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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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Dear ISPATians,

Greetings of the day !

On behalf of ISPAT, it gives us immense pleasure to introduce the ***'ISPAT-ENewsletter'*** in 2017- the post silver jubilee era,- nevertheless the idea was conceived a few years back & discussed several times during meetings. With a vision of cultivation and promotion of the study and practice of prenatal diagnosis, medical genetics & therapy in India, a small group of Obst & Gynaecologists & like-minded research professionals formed ISPAT in 1989 in Mumbai from where the Registered office & all activities have been coordinated since its inception as per the Bye-Laws. The aim & vision of ISPAT is well depicted by our present dynamic President- Nr. N. M. Malhotra in this issue highlighting the functioning & vast spectrum of specialities involved in care of the 'Unborn'. We are extremely fortunate to have the message to our young ISPATians from the visionary Founder President Dr. R. P. Soonawala.

Over the decades, we have witnessed, a tremendous revolution in ways and means of clinical practice in fetal medicine, translational research in genetic & non-genetic birth defects & advanced laboratory technology used globally for the benefits of 'fetus as a patient'. This is an era of laser,

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president **MALHOTRA**

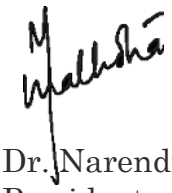
Dear ISPATians

Greetings on the launch of first ISPAT e-news letter.

ISPAT(Indian society of prenatal diagnosis and therapy) was established in 1989, to promote, educate and train medical personnel, paramedical staff from various interrelated specialities in management of high risk pregnancy. Salute to the far sight of our founder president Prof. R.P.Soonawala.

Today ISPAT has grown and we all keep on growing so that we can help to decode the genetics of high risk pregnancy and help to give HEALTHY BABIES TO HEALTHY MOTHERS.

This is your news letter, compiled by a team of young enthusiastic ISPATians. Do contribute and motivate your colleagues to join ISPAT.



Dr. Narendra Malhotra
President

the aim and vision of **ISPAT**

The Indian society for Prenatal Diagnosis and Therapy is a Multidisciplinary society established in 1989 by like minded Doctors and Scientists, interested in detection, prevention and management of Birth Defects of Genetic and Non Genetic origin.

The Society was set with purpose, ideas and functioning similar to the International Society for Prenatal Diagnosis and Therapy.

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non-invasive, genomic & proteomic, bioinformatics-integrated medical diagnostic services which are growing in leaps & bound. The knowledge about new genes, their functions and expressions, new insights into disease causation and potential fetal therapies is growing at astonishing pace. It is beyond the doubt that 'Golden Age' of child & maternal healthcare evolving around the unborn fetus has arrived & we as fetal medicine specialists, both physicians & researchers, should be well equipped with wisdom to welcome it. In this age of "Dr. Google", it is a mammoth task to cope with the latest updates in the field of prenatal diagnosis & fetal therapy, and not only remain connected with the world but also with our **Fellow ISPATians**.

'ISPAT-ENewsletter' is a small effort to bring our fellow friends, colleagues & young researchers closer by offering the common platform to discuss & exchange the recent applications, biomedicine developments, events & ideas to take ISPAT to a great height. In this first issue, we take the privilege of introducing ISPAT and the manpower efforts silently working for more than 2 decades. The new ideas & voluntary contribution of ISPAT members is most welcome to make this electronic on-line issue not only knowledge-rich but also attractive, interesting & coping with the expectations of everyone. An article by Dr. Raju Sahetya, President (2014-16) has enlightened us on *'Paradigm Shift in Prenatal Diagnosis'* over the last decades.

Finally, we wish to express our gratitude to our 'Editorial Team' for their creative & constant support to make this dream of ISPAT News letter a reality. *All Best Wishes !*

The society had released a document called 'Sabarmati Declaration' at the 7th ISPAT Biennial Conference at Ahmedabad, by the hands of, the then CM of Gujarat Narendra Modi. This states the philosophy by strongly condemning the deplorable practice of female

founder president **SOONAWALA**

Genetics is one of the most fascinating branches of medicine. It also is a must for good obstetric practice with deep understanding of foetal problems and their management. Because of this, in 1989, Indian Society for Prenatal Diagnosis & Treatment came into existence and like-minded people got together to form ISPAT Obstetricians, Neonatologists, Paediatricians, Sonologist and Geneticists.

I am very happy and congratulate the present managing committee for Newsletter Talk Back which will go a long way to spread the awareness.

