The Journal

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Address for Correspondence

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## Instructions to Authors


Dr Sulochana Gunasheela, FRCS (Edinburgh), FRCOG (London), and DA (London), founded the Gunasheela Surgical and Maternity Hospital and IVF center, Bangalore in 1985 and served as a managing partner.

It is with profound sorrow that we convey the sad demise of Dr Gunasheela who was a pioneer in the fields of obstetrics, gynecology, and infertility as well as a member of the editorial board of Perinatology. She was a national icon in her field and has an array of achievements to her credit. Following are a few of her achievements:

- She was the first to successfully employ the technique of embryo transfer (freezing and thawing of an immature oocyte) to produce a live baby (2011).
- She was the first in India (2003) to successfully use the technique of in-vitro maturation (IVM) of immature oocytes to produce a baby. This baby is one of the first 300 babies reported to be born by this technique in the whole world and the first IVM baby in India.
- She pioneered the in-vitro fertilization (IVF) technique in south India and used it effectively to produce the first baby in 1988.
- She introduced mass laparoscopic sterilization camp services in Karnataka and Tamil Nadu with the help of NGOs in 1982. These NGO camps eventually received government recognition and support.
- She introduced obstetric and gynecologic ultrasound in Bangalore in 1982.
- She was also the first to introduce the skill of hysteroscopy to the state of Karnataka.

She was the member of National Committee for drafting National Guidelines for Accreditation, Supervision and Regulation of ART clinics in India (by ICMR) - 2002; the Chairperson of All India Co-coordinating Committee of Royal College of Obstetricians and Gynecologists, London - 1999. She was associated with various other esteemed organizations and committees both at the national and international levels.

Dr Gunasheela has authored several books, contributed to several others, and has innumerable publications in national and international journals.

She has won many awards in recognition of her academic achievements, sterling work, and selfless service. Few of them are, the:
- Karnataka Rajyothsava Award, 1990
- IMA – Dr BC Roy Day’s Award
- Appreciation award for outstanding achievements - BSOG
- ISAR Award 2004 – for pioneering the IVF program in India

Her penchant to learn, share, contribute, and innovate was very much there until the very last day of her life. She was a great teacher and has inspired a whole generation of budding obstetricians and gynecologists.

May her soul rest in peace
Dear friends,

I am glad to present the 3rd issue of this volume.

Do note the introduction of 2 new features, “Perinatology through Philately” and “Dysmorphism and Syndromes,” in this issue.

The health scene of India seems to be in a pretty bad shape. The target of reducing the infant mortality rate to 28 per thousand live births by 2012 (end of the 11th 5-year plan) is yet to be attained. A latest report by the National Institute of Medical Statistics (NIMS), which is a part of the Indian Council of Medical Research (ICMR), shows that it is difficult for India to reach its target till as late as 2016. Also, the target of reducing the under-five mortality rate to 39 per thousand live births by 2012 cannot be reached before 2015. States such as Kerala, Tamilnadu, Goa, Maharashtra, and Punjab are doing a fair job, whereas many others are performing below par to bring down the national figures.

The reasons for this are varied, including lack of health awareness, failure to deliver health programs due to lack of infrastructure, personnel and motivation, etc. China, which had similar health indices to India in the 1950s, has marched way ahead in this regard. In addition, many of our neighboring countries such as Sri Lanka have also attained much better health indices.

It is time that we, including the Government, healthcare fraternity, nongovernmental agencies, private sector, and public wake up to this stark reality. Parameters such as concerted effort, proper planning, coordination, and hard work are required to improve our health indices.

Do send us your contribution and feedback to further improve the quality of the journal.

I hope you will enjoy reading this issue.

With regards,

Dr Ranjan Kumar Pejaver
Editor in chief
Email: rpejaver@yahoo.com
Preventing Child Mortality through Immunization

World immunization day is observed on 10th November, every year, with the goal of preventing childhood illness and diseases. Immunization is a low-tech, cost-effective, and highly successful method by which an individual's immune system becomes fortified against an immunogen.

Children are susceptible to 6 deadliest childhood diseases including, measles, tuberculosis, polio, tetanus, diphtheria, and pertussis. More than 19 million children, constituting almost 20% of them born each year are not immunized against preventable illnesses that could lead to disability or even death. A large number of these deaths can be prevented through vaccination.

Each year, more and more children are being reached out through this program. In 2010, an estimated 109 million children under the age of 1 year were vaccinated with 3 doses of diphtheria-tetanus-pertussis (DTP3) vaccine. Global efforts by means of mass vaccination programs have certainly resulted in successfully mitigating childhood mortality rates.

Global measles mortality has been reduced from an estimated 535,300 deaths in 2000 to 139,300 in 2010. Polio cases have decreased almost 99%, from an estimated 350,000 cases in 1988 to 1352 reported cases in 2010. Neonatal tetanus deaths have declined to an estimated 59,000, down from 790,000 deaths in 1988. These reductions are the result of the global effort to eradicate the diseases.

Immunization programs not only protect children from a number of preventable diseases, but also serve as an opportunity to deliver other life-saving measures, such as vitamin-A supplements to prevent malnutrition, insecticide-treated nets for protection against malaria, and deworming medicine to rid children of intestinal worms.
Perinatal Toxoplasmosis
Indu S Nair*

*Correspondence
Dr Indu S Nair
Consultant neonatologist
Manipal Hospital
98, old airport road
Bangalore 560017, Karnataka
India
Email: drindu_nair2000@yahoo.co.in

Introduction
Toxoplasmosis is a disease caused by the ubiquitous protozoan *Toxoplasma gondii*; and has a seroprevalence of 24.3% in India. Although these infections are usually asymptomatic or associated with self-limited symptoms in adults (fever, malaise, and lymphadenopathy) primary infection acquired during pregnancy can cause congenital toxoplasmosis with severe sequelae.

*T gondii* infection is most frequently caused by ingestion of raw or undercooked meat, infected water or food, which carry tissue cysts. Congenital toxoplasmosis occurs from the transplacental passage of the parasite from mother to fetus.

Once serological diagnosis of acute infection is established during pregnancy, prenatal diagnosis of fetal infection is done using amniotic fluid PCR and ultrasoundography. Further, the IgG avidity test helps to discriminate between past and recently acquired infection during pregnancy. Antenatal treatment is with spiramycin if PCR negative and with pyrimethamine, sulfadiazine if PCR positive until delivery. Congenital toxoplasmosis, whether symptomatic or not should be treated with pyrimethamine and sulfadiazine for 1 year. Prevention of congenital toxoplasmosis is through health education and awareness to avoid personal exposure to the parasite during pregnancy.

Toxoplasmosis is one of the most common parasitic infections of man and other warm-blooded animals; with definite hosts being felines. It is one of the most prevalent chronic infections affecting one third of the world’s human population.

Epidemiology
In the US, 15% of females at childbearing age were found to be seropositive. Serological survey by Tender, et al. has reported a positive sero-prevalence of 58% in central European countries, 51% to 72% in several Latin American countries, 54% to 77% in west African countries, and a low seroprevalence of 4% to 39% in southwest Asia, China, and Korea.

In India the average seroprevalence of *T gondii* infection is reported to be 24.3%; the lowest in the northern parts of India, highest in the south; and a seroconversion rate of 1.5% has been reported. In a study conducted in 2005-2006, a seroprevalence of 15.33% is reported in pregnant women in India.
Diagnosis of Toxoplasmosis in Pregnancy

For clinical purposes, toxoplasmosis can be divided for convenience into 5 infection categories, namely, (i) acquired by immunocompetent patients, (ii) acquired during pregnancy, (iii) acquired congenitally, (iv) acquired by or reactivated in immunodeficient patients, (v) ocular infections.

Incidence of Toxoplasma infection during pregnancy has been estimated at about 0.2% to 1% and incidence of congenital infection ranges from 1 in 1000 to 1 in 8000 live births.5,6 Toxoplasmosis can cause significant morbidity and mortality in the developing fetus if the mother acquires acute infection during pregnancy.7

The decision to perform *T. gondii* serological tests during pregnancy should not be based solely on clinical evidence (presence or absence of symptoms) or epidemiological evidence (history of exposure to *T. gondii*) as transmission can still occur even without clinical symptoms or exposure.

Serological tests should identify if the infection is acute or chronic and whether it was acquired during pregnancy or before conception.

For serological diagnosis, IgG, IgM, IgA, and IgE antibodies are detected; IgG avidity; and differential agglutination using acetone and formalin (AC/HS) have been employed successfully in an attempt to distinguish acute versus chronic stages of the infection.8 Except for quantification of IgG and IgM antibodies, most of these tests are performed only in reference laboratories.

Sera that are positive in the Sabin Feldman dye test (DT), but negative in the IgM, IgA, and IgE ELISAs, and reveal a chronic pattern in the AC/HS test are typically found in patients infected in the most distant past.8 The combination of high titers in the DT with positive IgM, IgA, and IgE ELISAs, and an acute pattern in the AC/HS test is highly suggestive of a recently acquired infection. In contrast, the presence of positive DT and IgM ELISA results but a negative, low-positive, or equivocal result in the IgA and IgE ELISAs and an equivocal pattern in the AC/HS test is more difficult to interpret.8

Criteria for evaluation of maternal serology

Adapted from the European Research Network on Congenital Toxoplasmosis9

<table>
<thead>
<tr>
<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
<th>IgG avidity</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-ve</td>
<td>-ve</td>
<td>-ve</td>
<td>-ve</td>
<td>Seronegative</td>
</tr>
<tr>
<td>+ve (&lt; 200 UI)</td>
<td>-ve</td>
<td>-ve</td>
<td>-ve</td>
<td>Previous infection</td>
</tr>
<tr>
<td>+ve</td>
<td>+ve</td>
<td>+ve</td>
<td>&lt;15%</td>
<td>Acute infection</td>
</tr>
<tr>
<td>+ve (&gt; 300 UI)</td>
<td>+ve</td>
<td>-ve</td>
<td>-ve</td>
<td>Probably recent</td>
</tr>
<tr>
<td>+ve (&lt; 300 UI)</td>
<td>+ve</td>
<td>-ve</td>
<td>-ve</td>
<td>IgM chronic carrier</td>
</tr>
<tr>
<td>+ve (&gt; 300 UI)</td>
<td>-ve</td>
<td>-ve</td>
<td>&gt;30%</td>
<td>Probably reinfection</td>
</tr>
<tr>
<td>-ve</td>
<td>+ve</td>
<td>-ve</td>
<td>-ve</td>
<td>Natural IgM</td>
</tr>
</tbody>
</table>

Serum IgG avidity test

This method was originally developed by Hedman and his associates in Finland.10 It has been observed that the functional affinity of specific IgG antibodies is initially low after primary antigenic challenge and that it increases during subsequent weeks and months by antigen-driven B-cell selection. Protein-denaturing reagents including urea are used to dissociate the antibody-antigen complex. The avidity result is determined using the ratios of antibody titration curves of urea-treated and urea-untreated samples.

The IgG avidity test was developed to help discriminate between past and recently acquired infections. Results are based on the measurement of the avidity (functional affinity) of Toxoplasma-specific IgG antibodies; a high avidity has been stated to exclude that the infection occurred in the previous 12 weeks. Thus, its greatest value is in sera obtained from pregnant women in their first trimester of gestation.

Once the diagnosis of acute acquired infection during pregnancy has been presumptively established, diagnostic efforts should focus on determining whether
the fetus has been infected. This can be done using amniocentesis, amniotic fluid PCR, and prenatal ultrasonography.

Guidelines for serological testing and management of toxoplasmosis during pregnancy, adapted from Jose, et al11 is represented in Figure 1.

