preparation for delivery

Ensure minimum trauma and complete placental removal

Transfusion of platelets should be initiated during or after delivery but not too early; no prophylactic platelets far ahead of delivery as placental concentration is sustained only for a few hrs in critical phase.

Do not wait for blood loss to fall below 500 cc or hematocrit to fall to a low level

Transfuse as soon as possible,but low trigger for blood replacement

Commence Oxytocin and Misoprost for ppl prophylaxis early

Delivery

Close monitoring of mother and neonate as vertical transmission high especially if dengue fever is around perinatal period.

During this period severe fetal illness and death may occur as insufficient time for production of maternal antibodies.

Recommendations

For initial resuscitation use normal saline.

No Dextrose.Colloids only after 2 fluid boluses in patients of shock.

Fresh blood if there is overt blood loss.

No prophylactic platelet transfusion. If less than 50000 then transfuse or in case of planned surgery and platelets less than 75000, again transfuse.

No role of steroids or immunoglobulins/prophylactic antibiotics /or tocolytics

Operative delivery for obstetric indications

Skilled team for operative delivery in a hospital.

Dr. Mohan Nair, Sr. Consultant and Chief of Cardiology Department participated as a TCT Advisory Faculty Member for the 30th Annual Scientific Symposium of Transcatheter Cardiovascular Therapeutics, (TCT 2018) held at the San Diego Convention Center in San Diego, California, from September 21 through September 25, 2018.

Dr.RoliGautam, Sr. Consultant, Obs.&Gyne. Department received Distinguished Doctors Award by Indian Medical Association South Delhi Branch.

QUIZ

A 10 year old child presents with recent onset headache, bodyaches, low grade fever and cough. Examination findings include mild tachypnea, bilateral wheezing, and erythema multiforme. What is the most likely diagnosis and management?

Kindly send your answers at : Newsletter@holyfamilyhospitaldelhi.org

Answer to previous quiz : Nephrocalcinosis.

Laughter Moments:

Patient: 'Doctor, doctor, will I be able to play the violin after the operation?'
Doctor: 'Yes, of course…'
Patient: 'Great! I never could before!'

A man goes to the doctor and says, "Doctor, wherever I touch, it hurts."
The doctor asks, "What do you mean?"
The man says, "When I touch my shoulder, it really hurts. If I touch my knee - OUCH! When I touch my forehead, it really, really hurts."
The doctor says, "I know what's wrong with you - you've broken your finger!"

The CT revolution

Dr. Rajesh Gothi Sr. Consultant, Radiology

The new128 slice CT scan, called Revolution,made by GE, has recently been installed in the hospital, replacing the old workhorse, the 16 slice CT scanner.With this new updated version, the department is now equipped to perform all CT investigations with considerable improvement in the image quality.

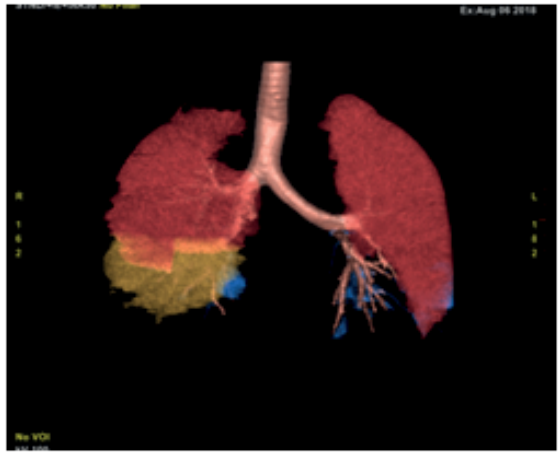
How is this new scanner different from the previous one and how is it likely to benefit patients and different clinical specialties?

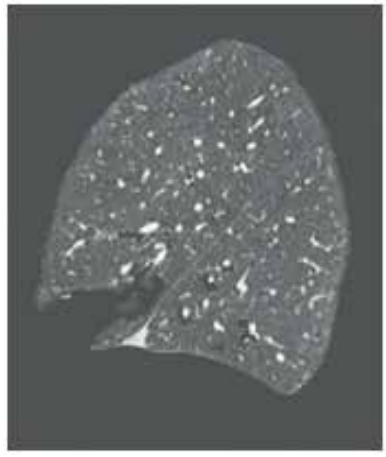
The new CT scanner has several upgraded features. The speed at which the scanning can be done is probably the most important upgrade. It makes possible evaluation of the beating heart, quick scanning a very sick patient who cannot hold his breath or stay still even for a few seconds. The radiation dose is much less as compared to the earlier scanner by virtue of the vastly improved scanning protocols.

