

Certification course with
Fetal Medicine Foundation &
Medical Ultrasound Educators

VENUE:

THE SAUJANA
12 km,
Off Sultan Abdul Aziz Shah
Airport Highway Saujana
47200 Subang,
Selangor D.E., Malaysia.
www.thesaujanahotel.com

TIME:

0830 hours - 1700 hours

FIRST TRIMESTER
PREGNANCY SYMPOSIUM

29-30 MARCH 2008 (SATURDAY & SUNDAY)



In Conjunction with:



S o u v e n i r P r o g r a m

Though a teeny bit anti-social, it's something all kids do. But worry not. It's really quite alright.

At least according to Dr. Friedrich Bischinger, an Innsbruck-based lung specialist who claims nibbling on you-know-what makes kids healthier.

In short, a shot of snot he says, boosts body resistance.

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Friso Gold. The little bodyguard that works for mum.

*Niers L, Stasse-Wolthuis M, Rombouts FM and Rijkers GT. Nutritional Support for the Infant's Immune System. Nutrition Reviews, 2007; 65: 347-360

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The gold standard formulation.

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WELCOME NOTE

The advantages of earlier prenatal diagnosis are obvious. High resolution ultrasound scan has largely been responsible for giving us a glimpse at the normal embryonic development. This has brought prenatal testing into the first trimester of pregnancy, together with all its medical, ethical and also financial dilemmas. The symposium aims to discuss the role of ultrasound in the first trimester of pregnancy, with particular emphasis in the detection of fetal abnormalities and the management of problematic pregnancies.

The speakers will highlight essential topics such as the practicalities of the nuchal translucency measurement and the future intricacies of prenatal testing such as pre-implantation genetic diagnosis. There will be a few Live Demo session, where speakers will show participants certain aspects of first trimester scanning. The symposium culminates with a theory and practical assessment, for those who wish to be certified by the Fetal Medicine Foundation (FMF), UK.

It is a pleasure to welcome Dr Pranav Pandya, who is the Director of Fetal Medicine in a renowned hospital in the heart of London. Also, we bid a warm welcome to Professor TK Lau from the Chinese University in Hong Kong. He is the Head of Fetal Medicine Team. Prof TK Lau's enthusiasm and passion in fetal medicine is exemplary.

Selamat Datang! Welcome to all participants and colleagues.

I trust will have an enjoyable and educational weekend.

A handwritten signature in black ink, appearing to read 'PA 3', with a long horizontal line underneath.

Patrick Chia
Course Director
Medical Ultrasound Educators

PROGRAMME SCHEDULE

Day 1

0830-0900	REGISTRATION OF PARTICIPANTS	
0900-0930	Welcome Remarks & Introduction to Course + FMF regulations for certification	pchia
0930-1000	Principles of Screening	pran
1000-1030	COFFEE BREAK	
1030-1100	Nuchal Translucency and chromosomal defects	pran
1100-1120	Live Demo [GE/Medison]	pran
1120-1150	Predicting pregnancy outcomes with Ultrasound (miscarriages & ectopic)	mjyap
1150-1200	Questions & Answers	
1200-1245	Increased Nuchal Translucency with normal karyotype	pran
1245-1345	LUNCH	
1345-1415	Early embryonic development and the normal ultrasound features (2D & 3D)	d ong
1415-1445	Detection of structural abnormalities	pran
1445-1515	Advances in laboratory techniques (QF-PCR: ChromosomesCheck, PGD, free fetal DNA)	yw wong
1515-1545	First trimester biochemistry	sraman
1545-1630	Live Demo [Siemens/Toshiba]	faculty
1630-1700	TEA BREAK	

PROGRAMME SCHEDULE

Day 2

0900-0930	Scanning for aneuploidies – other markers - nasal bone, Tricuspid Flow, Ductus Venosus, Fronto Maxillary Facial Angle	tk lau
0930-1000	Live Demo [Siemens/Toshiba]	tk Lau
1000-1030	3D/4D in the first trimester	pchia
1030-1100	COFFEE BREAK	
1100-1130	Multiple pregnancies and their problems	tklau
1130-1200	The management of pregnancy complications in multiple pregnancy	tklau
1200-1210	Questions & Answers	
1210-1240	Invasive antenatal tests	pchia
1240-1400	LUNCH	
1400-1430	FMF Certification: Hands-on Practical session [GE/Medison]	faculty
1430-1600	FMF Certification: Theory Examination	faculty
1600-1630	TEA BREAK	

THE FACULTY



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Scientific Director
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Bangi, Selangor
Email: yw.wong@dna-laboratories.com

SPEAKERS' PROFILE

Pranav Pandya BSc, MRCOG, MD

Dr Pandya graduated from University College & Middlesex School of Medicine, London in 1988 and worked mainly in London thereafter. He was the MRCOG Gold Medallist in 1997 and was awarded his MD on his original work done in describing the nuchal translucency in the screening Down syndrome in the first trimester of pregnancy. Subsequently, he went to the University of Toronto, Canada, where he stayed for two years as a fellow in maternal-fetal medicine.

Dr Pandya was appointed as a Consultant in Fetal Medicine and Obstetrics in January 2001. Upon Professor Charles Rodeck's retirement, Dr Pandya was recently appointed the Chair of Fetal Medicine in the Department of Obstetrics & Gynaecology, UCL Hospitals, London.

His special interests include first trimester ultrasound and fetal echocardiography. He has published extensively in peer review journals, review articles and chapters in books.

Lau Tze Kin MD, FHKCOG, FRCOG, MBChB

Professor TK Lau graduated from the Chinese University of Hong Kong in 1988. He obtained his M.Med (O&G) from the National University of Singapore in 1993. During the same year he obtained his MRCOG and MHKOG. He was awarded his MD from the Chinese University of Hong Kong with merit in 1999.

Professor Lau currently heads the Fetal Medicine team at the Chinese University of Hong Kong. His current areas of interests include of obstetrics ultrasound in clinical practice, different aspects of prenatal diagnosis and in-utero therapy and also non-invasive prenatal diagnosis. He has published a few hundred papers in peer review journals, reviews and chapters in books.