**Figure 1.** Guidelines for serological testing and management of toxoplasmosis during pregnancy on the basis of initial results obtained from *T gondii* IgG and IgM antibody tests

1. Initial serological screening with IgG and IgM tests usually can be reliably performed at nonreference laboratories
2. The interval for serological screening varies by the center and country where systematic serological screening is performed (eg, every month in France)
3. Consider consultation with a physician expert in management of toxoplasmosis during pregnancy
4. Consider sending samples to a reference laboratory
5. Treatment with spiramycin or with pyrimethamine, sulfadiazine, and folic acid
6. Amniotic fluid PCR should be performed at 18 weeks of gestation (not before) or later

**Figure 2.** Approach for pregnant women suspected or confirmed to have toxoplasmosis acquired during gestation

1. Consultation with a reference laboratory or physician expert in toxoplasmosis is suggested
2. Gestational age at which maternal infection was suspected or confirmed to have been acquired
3. Dosages of spiramycin, pyrimethamine, sulfadiazine, folic acid are as follows3:
   - Spiramycin: 1 g (3 million U) every 8 h (for a total of 3 g or 9 million U per day)
   - Pyrimethamine: 50 mg every 12 h for 2 days followed by 50 mg daily; until delivery
   - Sulfadiazine: initial loading dose of 75 mg/kg, for 2 days (max 4g/day) followed by 50 mg/kg every 12 h (maximum, 4 g/day); until birth
   - Folic acid (leucovorin): 10–20 mg daily (during and 1 week after completion of pyrimethamine therapy)

In immunocompetent patients with *T gondii* infection most likely acquired more than 6 months prior to conception, no treatment is indicated and no prenatal diagnosis advised because incidence of congenital infection is low in such cases.
If mother has coexistent HIV, then they are at a high risk of developing severe toxoplasmosis (ie, toxoplastic encephalitis, pneumonia, etc.), and/or rarely transmit the parasite to their offspring. Toxoplasma seropositive pregnant women with coexistent HIV infection and CD4 cell count < 200 cells/mm³ receive trimethoprim-sulfamethoxazole treatment (80 mg trimethoprim and 400 mg sulfamethoxazole in a single-strength tablet, 1 tablet per day); this treatment is commonly used to prevent Pneumocystis pneumonia in such patients and also prevent vertical transmission. For HIV infected women whose CD4 cell count is > 200 cells/mm³ and for non-HIV infected, but immunocompromised women, spiramycin treatment is suggested for the entire duration of the pregnancy. Spiramycin has a potential to prevent vertical transmission of the parasite and to reduce severity of infection by delaying transmission. Instead, the combination of pyrimethamine and sulfadiazine is highly active against \( T. gondii \) and is widely used as a treatment to reduce the risk of clinical manifestation in infected children.

The effectiveness of this treatment was contested by The SYROCOT study group in 2007, who performed an individual data meta-analysis of 20 European cohort studies, in which universal screening was conducted for toxoplasmosis in pregnancy.

In 1438 treated mothers identified by prenatal screening, European researchers found weak evidence that treatment started within 3 weeks of seroconversion reduced mother-to-child transmission of infection compared with treatment started after 8 or more weeks. So using the potentially toxic pyrimethamine and sulfadiazine in combination throughout pregnancy, is debatable and needs more randomized control trials. There was no evidence that prenatal treatment significantly reduced the risk of congenital toxoplasmosis. Gestational age at seroconversion was strongly associated with mother-to-child transmission and with the risk of intracranial lesions but marginally with eye lesions.

Other drugs with activity against toxoplasmosis include atovaquone or fluoroquinolones, but they cannot be used during pregnancy because their potential harmful effects on the embryo and fetus have not yet been well evaluated.

Azithromycin, has shown to be capable of inhibiting the vertical transmission of \( T. gondii \) in mice model of CT, and thiolactomycin analogues have demonstrated anti-\( T. gondii \) in vitro activity.

Encouraging results were observed using spiramycin- cotrimoxazole association, primarily for its safety and also because it showed effects on reducing the mother-to-child transmission rate and on preventing the risk of clinical sequelae.

### Congenital Toxoplasmosis

The disease is caused by vertical transmission of \( T. gondii \) from a seronegative pregnant woman who is acutely infected with \( T. gondii \) to her fetus. Worldwide, 3 to 8 infants per 1000 live births are infected in utero.

Congenital toxoplasmosis results from a primary infection acquired during pregnancy, but not from the reactivation of a latent infection in immunocompetent pregnant women. However, latent toxoplasmosis could reactivate and cause a congenital transmission of the parasite to infants who then become infected in utero.

Maternal infection prior to conception normally excludes the risk of fetal infection. However, this may not be the case when maternal seroconversion occurs a few weeks (or perhaps a few months) before conception and is accompanied by cervical adenopathies.

The risk of fetal involvement is highest when maternal infection occurs in the third trimester. Women infected at the very end of pregnancy though may remain seronegative at delivery yet have materno-fetal transmission.

The mother-to-child transmission rates rise from 7% in the first trimester to 24% in the second and 59% in the third, while the incidence of severe fetal infection falls from 75% to a negligible risk in late pregnancy.
Clinical presentation

The clinical manifestations are usually nonspecific and most cases reveal no pathological findings. Most common is the ultrasonographic findings of hydrocephalus, even in cases with negative PCR. Other findings are intracranial calcifications, microcephaly, ventriculomegaly on neurosonogram; abdominal ultrasonographic findings may include hepatomegaly, splenomegaly, ascitic fluid, cardiomegaly, and placental abnormalities.

Safadi, et al followed 43 children with congenital toxoplasmosis for a period of at least 5 years and their studies showed that most of them (88%) had sub-clinical presentations at birth; the most common neurological manifestation was a delay in neuro-psychomotor development and the most common ocular presentation was chorioretinitis. Freeman, et al found that congenital infection is associated more with preterm deliveries, especially when seroconversion is before 20 weeks but not associated with small for gestational age (SGA) or low birth weight (LBW) babies. Highest frequency of severe abnormalities at birth is seen in children whose mothers acquired a primary infection between the 10th and 24th week of gestation.

Neonatal manifestations are mainly nonspecific and may include a maculopapular rash, generalized lymphadenopathy, hepatomegaly, splenomegaly, hyperbilirubinemia, anemia and thrombocytopenia. The classic triad of chorioretinitis, intracranial calcifications, and hydrocephalus is found in fewer than 10% of infected infants. Hydrocephalus and/or microcephaly may develop when intra-uterine infection results in meningoencephalitis.

The most frequent ocular finding was chorioretinitis at 92% together with other ocular lesions in 71% of cases, and the second most common finding was microphthalmia with strabismus.

Wallon, et al studied the evolution of ocular lesions over 14 years in a prospective cohort study; they found the vision to be normal in two-thirds of children with lesions in one eye and half the children with lesions in both eyes and none had bilateral visual impairment. Overall ocular prognosis of congenital toxoplasmosis seems satisfactory when infection is identified early and appropriately treated.

Prenatal diagnosis

Prenatal diagnosis of congenital toxoplasmosis is currently based on ultrasonography and amniocentesis.

PCR on amniotic fluid for detection of *T. gondii*-specific DNA performed from 18 weeks of gestation should be used in all cases of established acute maternal infection or cases with serologic test results highly suggestive of acute acquired infection during pregnancy. If done at the 18th week, this test has an overall sensitivity of 64%, a negative predictive value of 88%, and specificity and positive predictive value of 100%. Sensitivity of prenatal diagnosis with PCR is significantly higher when maternal infection occurs between 17 and 21 weeks of gestation compared with infection occurring before 17 or after 21 weeks of gestation (*P* < .02); reliability of PCR at < 18 weeks of gestation is unknown.

Diagnosis of toxoplasmosis in newborns

Demonstration of IgA antibodies in peripheral blood appears to be more sensitive than detection of IgM antibodies for establishing infection in the newborn. *T. gondii*-specific IgA may be present when there is no *T. gondii*-specific IgM and the converse may also occur. If IgA are detected in the newborn, the test should be repeated at about 10 days after birth to ascertain that what is being measured is not contaminating maternal IgA antibodies. Isolation of toxoplasma by PCR in body fluids is diagnostic at all times.

Maternally transferred IgG antibodies should disappear within the first 6–12 months of life. A negative *T. gondii*-specific IgG test result at 1 year of age essentially rules out congenital toxoplasmosis.

Although not clinically available, antigen-specific lymphocyte transformation and lymphocyte typing in response to exposure to *T. gondii* antigens has been used successfully to diagnose congenital infection in infants.
Specific lymphocyte anergy to the organism may also occur in congenitally infected infants. Specific lymphocyte anergy to the organism may also occur in congenitally infected infants.46

Guidelines for Treatment of Congenital Toxoplasmosis in Infants
Adapted from Feigen, et al24

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrimethamine</td>
<td>Loading dose: 2 mg/kg per day for 2 days followed by 1 mg/kg per day for 2 or 6 months; and then 1 mg/kg every Monday, Wednesday, Friday</td>
<td>1 year</td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>100 mg/kg per day in two divided doses</td>
<td>1 year</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>10 mg thrice per week</td>
<td></td>
</tr>
</tbody>
</table>

Every case of congenital toxoplasmosis, symptomatic or not, needs to be treated even though there are no sufficient data available to properly evaluate treatment options in asymptomatically infected infants. Therapy at present is beneficial against the tachyzoite form, but none has been shown to effectively eradicate the encysted form, especially from central nervous system and eyes.

Pyrimethamine and sulfadiazine have been “gold standards” in treating toxoplasmosis and both together are 8-fold more active and associated with resolution of signs of active lesions usually within the first weeks after initiation of therapy. Two other studies also have documented good outcomes. Pyrimethamine toxicity needs monitoring of peripheral blood cell and platelet counts twice every week and coadministration of folinic acid (in the form of leucovorin calcium).

Newer drugs like atovaquone tested in animal models have reported significantly increased survival and reduction in brain cyst burden. The same can be said for azithromycin, that has also been found to have a partial effect on T. gondii tissue cysts.

To conclude children born with symptomatic T. gondii infection should be treated, but the benefit of treatment in children without symptoms at birth is debatable because there is lack of evidence.

Primary prevention
Prevention of congenital toxoplasmosis has been primarily directed toward health education focused on avoiding personal exposure to the parasite (general hygiene along with tidy culinary practices).

Secondary prevention
Screening
Routine screening programs for T. gondii are in practice in France, Austria, and Brazil as recommended by experts. But, the cost effectiveness of these programs and patient compliance needs to be considered and tailored as per disease prevalence.

Vaccination
Live attenuated S48 strain is in use for vaccination of sheep in Europe and New Zealand, which is unsuitable to humans. Development of vaccines against T. gondii surface antigen SAG1 expressed on tachyzoites, bradyzoites and oocytes is under evaluation.

References
Perinatal Toxoplasmosis

Neonatal Resuscitation Guidelines 2010: An Update

Naveen Bajaj*

*Correspondence
Dr Naveen Bajaj
Consultant neonatologist
Deep Hospital
481, Model town
Ludhiana 141002, Punjab
India
Email: bajajneo@yahoo.com

The American Heart Association (AHA) and the American Academy of Pediatrics (AAP) have published the revised Neonatal Resuscitation Guidelines 2010.1,2 These guidelines are based on the evidence presented in the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations.2 The major changes in the 2010 guidelines in comparison with the 2005 guidelines3,4 are presented here.

<table>
<thead>
<tr>
<th>Resuscitation Sequence</th>
<th>2005 Guidelines3,4,5</th>
<th>2010 Guidelines1,2,6</th>
<th>What’s New?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Scope of the NRP</td>
<td>Encompass new borns and neonates during first few weeks to months after birth</td>
<td>Encompass new borns and neonates during first few weeks to months after birth</td>
<td>Have similar applicability</td>
</tr>
<tr>
<td>B. Preparation for resuscitation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Resuscitation team</td>
<td>Introduced the concept of “Resuscitation Team” with a specified leader and an identified role for each member</td>
<td>Retains the concept of “Resuscitation Team” and emphasizes teamwork, leadership, efficient communication, and behavioral skills</td>
<td>Indicate behavioral skills and communication skills as keys to the success of a neonatal resuscitation</td>
</tr>
<tr>
<td>2. Equipment</td>
<td>Practitioners are to be provided with the complete list of “Neonatal Resuscitation Supplies and Equipment”</td>
<td>In addition to “Neonatal Resuscitation Supplies and Equipment” list, practitioners are to be provided with the “NRP Quick Pre-resuscitation Checklist.”</td>
<td>Emphasize on ensuring the presence and function of resuscitation equipment and supplies in the same order as they are used in NRP flow diagram</td>
</tr>
</tbody>
</table>
### C. Assessment of need for resuscitation

<table>
<thead>
<tr>
<th>Question(s) to be answered</th>
<th>Routine Care</th>
<th>Baby receives one or more of the 4 categories of action in sequence:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term gestation?</td>
<td>Provide warmth</td>
<td>a. Initial steps in stabilization</td>
</tr>
<tr>
<td>Is the amniotic fluid clear?</td>
<td>Clear airway, if necessary</td>
<td>b. Ventilation</td>
</tr>
<tr>
<td>Breathing or crying?</td>
<td>Dry</td>
<td>c. Chest compressions</td>
</tr>
<tr>
<td>Good muscle tone?</td>
<td>Assess skin color</td>
<td>d. Administration of epinephrine and/or volume expansion</td>
</tr>
</tbody>
</table>

1. If the answer to all the questions is YES

Routine care

- Provide warmth
- Clear airway, if necessary
- Dry
- Assess skin color

Routine Care

- Provide warmth
- Clear airway, if necessary
- Dry
- Ongoing evaluation

2. If the answer to any of the above questions is NO

Baby receives one or more of the 4 categories of action in sequence:

- a. Initial steps in stabilization
- b. Ventilation
- c. Chest compressions
- d. Administration of epinephrine and/or volume expansion

Baby receives one or more of the 4 categories of action in sequence:

- a. Initial steps in stabilization
- b. Ventilation
- c. Chest compressions
- d. Administration of epinephrine and/or volume expansion

### D. Initial steps

<table>
<thead>
<tr>
<th>Action</th>
<th>Lung assessment</th>
<th>Skin color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide warmth</td>
<td>No routine suctioning; suctioning only for babies:</td>
<td>No routine suctioning; suctioning only for babies:</td>
</tr>
<tr>
<td>Position; clear airway (as necessary)</td>
<td>Who have obvious obstruction to spontaneous breathing</td>
<td>Who require PPV</td>
</tr>
<tr>
<td>Dry, stimulate, reposition</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Temperature control in VLBW preterm (<1500 g) babies

VLBW babies are at an increased risk of hypothermia. Additional warming techniques like covering in a plastic wrap without drying and then placing under a radiant warmer is recommended in babies <28 weeks of gestation.