We can do cardiac CTs, thoracic emphysema and bronchial tree CTs, Dental CT and precision angiographies. We are also looking towards doing virtual colonoscopies and bronchoscopies with the new machine.

The scanner has a software called Thoracic VCAR for the chest. It enables quantification of emphysema in different

The bronchial tree derived from the software called " Thoracic VCAR".





The lung lobes, derived from the " Thoracic VCAR" software.

lung lobes, visualization of the bronchial anatomy in multiple planes and angles, eases the performance of maximum, minimum intensity projection and virtual bronchoscopy. We can now perform high quality of thoracic work.Our coronal, sagittal and axial reconstructions for abdominal disorders are now at par with the best centers .

You should also see our temporal bone, skeletal and PNS CTs for their ultra sharp images. The metal reducing software comes in handy when dealing with metallic implants. The bone subtracting software removes bones and clearly demonstrates blood vessels in angiographic studies.Our dental CT will probably meet the expectations of dentists also who are into implants

We have in addition, made changes at our end by using techniques to further lower radiation dose especially to children, women of child bearing age and patients

needing repeated scanning.

Our technique of replacing positive oral contrast with neutral contrast like Mannitol and water, completely doing away with oral contrast especially in the acutely ill and trauma cases has shown considerable improvement in the image quality with the machine's advanced multiplanar reconstruction capabilities.

Dose of IV contrast needed

The IV contrast dose needs for CECT is also greatly reduced, thus saving costs and increasing patient safety. The IV contrast dose administered has also touched low levels without any detrimental effect on the image quality because of the superior resolution of the machine. We have reduced doses by almost half, in a good number of cases.

Challenges ahead!

The new machine has also thrown challenges.The coronary cardiac CT, one of the investigations now possible with the system has a steep learning curve both for the technicians and radiologists.

The technicians are already getting a feel and have shown quick adaptation to this machine. They are probably the best technicians in the city, eager to learn and are living up to their reputation.When radiologists in the department, are also trying and be with the front runners in our speciality. Our challenge is to work with and know something about so many different specialties in the hospital. There are probably 15 specialities to deal with on a given day!

Needless to say, that we will learn more as we go along, improve our skill, stand tall and be counted in the fraternity of doctors and technicians.

We will be looking forward for your help, sharing of knowhow,words of encouragement ,both positive as well as negative feedback to reach our goal of excellence in imaging.

A few images from our image gallery for you to savour.

EARLY INTERVENTION IN NEONATES

Dr. Sona Chawdhary,
Sr. Consultant,
Paediatrics

Preterm infants, especially those born with a very low birth weight (VLBW < 1500gm) and those with perinatal insults like birth asphyxia, sepsis etc are at a risk for long term cognitive, behavioral and physical limitations. Studies reveal that 25% of infants born between 28 and 32 weeks of gestation have neurodevelopmental disabilities. Early detection and treatment of these problems offers the best opportunity to improve outcome.

DIAGNOSTIC AND DESIGN CHALLENGES

Diagnosis and designing new therapies is complicated by:

a. Complexity of development.

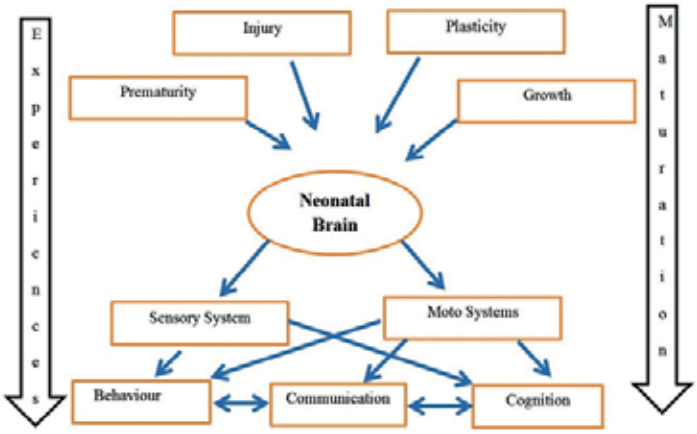
b. Variability and delays in neurological impairment after initial insult.

c. Unique characteristics of assessment in infants and young.

d. Establishing a diagnosis in the first two year of life.