Amidst his busy schedule he holds many honorary positions of professional bodies including the Chairman of the Hong Kong Fetal Medicine Foundation, Board Member of the Fetus As A Patient International Society and a council member of the Hong Kong College of Obstetricians and Gynaecologists, to name a few.

Douglas Ong MRCOG

Dr Douglas Ong is a consultant Obstetrician & Gynaecologist at the Mount Elizabeth Medical Centre in Singapore. An internationally recognized expert in fetal medicine and an avid proponent of ultrasound, Dr Ong is the founding member of the Medical Ultrasound Society of Singapore where he remains active as the current Honorary Secretary. He is an examiner in postgraduate ultrasound of the Graduate School of Medical, National University of Singapore. He also sits on the board of the Postgraduate Diploma in Ultrasound. He is a clinical tutor of the Faculty of Medicine, National University of Singapore and is a member of numerous professional bodies. He has an interest in ultrasound education, particularly with his wide experience in Obstetrics and Gynaecology. He has published widely in peer review journals and has written articles and chapters in books.

Despite running a highly successful private practice, he continues to spend a good deal of time imparting his ultrasound and fetal medicine skills on the international circuit.

Raman Subramaniam MD, FRCOG, FRCPI

Dr Raman had been a lecturer, Associate Professor and Professor at the Department of Obstetrics & Gynaecology, University Malaya. After many years, he left that institution to work as the Clinical Dean of the International Medical University, where, together with a team, pioneered the establishment of the Clinical School in Seremban, Negeri Sembilan, Malaysia.

He sits on the Editorial Board of the Journal of Paediatrics, Obstetrics & Gynaecology and the Journal of Ultrasound. He has published extensively and has authored more than a hundred research papers, articles and chapters in books.

His interest had been the fetal growth patterns in Malaysian women, where he obtained his MD thesis. The growth charts from this work are now commonplace in many obstetric units in Malaysia. He continues his avid interests in fetal medicine and left the IMU in July 2002, when he joined the Fetal Medicine & Gynaecology Centre. His other area of interest is the menopause. Apart from his clinical commitments, he has frequent invitations to speak at various conferences both locally and abroad.

Wong Yong Wee PhD

In 1995, Dr Wong graduated from University Kebangsaan Malaysia with a BSc (Hons) in Microbiology. He obtained his PhD from the University of Singapore and was a post-doctoral fellow in the Centre of Molecular Neurobiology, Hamburg for 3 years. During his time in Germany, he was awarded the Postdoctoral Fellowship, ZMNH Hamburg and the Long Term research Fellowship, Alexandra von Humboldt Foundation. He worked at the Singapore Eye Research Institute for 3 years as a Research Fellow. He is well experienced in setting up molecular medicine laboratories and well trained in various DNA microarray platform technology. He specializes in real time PCR and has extensive hands-on experience in molecular biology techniques including DNA and RNA.

He is currently the Scientific Director of DNA Laboratories. With the help of his colleagues, DNA Laboratories was awarded the Bionexus status recently and managed to secure RM 2.5 million to further his work in areas of women's health, offering DNA analyses and diagnoses.

Yap Moy Juan MRCOG

Dr Yap graduated from Manipal Academy of Higher Education, India in 1998. She went on to obtain her MRCOG in 2002. Her training in obstetrics and gynaecology was mainly done in Seremban Hospital. It was in Seremban Hospital that her interests in fetal medicine blossomed and later joined the Fetal Medicine and Gynaecology Centre in 2005. Her main interests are in the management of high risk obstetric cases, fetal medicine and laparoscopic surgery.

She has published widely in peer review journal, review articles and books. She has also translated medical books and articles into Mandarin.

Patrick Chia MRCOG

Having spent more than 15 years in the United Kingdom, where he obtained both his undergraduate and postgraduate degrees, Dr Chia returned to Malaysia in 1995. He served as

a Lecturer in the Department of Obstetrics & Gynaecology, University Malaya Medical Centre (UMMC). At UMMC, he was pivotal in setting up the Maternal-Fetal Division. After spending 3 years at UMMC, he was appointed Associate Professor in the Department of ObGyn at International Medical University. Together with a small team in the faculty, he saw the pioneering batch of graduates from the Clinical School recently.

He has contributed many publications in peer review journals, chapters in books and review articles. He has edited and authored several books. His passion includes the teaching of ultrasound and promoting awareness and excellence in the field of fetal medicine. His other areas of interest include recurring pregnancy loss.

Dr Chia currently works in Fetal Medicine & Gynaecology Centre.

ABSTRACTS

Predicting pregnancy outcomes with ultrasound

Yap Moy Juan, Fetal Medicine & Gynaecology Centre, Kuala Lumpur

Ultrasound plays a crucial role in the evaluation of normal and abnormal pregnancies. Improved image resolution has been mainly responsible for the increase in diagnostic accuracy, therefore helping clinicians manage their patients better. Vaginal bleeding is an early symptom that something is wrong with a pregnancy. Often patients seek reassurance from their doctors.

Early ultrasound findings will prognosticate a pregnancy and certain features will determine which of these pregnancies are more likely to fail and which are likely to progress normally. The lecture will highlight the normal ultrasound features of a viable pregnancy and will also discuss the predictors of pregnancy failure.

The diagnosis of an ectopic pregnancy can be made early with the help of hormonal markers. This would invariably reduce the maternal mortality and morbidity associated with it.

Early embryonic development and the normal ultrasound features (2D & 3D)

Douglas Ong, Mount Elizabeth Hospital, Singapore

Sonoembryology has been used to describe the developmental changes seen on ultrasound scan in the first trimester of pregnancy. This detailed anatomical survey is now possible due to the high resolution transducers utilized with transvaginal sonography. It is crucial to be familiar with the "normal" development of the embryo and fetus for those embarking in first trimester ultrasound. This lecture will highlight the major embryological landmarks during the first trimester of pregnancy. The 2D and 3D features of the normal fetus in the first trimester will be discussed.