VLBW babies are at an increased risk of hypothermia. Additional warming techniques like placing on exothermic mattress, covering in plastic wrap without drying and pre-warming the delivery room to at least 26°C is recommended in babies <28 weeks of gestation.

Preterms/babies <28 weeks of gestation, immediately after birth, should be completely covered in a polythene wrap or bag up to their necks without drying and then placed under a radiant heater. Delivery room temperatures should be at least 26°C for these infants.

2. Neonates born to mothers with MSAF

No intrapartum suction.

No intrapartum suction.

No change

1.1. Vigorous baby

Use a bulb syringe or large-bore suction catheter to clear secretions and meconium from the mouth and nose as needed and keep the baby under observational care.

Use a bulb syringe or large bore suction catheter to clear secretions and meconium from the mouth and nose as needed. Allow the baby to stay with the mother; give it routine care and keep under ongoing evaluation.

Assessment of vigorous meconium stained babies can be done while the babies stay with the mothers.

2.2. Nonvigorous baby

Endotracheal suctioning recommended

Endotracheal suctioning recommended

Current practice of endotracheal suctioning of nonvigorous babies with MSAF can be continued. However, if attempted intubation is prolonged or unsuccessful, or there is persistent bradycardia, resort to bag-mask ventilation.
### E. Progression to next resuscitation step following initial steps

<table>
<thead>
<tr>
<th>Step</th>
<th>Methods</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Heart rate assessment</td>
<td>Palpation of umbilical cord pulse</td>
<td>Auscultation of heart at the precordium is most accurate. Precordium auscultation is preferred to umbilical cord palpation for assessing heart rate. When pulse is detectable, palpation of umbilical pulse provides a rapid estimate of heart rate and is more accurate than palpation at other sites.</td>
</tr>
</tbody>
</table>
| 2. Use of pulse oximeter | Pulse oximeter is recommended for resuscitation of preterm babies (<32 weeks) | Pulse oximetry is recommended for both term and preterm babies, when:  
- Resuscitation can be anticipated  
- PPV is administered for more than few breaths  
- Cyanosis is persistent  
- Supplementary oxygen is being administered  
Apply neonatal probe to right hand or wrist (measure preductal saturations) of the baby before connecting it to machine, reliable reading can be obtained within 1–2 min. Target preductal SpO2 ranges:  
1 min: 60%–65%  
2 min: 65%–70%  
3 min: 70%–75%  
4 min: 75%–80%  
5 min: 80%–85%  
10 min: 85%–95%  
(same for both term and preterm) |

### F. Assessment of oxygen need and use of supplementary oxygen

<table>
<thead>
<tr>
<th>Method</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on skin color</td>
<td>Cyanosis can be normal for the first few minutes following birth; and skin color is a poor indicator of oxygen saturation. Hence, use pulse oximetry to assess oxygenation and titrate the percentage of inspired oxygen concentration so as to achieve the target SpO2 values (as mentioned in E2).</td>
</tr>
<tr>
<td>Supplementary (free flow) oxygen to babies who are breathing but have central cyanosis</td>
<td></td>
</tr>
<tr>
<td>Based on pulse oximetry</td>
<td>Attach a pulse oximetry probe to determine oxygenation, if levels are low and not increasing, provide supplemental oxygen.</td>
</tr>
</tbody>
</table>
| If labored breathing or persistent cyanosis is observed, resort to:  
  - Airway clearing  
  - SpO2 monitoring  
  - CPAP |  
| Any 1 out of 3 |  
- Apnea or gasping  
- Heart rate < 100/min  
- Persistent central cyanosis despite administration of supplementary oxygen |

### G. PPV

<table>
<thead>
<tr>
<th>Indication for PPV</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any 1 out of 3</td>
<td>Use SpO2 instead of skin color to assess oxygenation and start PPV if SpO2 values are below the target range despite increasing the delivered oxygen concentration to 100%.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- Apnea or gasping  
- Heart rate < 100/min  
- Persistent central cyanosis despite administration of supplementary oxygen |  
| Any 1 out of 3 |  
- Apnea or gasping  
- Heart rate < 100/min  
- SpO2 below target values despite increasing supplemental oxygen flow to 100% |
### 2. PPV strategies

#### 2.1 Inflation pressure
- Average initial peak inflation pressure of 30 to 40 cm H₂O for term and 20 to 25 cm H₂O for preterm babies is adequate.
- Start with an inspiratory pressure of about 20 cm H₂O, which is usually effective in both term and preterm babies. Inflation pressure of 30 to 40 cm H₂O may be required in some term babies.
- The emphasis is on monitoring of inflation pressure. If pressure is not being monitored, use the minimal inflation required to achieve an increase in heart rate.

#### 2.2 PEEP
- Not recommended
- PEEP is likely to be beneficial for initial stabilization of apneic preterm infants requiring PPV and should be used.
- PEEP should be used in preterm infants with suitable equipment (T-piece resuscitator or flow inflating bags).

#### 2.3 Indicators of adequate inflation pressure and ventilation
- Improvement in:
  - Heart rate
  - Color
  - Muscle tone
- • Rising heart rate
- • Rising SpO₂
- • Audible bilateral breath sounds
- Rising heart rate is the most important indicator of successful PPV. Use SpO₂ instead of skin color to assess oxygenation.

#### 2.4 Initial oxygen concentration for resuscitation with PPV
- For term infants:
  - Begin with 100% O₂
  - If resuscitation is initiated with room air and there is no improvement within 90 s after birth, give supplemental O₂ up to 100%
  - In case of non-availability of O₂, start resuscitation with room air
- For term infants:
  - Best to begin with room air rather than 100% O₂
  - Despite effective ventilation if there is no increase in heart rate or if oxygenation as guided by pulse oximetry remains unacceptable, use higher oxygen concentration of up to 100%
- For preterms, <32 weeks of gestation:
  - Start PPV with an O₂ concentration somewhere between 21% to 100% by using blender
  - In the first few minutes, SpO₂ of 70% to 80% is acceptable as long as heart rate and SpO₂ increase with ventilation, then adjust oxygen to target SpO₂ between 85% to 95%
- For preterms, <32 weeks of gestation:
  - Begin with O₂ concentration of 30% or 90% by using blender, then titrate O₂ concentration up or down to achieve target SpO₂
  - • For preterms start with an O₂ concentration of 30% or 90% and then increase or decrease O₂ concentration so as to achieve saturation values (as mentioned in E2).
  - • There is insufficiency of evidence to define the appropriate oxygen strategy for babies between 32 and 37 weeks of gestation.

#### 2.5 PPV Rates
- 40 to 60 breaths/min
- 40 to 60 breaths/min
- No change

#### 2.6 Ventilation corrective steps
- Are mentioned, but not in the form of a flow diagram
  - Inadequate seal
  - Blocked airways
  - Not enough pressure
- An additional step has been inserted in the flow diagram, involving a new pneumonic (MR SOPA), to ensure provision of adequate ventilation before initiating chest compressions
  - M: Mask adjustment
  - R: Reposition airway
  - S: Suction mouth and nose
  - O: Open mouth
  - P: Pressure increase
  - A: Airway alternative

#### 2.7 CPAP during resuscitation
- Consider CPAP if a preterm is breathing spontaneously with a heart rate above 100/min but has labored respirations, persistent cyanosis or a low SpO₂
- CPAP is beneficial, if a baby is breathing spontaneously with a heart rate above 100/min, but has labored respirations, persistent cyanosis or a low SpO₂ and particularly, if the baby is preterm
  - • Spontaneously breathing preterm infants who have respiratory distress may be supported with CPAP or intubation and mechanical ventilation as guided by local expertise.
  - • There is no evidence either to support or refute the use of CPAP in term babies.
### H. Assisted ventilation devices

<table>
<thead>
<tr>
<th>Effective ventilation can be achieved with a self-inflating bag, flow-inflating bag or T-piece resuscitator.</th>
<th>Effective ventilation can be achieved with a self-inflating bag, flow-inflating bag or T-piece resuscitator. Mouth-to-mask or tube-to-mask ventilation can be used when bag-mask devices are not available.</th>
<th>Bag-mask ventilation is preferable to mouth-to-mask ventilation or tube-to-mask ventilation.</th>
</tr>
</thead>
</table>

1. **LMA**

| LMA may be useful if bag-mask ventilation is unsuccessful and endotracheal intubation is unsuccessful or not feasible. | Considered as an alternative, if face mask ventilation is unsuccessful and endotracheal intubation is unsuccessful or not feasible for resuscitation of newborns weighing >2000 g or delivered >34 weeks of gestation. | There is limited evidence to support the use of LMA in newborns weighing <2000 g or delivered at <34 weeks of gestation. Its use has not been evaluated in instances of MSAF, chest compressions, or administration of medications. |

2. **Upper airway interface devices**

| Rounded, cushioned or anatomical shaped mask can be used. | Conflicting evidence about ability to maintain seal with anatomical shaped mask compared with rounded mask. Nasal prongs are an alternative way of giving respiratory support. | Whichever is the interface used, care providers should ensure that they are skilled at using the necessary devices. |

### I. Endotracheal intubation

1. **Indications**

<table>
<thead>
<tr>
<th>• Tracheal suctioning of nonvigorous babies with MSAF.</th>
<th>• Tracheal suctioning of nonvigorous babies with MSAF.</th>
<th>Indications for endotracheal intubation are same except that there is de-emphasis on intubation for epinephrine administration.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ineffective or prolonged bag-mask ventilation.</td>
<td>• Ineffective or prolonged bag-mask ventilation.</td>
<td></td>
</tr>
<tr>
<td>• When chest compressions are performed.</td>
<td>• When chest compressions are performed.</td>
<td></td>
</tr>
<tr>
<td>• When endotracheal administration of medications is desired.</td>
<td>• For special resuscitation circumstances, such as congenital diaphragmatic hernia or ELBW (&lt;1000 g) babies.</td>
<td></td>
</tr>
</tbody>
</table>

2. **Confirmation of endotracheal tube placement**

| Exhaled CO₂ detection is the recommended method of confirming the placement of the endotracheal tube except in cases of low or no cardiac output (cardiac arrest). | Exhaled CO₂ detection is the recommended method of confirming the placement of the endotracheal tube except in cases of low or no cardiac output (cardiac arrest). | No change |

### J. Chest compressions

1. **Indications**

| Heart rate < 60/min despite 30 s of effective PPV. | Heart rate < 60/min despite 30 s of effective PPV. | No change |

2. **Compression–ventilation ratio**

| 3:1 | 3:1 | Ratio is the same, except when an arrest is clearly of a cardiac origin especially, in babies who are beyond immediate newborn period, where a higher ratio (eg, 15:2) may be used. |
### Review Articles

#### Bajaj N. Neonatal Resuscitation Guidelines 2010

<table>
<thead>
<tr>
<th>3. Technique</th>
<th>Thumb technique preferred to two finger technique</th>
<th>Thumb technique preferred to two finger technique</th>
<th>Thumb technique preferred even when umbilical access is desired</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Site</td>
<td>Lower one-third of the sternum</td>
<td>Lower one-third of the sternum</td>
<td>No change</td>
</tr>
<tr>
<td>5. Depth</td>
<td>One-third of AP diameter of chest</td>
<td>One-third of AP diameter of chest</td>
<td>No change</td>
</tr>
<tr>
<td>6. Reassessment of heart rate</td>
<td>After 30 s of well-coordinated chest compressions and ventilation</td>
<td>After 45 to 60 s of well-coordinated chest compressions and ventilation</td>
<td>Once chest compressions are started, return of spontaneous circulation may take a minute or so, and there may be a delay of 45 s or longer before the coronary perfusion pressure returns to its previous value.</td>
</tr>
</tbody>
</table>

#### K. Medications

##### 1. Epinephrine

<table>
<thead>
<tr>
<th>1.1. Indication</th>
<th>Heart rate &lt; 60/min after 30 s of effective assisted ventilation and another 30 s of coordinated chest compressions and ventilation</th>
<th>Heart rate &lt; 60/min after 30 s of effective assisted ventilation (preferably after endotracheal intubation) and at least another 45 to 60 s of coordinated chest compressions and effective ventilation</th>
<th>Instead of 30 s, wait at least 45 to 60 s of coordinated chest compressions and effective ventilation before decision to administer epinephrine is made.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 IV dose</td>
<td>0.1 to 0.3 mL/kg of 1:10,000 concentration of epinephrine</td>
<td>0.1 to 0.3 mL/kg of 1:10,000 concentration of epinephrine</td>
<td>Stronger emphasis on IV use</td>
</tr>
<tr>
<td>1.3 Endotracheal dose</td>
<td>0.3 to 1 mL/kg, only if IV access is not available</td>
<td>0.5 to 1 mL/kg, only if IV access is not available</td>
<td>De-emphasis on endotracheal administration of epinephrine</td>
</tr>
</tbody>
</table>

##### 2. Volume expansion

Consider when blood loss is suspected and baby appears to be in shock and is not responding to resuscitation.