Developing infants' brain and its interactions with environment and the sequelae can be summarized in the diagram

Preterm (31 weeks) DEVELOPING INFANT BRAIN



Early Intervention Rehabilitation is required in the following fields:

A. Neurosensory Rehabilitation

(i) Hearing : Early OAE/ABR to be done for diagnosis of hearing loss.

(ii) Vision

(a) ROP (Retinopathy of Prematurity) Early detection and treatment (Laser, Bevacizumab injection).

(b) Amblyopia (Reduced visual function due to discrepancy of function between eyes associated with squint)

Treatment: Neural stimulation to the amblyopic eye by patching normal eye and correction visual acuity.

(c) Strabismus: Treatment by surgery.

B. Somatosensory Rehabilitation:

Exposure to painful stimuli while in NICU can cause internalizing behaviour, which may be evident by 18-22 months of age, in form of anxiety, depression and withdrawal.

These may be prevented / corrected by

(i) Decreasing the number of painful ailments to the baby e.g. clustering of investigations

(ii) Low noise levels in the nursery

(iii) Emotional availability of parents (Kangaroo mother care, singing to the baby)

C. Motor Rehabilitation:

I. Motor rehabilitation treatment should be based on:

(i) Infant directed learning and initiation of actions.

(ii) Goal directed movements

(iii) Positive reinforcements

II. Oromotor Rehabilitation:

Preterm and neonates with encephalopathy have poor suck swallow breath co-ordination. Measures to improve this are:

(i) Non nutritive sucking (NNS).

(ii) Oral and perioral stimulation.

(iii) Manual assistance to shape movement necessary

for feeding.

D. Cognitive Rehabilitation:

Interventions in NICU to improve cognition are:

(i) Improvement in parent – infant interaction

(ii) Newer methods of using computer generated tasks to improve sustained attention.

E.Communication, Speech and Language Rehabilitation

(i) Parental education to recognize and minimize stress response in infants

(ii) Non verbal communication tools such as touch, movements and multisensory interactive.

(iii) Speech therapy at a later age.

Conclusion:

Early Intervention targeted towards early recognition of symptoms and their treatment in the high sick NICU graduates is important as the brain goes through a period of critical growth between 24 to 40 weeks.

DIAGNOSIS AND TREATMENT OF MALARIA

Malaria is the most important parasitic disease of humans, affecting millions of people and causing approximately 2000 deaths each day. The disease is endemic in most of the tropics, including much of South and Central America, Africa, the Middle East, the Indian subcontinent, Southeast Asia, and Oceania. Transmission, morbidity, and mortality are greatest in Africa, where most deaths from malaria are in young children. Although the disease remains a major problem, impressive advances have been made in many regions. A 2016 study estimated a 57% decrease in the malaria death rate and 37% decrease in the annual number of malaria deaths in the past 15 years.

Dr. Puneet Uberoi
Sr. Consultant, Medicine

Cause of malaria

Malaria is transmitted by the bite of infected female anopheline mosquitoes. Four species of the genus Plasmodium classically cause human malaria. Plasmodium falciparum is responsible for nearly all severe disease. It is endemic in most malarious areas and is by far the predominant species in Africa. Plasmodium vivax is about as common as P falciparum, except in Africa. P vivax uncommonly causes severe disease, although this outcome may be more common than previously appreciated. Plasmodium ovale and Plasmodium malariae are much less common causes of disease, and generally do not cause severe illness.

Who is at risk?

In highly endemic regions, where people are infected repeatedly, antimalarial immunity prevents severe disease in most older children and adults. However, young children, who are relatively nonimmune, are at high risk for severe disease from P falciparum infection, and this population is responsible for most deaths from malaria. Pregnant women are also at increased risk for severe falciparum malaria. In areas with lower endemicity, individuals of all ages commonly present with uncomplicated or severe malaria.

Clinical features of uncomplicated malaria

Prodrome of headache and fatigue, followed by fever.

Classic malarial paroxysm includes chills, high fever, and then sweats.

Patients may appear to be remarkably well between febrile episodes.

Headache, malaise, myalgias, arthralgias, cough, chest pain, abdominal pain, anorexia, nausea, vomiting, and diarrhea are common. Physical findings may be absent or include signs of anemia, jaundice, splenomegaly, and mild hepatomegaly.

Severe malaria

Characterized by signs of severe illness, organ dysfunction, or a high parasite load (peripheral parasitemia greater than 5% or greater than 200,000 parasites/mcL).