Advances in laboratory techniques

(QF-PCR: ChromosomesCheck, PGD, free fetal DNA)

Wong Yong Wee, DNA Laboratories, Bangi, Selangor.

With widespread screening of the fetus, the pattern of referral for prenatal diagnosis has changed. When invasive prenatal diagnosis is carried out, genetic analysis of the tissue extracted is essential in establishing a diagnosis. This occurs in about 1 in 200 newborns and is responsible for a significant number of congenital malformations and mental subnormality. Karyotyping is still the gold standard and is highly reliable for aneuploidy and large structural rearrangement (>5-10 million base pairs). For amniotic fluid, the accuracy is between 99.4 to 99.8% and for cvs, 97.5 to 99.6%. Its main limitation, however, is the delay of having to culture the cells. RAD (Rapid Aneuploidy Diagnosis) consists of FISH and QF-PCR and can be done in 2 working days. Both are highly sensitive and specific for aneuploidies. QF-PCR can identify maternal cell contamination and 20 to 30% of mosaics. It is more cost effective and is currently widely used across Europe. With sensitive PCR methods to detect single copy of DNA, the detection of chromosomal abnormalities in Pre-implantation Genetic Detection (PGD) with single cell is now possible. Newer techniques are multiplex ligation-dependant probe amplification (MLPA) and Bacterial artificial chromosome (BAC). BAC uses array-based comparative genomic hybridization (aCGH). These techniques require further evaluation and needs to be cost effective. The identification of fetal DNA in maternal circulation, first reported in 1997, has opened up a new frontier in non-invasive sampling & prenatal diagnosis. The benefits are obvious and the possibility of non-invasive prenatal diagnosis of genetic disorders will become commonplace in the near future.

First trimester biochemistry

S Raman, Fetal Medicine & Gynaecology Centre, Kuala Lumpur.

An important cause of perinatal deaths and childhood handicaps is chromosomal abnormalities. Definitive diagnostic methods are invasive. By contrast, the screening tests are non invasive and involves estimation of maternal serum fetoplacental products. Traditionally, this is done in the second trimester and is capable of detecting 90% of opened neural tube defects, 68% of Down syndrome and 65% of Trisomy 18.

The current first trimester screening uses the ultrasound scan to measure nuchal translucency, detect the nasal bone, assess for tricuspid regurgitation and ductus venosus Doppler. The ultrasound combined with maternal serum biochemistry consisting of PAPP-A and free Beta-hCG has been shown to increase the detection rate of Trisomy 21, 18 and 13. More recently a new marker, ADAM 12 which is a disintegrin and metalloprotease has emerged as a potential marker for the first trimester screening for Trisomy 18 and 21. Its potential as a second trimester marker is also being evaluated.

Scanning for aneuploidies – other markers - nasal bone, Tricuspid Flow, Ductus Venosus, Fronto Maxillary Facial Angle

TK Lau, Department of Obstetrics and Gynaecology, Chinese University of Hong Kong

Nuchal translucency in the first trimester has been shown to be a very useful marker for fetal Down syndrome. Using this marker alone, it is possible to achieve a 75-80% detection rate at a 5% false positive rate for fetal Down syndrome. The discovery of newer first trimester markers enables us to further increase the detection rate, or to lower the FPR. Among the newer markers, absence of fetal nasal bone is probably the most important. In the talk, I will show you the evidence of how fetal nasal bone assessment could improve the screening program, and how fetal nasal bone should be assessed. In this talk, I will also discuss briefly on other markers in particular tricuspid regurgitation and abnormal waveform of the ductus venosus.

3D 4D in the first trimester of pregnancy

Patrick Chia, Fetal Medicine & Gynaecology Centre, Kuala Lumpur

Three-dimensional ultrasonography has recently become fully established mainly due to the development of exceptionally fast computer processors. This has allowed the clinician to catch a detailed glimpse at the developing embryo and therefore the diagnosis of fetal anomalies can be made much earlier.

The newer technology of the four-dimensional or the live three-dimensional ultrasound, opens new opportunities to observe fetal movements, behavior and facial expressions. The lecture will discuss the value of the 3D and 4D technologies in assessing the fetus in early pregnancy.

Multiple pregnancies and their problems and the management of pregnancy complications in multiple pregnancies

TK Lau, Department of Obstetrics and Gynaecology, Chinese University of Hong Kong

In this talk, I will focus on the complications of monochorionic (MC) twin pregnancies. Compared to dichorionic twins, MC twins not only have higher perinatal mortality and morbidity rates, but also are associated with the development of MC-twin specific complications, which include twin-twin transfusion, discordant fetal growth, discordant fetal abnormalities, monochorionic

twin, conjoint twin and acardiac twin. In this talk, I will discuss in details the pathology, diagnosis, monitoring and management of these complications.

Invasive Antenatal tests

Patrick Chia, Fetal Medicine & Gynaecology Centre, Kuala Lumpur

Invasive antenatal tests include amniocentesis, chorionic villous sampling and fetal blood sampling. The three procedures will be discussed in detail during the course of the lecture. Data from the years 2000 to 2007 will be presented. During the seven year period, there were 1285 invasive diagnostic procedures done at the Fetal Medicine and Gynaecology Centre. Nine hundred amniocenteses, 335 chorionic villous sampling and 50 fetal blood sampling were performed. Cultural differences were obvious, with almost 80 % (1002/1285) uptake of invasive procedures from the Chinese ethnic group. There had been a gradual decline in amniocentesis done because of advanced maternal age and a positive triple or double test still remains as one of the major indications for amniocentesis. CVS was done mainly for thalassaemia diagnosis and the need to perform fetal blood sampling has decline dramatically over the years. Complication rates were 1.5% for cvs (5/335) and 0.3% (3/900) which is in tandem with the internationally quoted rates.

Principles of screening; Nuchal Translucency and chromosomal defects; Increased Nuchal Translucency with normal karyotype; Detection of structural anomalies

Pranav P Pandya, University College London Hospitals, Huntley Street London WC1E 6DH

[The notes of these lectures are found in the relevant chapters of the accompanying book; The 11-13⁺⁶ weeks scan published by the FMF].