Dr. Rustom Soonawala
Founder President

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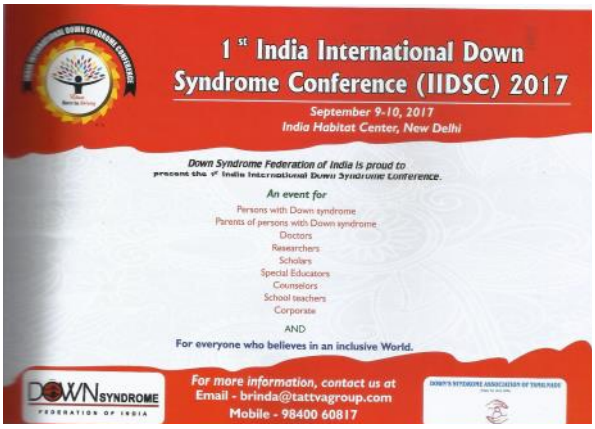
feticide, sex selection at pre and post conception stage.

So far thirteen ISPAT Biennial Conferences and several Training Workshops across the country and one International Conference at Goa have been done.

Genetics and prenatal diagnosis is not taught with special emphasis in medical graduate and post graduate courses, it is therefore responsibility of societies like ours to promote, educate, and train all the related medical personnel in this Multi Disciplinary (Obstetrician, Paediatrician, Obstetric Ultrasonologist, Geneticist, Genetic Counsellor, Neonatologist, Paediatric Surgeon, Cardiologist, Urologist, Haematologist) field of fetal diagnosis and management of the Fetus as a Patient.

upcoming **EVENTS**



quiz of the **MONTH**

1. The first disease to be diagnosed prenatally.
2. Till date how many diseases we are able to diagnose prenatally?
3. First amniocentesis, when, where by whom?
4. First CVS, when, where, by whom?
5. Soft markers to be looked for Down's syndrome in first trimester scan?

Answers: Next Issue

Paradigm shift in Prenatal Diagnosis

by Dr. Raju Sahetya

We are in the midst of a paradigm shift in the way that prenatal screening and diagnosis are performed around the world.

This change is occurring in real time at an extremely rapid pace that is unprecedented in the history of prenatal care.

Prenatal Care

The quest for a less invasive approach to prenatal diagnosis has been the focus of much research over recent decades.

In late 70s, the introduction of ultrasound and the possibility to visualize the fetus in utero brought about a true revolution in two respects.

For doctors, it allowed to diagnose in fetal life problems that until then had been only known in the newborn.

For parents, it facilitated the recognition of the fetus as a person.

The combination of these two factors resulted in the development of a new concept, "**The Fetus as a Patient**", and with it, the beginning of a subspecialty that we know today as "**Fetal Medicine**".

The Fetal Medicine Team

Roles and responsibility of the team members:

Obstetrician, who manages the pregnancy regularly and who may perform minimally invasive interventional procedures for diagnostic tests like Chorionic Villus Sampling and Amniocentesis and therapeutics procedures such as percutaneous shunt and catheter placement. Intra uterine transfusion IUT, for Rh issoimunisation and fetal anemia.

Maternal-fetal medicine specialist, a perinatologist, who specializes in diagnosis and treatment of the high-risk maternal-fetal disease.

Geneticist or genetic counselor, who takes responsibility for prenatal genetic counselling, diagnosis, prognosis, talks to the parents to be and family and make them prepared for the consequences, and above all the laboratory procedures and investigations involved in prenatal diagnosis.

Neonatologist, who counsels the pregnant patient and her family prenatally with respect to expectations and outcomes and prepares to continue care for the baby after birth.

Pediatric surgeon, who, with the neonatologist, continues postnatal management of the fetal disease and makes the fetal treatment plan.

Obstetric sonologist who has expertise in the fetal diagnosis and its severity and guiding diagnostic and therapeutic procedures.

Pediatric super-specialists, such as cardiologists, cardiothoracic surgeons, neurosurgeons, and urologists, depending on the lesion

In the Past

Invasive Procedures and Karyotype was a rule in the following circumstances

Late Maternal Age

Positive History

In the Rescent Past

Ultrasonograpghy, Serum Screening, Nuchal Translucency, Invasive Procedures followed by Metaphase Karyotype.

Ultrasonography

First trimester ultrasonic 'soft' markers for chromosomal abnormalities such as the absence of fetal nasal bone, an increased fetal nuchal translucency are now in common use to enable detection of Down syndrome fetuses.