##### 3. Naloxone

Use in case continued respiratory depression is seen even after PPV restores normal heart rate and skin color and if there is history of maternal narcotic administration within past 4 h of delivery.

Administration of naloxone is not necessary as long as the baby can be adequately ventilated. It may be considered in a baby with continued respiratory depression and when there is a history of maternal narcotic administration within the past 4 h of delivery. Not recommended as part of the initial resuscitation in babies with respiratory depression in delivery room; focus needs to be on effective ventilation.

#### L. Type of care

3 levels of care
- Routine care
- Observational care
- Postresuscitation care

2 levels of care
- Routine care
- Postresuscitation care

Observational care is removed from the algorithm

#### M. Post resuscitation management

##### 1. Glucose

Infants who require significant resuscitation should be monitored and treated to maintain glucose levels in the normal range.

IV glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia.

Due to paucity of data, no specific target glucose concentration range can be recommended.
2. **Therapeutic hypothermia**

Avoid hyperthermia; data available are inadequate to recommend routine use of modest systemic or selective cerebral hypothermia after resuscitation.

Therapeutic hypothermia is recommended for newborns ≥ 36 weeks of gestational age with evolving moderate to severe hypoxic-ischemic encephalopathy.

Therapeutic hypothermia should be implemented according to the studied protocols, which currently include commencement within 6 h following birth, continuation for 72 h, and slow rewarming over at least 4 h, in facilities with capabilities for multidisciplinary care and longitudinal follow-up.

---

N. **Timing of cord clamping**

No recommendation

Delaying cord clamping recommended for uncomplicated term and preterm births

Term: Delay cord clamping for a minimum time ranging from 1 min to the time the cord stops pulsating after delivery

Preterm: Delay cord clamping for a minimum time ranging from 30 s to 3 min after delivery

Evidence suggests that it is beneficial to delay umbilical cord clamping in both term and preterm babies not requiring resuscitation. However, there is insufficient evidence to support or refute a recommendation to delay cord clamping in babies requiring resuscitation.

---

O. **Guidelines for withholding resuscitation**

The following guidelines must be interpreted according to current regional outcomes:
- Gestational age
- < 23 weeks
- Birth weight < 400 g
- Major chromosomal anomalies (eg, trisomy 13)
- Anencephaly

The following guidelines must be interpreted according to current regional outcome:
- Gestational age < 23 weeks
- Birth weight < 400 g
- Major chromosomal anomalies (eg, trisomy 13)
- Anencephaly

i. No change in the guidelines

ii. Assessment of morbidity and mortality risks should take into consideration available data, and may be augmented by use of published tools based on data from specific populations.

---

P. **Guidelines for discontinuation of resuscitations**

Appropriate to consider when heart rate is undetectable after 10 min of complete and adequate resuscitation

Appropriate to consider when heart rate is undetectable after 10 min of complete and adequate resuscitation

Decision to continue resuscitation beyond 10 min with no heart rate should take many factors into consideration

When heart rate is < 60/min at birth and persists 10 to 15 min after adequate resuscitation, there is no sufficient evidence to guide the decision of withholding or continuing resuscitation.

---

Q. **Structure of educational program to teach resuscitation**

Not mentioned

AHA/AAP NRP should adopt simulation, briefing–debriefing techniques in designing an educational program for acquisition and maintenance of skills necessary for effective neonatal resuscitation.

Recommends an effective and extensive NRP teaching and training program hitherto not mentioned

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AHA/AAP, American Heart Association/American Academy of Pediatrics; AP, anterior-posterior; CPAP, continuous positive airway pressure; ELBW, extremely low birth weight; IV, intravenous; LMA, laryngeal mask airway; MSAF, meconium-stained amniotic fluid; NRP, neonatal resuscitation program; PPV, positive-pressure ventilation; PEEP, positive end–expiratory pressure; VLBW, very-low birth weight.
Bajaj N. Neonatal Resuscitation Guidelines 2010

Newborn resuscitation algorithm (2010)

HR, heart rate; IV, intravenous; PPV, positive pressure ventilation.

References


Low-cost Warming Devices: Critical and Essential Component for Neonates

Arvind Shenoi*

*Correspondence
Dr Arvind Shenoi
Consultant Neonatologist and Medical Director
Cloud Nine Hospital
115, Kodihalli
Old airport road
Bangalore 560017, Karnataka
India
Phone: 98450 29956
Email: drarvindshenoi@cloudninecare.com

Introduction

The smallest patients need the greatest amount of care. The perinatal period is the time when the fetus, who is adapted to life inside its mother’s womb, must suddenly at birth be able to survive in a totally different environment. Warmth is one of the basic needs for the survival and well being of the newborn baby. Hence, it is vital to help them achieve thermoregulation to prevent morbidities and mortality. The World Health Organization recognizes newborn thermal care as a critical and essential component of essential newborn care. A healthy neonate is susceptible to heat loss by convection, radiation, evaporation, and conduction. Keeping the neonate warm or in the thermo-neutral zone along with asepsis and nutrition forms the tripod of neonatology. Low-cost methods of achieving this need have been detailed in an excellent review by Kumar et al. A premature, low-birth weight or a sick term neonate, however, needs extra warmth and if nursed naked, a thermo-neutral environment within a narrow range.

In this article, we will discuss some low-cost strategies that can aid in providing warmth to the neonate even in cost-constrained circumstances.

Devices providing extra warmth can be classified based on the heat source. An ideal heat source, in addition to being low cost, must fulfill the following criteria:

1. It should keep the body temperature of the neonate within the physiological range
2. There should be no danger of overheating or excessive cooling – a servo mechanism is ideal, but it increases the cost
3. The energy source should be clean and not subject to toxic emissions
4. The warming device should facilitate the care of sick and convalescent neonates.

The best and low-cost heat source is the mother, and hence, kangaroo mother care (KMC) is probably the best low-cost source.
Kangaroo mother care
Numerous studies have shown the benefits of the Kangaroo Mother Care (KMC) for nursing a stable and convalescent neonate. In this case, the mother acts like a heat source as well as a source of nutrition. This method could be the method of choice in all cost constrained circumstances. It has been shown to be of benefit in low and high technology settings in developing countries. KMC may not be applicable in the case of a sick ventilated neonate.

Warm water bottle or a warm water mattress
Water is a heat sink with an ability to provide heat for over a prolonged period of time. However, water bottles can cause burns or scalds if the water is too warm followed by leakage. Therefore, direct contact between the baby’s skin and the water bottle should be avoided. In addition, as a safety measure the temperature of the water should not be more than 40°C. Warm water tends to cool variably based on environmental temperature, thickness of the rubber, and additional coverings, if any. Thus, there is a need to monitor the water temperature, and periodically top up or refill with warm water. This makes the hot water bottle a low cost but difficult-to-use device.

The heated water-filled mattress is a safe and more economical device for keeping low birth weight/sick babies warm than an incubator. The mattress is placed on an ordinary cot and filled with 5 L of water. An electric heating plate and control unit is fitted into a compartment at the bottom of the mattress; and the temperature of the water is maintained at 35°C to 38°C (95°F–100.4°F). The baby is kept clothed and covered with a blanket on the cot. A reliable electricity supply is needed for this method. However, the mattress will maintain a constant temperature for several hours even if the electricity fails. The device does not create much barrier between the mother and baby as compared with an incubator.

Warm water incubator
A relatively low-cost incubator prototype was trialed at PGI, Chandigarh, many years ago. It consisted of a wooden incubator with 2 compartments. The first compartment had a water tank with a 10-L capacity. A wooden partition separated it from the baby care area. The water tank would warm the air in the first compartment, which then circulates into the baby care area. This incubator kept the baby in the thermo-neutral range for about 6 h, before needing a warm water top-up. The drawbacks of this incubator were that it was never marketed commercially and its safety and long-term durability were never tested.

Warm cotton wrap
The study carried out by Professor Daga in tribal areas of Dahanu, Maharashtra, have shown that low birth weight and very-low birth weight neonates can be nursed in cotton warmed over a tawa and wrapped around the baby, with a continuous monitoring of the temperature of the cotton and the baby needs just as in the water bottle example above.

Thermopod or wax-based warming device
An innovative idea designed by students at the Stanford University uses a wax or a phase change material that melts at 37°C. The wax is sealed in a puncture proof plastic cover and warmed on an electrical warmer. The wax packet is then inserted into a sleeve of a cloth jacket. The baby is made to lie inside the jacket. The wax hardens, thus liberating heat and gently warms the baby. This device has undergone some clinical trials in our country, but the need for electricity to warm the wax packet is its limiting factor.

Electric warmer based on electric bulbs
Professor Bhakoo designed a simple low-cost warmer that used an array of 40 W light bulbs under a plastic baby mattress at Chandigarh. The heat output could be increased by switching on all the bulbs and decreased by switching off some of them. The obvious disadvantages of this system were the need of 24-h electricity and monitoring of the baby’s temperature. The light bulbs emit more light than heat energy and hence this system seemed to be energy inefficient. The major
drawback of this warmer was that the bulbs required periodic replacement as they burn out adding to the maintenance cost equipment.

**Bakery lamp**

The modification of the above principle is the bakery lamp. Bakery lamps emit more light than heat and hence a single lamp can be used as a radiant warmer in the nursery. However, as there is no servo system, the baby needs to be monitored for thermal injury and overheating. Just as the electrical warmer bed, this equipment also needs continuous electric supply and replacement of the bulb when it wears out.

**Simple ceramic warmer**

Further development of a simple warming device came about with the development of ceramic warmers. These were fixed above the cot of the baby and had a simple regulator like in the household fan, which could increase or decrease the heater output. The cost was moderate and this device was known as the NNF cot in our country. It did not have servo control and hence monitoring the baby was essential. These cots are no longer available, but could be fabricated at a fraction of the cost of their high-tech cousins.

**Solar heating**

The unit established at the Sir JJ hospital in Mumbai was Professor SN Daga’s brain child. A solar panel on the roof heated the water that circulated in pipes placed along the walls of the nursery. Thus, the entire nursery became an incubator. This innovation required only the initial investment with very little running costs. The only disadvantage in this case was that the staff had to work in high ambient temperatures.

**Incubator constructed using auto parts**

NeoNurture is an incubator that has been constructed using auto parts with an ease of repair and maintenance. In terms of design standards it is pretty similar to its expensive cousins. The rationale used here is the availability of auto parts and mechanics even in the remotest parts of the world. Therefore, running and maintenance could be handled very easily even by relatively untrained people. It is not known if this incubator has undergone any clinical testing. Also, the purchase and running costs to the consumer remains unclear.

**Conclusion**

Prevention of neonatal hypothermia is one of the tripods of neonatal care. In resource constrained surroundings this is an important area of care. As research continues, more and more methods and innovations will emerge into the market. As in most medical equipments, the initial cost, ease of use, cost of maintenance and repair, and availability of spare parts will determine their widespread. This article summarizes the currently available strategies for providing warmth to neonates and also in aiding cost-constrained circumstances.

**References**

Outcome of Fetal Megacystis Diagnosed Between 11 and 13+6 Weeks of Gestation
Shettikeri A, Acharya V, Radhakrishnan P*

Abstract

Aim: To determine the incidence of chromosomal defects and outcome of fetuses with megacystis diagnosed antenatally between 11 and 13+6 weeks of gestation

Patients and Methods: Twenty fetuses diagnosed with megacystis from 11 to 13+6 weeks of gestation, between August 2005 and July 2012, were included for the study. Fetal megacystis was detected through ultrasound imaging; fetal karyotyping was done to check for chromosomal anomalies; and vesicocentesis and vesicoamniotic shunts were used as treatment methodologies.

Results and Discussion: Of the 20 cases of fetal megacystis under study, there were 2 cases of spontaneous resolution, 2 cases with chromosomal abnormalities, 6 cases with multiple fetal defects, 1 case of intrauterine death, 1 case of neonatal death and 1 case of declined evaluation; the remaining 7 instances, the parents opted for termination of pregnancy in view of bad evolution.

Prognosis relies on early detection of fetal megacystis, associated chromosomal anomalies, if any, followed by suitable fetal interventions.