The following are the more recent references:

Increased nuchal translucency thickness and normal karyotype: time for parental reassurance. *Bilardo CM, Müller MA, Pajkrt E, Clur SA, van Zalen MM, Bijlsma EK. Ultrasound Obstet Gynecol. 2007 Jul;30(1):11-8.*

Long-term outcome of children born after a first-trimester measurement of nuchal translucency at the 99th percentile or greater with normal karyotype: a prospective study. *Senat MV, Bussières L, Couderc S, Roume J, Rozenberg P, Bouyer J, Ville Y. Am J Obstet Gynecol. 2007 Jan;196(1):53.e1-6.*

By how much does increased nuchal translucency increase the risk of adverse pregnancy outcome in chromosomally normal fetuses? A study of 16,260 fetuses derived from an unselected pregnant population. *Westin M, Saltvedt S, Almström H, Grunewald C, Valentin L. Ultrasound Obstet Gynecol. 2007 Feb;29(2):150-8.*

Frontomaxillary facial angle in chromosomally normal fetuses at 11⁺⁰ to 13⁺⁶ weeks. *Borenstein M, Persico N, Kaihura C, Sonek J, Nicolaidis KH. Ultrasound Obstet Gynecol. 2007 Oct;30(5):737-41.*

FMF REGULATIONS

CERTIFICATION OF COMPETENCE in the 11-13⁺⁶ weeks scan

The Fetal Medicine Foundation (FMF) has set up a process for certification in the 11-13⁺⁶ week scan, to ensure that all those performing this scan have been adequately trained, and that high standards are maintained by continuous education and audit.

Having obtained the Certificate of Competence in the 11-13⁺⁶ weeks scan, the doctor/sonographer will be entitled to receive the FMF software for the calculation of risk of Down syndrome by a combination of maternal age, nuchal translucency measurement, nasal bone, and first trimester maternal serum biochemistry, serum β -hCG and PAPP-A. The accredited doctor/sonographer be included on the FMF's list of "Accredited Sonographers" and the hospital/clinic of the doctor/sonographer will be included in the FMF's list of "Registered Centres".

The only condition for ongoing certification and use of the software is provision of NT data and images by the Centre and / or sonographer for the purposes of audit.

The Certification process

The requirements for Certification are:

1. Attendance of an FMF recognised theoretical course and successful completion of the course exam;
2. Submission of a logbook of 10 images demonstrating your measurement of nuchal translucency;
3. Practical assessment.

The theoretical course

The aim of this is to introduce you to the concepts of screening for chromosomal abnormalities in the first trimester, and other issues that arise from the 11-13⁺⁶ weeks scan. The course content will include:

- Nuchal translucency and chromosomal defects;
- Increased nuchal translucency with normal karyotype;
- Pathophysiology of nuchal translucency;
- Diagnosis of fetal abnormalities at the 11-13⁺⁶ weeks scan;
- Determination of chorionicity and diagnosis and management of multiple pregnancy at the 11-13⁺⁶ weeks scan
- Assessment of Nasal Bone
- Assessment of Tricuspid Flow

The course study material is "The 11-13⁺⁶ week scan" book (Edited by the FMF) and this will be given to you at the beginning of the course.

At the end of the course there is a short multiple choice questionnaire. This is designed to ensure that you have understood the concepts of the course, rather than to test your memory of the information and the course book can be used for reference!

The logbook

This consists of ten thermal images, placed loosely in an envelope, and submitted to the FMF. Each image is assessed on the following criteria:

1. Image size (only the fetal head, neck and upper thorax on screen)
2. Head position (neutral, not flexed or extended)
3. True sagittal section obtained (rather than oblique)
4. Caliper position (on the borders of the translucency)
5. Area of measurement (at the widest point of the translucency thickness)

It is expected that each of the above criteria are met in at least 8 of the 10 images before the logbook can be passed. If this standard is not met in 3-5 images, the sonographer will be asked to submit another 5 images demonstrating a definite improvement before the logbook can be passed. If this standard is not met in more than 5 images, another 10 images will be required.

If you have not yet registered with the FMF please use the form on page 15. Complete the form and send it to the specified address together with any other information you are sending to us. It is vital that this form should be completed accurately to enable us to identify you in the future.

Once completed, the logbook should be sent to Patricia Colombo who co-ordinates the certification process. Please indicate clearly and legibly your name, address and which theoretical course you have attended on your logbook.

Certification

After attendance of the theoretical course and practical training and successful completion of the logbook, the doctor/sonographer will be sent the Certificate of Competence in the 11-13⁺⁶ weeks scan.

Please also note:

- All the sonographers performing scans and using the FMF software must hold the FMF Certificate of Competence in the 11-13⁺⁶ weeks scan
- NT data and images must be sent to the FMF for ongoing audit after the first 6 months of use and periodically thereafter.

Once the Sybase Anywhere license fee has been paid, the centre will receive the FMF risk calculation software and entered onto the FMF list of Registered Centres.

In order to obtain the FMF risk calculation software you must first purchase a Sybase Anywhere license (see below).

The practical assessment

Assuming your logbook is satisfactory, you will be asked to attend a practical session for practical assessment. This can be done at a training centre or with a FMF certified trainer. The training centres and certified trainers are units and/or individuals with extensive experience in performing the 11-13⁺⁶ weeks scan that have consistently demonstrated good results from their audit. Each has agreed to act as training centres on behalf of the FMF in order to give you the opportunity to see at first-hand how the 11-13⁺⁶ weeks scan is conducted, particularly with regard to the pre and post test counseling of the patient, and to enable your own technique to be assessed in practice. This will be an informal assessment, but you will be expected to scan at least one patient to demonstrate your competence in the 11-13⁺⁶ weeks scan. Having

successfully completed the practical assessment, a form recommending you for Certification will be completed by your examiner and sent to the FMF. On receipt of this, you will be issued with the Certificate of Competence in the 11-13⁺⁶ week scan and you will be offered the FMF software (free-of-charge). However you will be required to acquire the FMF license in order to use the software.