Screening Options

Test	When Done	Detection Rates
1st trimester (NT + 2 serum)	10-14 weeks	T21 -- 83% T18 – 80%
Ultrasound	18-20 weeks	T21 -- 60%; T18 -- 85% NTD -- 70-98%
Quadruple screen (4 serum analytes)	15-21 weeks	T21 -- 75-80%; T18 -- 60% NTD -- 80-90%
*Integrated screen (1st trimester screen + quadruple screen)	10-14 weeks 15-21 weeks	T21 -- 92% T18 -- 90% NTD -- 80%
Maternal serum	>7 weeks	T21 - >99% Other aneuploidy?

Ultrasound can also assist in other Prenatal Diagnostic Procedures such as Amniocentesis, Chorionic Villus Sampling, Cordocentesis and in Fetal therapy.

Many structural abnormalities in the fetus can be reliably diagnosed by an ultrasound scan, and

MELISSA Trial Results: Overall MPS Performance

Bianchi et al., Obstet Gynecol 2012; 119:890-901

Classified	Sensitivity (%)	95% CI	Specificity (%)	95% CI
Trisomy 21 (n=493)	100·0 (89/89)	95·9 - 100·0	100·0 (404/404)	99·1 - 100·0
Trisomy 18 (n=496)	97·2 (35/36)	85·5 - 99·9	100 (460/460)	99·2 - 100·0
Trisomy 13 (n=499)	78·6 (11/14)	49·2 - 99·9	100·0 (485/485)	99·2 - 100·0
Monosomy X (n=433)	93·8 (15/16)	69·8 – 99·8	99·8 (416/417)	98·7 - >99·9

2.8% of cases were unable to be classified

these can usually be made before 20 weeks.

Common examples include Hydrocephaus, Anencephaly, Menigomyelocoele, Achondroplasia and other dwarfism, Spina bifida, Exomphalos, Gastroschisis, Duodenal atresia and Fetal hydrops.

With more recent equipment, conditions such as cleft lip / patate and congenital cardiac abnormalities are more readily diagnosed and at an earlier gestational age

Invasive Diagnostic Techniques

CVS

Amnio

Cordocentesis

Metaphase Karyotyping

Trisomy 21

Present

Ultrasonography

Serum Markers

Genetic Counseling

Reduced Invasive Procedures

FISH + Karyotype

Sequencing of Maternal Plasma DNA for Aneupoidy

Initially this was focused on the potential of fetal cells in maternal blood. Intact fetal cells have been difficult to isolate and analyze, although research in this area continues.

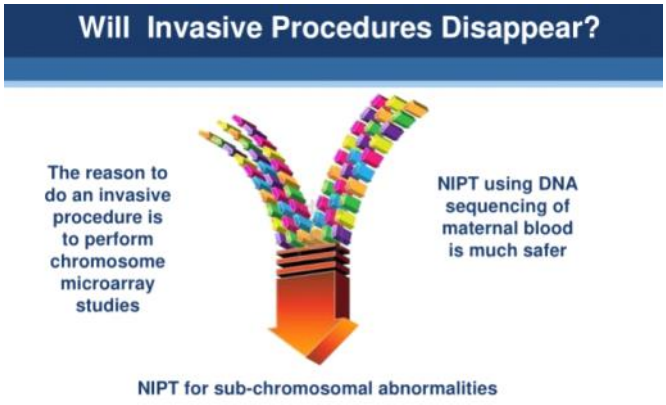
When Lo and colleagues identified male cell-free fetal DNA (cffDNA) in the blood of pregnant women in 1997, this allowed the dream to be realized.

It then took less than 5 years for this observation to be translated into the management of pregnancies at high risk of sex-linked diseases

In less than 15 years later, noninvasive fetal Rhesus D disease typing is routinely offered in Europe to facilitate targeted immuno-prophylaxis by using anti-D immunoglobulin and reducing maternal exposure to human blood products.

Identification of Y-chromosome specific sequences is also standard practice in many European countries for fetal sex determination in pregnancies at risk of serious sex-linked disorders and congenital adrenal hyperplasia.

However, it took major advances in DNA sequencing



NIPT for sub-chromosomal abnormalities

technology that occurred in the first decade of the new millennium before it was possible to detect fetal chromosomal abnormalities without either isolating pure fetal DNA or amplifying a uniquely fetal sequence in maternal blood.