Key words: Congenital megacystis, antenatal, chromosomal anomalies, bladder, vesicocentesis, vesicoamniotic shunt
Introduction

Fetal bladder is readily visualized in the first trimester of pregnancy as a hypoechoic area in the fetal pelvic region. Longitudinal diameter of the fetal bladder under normal conditions is $< 7$ mm (Figure 1). An abnormally enlarged bladder with a longitudinal diameter $> 7$ mm constitutes fetal megacystis. Fetal megacystis is classified into 2 categories based on the longitudinal diameter of the bladder: 7 to 15 mm in diameter (Figure 2) and $> 15$ mm in diameter (Figures 3 and 4). The longitudinal diameter of the bladder determines the prognosis.\textsuperscript{1,6,7}

Megacystis, with a longitudinal diameter of bladder $> 15$ mm is usually obstructive in nature causing Lower Urinary Tract Obstruction (LUTO); the risk of chromosomal anomalies is about 10\%. In other cases, the condition is invariably associated with progressive uropathy and perinatal mortality rates of almost 100\%.\textsuperscript{1,3-5} Therefore, fetal interventions such as vesico-centesis and vesicoamniotic shunt have been proposed for the treatment of this condition during its early stages. However, the results thus far have been disappointing. Besides, percutaneous vesicoamniotic shunts lead to non-physiological rerouting of urinary drainage, which may not prevent bladder dysfunction completely.\textsuperscript{9}

Fetal cystoscopy has been proposed as another therapeutic option for the in-utero treatment of LUTO, especially after 18 weeks of gestation, with possible advantages over the other procedures of promoting physiological urinary release. Fetal cystoscopy allows the correct prenatal diagnosis of obstructive uropathy, such as urethral atresia and posterior urethral valves.
Shettikeri A. Diagnosis and Outcome of Fetal Megacystis

(PUV). Although this procedure seems to improve neonatal survival and prevent renal impairment when performed after 18 weeks of severe megacystis, its effectiveness for preventing bladder damage may be low because of the prolonged bladder distension. In this regard, early fetal cystoscopy performed at 16 weeks of gestation may have a role in preventing renal and bladder dysfunction.9

In megacystis, with a longitudinal diameter of bladder in the range of 7 to 15 mm, the incidence of chromosomal anomalies is 20%; if the chromosomes are normal, then 90% of them undergo spontaneous resolution. In cases where the longitudinal diameter of the bladder is >15 mm, the incidence of chromosomal anomalies is 10%; and if chromosomes are normal, most of them do develop progressive obstructive uropathy.3-5

The incidence of fetal megacystis is found to be about 1 in 1,500 pregnancies.

Aim
To determine the incidence of chromosomal defects and outcome of fetuses with megacystis between 11 and 13+6 weeks of gestation

Materials and Methods
In the period from August 2005 to July 2012, 20 fetuses between 11 and 13+6 weeks of gestation diagnosed with megacystis, at the Bangalore Fetal Medicine Centre were included in the study. Fetal megacystis was diagnosed if the longitudinal diameter of the fetal bladder exceeded 7 mm. Fetal karyotyping was done to check for the associated chromosomal abnormalities. Vesicocentesis and vesicoamniotic shunting were used as treatment modalities. Renal function was evaluated using urinalysis for urine sodium and beta-2 microglobulin. Outcomes were obtained from the patients themselves or through their Obstetricians.

Results
Table 1 summarizes the results obtained in this study.

In this study, 5 fetuses with a longitudinal bladder diameter of 7 to 15 mm were identified (Figure 2).

Table 1. Outcome of Fetal Megacystis Between 10 and 13+6 Weeks of Gestation

<table>
<thead>
<tr>
<th>Longitudinal diameter of bladder: 7–15 mm</th>
<th>Longitudinal diameter of bladder: &gt;15 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases, N</td>
<td>5</td>
</tr>
<tr>
<td>Abnormal karyotype, n (%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Karyotype declined, n</td>
<td>1</td>
</tr>
<tr>
<td>Normal karyotype with further follow-up available, n/N</td>
<td>4/5</td>
</tr>
<tr>
<td>Spontaneous resolution, n (%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Increased NT, n/N</td>
<td>2/5</td>
</tr>
<tr>
<td>Renal functional abnormalities, n</td>
<td>0</td>
</tr>
<tr>
<td>Vesicocentesis, n/N</td>
<td>1/5</td>
</tr>
<tr>
<td>Intrauterine death, n</td>
<td>0</td>
</tr>
<tr>
<td>Termination of pregnancy, n/N</td>
<td>3/5</td>
</tr>
<tr>
<td>Live births</td>
<td>2/4</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>0</td>
</tr>
</tbody>
</table>

NT, nuchal translucency
*One fetus of a monochorionic pair

Of these, 1 fetus was confirmed to have an abnormal karyotype (trisomy 16); in another fetus, an increase in longitudinal bladder diameter was noted in a subsequent follow-up scan. Serial vesicocentesis confirmed deterioration of renal function before 16 weeks of gestation and therefore, the parents opted to terminate the pregnancy. Of the other 3 fetuses diagnosed with this condition, in 2 fetuses, at subsequent follow-up scans, the megacystis resolved spontaneously and the prospective mothers continued the pregnancy. Both these pregnancies resulted in live births with no residual renal functional abnormality. One pregnancy was terminated with no investigations or follow-up.

In addition, the study also revealed 15 fetuses with a longitudinal bladder diameter >15 mm at the time of diagnosis in the first trimester (Figures 3 and 4). There was 1 fetus with an abnormal karyotype (translocation Down syndrome). There was no spontaneous resolution in this group. Serial vesicocentesis was performed in 6 cases; all of them showed deterioration in renal func-
tion. Hence, no further interventions were offered and all pregnancies were terminated. One case of a monochorionic pair continued the pregnancy, which resulted in a neonatal death due to poor renal function.

Ultrasound appearances of megacystis

Fetal pelvic cyst seen in the first trimester is megacystis, unless proved otherwise. This can be differentiated from other cysts by using color Doppler to identify the umbilical vessels running alongside the bladder (Figure 5).

Fetal interventions for megacystis

Although the incidence of fetal megacystis is 1 in 1,500 pregnancies, it presents a dilemma in terms of its management. In the absence of timely intervention, the condition may resolve spontaneously or progress to obstructive uropathy (Figure 6).²

The aim of a fetal vesicoamniotic shunt in the management of LUTO is to decompress the obstructed bladder and restore amniotic fluid dynamics and volume, thereby preventing oligohydramnios and consequent pulmonary and renal dysplasia.⁹ Resolution of megacystis in some cases, following vesicocentesis, may be explained by a decompression mediated improvement in the bladder outlet urethral valve function; decompression results from correction of acute vesico-urethral angle (caused by severe enlargement of the bladder). However, with urethral agenesis, the bladder can remain empty only with a vesicoamniotic shunt.⁸

It has not been possible, in the prenatal stage, to determine the precise cause of megacystis. Paradoxically, recurrence of megacystis soon after aspiration may not necessarily signify urethral agenesis. Performing fetal urinary biochemical analysis would be useful, in all cases, to assess deteriorating renal function prior to the insertion of vesicoamniotic shunt or advanced fetoscopic procedures. High fetal urinary sodium levels are associated with renal dysplasia or subsequent development of renal failure.

Fetal lower urinary tract obstruction

LUTO is characterized by proximal urethral obstruction, enlarged bladder, bilateral hydronephrosis and normal/oligo/anhydramnios. In male fetuses, the common causes of megacystis are PUV, urethral atresia or prune belly syndrome. In female fetuses, LUTO is mostly associated with cloacal abnormalities.

The megacystis microcolon hypoperistalsis is another cause of urinary obstruction; and is difficult to be distinguished from the other causes of urinary obstruction. However, it is important to be identified after birth as it is an autosomal recessive condition and has a 25% recurrence risk.
Embryology and genetics

PUV are derived from the remnants of the müllerian duct or the cloacal membrane between 7th and 11th week of pregnancy. PUV and urethral atresia are sporadic in origin. Recurrence risk of PUV is no greater than in the general population.

Management

Once a case of LUTO is diagnosed, a thorough examination for other associated anomalies is performed. Parents are counseled regarding its possible association with chromosomal abnormalities. If the karyotype is normal, the family may be counseled that the fetus is likely to face a 50% or greater risk of perinatal mortality and substantial pulmonary and renal morbidity even if conservative management is employed.

Serial vesicocentesis is done 72 hours apart to study the urinary biochemistry, sodium and beta-2 microglobulin levels in order to assess the renal function. Urinary sodium <100 mmol/L and beta-2 microglobulin <6 mg/L indicates normal renal function and hence better prognosis. These fetuses may be eligible for fetal intervention therapy, that is, vesicoamniotic shunting. The aim of vesicoamniotic shunting is to decompress the bladder antenatally, restore the amniotic fluid levels and hence prevent renal dysplasia by avoiding prolonged back pressure on the renal system.

Weekly ultrasound monitoring is suggested following shunt placement to assess shunt position, bladder size, kidney appearance, and amniotic fluid volume as required. Up to 40% of shunts become displaced and may require replacement if oligohydramnios recurs at mid-gestation. Following confirmation of successful shunt positioning over the next three weeks, the patient may be assessed every 2 weeks as required. In patients with partial obstruction, not undergoing shunt placement, amniotic fluid volume is measured and renal parenchyma is assessed for evidence of cystic dysplasia every 1 to 2 weeks as needed.

Surgery for lower urinary tract obstruction

Surgical intervention is indicated in most cases where megacystis is persistent and shows evidence of obstruction that threatens renal function. Minimally invasive decompression through transurethral or suprapubic catheter placement may be employed as a temporary measure until definitive surgical repair can be performed. PUV and obstructing ureterocele may be amenable to cystoscopic therapy, though further surgical intervention may be necessary in the newborn period or early in infancy. Long term outcome of these babies is dependent on the residual renal function.

Research

The newer aspect which is still under evaluation is laser fulguration of the posterior urethral valves, where the proximal urethral valves are identified directly using a microcystoscope and laser ablation or mechanical disruption is then performed. This has shown mixed results and has its own complications. But laser fulguration is promising, in that, it overcomes the drawbacks of the shunt placement and migration. Most importantly, the bladder functions like bladder storage and voiding are restored.

Conclusions

An abnormal karyotype is most likely to be associated with an increased bladder diameter of 7 to 15 mm. Physiological megacystis may be a consequence of temporary malfunction during critical stages in the development of bladder function. Autonomic innervations and the appearance of the smooth muscle in the bladder occur only after 13 weeks of gestation. Hence spontaneous resolution is more likely to occur when the bladder diameter is <15 mm; when bladder diameter is >15 mm, none show spontaneous resolution.

Vesicocentesis can be offered to temporarily alleviate over distention of the bladder. Meanwhile, the karyotype can be assessed for anomalies, which can aid in proper planning of fetal therapeutic interventions. Fetal urinary biochemical analysis must be carried out prior to planning any fetal intervention and completion of investigations for fetal megacystis.

Early detection followed by suitable fetal interventions play crucial roles in saving the life of the fetus. Following detection, parental counseling by fetal medicine specialists and pediatric urologists is essential in the management of megacystis.
Summary

- Fetal megacystis is easily detectable on antenatal ultrasound from 11 to 13th weeks of gestation by identification of a longitudinal bladder diameter of >7mm.
- Longitudinal bladder diameter of 7 to 15 mm is more likely to be associated with chromosomal anomalies and is also more likely to resolve spontaneously in the antenatal period.
- Longitudinal bladder diameter >15 mm is due to obstructive uropathy (PUV/Urethral atresia) and is less likely to resolve in the antenatal period.
- Following the detection of megacystis, parents should be counseled regarding the prognosis depending on the maximal bladder length and its association with chromosomal and structural abnormalities.
- Serial vesicocentesis allows to further prognosticate these pregnancies based on preservation of renal function.
- Following confirmation of reasonable renal function, fetal palliative and therapeutic renal function like vesicoamniotic shunting and fetoscopic laser fulguration of PUV may be considered.
- Postnatal surgical procedures for PUV have reasonable survival and reduced morbidity in units where such expertise is available.
- Individualizing the fetus, based on associated findings, systematic approach, and thorough antenatal counseling in a multidisciplinary setting is absolutely vital for such babies to allow for early termination of very sick babies and continuation of pregnancies where postnatal outcome may not be bad after all.

References

Global Handwashing Day (GHD) is a campaign conducted to motivate and mobilize millions of people around the world to wash their hands with soap. It is conducted on the 15th of every October, every year. The campaign is dedicated to raising awareness of handwashing with soap as a key approach to disease prevention.

The World Health Organization (WHO) defined “handwashing” as washing hands with either plain or antimicrobial soap and water. The Centers for Disease Control and Prevention, USA, stated that “Handwashing is the single most important means of preventing the spread of nosocomial infections.”

The GHD campaign was first initiated at the Annual World Water Week, held in Stockholm, Sweden, from August 17 to 23, 2008. The Public–Private Partnership for Handwashing initiated the GHD, for the first time, on October 15, 2008 (date appointed by UN General Assembly in accordance with the year 2008 as the International Year of Sanitation) as an innovative way to raise awareness and foster the practice of handwashing with soap.