Sybase License Fee

The FMF risk calculation software requires a license for Sybase Anywhere. This one off cost of Euro50 per license can be paid online using a credit card.

NT Quality Review and Ongoing Certification

Each registered centre must be audited by the FMF six-months after the NT screening programme is launched.

The audit involves:

- Assessment of the distribution of measurements of each sonographer
- Examination of the quality of five random images from each sonographer

An audit is considered to be satisfactory if 40-60% of NT measurements are above the median and the images are of a high quality. Sonographers or centres passing their audit will be re-audited and re-licensed on an annual basis thereafter. The NT distribution cannot be assessed if fewer than 30 scans have been performed, but in this situation an individual can still pass their audit if their images are satisfactory.

Accredited Sonographers list

All sonographers passing their FMF audit will be included on the Accredited Sonographers list. Individuals performing less than 30 NT scans per year and those that are not actively involved in an NT screening service can remain accredited, as long as they submit five satisfactory NT images annually.

Registered Centres list

Centres scanning more than 50 patients per year and where more than 75% of the scans are performed by sonographers who have passed their audit and are on the Accredited Sonographers list will be included on the FMF Registered Centres list. Those performing less than 50 scans a year can continue to have the programme license if the images that they submit are of acceptable quality, but they will not be included on the FMF Registered Centres list.

Management of the Under-performing Sonographers

If the NT distribution falls outside the satisfactory range:

- Advice will be given on how to improve NT technique, based on the review of images
- The name of the sonographer will be removed from the Accredited Sonographer list
- A new audit will be carried out in three to six months
- The sonographer will only be reinstated on the Accredited Sonographer list once the audit is considered satisfactory

- The programme license will be extended on the first occasion that it is due for renewal after the audit is noted to be sub-standard, but it will not be renewed the following year if there has been no improvement to achieve an acceptable standard

Centres excluded from the Registered Centres list will only be reinstated once efforts are made to ensure that everyone is accredited. The centre license will not be renewed the following year if they fail to do so. In centres with more than one sonographer where an individual sonographer fails to achieve the required standard, it will be the responsibility of the other sonographers to retrain and supervise the underperforming sonographer until a satisfactory level is achieved.

Re-licensing Arrangements

Once the programme license has been revoked, it is suggested that selected sonographers within that centre undergo a period of retraining and re-certification. Once this has been done, they may re-apply for the programme license, but it must be clearly noted that only they, and not unaccredited colleagues, may use the risk calculation software and that the above stringent audit policy will apply to all subsequent audits.

Internal Audit

In addition to the FMF audit, all centres are encouraged to perform their own internal quality assurance on a monthly basis by:

- “Spot-checking” three images from each sonographer, selected entirely at random
- Examining the NT distribution of each individual sonographer using the automated audit module incorporated within the FMF risk calculation software.

The FMF is willing to provide additional support to facilitate this process and advise if the results are suboptimal.

Contact details

Submission of logbooks and any questions or comments about the 11-13⁺⁶ weeks scan, should be addressed to:

NT Certification
The Fetal Medicine Foundation
137 Harley Street
London W1G 6BG, UK

Tel +44 (0)20 7034 3070
Fax +44 (0)20 7034 3071
Email: certification@fetalmedicine.com



Fetal Medicine Foundation

137 Harley Street
London
W1G 6BG
United Kingdom

Registration Form

Please complete this form and return it to us at the address supplied below. Please note that the information supplied here will remain confidential and will only be used by us in order to correspond with you. It is important therefore that the contact details you supply here are accurate and as complete as possible because this will be the information which we will use to communicate with you.

PLEASE INFORM US OF ANY CHANGE OF ADDRESS OR OTHER CONTACT DETAILS.

(Please print clearly)

Title (tick one box only) Mr Ms Dr Prof

Surname/Last Name

Occupation (tick one box only) Ob/Gyn Radiologist Sonographer
 Dr-Sonographer Midwife-Sonographer Nurse-sonographer

Home Address

Postcode Country

Home Tel* Home Fax*

Mobile

Email

* Please supply area code and number only e.g. (012) 3456 7890

If you already know the scanning centre that you will be working in, please provide the centre name, address and the 4-digit FMF Centre ID which will enable us to add your name to the FMF risk calculation software license for that centre.

Centre Name

FMF Centre ID (This is a 4-digit number – please check with the centre coordinator)

Centre Address

Postcode Country

Please post this form together with your logbook images or any other information to:

The Fetal Medicine Foundation
Attn: Certification Team
137 Harley Street
London W1G 6BG
United Kingdom

ACKNOWLEDGEMENTS

We wish to thank the following companies for their support (in alphabetical order)

1. Abex Toshiba
2. Cryocord
3. DNA Lab / Perkin Elmer
4. Diagnostica GE
5. Fonterra
6. Gideons Medison
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Information for patients:

First Trimester Screening for Down's syndrome

What is Down's syndrome?

Down's syndrome is genetic disorder caused by the presence of an extra or part of chromosome 21 (Trisomy 21). It is the commonest cause of severe learning disability in children. It is characterized by both mental and physical impairment. Individuals with Down's syndrome have the typical facial features including oblique eye fissures with epicanthic folds on the inner corner of the eyes, flat nasal bridge (due to absent nasal bone), white spots on the iris known as Brushfield spots and a protruding tongue. About 30% of babies with Down's syndrome are born with a serious heart defect. Most individuals have mental retardation in the mild (IQ 50–70) to moderate (IQ 35–50) range.

About 50% of Down's syndrome pregnancies will not survive to term. However, nine out of ten affected babies who reach term will survive their first year. Most people with Down's syndrome live beyond 50 and most develop pathological changes in the brain associated with Alzheimer's disease after the age of 40.