Principally a result of P falciparum infection because this species uniquely infects erythrocytes of all ages and mediates the sequestration of infected erythrocytes in small blood vessels, thereby evading clearance of

infected erythrocytes by the spleen.

Severe falciparum malaria can include dysfunction of any organ system, including neurologic abnormalities progressing to alterations in consciousness, seizures, and coma (cerebral malaria); severe anemia; hypotension and shock; noncardiogenic pulmonary edema and the acute respiratory distress syndrome; acute kidney injury due to acute tubular necrosis or, less commonly, severe hemolysis; hypoglycemia; acidosis; hemolysis with jaundice; hepatic dysfunction; retinal hemorrhages and other fundoscopic abnormalities; bleeding abnormalities, including disseminated intravascular coagulation; and secondary bacterial infections.

Laboratory Findings

Giemsa-stained blood smears remain the mainstay of diagnosis, although other routine stains (eg, Wright stain) will also demonstrate parasites.

Thick smears provide efficient evaluation of large volumes of blood, but thin smears are simpler for inexperienced personnel and better for discrimination of parasite species.

Single smears are usually positive in infected individuals, although parasitemias may be very low in nonimmune individuals.

If illness is suspected, repeating smears at 8 to 24 hour intervals is appropriate.

The severity of malaria correlates only loosely with the quantity of infecting parasites, but high parasitemias (especially greater than 10–20% of erythrocytes infected or greater than 200,000–500,000 parasites/mcL) or the presence of malarial pigment (a breakdown product of hemoglobin) in more than 5% of neutrophils is associated with a particularly poor prognosis.

Other modalities of diagnosis include rapid diagnostic tests to identify circulating plasmodial antigens with a simple “dipstick” format.

They offer sensitivity and specificity near that of high-quality blood smear analysis and are simpler to perform.

Serologic tests indicate history of disease but are not useful for diagnosis of acute infection.

PCR and related molecular tests are highly sensitive but not available for routine diagnosis.

Treatment

Symptomatic malaria is caused only by the erythrocytic stage of infection. Available antimalarial drugs act against this stage, except for primaquine, which acts principally against hepatic parasites.

A. Non-Falciparum Malaria

The first-line drug for non-falciparum malaria from most areas remains Chloroquine.

Due to increasing resistance of P vivax to Chloroquine, alternative therapies are recommended when resistance is suspected.

These infections can be treated with artemisinin-based combination therapies (ACTs) or other first-line regimens for P falciparum infections.

For P vivax or P ovale, eradication of erythrocytic parasites with Chloroquine should be accompanied by treatment with Primaquine (after evaluating for glucose-6-phosphate dehydrogenase [G6PD] deficiency) to eradicate dormant liver stages (hypnozoites), which may lead to relapses with recurrent erythrocytic infection and malaria symptoms after weeks to months if left untreated.

Tafenoquine, the new drug related to Primaquine, appears to offer similar efficacy with simpler dosing (300 mg single dose above 16 years), but it also engenders potential toxicity in those with G6PD deficiency. P malariae infections need only be treated with Chloroquine.

B. Uncomplicated Falciparum Malaria

P falciparum is resistant to chloroquine and sulfadoxinepyrimethamine in most areas.

Falciparum malaria from other areas should not be treated with these older drugs, and decisions regarding chemoprophylaxis should follow the same geographic considerations.

ACT, including a short-acting Artemisinin and longer-acting partner drug, are first-line therapies in nearly all endemic countries.

WHO recommends ACT to treat falciparum malaria.

Quinine generally remains effective for falciparum malaria, but it must be taken for an extended period to

cure disease and is poorly tolerated, and should best be reserved for the treatment of severe malaria and for treatment after another regimen has failed.

C. Severe Malaria

Severe malaria is a medical emergency.

Parenteral treatment is indicated for severe malaria and with inability to take oral drugs.

With appropriate prompt therapy and supportive care, rapid recoveries may be seen even in very ill individuals.

The standard of care for severe malaria is intravenous Artesunate, which has demonstrated superior efficacy and better tolerability than Quinine.

The drug is administered in four doses of 2.4 mg/kg over 3 days, every 12 hours on day 1, and then daily.

If Artesunate cannot be obtained promptly, severe malaria should be treated with intravenous Quinine (available in most countries) or Quinidine.

In endemic regions, if parenteral therapy is not available, intrarectal administration of Artemether or Artesunate is also effective.