The WHO launched a program entitled “Clean Care is Safer Care” that aimed at improving healthcare-associated infections worldwide.

Experts suggest that by rubbing hands vigorously with soap water, the dirt and oily soils are pulled away from the skin. The soap lather suspends both the dirt and germs trapped inside and quickly washes them away. They also suggest that simple handwashing can save more lives by reducing the germs that cause infections in the developing world than any single vaccine or medical intervention.

A logo showing water, soap, and hand was developed for representing the GHD around the world (Figure 1).

The symbols used in the logo aim to motivate children to embrace and share proper handwashing practices, and ingrain this habit to save lives.

The theme for the inaugural year of GHD was “Focus on School Children.” The members pledged to get maximum number of school children wash their hands with soap, in more than 70 countries. Encouraging these simple habits at critical times can make a
vital difference to a child’s life. The day streamlines the significance of the caregivers such as young mothers, teachers, elder siblings, and medical professionals who can adopt these practices and keep diseases away.

Ideally, use of soap and warm running water to wash away all of the surfaces, including that beneath the fingernails, thoroughly seem to be necessary. One should rub their wet soapy hands together outside the stream of running water for at least 20 s before rinsing it thoroughly, followed by drying with a clean towel, disposable, or otherwise. The use of a clean towel is a necessary part of effective contaminant removal as the washing action separates the contaminants from the skin but does not completely flush them from the skin. Thus, removing excess water using a towel helps remove the suspended contaminants. This hygienic behavior has shown to cut down the number of child deaths due to diarrhea by almost half and from pneumonia by one-quarter.

Handwashing with soap and/or a hand antiseptic after critical times, such as after using the bathroom; after changing a diaper; before feeding a child; before eating and preparing food; while handling raw meat, fish, or poultry; before and after tending to a sick person or any other situation leading to potential contamination is vital in order to prevent fecal-oral transmission and reduce the spread of germs.

Children learn good handwashing techniques by observing their parents. Therefore, it is important for the parents to encourage their children to wash hands before eating, after playing outdoors or with pets, after using the bathroom, and after blowing their nose.

Although this campaign was initiated to reduce mortality rates related to diarrheal diseases in children aged below 5 years, by introducing simple behavioral changes such as handwashing with soap, it is equally, if not more, relevant to perinatology and neonatology with some refinement. The WHO has published a pictorial sheet demonstrating standard handwashing and handrubbing in health-care sectors.²

In each country, where GHD activities are planned, a convening institution brings together other organizations with an interest in handwashing to coordinate activities.

For example, in Nepal, the GHD was celebrated with multi-dimensional efforts, one among them being the release of a stamp and postmark on the theme of handwashing, which created a philatelic history (Figures 2–4). The Nepal General Post Office used a postmark with a special handwashing message to stamp all the letters and documents posted for 15 days.

Figure 2. Postage stamp of Nepal, 2010

Figure 3. Nepal, “Handwashing” postmark

Figure 4. The first “Handwashing Day” post cover with stamp and postmark, released in Nepal, dated December 30, 2010

The Department of Postal Service, Nepal, issued a unique stamp (Figure 1) carrying the slogan “Always Keep Hands Clean for Healthy Life” on December
The multicolored stamp depicted traditional steps of handwashing and also the GHD logo. A pictorial postmark showing handwashing (Figure 2) and a matching first day cover (Figure 3) were also issued. It is the first stamp in the world on GHD that carried such a hygiene-related message. It forms part of the “Global Handwashing” campaign, promoted in Nepal in November, and is designed to reinforce the call for improved hygiene practices across the country. A small stamp has so much of power! No other country is known to follow this philatelic example so far.

In India, among other programs, cricket legend Sachin Tendulkar and his teammates joined an estimated 100 million school children around the country in lathering up for better health and hygiene as part of the first GHD.

The driving theme for GHD in the year 2009 was “Children and Schools” and in the year 2010, it was “More Than Just a Day.” In the year 2011, there was no global theme; thus, organizations had the flexibility to choose their own theme. They could continue to use the theme “More Than Just a Day” or select a theme that addresses specific needs about handwashing.

References
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2. WHO. How to handwash? With soap and water, 2006 (Version 1)
3. WHO. Guidelines on Hand Hygiene in Health Care, 2009
4. Philatelic Information Sheet on Global Handwashing Day stamp, Nepal
Dysmorphology and the Hand

Meenakshi Bhat*

*Correspondence
Dr Meenakshi Bhat
Consultant clinical geneticist and associate professor
Center for Human Genetics
Biotech Park, Electronic City phase I main road
Bangalore 560100, Karnataka
India

Introduction

Dysmorphology is the study of malformations affecting the anatomy of an individual; structural defects could be of chromosomal or idiopathic origin. There is a notion that when a child is referred to as being “dysmorphic” it describes the unusual facial features. However, careful observation of the entire body, noting if there is an alteration of form or shape in any part of the body may reveal the other deformities. In this article, a number of common hand anomalies are discussed, which may indicate a diagnosis or a small list of differential diagnoses. For any child with congenital hand anomaly, it is important to observe the following:

• Unilateral or bilateral hand involvement
• Identical or asymmetric involvement in both hands
• Elbow and other arm bones
• Involvement of feet

Hand Anomalies

Arachnodactyly

Under normal conditions, the length of the middle finger is usually proportional to the length of the palm. Abnormally long and flexible fingers (Figure 1) and toes are characteristically seen in Marfan syndrome. Marfan syndrome is an autosomal dominant disorder caused by mutations in the fibrillin gene. It is characterized by a triad of skeletal manifestations; ocular abnormalities including lens subluxation; and cardiac complications such as aortic root dilatation and dissecting aortic aneurysms. Other conditions in which arachnodactyly is seen are Ehlers-Danlos syndrome, homocystinuria, Beals syndrome, and Shprintzen-Goldberg syndrome.

Figure 1. Arachnodactyly of the hand as seen in an individual with Marfan syndrome
Single transverse palmar creases

Single transverse palmar crease (STPC) is also called simian crease; and is the most commonly described hand anomaly, yet its significance is unclear to many. It occurs both unilaterally and bilaterally (Figure 2). Believed to originate between the 2nd and 3rd month of embryonic life, its importance is most closely linked to its association with Down syndrome. From various studies, it is noted that single transverse palmar creases are present in approximately 60% of individuals with Down syndrome and 3% of normal individuals as well. Males are twice as likely to have STPC as females. It is regarded as a minor marker for chromosomal disorders and is also seen in arthrogryposis syndrome.

Broad misshapen thumbs

Broad misshapen thumbs (Figure 3) along with broad great toes are usually seen in Rubinstein-Taybi syndrome. This is a rare autosomal dominant syndrome with mutations in the CREBBP gene; characterized by distinctive facial features, overhanging medial nasal septum, short stature, moderate to severe mental retardation, hirsutism, and congenital heart disease.

Duplication of thumbs

Duplication of thumbs (Figure 4) is seen in Holt-Oram syndrome, usually bilateral with asymmetric radial defects and normal feet. It is a rare autosomal dominant disorder caused by a mutation in TBX5 gene with congenital heart disease (CHD), usually atrial septal defect, cardiac rhythm abnormalities and a normal looking face. Duplication of thumb is also seen in some chromosome rearrangements and therefore chromosome analysis is a must in all children with unilateral or bilateral thumb duplication.

Radial deformity and/or hypoplastic thumb

Radial deformity and/or hypoplastic thumb is usually bilateral and often asymmetrical. The radius in the forearm may be hypoplastic or absent; the thumb is either absent (Figure 5A), rudimentary, hypoplastic (Figure 5B) or in mild cases may lack creases or may
just manifest with a flattening of the thenar curvature. A number of genetic conditions may be associated with radial deformities.

**Fanconi pancytopenia**

Fanconi pancytopenia is also called Fanconi anemia; associated with developmental delay, short stature, multiple café au lait patches, and a tendency toward hematological malignancies. It is inherited as an autosomal recessive condition with a 25% recurrence in subsequent pregnancies. A history of parental consanguinity is often elicitable. Mitomycin induced chromosome breakages are characteristic in karyotype studies.

**Holt-Oram syndrome**

Holt-Oram syndrome with CHD as described elsewhere in this article.

**VACTERL association**

VACTERL association is a disorder that affects many body systems; it signifies vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities. While VATER association is usually a sporadic occurrence, VACTERL association may be a manifestation of Fanconi pancytopenia with an autosomal recessive inheritance.

**TAR syndrome**

Thrombocytopenia-absent radius (TAR) syndrome is characterized by the absence of the radius bone in the forearm; 50% of the manifestations also show cow’s milk allergy; but with normal intellectual development. Bilateral radial involvement with normal lower limbs is the norm. TAR syndrome is caused by a micro-deletion of the long arm of one copy of chromosome 1.

**Ellis-van Creveld syndrome**

Ellis-van Creveld (EVC) syndrome is also called chondroectodermal dysplasia. Figure 6 shows all the typical radiological findings described in EVC syndrome—post axial polydactyly, shortening of the middle and distal phalanges, and the fusion of the capitate and hamate bones in the wrist; also seen is the 4th finger clinodactyly. Disproportionate and short stature due to chondrodystrophy of bones; anomalies of teeth and oral frenulae; congenital heart defects; ectodermal dysplasia and polydactyly are the characteristic features. EVC is a rare syndrome caused by mutations in the *EVC1* and *EVC2* genes and is inherited in an autosomal recessive pattern with a 25% recurrence risk in subsequent pregnancies.

**Postaxial polydactyly**

Postaxial polydactyly is a common congenital anomaly seen 1 in 500 births. An additional finger on the ulnar or little finger side of the hand or foot may occur in one or both hands (Figure 7) and feet. Polydactyly may occur as an isolated finding or as part of several genetic syndromes. As an isolated finding in one or more limbs, it is usually caused due to a mutation on
the short arm of chromosome 7 and is inherited in an autosomal dominant pattern. There are 50% chances of an affected individual passing-on the anomaly to each of the descendents.

The common syndromic associations of postaxial polydactyly are trisomy 13, trisomy 18, and Greig polydactyly (autosomal dominant). Bardet-Biedl, Meckel-Gruber, Smith-Lemli-Opitz, EVC, and short rib polydactyly syndromes are autosomal recessive syndromes associated with polydactyly and occur more frequently in highly inbred populations. A full systemic examination is therefore mandatory in all cases with four-limbed polydactyly.

**Short 4th metacarpal bone**

Short 4th metacarpal bone is best seen on fisting the hand and observing the knuckles (Figure 8). This is usually a bilateral finding, often accompanied by short fourth metatarsals in the feet. This is commonly seen in females with Turner syndrome, which is caused by an absence and/or abnormality of the 2nd X chromosome. Evidence of short stature, webbed neck, increased carrying angle at elbows, cardiac anomalies, ultrasound findings of streak ovaries, and renal anomalies are supportive findings in Turner syndrome. This can be ascertained through chromosomal analysis of the individual’s blood sample. Short fourth metacarpals may also be seen in individuals with pseudohypoparathyroidism (PHP) (also called Albright’s hereditary osteodystrophy; manifested by low serum calcium, high phosphate, and parathyroid hormone levels) and pseudo-PHP.

The hand anomaly alone may either cause little effect (as in postaxial polydactyly) or severe restriction of function (as in thumb anomalies). Many are distinct enough to suggest evaluation for specific genetic syndromes, which are highlighted by the examples listed in this article. This is by no means a comprehensive list of hand anomalies or associated syndromes but, serves as an attempt to encourage all medical specialists to observe an individual in detail and take into account all physical clues toward an underlying systemic disorder.
Picture Quiz

Can you make the correct diagnosis?

- Figure 1
- Figure 2
- Figure 3
- Figure 4
Self-assessment Quiz

1. **In the fetus at term**
   a. hemoglobin has a higher affinity for oxygen than in adult
   b. there is no adult hemoglobin
   c. erythropoiesis is mainly hepatic
   d. the hemoglobin concentration is greater than in the adult
   e. hemoglobin is more resistant to acid denaturation than adult hemoglobin

2. **At birth**
   a. pressure in the right side of the heart increases
   b. the foramen ovale closes immediately
   c. pulmonary vascular resistance falls
   d. increased arterial oxygen tension causes closure of the ductus arteriosus
   e. increased prostaglandin release causes closure of the ductus arteriosus

3. **Breast feeding is more likely to succeed if**
   a. the nipples are everted
   b. initial sucking is delayed until the mother has rested after delivery
   c. oral estogens are administered
   d. baby and mother share the same room
   e. supplementary cow’s milk feeds are given

4. **Human breast milk contains**
   a. less protein than cow’s milk
   b. less iron than cow’s milk
   c. immunoglobulins which protect the infant from gastroenteritis
   d. alcohol if the mother drinks alcohol herself
   e. a constant balance of constituents

5. **During lactation**
   a. prolactin causes the myoepithelial cells of the breast to contract
   b. ovulation is often delayed
   c. prolactin secretion is stimulated by suckling
   d. the administration of progestogen will suppress milk production
   e. oxytocin secretion is stimulated by suckling

6. **The following drugs are safe to use in breast-feeding mothers**
   a. labetalol
   b. warfarin
   c. carbimazole
   d. insulin
   e. rifampicin

7. **In labour, fetal heart rate patterns that are indications for fetal blood sampling include**
   a. a persistent rate of 175 bpm
   b. accelerations with contractions
   c. late decelerations
   d. a persistent rate of 125 bpm
   e. a baseline variability of 10 bpm
Picture Quiz Answers

**Figure 1: Polydactyly**
This may be familial and associated with a number of congenital syndromes. If the extra digit contains bone, its removal should be delayed until ossification can be defined, toward the end of the first year.