Genetics

A typical human karyotype is designated as 46,XX, or 46,XY, indicating 46 chromosomes (or 23 pairs) with an XX in females and 46 chromosomes with an XY in males. Approximately 95% of observed Down syndrome is caused by a meiotic non-disjunction event (due to maternal age). This means that a gamete (i.e., a sperm or egg) is produced with an extra copy of chromosome 21; the gamete (usually maternal) thus has 24 chromosomes. When combined with a normal gamete from the other parent, the embryo now has 47 chromosomes, with three copies of chromosome 21 (Trisomy 21; 47XX, +21) (See Figure 1).

2-3% of observed Down's syndrome do not show the maternal age effect. In these cases the extra chromosome material results from Robertsonian translocation. The long arm of chromosome 21 is attached to another chromosome, often chromosome 14 (45,XX, t(14;21q)) or itself (called an isochromosome, 45,XX, t(21q;21q)), giving rise to a gamete with an extra chromosome 21. This is often referred to as familial Down syndrome. On the other hand, when some of the cells in the body are normal and other cells have trisomy 21, it is called mosaic Down syndrome (46, XX / 47, XX, +21). This is the cause of 1–2% of the observed Down syndrome.

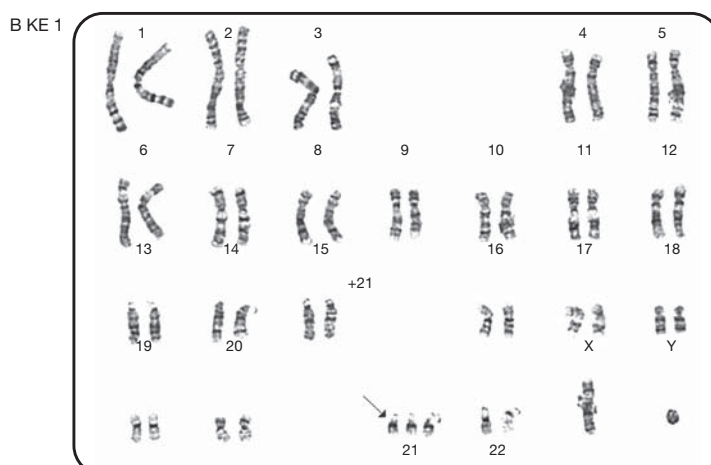


Figure 1: A Karyogram showing an embryo with three copies of chromosome 21 (Trisomy 21; 47XX, +21)

Incidence

The incidence of Down syndrome is estimated between 1 in 800 and 1 in 1000. Maternal age influences the chances of conceiving a baby with Down syndrome (*Figure 2*). At maternal age 20 to 24, the probability is 1 in 1500; at age 40 the probability is 1 in 60, and at age 49 the probability is 1 in 11.

Although the probability increases with maternal age, 80% of children with Down syndrome are born to women under the age of 35, reflecting the overall fertility of that age group. Recent data also suggest that paternal age also increases the risk of Down syndrome manifesting in pregnancies in older mothers.

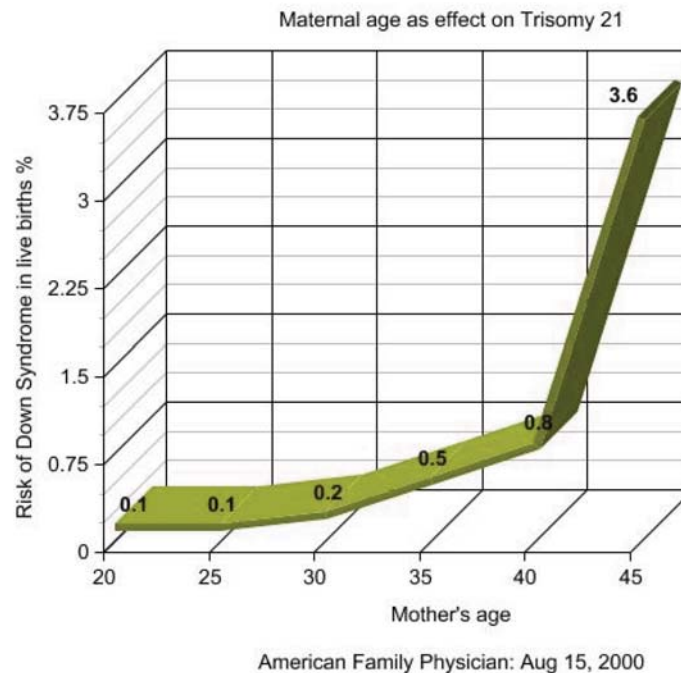


Figure 2: The risk of Down syndrome with maternal age

Prenatal testing

Prenatal testing (*Figure 3*), involves both non-invasive and invasive tests. The invasive tests include amniocentesis, chorionic villous sampling and fetal blood sampling. They are called diagnostic tests and involve sampling the fetal DNA for analysis. Since they are invasive tests there is a risk of miscarriage (between 0.5-2 %).

The non-invasive tests are the screening tests. They are not 100% accurate (sensitive) and have a false positive rate of 5%. However, the screening tests do not jeopardize or pose any risks to the pregnancy as they are non-invasive. Examples of non-invasive tests include ultrasound scan and maternal serum biochemistry.

Historically, maternal serum biochemistry measures levels of chemicals or hormones in maternal blood in the second trimester of pregnancy. These tests include the triple test and the quadruple test. A small amount of maternal blood is taken and analysed for the concentration of different chemicals or hormones. The triple test measures the maternal serum alpha-fetoprotein (a fetal liver protein), estriol (a pregnancy hormone), and human chorionic gonadotropin (hCG, a pregnancy hormone). The quadruple test measures maternal serum alpha-fetoprotein, estriol, human chorionic gonadotropin, and inhibin-A. The accuracy (sensitivity) is 71% for the triple test and 78% for the quadruple test. This means that the triple test will pick up 2 out of 3 Down syndrome but misses 1 in 3. On the other hand, the quadruple test will detect almost 80% of Down syndrome but misses 1 in 5 cases of Down syndrome (*Table 1*).

