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Healthy Babies to Healthy Mothers

ESTD 1989
ISPAT

# talkBACK

## Newsletter of the Indian Society for Prenatal Diagnosis and Therapy



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## editor's DESK

Dear ISPATIAN friends,

Newborn screening (NBS)is the practice of testing all new- born babies in their first days of life for certain disorders and conditions that can compromise their normal development later. If we believe in this data from USA then each year, over 12,000 babies are born with one of the conditions included in state newborn screening panel and More than 1 in 300 newborns have a treatable condition. September is Newborn Screening Awareness Month! With a small beginning in 1960s by Robert Guthrie, NBS program in well-developed nations has now become a preventive public health policy & mandatory in many countries to save life of thousands of babies.

Guidelines from these developed countries recommend newborn screening before discharging the baby and mother after birth, because of the high prevalence of certain endocrinopathies, metabolic errors and hearing loss which, if recognized later, contribute to significant morbidity. Although the exact list differs among, and sometimes within countries, testing for phenylketonuria (PKU) and congenital hypothyroidism (CH) is universal in all the programs. However, neonates are not screened in India because the health policies have typically targeted mortality and infectious morbidities and disabilities due to genetic causes is not the priority, probably due to paucity of resources. Nevertheless, these policies have been successfully offered evidence of lowering infant mortality rates, but the net effect of these gains has been somewhat offset by an increase in disability. One of the basic requisites for a screening program is the availability of the epidemiological data regarding candidate NBS disease and we the Indians lack badly in collecting it. As of now CH , congenital heart disease, and hearing loss along with certain organic, & amino acid disorders are the diseases which if we screen and intervene earlier, we can prevent the consequences and financial burden it is associated with. One ethical and economical question is how useful these screenings programs are and are we in a state of implementing holistic NBS program with diet

president **N MALHOTRA**

president **J MALHOTRA**

# Prenatal Diagnosis and care Yesterday Today and Tomorrow

**Prof. Narendra Malhotra, Prof. Jaideep Malhotra**
**I.S.P.A.T. – FOGSI**
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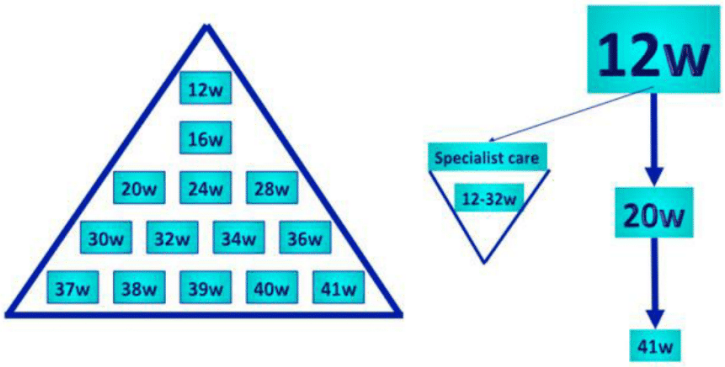
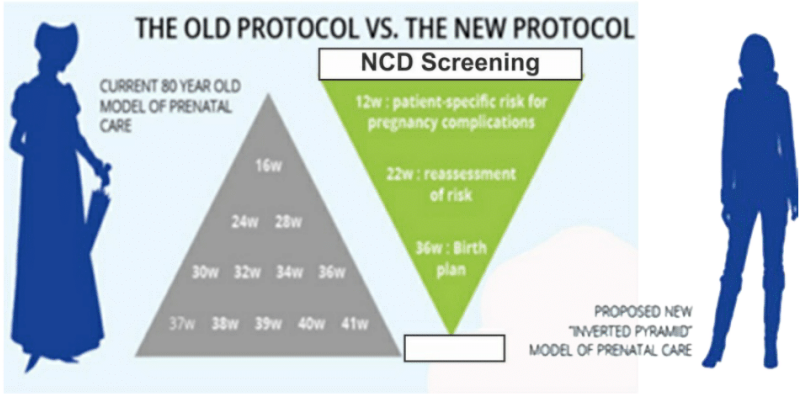
Approximately 3% of viable fetuses would be born with an anomaly. Today reversing of the diagnostic triangle of Prenatal diagnosis will ensure that we pick up these anomalies as early as possible.