Patients receiving intravenous Quinine or Quinidine should receive continuous cardiac monitoring; if QTc prolongation exceeds 25% of baseline, the infusion rate should be reduced. Blood glucose should be monitored every 4–6 hours, and 5–10% dextrose may be coadministered to decrease the likelihood of hypoglycemia.

Appropriate care of severe malaria includes maintenance of fluids and electrolytes; respiratory and hemodynamic support; and consideration of blood transfusions, anticonvulsants, antibiotics for bacterial infections, and hemofiltration or hemodialysis.

With high parasitemia (greater than 5–10%), exchange transfusion has been used, but beneficial effects have not clearly been demonstrated and it is generally no longer recommended.

Clinical Setting	Drug Therapy[1]	Alternative Drugs
Chloroquine-sensitive *Plasmodium falciparum* and *Plasmodium malariae* infections	Chloroquine phosphate, 1 g at 0, followed by 500 mg at 6, 24, and 48 hours –or– Chloroquine phosphate, 1 g at 0 and 24 hours, then 0.5 g at 48 hours	
Plasmodium vivax and *Plasmodium ovale* infections	Chloroquine (as above), then (if G6PD normal) primaquine, 30-mg base daily for 14 days	For infections from Indonesia, Papua New Guinea, and other areas with suspected resistance: therapies listed for uncomplicated chloroquine-resistant *P falciparum* plus primaquine
Uncomplicated infections with chloroquine-resistant *P falciparum*	Coartem (artemether 20 mg, lumefantrine 120 mg), four tablets twice daily for 3 days –or– Malarone, four tablets (total of 1-g atovaquone, 400-mg proguanil) daily for 3 days –or– Quinine sulfate, 650 mg three times daily for 3–7 days Plus one of the following (when quinine given for < 7 days) Doxycycline, 100 mg twice daily for 7 days –or– Clindamycin, 600 mg twice daily for 7 days	Mefloquine, 15 mg/kg once or 750 mg, then 500 mg in 6–8 hours –or– Dihydroartemisinin-piperaquine[2] (dihydroartemisinin 40 mg, piperaquine 320 mg), 4 tablets daily for 3 days –or– ASAQ[2] (artesunate 100 mg, amodiaquine 270 mg), two tablets daily for 3 days
Severe or complicated infections with *P falciparum*	Artesunate 2.4 mg/kg intravenously every 12 hours for 1 day, then daily[3,6]	Quinidine gluconate,[4–6] 10 mg/kg intravenously over 1–2 hours, then 0.02 mg/kg intravenously/min –or– Quinidine gluconate,[4–6] 15 mg/kg intravenously over 4 hours, then 7.5 mg/kg intravenously over 4 hours every 8 hours –or– Quinine dihydrochloride,[2,4–6] 20 mg/kg intravenously over 4 hours, then 10 mg/kg intravenously every 8 hours –or– Artemether,[2,6] 3.2 mg/kg intramuscularly, then 1.6 mg/kg/day intramuscularly

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Anaesthesia / Pain Management	Neurology with Neurosurgery
Dental Clinic	Obstetrics and Gynaecology with Laparoscopic Surgery
Comprehensive Cardiology Service (Including Interventions)	Orthopaedics, Trauma and Joint Replacements
Dermatology	Paediatrics with IPCU & NICU
Emergency Services	Physiotherapy
Eye and ENT Surgery	Plastic and Vascular Surgery
Gastroenterology with Endoscopy	Psychiatry with Clinical Psychology
General, Laparoscopic and Paediatric Surgery	Radiology with CT and MRI
Intensive Care (ICU/IPCU/NICU)	Respiratory Medicine (Bronchoscopy, Sleep Lab, EBUS,
Laboratory Services	Thoracic Surgery
Medicine with ICU	Urology and Urosurgery
Nephrology and Dialysis	Alternative Medicine Including Homoeopathy & Ayurveda

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Editorial

In the fag end of monsoon, the national capital is witnessing a spurt in diseases. As seen in past this year also at least 50 per cent of the OPD patients are suffering from viral fever and flu infection, some of those later diagnosed as dengue and malaria cases. One of the reason for this spurt is heavy rains and the intense humidity in the city and failure of civic agencies in not taking preventive measures to control mosquito-borne diseases. Delhi has been witnessing a spike in dengue, malaria and chikungunya cases in the past four years. As the symptoms of dengue are seen in many other diseases as well, its diagnosis is confirmed by detecting dengue antibodies in patients' serum.

Therefore this issue of newsletter is dedicated to the seasonal infections to refresh our knowledge and dos and don'ts in various conditions during these fevers.

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