**Figure 2: Funnel chest (pectus excavatum)**
This is usually congenital but may follow chronic respiratory obstruction or rickets. Cardiopulmonary embarrassment is unusual.

**Figure 3: Cystic hygroma**
There is a large lymphangiomatous swelling of the face and neck. The mass is fluctuant and transilluminates. It may cause obstruction of the upper airways at birth or in later life, due to enlargement during upper respiratory tract infections or hemorrhage into the lesion.

**Figure 4: Third nerve palsy**
A paralytic squint is present, with downward and outward deviation of the right eye whatever the direction of gaze of the left. The right pupil is enlarged and a right ptosis is present.
Self-assessment Quiz Answers

1. Question 1: a, d, e
Hemoglobin F (HbF) has a higher affinity for oxygen than adult hemoglobin. It co-exists with adult hemoglobin at birth and is gradually replaced by it in the first year of life. The resistance of HbF to acid or alkali denaturation is the basis of the Kleihauer test. Erythropoiesis is mainly hepatic in the second trimester of pregnancy. The hemoglobin concentration at birth is usually approximately 17 g/dL.

2. Question 2: c, d
When the umbilical vessels are occluded there is a decreased venous return, lowering the pressure in the right side of the heart. The foramen ovale gradually closes. Pressure in the pulmonary vasculature falls as the first breath is taken. The ductus arteriosus is sensitive to arterial oxygen tension, an increase causing it to close. Prostaglandin synthetase inhibitors, such as aspirin or indomethacin, may also cause closure prematurely in some cases when these drugs are given in pregnancy in sufficient dose.

3. Question 3: a, d
Successful breast feeding depends upon the enthusiasm of the mother as well as encouragement and education from her attendants. The baby should be suckled as soon after delivery as possible, initially for 2 to 3 min on each side, and thereafter fed on demand. Supplementary cow’s milk feed should be kept to a minimum. Oral estrogens are used to suppress lactation.

4. Question 4: b, c, d
The composition of breast milk varies throughout feed, the fat concentration rising towards the end. Furthermore, the composition may differ between two feeds on the same day, and milk of the early puerperium differs from that of established lactation. It is a better source of protein than cow’s milk but contains relatively less iron. The immunoglobulins present are one of several factors increasing the resistance of the baby to gastroenteritis. Many drugs including alcohol are transmitted into breast milk in significant quantities.

5. Question 5: b, c, e
Oxytocin and prolactin secretion are stimulated by suckling. The prolactin promotes milk synthesis while the oxytocin causes milk ejection. Estrogens block the action of prolactin and suppress lactation, progestogens have no effect. Ovulation is delayed but not reliably, and lactation is not to be recommended as an effective contraceptive measure.

6. Question 6: a, b, d, e
Labetalol does not enter breast milk in significant amounts, nor does insulin. Although minimal amounts of Warfarin pass into breast milk, it is generally considered safe except in case of vitamin K deficiency. Rifampicin also passes into breast milk, but does not harm the infant, whereas Carbimazole causes neonatal hypothyroidism or goiter.

7. Question 7: a, c
Fetal blood sampling should be performed when meconium is seen or when the fetal heart rate is abnormal. A normal fetal heart rate pattern has a baseline between 120 and 160 bpm, with a baseline variability of approximately 10 bpm and accelerations with contractions.
Pulse Oximetry Screening for Critical Congenital Heart Defects in Asymptomatic Newborn Babies: A Systematic Review and Meta-analysis

Thangaratinam S, et al


In newborn babies, early screening for critical congenital heart defects can aid in early recognition, with the prospect of improved outcome. In this systematic review, we assessed the performance of pulse oximetry as a screening method for the detection of critical congenital heart defects in asymptomatic newborn babies.

A systematic review of published literature in Medline (1951–2011), Embase (1974–2011), Cochrane Library (2011), and Scisearch (1974–2011) was done for relevant citations, with no language restriction. Studies that assessed the accuracy of pulse oximetry for the detection of critical congenital heart defects in asymptomatic newborn babies were selected. Two reviewers selected those studies that met the predefined criteria for population, tests, and outcomes. Sensitivity, specificity, and corresponding 95% confidence intervals were calculated for individual studies. A hierarchical receiver operating characteristic curve was fitted to generate summary estimates of sensitivity and specificity, with a random effects model.

Five-hundred and fifty-two studies were screened and 13 eligible studies, with data for 229,421 newborn babies, were identified. The overall sensitivity of pulse oximetry for the detection of critical congenital heart defects was 76.5% (95% CI: 67.7–83.5), whereas the specificity was 99.9% (95% CI: 99.7–99.9), with a false-positive rate of 0.14% (95% CI: 0.06–0.33). The false-positive rate for detection of critical congenital heart defects was found to be particularly low when newborn pulse oximetry was done 24-h post birth than when it was done 24-h prebirth (0.05% [0.02–0.12] vs. 0.50 [0.29–0.86]; P = .0017).

Therefore, it is interpreted that pulse oximetry is highly specific for the detection of critical congenital heart defects with moderate sensitivity that meets universal screening criteria.

Outcomes of Partogram Use on Women with Spontaneous Labor at term

Lavender T, et al


The partogram (sometimes known as partograph) is usually a preprinted paper form on which labor observations (before childbirth) are recorded. It often contains preprinted alert and action lines. An alert line represents the slowest labor progress (10%) of primigravid women, whereas an action line is placed a number of hours after the alert line (usually 2 or 4 h) to prompt effective management of slow progress of labor. In addition, partogram intends to provide an accurate record of the progress of labor, so that any delay or deviation from normal labor may be detected quickly and treated accordingly.

The present study was conducted to determine the effect of partogram-use on perinatal and maternal morbidity and mortality.

The Cochrane Pregnancy and Childbirth Group’s Trials Register (May 31, 2012) was searched for randomized and quasi-randomized controlled trials involving a comparison of partogram with no partogram or comparison among different partogram designs. The data collected were analyzed by 3 review authors independently for eligibility and quality before extraction.

The review included 6 studies involving 7706 women; 2 studies assessed partogram versus no partogram while the remaining studies assessed different partogram designs. There was no evidence of any difference between partogram and no partogram in cesarean section (risk ratio [RR]: 0.64; 95% confidence interval [CI]: 0.24–1.70), in instrumental vaginal delivery (RR: 1.00; 95% CI: 0.85–1.17), or in Apgar score of less than 7 at 5 min (RR: 0.77; 95% CI: 0.29–2.06) between the groups. When compared to a 4-h action line, women in the 2-h action line group were more likely to require
Abstracts from Literature

oxytocin augmentation (RR: 1.14; 95% CI: 1.05–1.22). When the 3-h and 4-h action line groups were compared, cesarean section rate was lowest in the 4-h action line group, and this difference was statistically significant (RR: 1.70; 95% CI: 1.07–2.70, n = 613, one trial). When partograms with a latent phase (composite) were compared to the one without a latent phase (modified), the cesarean section rate was found to be lower in the partograph without a latent phase (RR: 2.45; 95% CI: 1.72–3.50, n = 743, one trial).

On the basis of the findings of this review, routine use of the partogram as a part of the standard labor management and care seems irrational. Given the fact that the partogram is currently in widespread use and generally accepted, it appears reasonable, until stronger evidence is available, that use of partogram should be locally determined. Further trial evidence is required to establish the efficacy of partogram-use.

Human Milk Oligosaccharide Concentration and Risk of Postnatal Transmission of HIV Through Breastfeeding
Bode L, et al

The inefficiency of HIV transmission through breast milk may be due to the presence of immunologically active factors, including human milk oligosaccharides (HMOs). This nested case-control study aimed to investigate if HMO concentrations are associated with a reduced risk of postnatal HIV transmission.

The study was conducted within a larger cohort study of HIV-infected women and their infants (followed from birth to 24 months in Lusaka, Zambia). Breast milk samples (at 1 month) were collected from 81 HIV-infected women who transmitted the disease through breastfeeding, a random sample of 86 HIV-infected women who did not transmit the disease through breastfeeding, and 36 uninfected breastfeeding women. Total and specific HMO concentrations were measured by high-performance liquid chromatography and compared among groups with adjustment for confounders by using logistic regression.

HIV-infected women with total HMOs above the median (1.87 g/L) were less likely to transmit the disease through breastfeeding (OR: 0.45; 95% CI: 0.21, 0.97; P = .04) after adjustment for CD4 count and breast milk HIV RNA concentrations; a trend toward higher concentrations of lacto-N-neotetraose being associated with reduced transmission (OR: 0.49; 95% CI: 0.23, 1.04; P = .06) was also observed. The proportion of 3′-sialyllactose (3′-SL), per total HMOs, was higher among women transmitting the disease than among nontransmitting women (P = .003) and it also correlated with higher plasma and breast milk HIV RNA and lower CD4 counts. Neither Secretor nor Lewis status was distinguished between transmitting and nontransmitting women.

Higher concentrations of non-3′-SL HMOs were associated with protection against postnatal HIV transmission independent of other known risk factors. Further study of these novel, potentially anti-HIV components of breast milk are warranted. This trial was registered at clinicaltrials.gov as NCT00310726.
Esophageal Perforation in Preterm Neonates: A Complication to Remember

Vikram Singhal, Nutan Kamath,* Rathika D Shenoy

Abstract

Background and aim: Esophageal perforation (EP), a hole in the esophagus—the tube through which food passes from the mouth to the stomach, is a well-known entity in adults, while it is relatively uncommon in infants and children. Instrumental perforation and spontaneous perforation remain the 2 major causes of esophageal injury in infants and children. EP due to instrumentation is a life-threatening complication. Incidences of morbidity and mortality are directly related to delays in diagnosis and treatment. In the newborns, EP may be iatrogenic or noniatrogenic. We herein report our experience with the successful management of this complication in an infant.

Materials and methods: In this study, a 32-week preterm infant small for gestational age (SGA) was ventilated for hyaline membrane disease at the Department of Pediatrics, KMC Hospital (Attavar, Mangalore). The infant presented with fresh bleed during the change of blocked endotracheal tube with sudden cardiopulmonary deterioration and right-sided tension pneumothorax. In addition, a chest radiograph revealed coiling of the feeding tube in the right pleural cavity suggestive of EP. An infant feeding tube of 5 Fr (nasogastric tube) was passed into the stomach. An intercostal, extrapleural drain was then positioned close to the anastomosis. The nasogastric tube was removed after 10 days. The infant was managed conservatively throughout the study period.

Results: Upon a 9 year follow-up, the infant was found to be doing well with no evidence of esophageal stricture.

Conclusion: The patient was successfully treated using conservative measures.

Key words: Esophageal perforation, nasogastric tube, pneumothorax
Introduction

Esophageal perforation (EP) in the neonates can be spontaneous, instrumental, or anastomotic. With advanced neonatal intensive care, EP becomes an important complication to consider in the event of deterioration after oropharyngeal procedures. Subtle features and radiographs with infant feeding tube in-situ are important in making an early diagnosis. Here, we present the case of a neonate with this complication and the outcomes.

Case Report

A 32-week preterm neonate small for gestational age (SGA), weighing 1400 g, was ventilated for hyaline membrane disease at the Department of Pediatrics, KMC Hospital (Attavar, Mangalore). On day 4 of ventilation, fresh bleed was noted during the change of blocked endotracheal tube along with sudden cardiopulmonary deterioration. Clinically, right-sided tension pneumothorax was also observed (Figure 1). A chest radiograph revealed coiling of the feeding tube in the right pleural cavity suggestive of EP (Figure 2). Subsequently, intercostal drainage was placed. When 5 Fr gauge infant feeding tube was passed fresh bleed was noted. After 48 h, 8 Fr nasogastric tube was placed under fluoroscopy. Sepsis was managed with appropriate antibiotics. Total parenteral nutrition was initiated. On day 10 of life, the infant was extubated and subsequently the chest tube was removed. Tube feeds were initiated 48 h after extubation and normal upper gastrointestinal contrast study. Nasogastric tube was removed after 10 days. Infant was managed conservatively throughout the study.

Upon a 9 year follow-up, the infant was found to be doing well with no evidence of esophageal stricture. After performing a needle aspiration the infant’s condition began to show further improvement.