Prenatal care triangle of the 1990's

Today, as suggested Prof. Kypros Nicalodis the prenatal care triangle has been reversed to diagnosing anomalies early and also to this triangle is added a basement and a penthouse for preventions of N.C.D.'s




We need to be aware of the "Fetal origins of adult diseases" and proper care of the mother during pregnancy will assure the birth of a healthy neonate. Nine months are windows of opportunity to us care providers (obstetricians) to assure a healthy next generation. FOGSI in 2018 will be propagating the concept of Devine mother and virtue baby which gives a complete

holistic approach to Pregnancy and incorporates healthy habits, meditation, Rajyoga and spiritual teachings and exposure to the mother and unborn fetus.

Yesterday we diagnosed problems in neonates after birth, Today we have advanced and very accurate screening tests like NIPT and tomorrow we are likely to do gene studies and manipulate defective genes in the unborn to assure the birth of a healthy disease fee new born.

We congratulate the FOGSI perinatology committee and editor Dr Reena Wani for revising the manual.

Happy Readings.

Prof. Narendra Malhotra
*MD, FICOG, FICMCH, FRCOG, FICS, FMAS, AFIAPM*

Prof. Jaideep Malhotra
*MD, FICOG, FICMCH, FRCOG, FICS, FMAS, FRCPI*

## What's in **NEWS** these days

**In a breakthrough two fetuses suffering from spina bifida were operated in utero in UCLA London, under the guidance of Prof. Anne David by 30 doctors team. Till now these surgeries were available post birth only.** *https://speciality.medicaldialogues.in/two-babies-with-spina-bifida-treated-while-still-in-womb/*

**Early pregnancy loss – ACOG updates guidelines**
*https://www.acog.org/Clinical-Guidance-and-Publications/Practice-Bulletins/Committee-on-Practice-Bulletins-Gynecology/Early-Pregnancy-Loss*

**Children born through Art techniques(IVF & ICSI) are at higher risk of developing essential hypertension in their teen years.**
*https://speciality.medicaldialogues.in/ivf-children-at-increased-risk-of-high-bp-in-their-teenage-years-jacc/*

## membership **UPDATE**

**TOTAL**

**860**

**Become an ISPATian**
**https://goo.gl/ExJQvv**

## secretary **SAURABH DANI**

### Digitization of Member's Records

ISPAT has been in existence since 1989 when the best way to communicate was by paper and post. Since then everything has changes except we members. This year we undertake to update all our members data and store it in digital format for easy retrival and easy of use for communicating and eVoting.

We intend to make the society environment friendly by reducing the use of paper and extensively use the digital platform.

**Between now and March 2019 all will be asked to verify/update the existing data with us and will be asked to upload latest photos/documents.**

We hope you co-operate and help your ISPAT become 100% Digital.

## Continued from **Pg1**

therapy? Wilson and Jungner have outlined specific criteria that serve as a template to decide what disorders to include in the screening at a national platform. These are: (a) biochemically well identified disorder; (b) known incidence in the population; (c) disorder associated with significant morbidity and mortality; (d) effective treatment available; (e) period before which intervention improves outcome; and (f) availability of an ethical, safe, simple and robust screening test.

Till we as a nation become equipped with all above, it is our duty to begin NBS at least at our regional centers or district centers to prevent childhood disabilities & mortality due to such congenital metabolic diseases. On this note, we wish you happy reading and a very happy Diwali and festive season ahead.