Furthermore, it took a significant change in the way sequencing results were interpreted to advance the field. Rather than to simply sequence the DNA

In 2007, two separate groups hypothesized that if you sequenced, mapped, and counted DNA molecules relative to a reference standard, fetal trisomy should be detectable even in the presence of large amounts of maternal DNA.

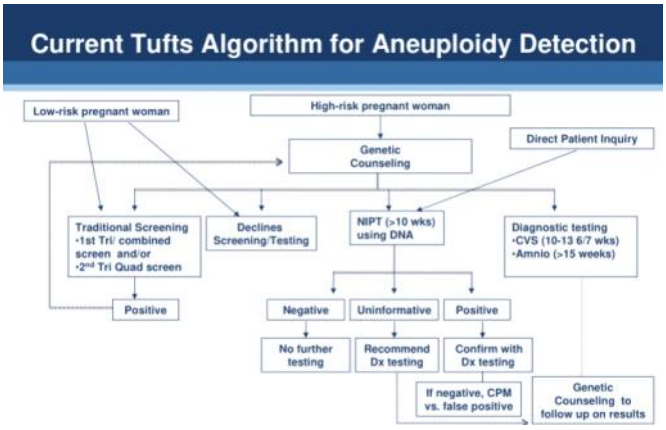
By 2008 proof of principle experiments had been published, which then gave way to large-scale blinded

clinical trials of noninvasively detecting aneuploidy by performing massively parallel sequencing of maternal plasma DNA.

On October 17, 2011, testing became clinically and commercially available in the USA (it had become available earlier in mainland China).

Non Invasive Prenatal Testing (NIPT)

The reason why noninvasive prenatal testing (NIPT) represents a paradigm shift is that it changes the



algorithm, of screening followed by invasive testing ,that has been in practice worldwide for the last 30 years.

Even in the first year of NIPT's integration into clinical care many medical centers are witnessing a significant decline in the number of invasive procedures being performed for aneuploidy.

In addition, every aspect of the current standard of care is being questioned – for example, do we still need to measure maternal serum biomarkers, and what is the place of nuchal translucency measurement?

There is little doubt that tests based on cffDNA provide a readily accessible and generally safer option for prenatal testing that can be offered from 10 until 40 weeks of gestation.

The challenge now is to translate this technology into practice that is accessible to all pregnant women, and in an ethical way that preserves informed parental choice and within the purview of PCPNDT Act

While not increasing overall costs to the heath care system.

Future

Sequencing of Maternal Plasma DNA for Aneupoidy

DNA Microarrays

Sequencing of maternal plasma DNA for the

whole fetal genome

Use of transcriptome to develop

novel fetal therapies

Take Home Message

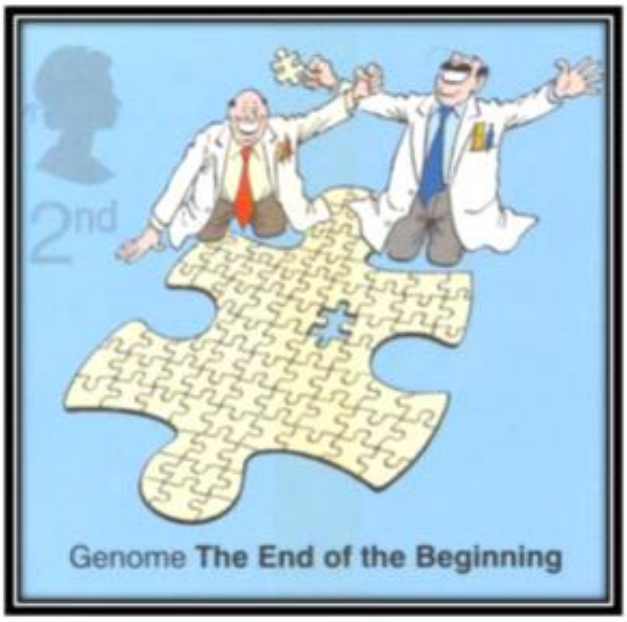
In the years to come, the demands for a high quality fetal medicine and therapy will steadily increase, due to the growth of the three factors:

(1) the continuous improvement in diagnostic and therapeutic capabilities,

(2) the increasing perception of the fetus as a person, resulting from better and more accurate imaging techniques, and

(3) increasing public awareness and demands for advanced fetal medicine and therapy solutions, in the context of the global information society.

The development of imaging techniques and of molecular medicine will allow diagnoses and treatments today unimagined.



talkBACK

MEMORIES

(more on ISPAT website)