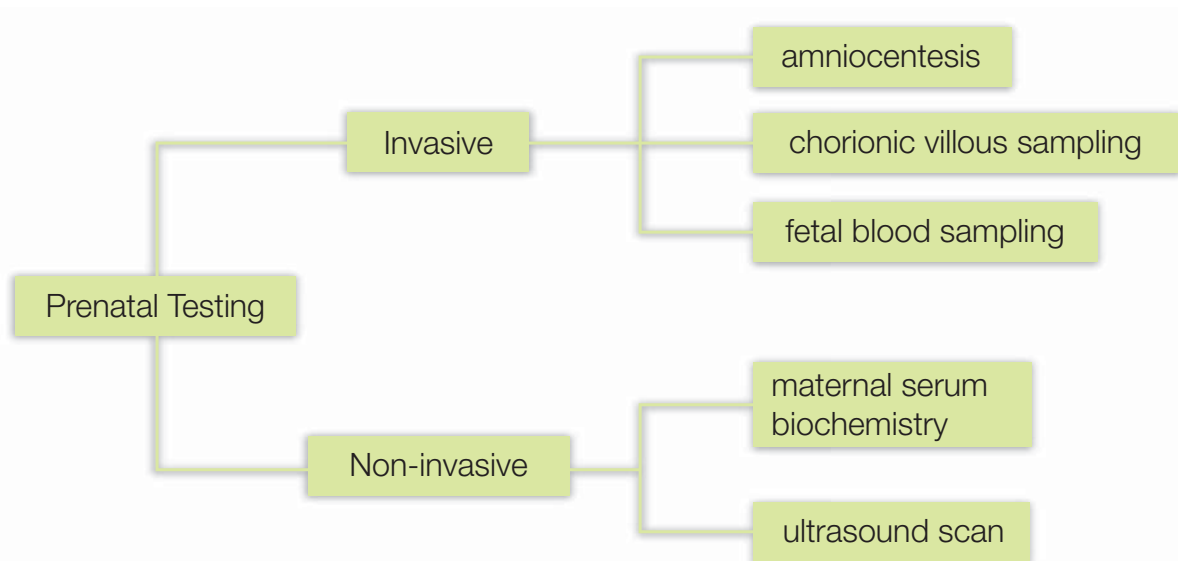


Figure 3: The extent of prenatal testing for Down syndrome

Method of screening	Timing of test (weeks)	Detection Rate (Sensitivity/Accuracy)
Maternal Age	14-22	30%
Maternal Age + AFP	14-22	40%
Double test (using free β -hCG)	14-22	62%
Triple test (using free β -hCG)	14-22	71%
Quadruple test (using free β -hCG)	14-22	78%

Table 1: The detection rates of different methods of Down syndrome screening in the second trimester

First trimester testing

Advances in computer technology have enabled the introduction of higher resolution ultrasound machines. This has allowed doctors to examine the normal developing embryo / fetus in detail very early on in pregnancy. Diagnosis of fetal abnormalities early in the first trimester is therefore, now possible.

Early ultrasound scan done between 11 and 13 weeks 6 days (crown-to-rump length between 45 and 84 mm) of pregnancy involves measurement of the nuchal translucency (fluid-filled space beneath the skin behind the neck – *Figure 4*). A large nuchal translucency measurement may be an indication of chromosomal abnormality (such as Down syndrome) or heart problem in the baby.

During the nuchal scan, the nasal bone is also checked to see if it is present. Recent studies have shown that the nasal bone is absent in 3 of 4 babies with Down syndrome during this time. The general anatomy will be checked to look for any physical (structural) abnormalities. The head, limbs, spine and the abdomen will be examined. The nuchal translucency is measured using the abdominal probe. This requires a relatively full bladder but not to the extent that you feel uncomfortable. However, a vaginal scan is done in some cases. You will be asked to empty your bladder and the measurement is repeated with a trans-vaginal probe.

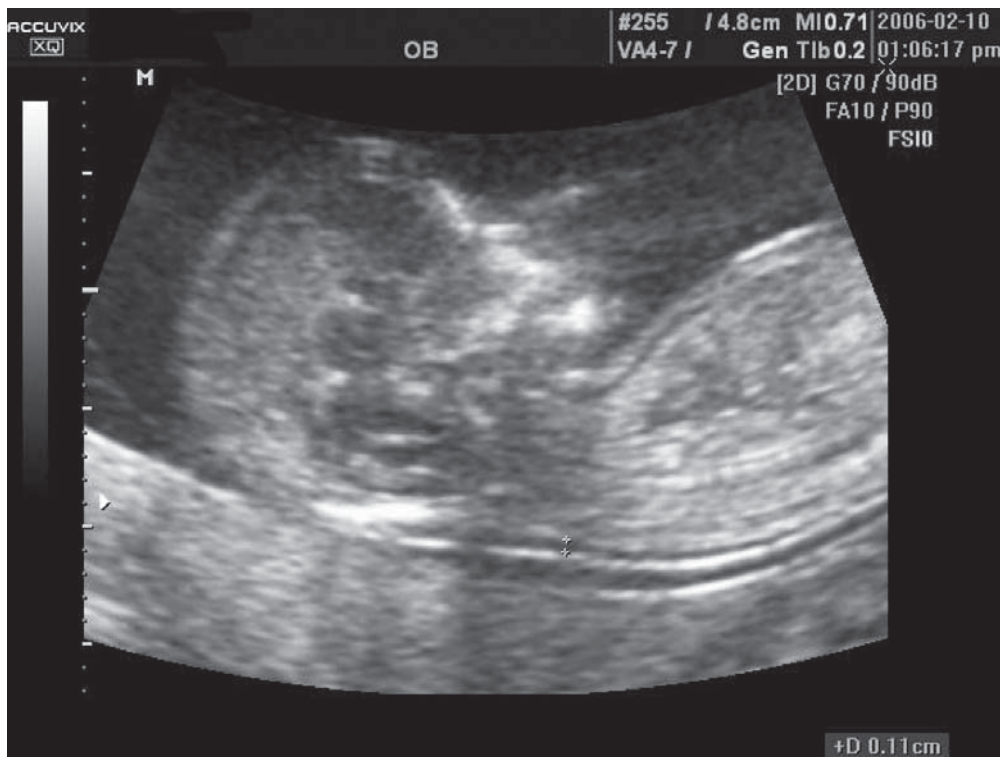


Figure 4: The nuchal translucency measurement

The combination of tests

Ten mls of blood is drawn from the arm to measure the levels of two proteins normally found in all pregnant women. Pregnancy Associated Plasma Protein-A (PAPP-A) and free beta-subunit of human Chorionic Gonadotrophin (free β -hCG) comes from the placenta. Their concentration in the blood varies with gestation (PAPP-A increases and free β -hCG decreases). However, in Down syndrome pregnancies, PAPP-A is low and free β -hCG is high.