Yours truly,

Dr. Usha Dave

Dr. Seema Pandey

## upcoming **EVENTS**

### First International Conference on Prenatal Development in India

**Date : 18/01/2019 - 20/01/2019**
**Venue : Lonavla, Maharashtra**
Contact Person : Dr Aruna Narvekar
Mobile : 9819010301
Email : drarunanarvekar@gmail.com
Website : https://conference.manashakti.org/

### UPCOG 2018: 30th Annual Conference of UP Chapter of Ob&Gy

**Date : 15-17 November 2018**
**Venue : Allahabad, Uttar Pradesh**

some **PAST EVENTS**

## FOGSI-ISPAT E-Connect - Complications in Pregnancy and Advancements in Nutrition for Women

**by Saurabh Dani**

FOGSI & ISPAT joined hands with GSK to conduct 30 CME's across India on the topics of Genetics, Nutrition, PIH, GDM, NBS & FGR. The CME's were conducted in all the zones on India. Each CME had an attendance of 50 delegates from the local region. The CME's focus was to create awareness on use of Genetics in day to day life of an Obstetrician, Recent advancements in GDM, PIH & FGR and also to understand the role of Obstetricians in Newborn Screening. The topics were selected to stimulate the thought process and upgrade the knowledge of fellow obstetricians, which in turn would help improve the health of pregnant women across India.


Excellent support was provided by the staff of Dialog India and GSK which made the mammoth task of fixing venue and faculty simple.

I would like to thank Dr. Narendra Malhotra for entrusting me with this program and also would like to thank my counter part of FOGSI, Dr. Neharika Malhotra for supporting me completely. It would have been impossible to do this without the support of FOGSI President Dr. Jaideep Malhotra and the office bearers of ISPAT.

Now that phase 1 is over we look forward to embark on phase 2 of the same e-Connect program in 2019.

## quiz of the MONTH

by Dr.Amitha Indersen

1) Which of the following anomalies have a strong association with history of maternal diabetes?
A: Common arterial trunk
B: Focal femoral hypoplasia
C: Sacral agenesis
D: All the above

2) Increased middle cerebral artery peak systolic velocity is seen in
A: Fetal sacro coccygeal teratoma
B: Fetal Cytomegalovirus infection
C: Fetal arterial calcinosis
D: None of the above

3) In Tetrology of Fallot diagnosed in the fetus which component of the Tetrology differs from the postnatal presentation?
A: Narrowing of the pulmonary artery.
B: Over-riding of aorta
C: Ventricular septal defect
D: Right ventricular hyperplasia

4) Binders facies can occur due to
A: Retinoic acid
B: Warfarin therapy
C: Severe oligohydramnios
D: Misoprostol

5) In the recent ASPRE trial the dose of prophylactic aspirin has been recommended as 150mg and not low dose aspirin. Why?
A: Many women on low dose aspirin developed resistance to aspirin at that dose and the higher dose overcomes the resistance.
B: Wrong dose was in use
C: Lower dose used for fear of sub chorionic haemorrhage.
D: All of the above

Answers: Last Page

# Noninvasive Prenatal Screening Test (NIPT)

by Usha P. Dave & Surendra K Chikara

In the era of genomic diagnostic technology, it becomes empirical to use the latest prenatal fetal screening & diagnostic tests for the benefit of our patients. ***"Noninvasive Prenatal Screening (NIPS) Test"*** is one such test based on "Next Generation Sequencing (NGS)" DNA technology to detect chromosomal aneuploidies during early pregnancy ( 10 weeks onwards) using maternal blood.

**What is NIPS/ NIPT TEST ?**

NIPT, which analyzes cell-free fetal DNA circulating in maternal blood, is a new option in the prenatal screening and testing paradigm for trisomy 21 and a few other fetal chromosomal aneuploidies (18, 13, X &Y). DNA from the fetus circulates in maternal blood. Unlike intact fetal cells in maternal blood, which can persist for years after a pregnancy, circulating cell-free fetal DNA (ccffDNA) results from the breakdown of fetal cells (mostly placental) and clears from the maternal system within hours. Fetal DNA detected during a pregnancy, therefore, represents DNA from the current fetus. Quantitative differences in chromosome fragments in maternal blood can be used to distinguish fetuses affected with trisomy 21, and a few other fetal aneuplodies, from those that are not affected.