Discussion

Spontaneous EP ruptures (Neonatal Boerhaave’s syndrome) in the newborn are mainly iatrogenic and rare. It is more commonly seen in premature and SGA infants. Usually, the most common site of injury is cervical esophagus. Low incidence, subtle features, and confusing radiographic findings can result in a critical delay of diagnosis and therapy. Iatrogenic EP should be suspected in the pharyngeal region after instrumentation, as there is a sudden deterioration with right-sided pneumothorax and difficulty in maneuvering the nasogastric tube with blood tinged oral secretions or fresh nasogastric bleed. The pneumothorax is usually right-sided as the aorta provides an additional support on the left. The initiating event may be a submucosal injury and cricopharyngeal spasm by laryngoscope.
blade or endotracheal tube that extends into a full-thickness perforation after a subsequent oropharyngeal suctioning or nasogastric tube insertion.4 Extension of the neck during intubation increases the risk as the posterior esophageal wall is compressed by the body in the cervical vertebrae.5 Upper gastrointestinal tract contrast study or esophagoscopy are indicated only when esophageal obstruction is suspected. The contrast study may be done after 7 to 10 days before initiation of feeds. Surgical intervention is required only when there is a complication.6,7 The overall mortality is usually around 30%.

Intubations should be performed by experienced physicians in a gentle manner using compliant tubes as hyperextension of the neck, application of excessive force, protruding stylets, and blind intubations predispose to iatrogenic injury. Hence, intubations should be performed by an experienced pediatrician in a skillful manner using appropriate equipment.

**Conclusion**

Most of the EPs are iatrogenic. Clinical presentation depends on the site of esophageal injury. Gentle intubation can prevent iatrogenic perforation. Most often, the management is conservative in nature.

**References**

Diagnosis of Shprintzen–Goldberg Syndrome

Naveen Bajaj,* Smruti Patel

Abstract

Shprintzen–Goldberg syndrome (SGS) is a rare disorder characterized by marfanoid habitus, dolichocephaly, and ocular proptosis. A male infant weighing 2605 g, and having a length of 57 cm (>97th percentile) and a head circumference of 36 cm (50th percentile) during admission was enrolled in this study. In this infant, features such as increased length at birth, longer arm span, arachnodactyly, facial features, and hypotonia were observed. Neurologic, ophthalmic, and radiologic examinations were found to be normal. The aim of this study was to present the first such case of the syndrome from India and describe in detail the findings.

Key words: Arachnodactyly, marfanoid habitus, Shprintzen–Goldberg syndrome

Introduction

Shprintzen–Goldberg syndrome (SGS) is a rare disorder characterized by marfanoid habitus, dolichocephaly, and ocular proptosis.1 In 1982, Shprintzen and Goldberg described a new syndrome in 2 unrelated males with craniosynostosis and marfanoid habitus.2 A patient with similar findings but lacking craniosynostosis was reported in a study by Sugarman and Vogel in 1981.3 Since then approximately 42 cases of this syndrome have been reported.4 The first case of SGS in India is reported in this study.

Case Report

A male infant on day 7 of life presented with irritability, difficulty in feeding, and intermittent episodes of cyanosis. He was born at term by normal vaginal delivery in a peripheral hospital and cried immediately after birth. He weighed 3050 g at birth (50th percentile) and had uneventful immediate neonatal period. Family history was unremarkable. On examination at admission, he was found to weigh 2605 g with a length of 57 cm (>97th percentile) and a head circumference of 36 cm (50th percentile). General physical examination showed prominent forehead, large anterior fontanel, upturned nose, micrognathia, and high-arched palate. The eyes had downward slanting palpebral fissures, proptosis, and hypertelorism. Ears were low-set and posteriorly rotated (Figure 1). Examination of extremities (Figure 2) revealed arachnodactyly, long hands (hand length >2 SD), and long feet (foot length >2 SD).
The SGS is a disorder of unknown cause comprising craniosynostosis, marfanoid habitus, and skeletal, neurological, cardiovascular, and connective-tissue anomalies. There are no pathognomonic signs for SGS, and diagnosis mainly depends on recognition of a characteristic combination of anomalies.5

On clinical basis, increased length at birth, longer arm span, arachnodactyly, facial features, and hypotonia suggest the diagnosis of SGS in the infant; and did not
show any clinical or radiological evidence of craniosynostosis during the neonatal period. However, onset of craniosynostosis in the later period of life cannot be ruled out. It should be stressed that, in contrast to Marfan syndrome (characterized by enophthalmos), SGS is characterized by proptotic eyes. Of the reported cases in the literature, almost 40% of patients were found to have craniosynostosis (may be late in onset).

In 2005, Robinson, et al carried out a clinical analysis in 14 German individuals and observed a characteristic facial appearance, with more than two-third of all individuals having hypertelorism, down-slanting palpebral fissures, high-arched palate, micrognathia, and apparently low-set and posteriorly rotated ears.5 In the present study, the infant had all the above-mentioned facial features suggesting the diagnosis of SGS. Other commonly reported manifestations include hypotonia (at least during the neonatal period), developmental delay, and inguinal or umbilical hernia. The degree of reported intellectual impairment ranges from mild-to-severe. The most common skeletal manifestations in SGS were arachnodactyly, pectus deformity, camptodactyly, scoliosis, and joint hypermobility. However, none of the skeletal signs alone is specific.5 Arachnodactyly was the only skeletal abnormality that could be found in this case.

Symptoms such as feeding difficulties, stridulous breathing during sleep, cyanosis, and respiratory difficulties are common during infancy period and may require gavage feeding.1 The infant enrolled in this study also had feeding difficulties in addition to drooling of milk during feeding and episodes of cyanosis during sleep that was resolved at 1 month of age.

The SGS mode of inheritance is unknown. Although, familial recurrences are rare, they have been reported in some studies.5,6 Germline mosaicism for a new autosomal dominant mutation, autosomal recessive inheritance, or cryptic structural abnormality of a chromosome may explain familial recurrence with unaffected parents. The risk to sibs of a proband is small, but greater than that of the general population. To date, all offspring of individuals diagnosed with SGS have been unaffected.4 Dietz, et al reported that SGS is associated with mutation of the fibrillin-1 gene, the same gene that causes mutation in the Marfan syndrome.7 The phenotype of SGS is still not clearly defined, but shows some overlap with Loeys–Dietz syndrome and Marfan syndrome.4

References
Instructions to Authors

Perinatology, one of the few journals dedicated to the emerging multidisciplinary field of perinatal medicine, is published quarterly. The journal publishes original articles, brief reports on clinical and laboratory observations, case reports of substantive value, invited editorials, invited papers on recent advances, clinical diagnosis, announcements of meetings, and summary reports of conferences.

The journal is multidisciplinary and welcomes articles in English from metabolic specialists, clinical biochemists, obstetricians, neonatologists, pathologists, geneticists, endocrinologists, neurologists, developmental pediatricians, and any other person whose work is related to metabolic disorders and genetics.

The articles should not exceed 2500 words, with not more than six figures, tables, and photographs. Brief reports and case reports should not exceed 1200 words, with not more than two tables and figures or photographs and six references. Brief accounts of new observations can also be presented as letters not exceeding 400 words.

Guidelines to be followed while preparing and submitting a manuscript are given below.

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  - If the subjects of the photographs are identifiable, either their eyes should be masked or their written permission to reproduce or adapt previously published illustrations and tables
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MANUSCRIPT FORMAT

Titles and subtitles
Titles should be short, concise, specific, and informative.

Abstract
Abstract of a research paper summarizes the main points of an article: (1) the study objective and background, (2) the study design and methods, (3) results, and (4) conclusion.

Key words
Key words are descriptors representing the key topics presented in the article.

Introduction
The introduction should provide the objective of the study and state the hypothesis or research question, how and why the hypothesis was developed, and why it is important.

Methods
This section includes a description of:
- Study design or type of analysis and period of study
- Condition, factors, or disease studied
- Details of sample (eg, study subjects and the setting from which they were drawn)
- Intervention(s)
- Outcome measures
- Statistical analysis

Results
The results given in the manuscript should be specific and relevant to the research hypothesis.

Discussion
This section should be a formal consideration and critical examination of the study. The results should be considered in this section in the context of other studies.

Conclusion
This section summarizes the consensus statement. It may include benefits and harms of the study. The type of future studies, if appropriate, should be mentioned here.

Acknowledgments
Acknowledgments are considered to be a continuation of the text and precede the references. Only those who have made substantial contributions to the study and/or preparation of the paper should be acknowledged. The source(s) of grant support, equipment, and drugs should be included.
Instructions to Authors

Some notes on the use of abbreviations are given below.

Abbreviations should not be introduced in titles. Some very common abbreviations need not be expanded. Abbreviations should not be introduced in titles. Some very common abbreviations need not be expanded. Abbreviations—such as PhD and pH—do contain lower case letters.

Figure caption in sentence case. (Note the full point at the end.)

For example:

Table caption in title case (no full point at the end)

For example:

Table 1. Table caption in title case (no full point at the end)

References

Authors cite a reference:

• To support their arguments or lay the foundation for their theses
• As a source of information or to credit other authors

General Style Points (US Spelling and Style)

• Use American English, “ize” spelling
• Numbers under 10 are spelled out, except for measurements with a unit (8 mmol/L) or age (6-week old), or when in a list with other numbers (14 dogs, 12 cats, and 9 gerbils)
• Use list comma. For example: The bishops of Durham, Canterbury, Bath and Wells, and York were invited. OR I used to help my mother with the cooking, cleaning, washing and ironing, and yard work
• Use double quotes: Generally, quotes are outside punctuation.

For example: poliomyelitis is commonly referred to as “polio.”

• For range use “to” in text, for example 40 to 50 mg, and “—” (en dash) in parenthesis (33–47 cm)

• Use P value as: P = .05, P < .005, P < .05 (no “0” before period and “P” is capital and italics; no space between the symbols (<, >, and “P”): rule of exception: insert space before and after the symbol “=”)

• Closed-up em dash “—” should be used for parenthetical phrases

• Parenthesis style: First priority is parenthesis followed by square bracket, that is, [()]. [World Health Organization [WHO]]

• Date: December 5, 2008 (US style)

• Foreign words listed in “Merriam-Webster’s” online dictionary should not be italicized and hyphenated (in vitro, in vivo, etc.)

• Italicize when used in singular: Species, variety or subspecies, genus (eg, first occurrence in text—Escherichia coli; following occurrences—E coli—without any period)

Use lowercase [unless it is not a beginning of the sentence] and nonitalic style for plural form of organisms

Bacillus cubelli
Staphylococcus staphylococci
Streptococcus streptococci

Tables

• All tables should be cited in the text and it should be in sequential order
• Table should be cited as Table 1/Tables 1 and 2/Tables 1 to 3 (or Tables 1–3, inside parenthesis)
• Table caption should be provided and its first part should be in bold form as given below

For example:

Table 1. Table caption in title case (no full point at the end)

Figures

• All figures should be cited in the text and it should be in sequential order
• Figure should be cited as Figure 1/Figures 1 and 2/Figures 1 to 3 (or Figures 1–3, inside parenthesis)
• Figure caption should be provided and its first part should be in bold form as given below

For example:

Figure 1. Figure caption in sentence case. (Note the full point at the end.)

Abbreviations

Most abbreviations should be spelled out at first mention (in text); some very common abbreviations need not be expanded. Abbreviations should not be introduced in titles.

Some notes on the use of abbreviations are given below.

• In general, use uppercase letters without period for acronyms and initialisms such as CHF, GFR, and WBC and also for routes of administration and dosage schedules such as PO, IV, BID, and TID. Some abbreviations—such as PhD and pH—do contain lower case letters.

Use abbreviations consistently. In general, write out the term or phrase at first mention, followed by the abbreviation in parentheses; use only the abbreviation thereafter

• Write lowercase abbreviations without period; “et al.” and “vs” are examples. Rule of exception: Use lowercase abbreviations, preceded by a comma and followed by a full point at the end of “etc.” For example: sun, moon, etc.

• Write “for example” or “that is,” preceded and followed by a comma, if it is not the beginning of the sentence, in a running text. Write “eg” or “ie” followed by a comma when used in parenthesis (ie, or eg.)

Genus and species

Italicize when used in singular: Species, variety or subspecies, genus (eg, first occurrence in text—Escherichia coli; following occurrences—E coli—without any period)

Use lowercase [unless it is not a beginning of the sentence] and nonitalic style for plural form of organisms

Bacillus cubelli
Staphylococcus staphylococci
Streptococcus streptococci

Units

Use standard abbreviations for units of measure.

References

All references should be cited in the text, tables, or figures in consecutive numerical order (as presented in the text) by means of superscript Arabic numerals, outside punctuation.

Articles in Journals

Typical entry for journal with more than two authors (if more than two authors, list first author, then et al).

For example:


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Author name: Same as journal.


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Do not include material that has been submitted for publication but has not yet been accepted. This material, with its date, should be noted in the text as “unpublished data,” as follows:

For example:

These findings have recently been corroborated (Mariman, unpublished data, January 1996).