The nuchal translucency measurement is entered into a dedicated computer program licensed by the Fetal Medicine Foundation (FMF UK), together with other parameters such as the crown-to-rump length, maternal age and weight. The blood levels of the 2 proteins are also entered into this program. The computer would then calculate a personalized risk based on these parameters.

The combination of tests is called “the first trimester screening” (FTS) and is much more accurate than the individual tests. The combination of tests improves the detection of Down syndrome (Table 2).

In many developed countries the maternal age is 35 years or more in about 20% of pregnancies. Consequently, screening for Down syndrome by maternal age could identify 50% of affected fetuses after amniocentesis in 20% of women. The alternative is to screen by a combination of maternal age, serum biochemistry and ultrasound examination at 11⁺⁰ to 13⁺⁶ weeks (FTS). This will allow a 10-fold reduction in the need for invasive testing with a doubling in detection rate of Down syndrome.*

* Nicolaidis KH. Some thoughts on the true value of Ultrasound. Editorial. *Ultrasound Obstet Gynecol* 2007; 30: 671–674

Method of screening	Detection Rate (Sensitivity/Accuracy)
Maternal Age + PAPP-A + free b-hCG	62%
Maternal Age + NT	72%
Maternal Age + PAPP-A + free b-hCG + NT (+ NB)	85% (>90%)

Table 2: The combination of tests improves the detection of Down syndrome in the first trimester.
 NT = nuchal translucency, NB =nasal bone

It is essential to know that a screening test does not provide a diagnosis. It predicts the likelihood of a problem. The FTS will therefore tell you if your risk of Down syndrome is increased.

Interpreting the results

The results can either be “screen-positive” or “screen negative”. A cut-off level (at a 5% false positive rate) of 1 in 250 is taken. Therefore, by combining maternal age together with the levels of PAPP-A, free β -hCG and the NT measurement, those in the high risk “screen positive” group have an estimated risk of 1 in 250 or greater.

About 1 in 33 women screened will have a “screen-positive” result. However, most of these women will not have affected pregnancies. Those with a “screen positive” result are offered a diagnostic test (see below) to confirm if the pregnancy is affected. A “screen positive” result does not mean that your baby has Down syndrome. It means that probability of a Down syndrome baby is increased.

A “screen-negative” result, however, means that the risk of a pregnancy with Down syndrome is not high but it does not exclude the possibility of an affected pregnancy.

Diagnostic tests

If the result is screen-positive for Down syndrome then diagnostic tests such as chorionic villous sampling or amniocentesis is offered.

“Diagnostic tests” are invasive tests which are offered to mothers considered to be at high risk of having a baby with a chromosomal problem. The diagnostic test provides you with a definitive answer as to whether your baby is truly affected.

Chorionic villous sampling (CVS) involves removing a small amount of cells from the placenta (afterbirth). Cells are obtained by passing a fine needle through the abdomen or occasionally through the vagina, into the placenta. It can be done from 11 weeks onwards. An advantage of this test is that a definitive result is available sooner. There is a 1-2% risk of miscarriage.

Amniocentesis (*Figure 5*) involves removing a small amount of the fluid that surrounds the baby (amniotic fluid). Skin cells from within this fluid are filtered and examined. Amniocentesis can be performed from 16 weeks onwards. It is also associated with a miscarriage rate of between 0.5 and 1%.



Figure 5: An amniocentesis involves removing a small amount of amniotic fluid which surrounds the fetus.

The Results

Samples of chorionic villous (placenta) or amniotic fluid, which contain DNA of the baby, are sent to the laboratory for analysis. The gold standard test is a process called karyotyping which involves culturing the baby's cells, and this takes about 10 to 14 days. This method of chromosomal analysis is very reliable and will exclude all chromosomal abnormalities including Down syndrome (Trisomy 21), Edward's syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13). Subtle abnormalities such as translocation, where part of a chromosome is transferred to another chromosome, may also be detected.

A newer method of laboratory testing called QF-PCR (Quantitative Fluorescence Polymerase Chain Reaction) takes only 2 to 3 days. However, this is very specific for the commonest abnormalities such as Trisomies 21, 18 and 13 including abnormalities of the X and Y chromosomes. Markers specific for chromosome 13, 18, 21, X and Y are used to measure the number of these chromosomes in the baby.

Other information from the Combined Test

FTS will identify a number of other birth defects in addition to Down syndrome. These include cardiac defects, other chromosome abnormalities such as Trisomy 18, Trisomy 13 and a variety of other rarer genetic disorders.

It is essential that those women with a normal chromosome analysis after an amniocentesis or cvs should be scheduled for a detailed fetal echocardiogram at 20 weeks gestation to look for cardiac abnormalities. These babies should also be monitored for growth problems in the third trimester.

Conclusions

Down syndrome is a genetic disorder where there is an extra chromosome 21 and is the commonest cause of mental and physical impairment. Any woman may have a baby with Down syndrome at any age. However, the chance in having a baby with Down syndrome gets progressively higher as a woman gets older.

Down syndrome can be diagnosed by analyzing the baby's DNA obtained from amniocentesis or chorionic villous sampling but these procedures carry a risk of miscarriage. A combination of tests (using ultrasound scan and maternal blood test) in the first trimester is now available to detect Down syndrome with over 90% sensitivity (accuracy) with no risk to the baby.

Patrick Chia © FMGC 2008

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