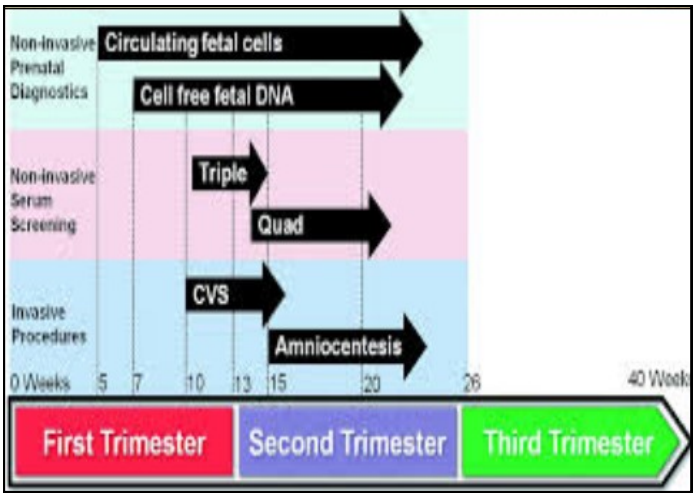



**Fig. 1**

**NIPS Testing** can be done any time after 10 weeks using about 10 ml of mother's blood in special tube ; typically it is done between 10-22 weeks which is sent to Genetic Laboratory using NGS technology/ or having the patented method or platform to conduct NIPS test. Results can take 8-10 working days.

**What are the techniques for Fetal Diagnosis ?-**

It can be summarized as below-

**A) Non-Invasive screening methods-** Biochemical Maternal Screening, Ultrasonography & Maternal Fetal DNA Tests

**B) Invasive methods-** Diagnostic tests for chromosomal & molecular tests

- Amniocentesis
- Chorionic villus sampling
- Fetal blood sampling
- Fetal tissue sampling

**A risk calculation from combination of below is conducted to predict the "Risk" in pregnancy for chromosomal aneuploidies-**

- Biochemical ( Dual or Quadruple ) Marker - Tests & USG values
- A risk calculation from combination of age, other risk factors & lab. tests results
- Biochemical Markers & USG values

**As shown in Fig.1, there are various options of First Trimester Screening & Second Trimester screening as both Invasive & Non-invasive tests.** However, these tests have their own limitations of specificity & high False Positive (FPR) detection rate. Secondly, the disorders screened are three most common fetal chromosomal abnormalities,

- Trisomy 21(Down's Syndrome),
- Trisomy 18 (Edwards' Syndrome) and,

- Trisomy 13 (Patau's Syndrome),

and having Detection Rate > 90% with 5% FPR ( False Positive Rate) when used combined values of all markers

**FETAL DNA & NIPT -**

The Cell-free fetal DNA (CffDNA) is genetic material that is released by the placenta and circulates in a woman's blood during pregnancy. It is present in small quantities starting in the first trimester and increases throughout pregnancy. CffDNA generally reflects the genetic makeup of the developing baby. **NIPS *is a Screening Test NOT a Diagnostic Test.***

The important difference between a screening & diagnostic tests (details shown in **Table 1)** must be understood by a practicing clinician. NIPT technologies have been validated in singleton pregnancies at high risk for trisomy 21 & recently there are almost all (22 autosomes +2 Sex chromosomes) trisomies are added to the list including a few chromosomal microdeletions/ duplication found in certain genetic syndromes offering the advantages of "Genome-wide Screening". Very few Genetic Labs offer this NIPS test in twin pregnancies, and for Turner syndrome (monosomy X) when the fetus presents with a cystic hygroma.

**Table 1 – Comparison of settings and criteria for screening and diagnostic testing**

| | Screening test | Diagnostic test |
|---|---|---|
| Purpose | To detect potential disease indicators | To establish presence/absence of disease |
| Sensitivity and specificity | Often chosen towards high sensitivity not to miss potential disease; may result in some false positives | Chosen towards high specificity (true negatives) |
| Patient population | Large numbers of asymptomatic, but potentially at-risk individuals | Symptomatic individuals to establish diagnosis, or asymptomatic individuals with a positive screening test |
| Test method | Simple and acceptable to patients | May be invasive and/or expensive. Accuracy and precision more important than patient acceptability |
| Cost | Generally cheap, given large numbers of people will need to be screened to identify a small number of potential cases | Higher costs often justified as necessary to establish a diagnosis |

**Table 1**

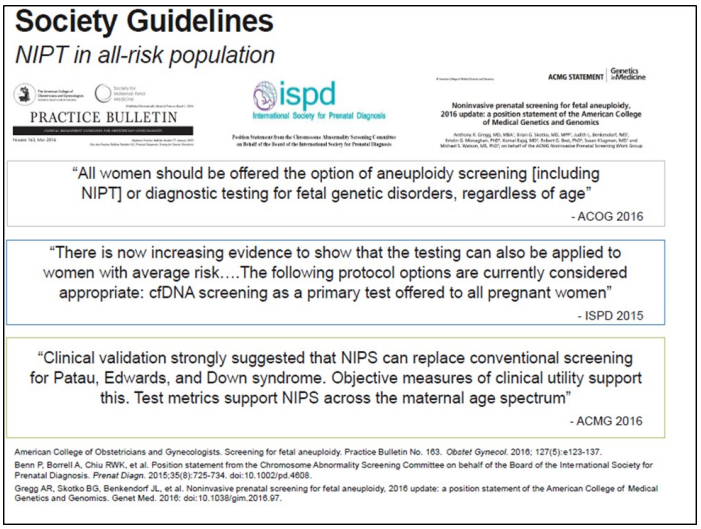



**Fig. 2**

**<u>Maternal Indications for NIPS Test-</u>**

- Advanced maternal age
- Abnormal maternal serum screen
- Personal/family history of aneuploidy
- Abnormal ultrasound findings

**No Risk pregnancy– As NIPS is a screening test advocated for all pregnant women for aneuploidy screen by various Societies, viz. ACOG, ACMD & ISPD as shown in Fig.2**

**<u>Highlights of NIPS test -</u>**

The testing is non-invasive, involving a maternal blood draw, so the pregnancy is not put at risk for miscarriage or other adverse outcomes associated with invasive testing procedures. NIPT Detection Rate and Accuracy is higher than biochemical & USG tests risk prediction

At present, NIPT provides information about specific fetal aneuploidies with 99 % specificity & sensitivity initially for 5 aneuploidies- Chr.13,18, 21, X & Y. NIPT does not typically provide any other genetic information about the genetic constitution of the mother or fetus. It accurately provides information regarding the fetus & hence the genetic counseling & support to couples for reproductive decisions. It helps to ease the burden on couples & is cost savings for the society.

Since, the time required for the NIPS result is shorter than conventional karyotyping, the couple

has enough time for reproductive option even in late pregnancy of 18-19 weeks. However, it does not predict the risk of Neural Tube Defects – eg. Spina bifida and Anencephaly.

**The limitation of this technology** is both pre- & post test genetic counseling is essential to explain the couple about the genetic screening test to be used. If the screening yields positive results, then a woman and her partner will have to deal with this new information and choose whether or not to act on it as per the international protocol as below-

**Genetic counseling** and prenatal **diagnostic tests** is required to more accurately detect whether the fetus actually has a genetic condition.

Genetic screenings can give false positive results, meaning they can be wrong and lead expectant parents to believe their unborn babies might have genetic abnormalities when they do not. There's also a chance the screening will not pick up a chromosomal abnormality when there is one.

As per the protocol, Genetic Counselor cannot advise the couple about MTP based on a positive NIPS screening result alone.

**Conclusion** – As described above, NIPS test is becoming more popular among High-Risk pregnancies. Nevertheless, being more reliable with more than 95 % specificity & sensitivity, it may soon replace conventional biochemical marker tests if used in conjunction with USG markers. It is already recommended worldwide to use in all pregnant women for aneuploidies, a tleast for basic 5 chromosomal aneuploidies as mentioned above. With advanced "Clin Exome" technology, NIPS test is proving significant in detection of prenatal specific chromosomal abnormalities & can prevent the certain genetic conditions in families.




Answers (November 2018): 1 D, 2 A, 3 D, 4 B, 5 A