

Early Pregnancy

Lecture for the Academic Year 2018 – 2019
Defined Learning Objectives

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Disclosure



G E S E A

**Chairman Gynaecological Endoscopic
Surgery Education and Assessment**



Womana Medical Services
Director
www.womana.com.cy



**European Academy
of Gynaecological Endoscopic Surgery**
Scientific Director
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**ESHRE Certification of Reproductive
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www.eshre.eu

Early Pregnancy Presentation & Learning Objectives

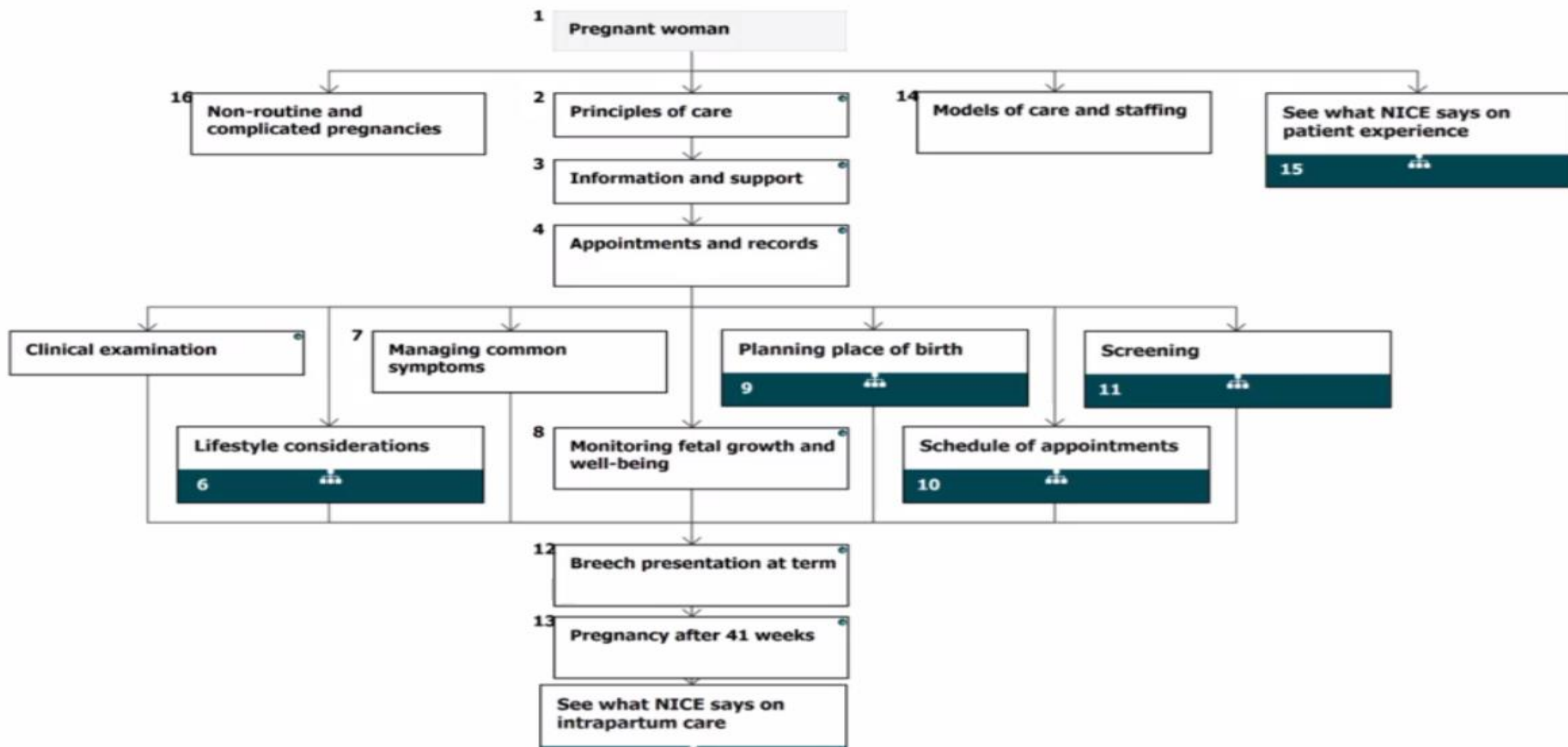
- Clinical manifestations
- Beta hCG and US findings – CRL
- Assessment of gestational age and embryo development
- Tween pregnancy
- Rule out chromosomal abnormalities
- Placental hormones, NIPT,
- Chorion villous sampling,
- Amniocentesis, Cordocentesis

Antenatal care quality standard

1. Services – access to antenatal care
2. Services – continuity of care
3. Risk assessment – body mass index
4. Risk assessment – gestational diabetes
5. Risk assessment – intermediate risk of venous thromboembolism
6. Risk assessment – high risk of venous thromboembolism



NICE National Institute for Health and Care Excellence



Antenatal care for uncomplicated pregnancies overview

- Crown–rump length measurement should be used to determine gestational age.
- If CRL length > 84 mm, the gestational age should be estimated using head circumference
- **Breast examination** - during antenatal care is not recommended for the promotion of postnatal breastfeeding
- **Pelvic examination** - Routine antenatal pelvic examination is not recommended
- **Female genital mutilation** - should be identified early in antenatal care through sensitive enquiry. will allow planning of intrapartum
- **Domestic violence** - be alert to the symptoms or signs of domestic violence
- **Mental disorders** - assessment and management of mental health problems up to 1 year after childbirth



Managing common symptoms

- **Nausea and vomiting** – resolves spontaneously within 16 to 20 w
- **Dyspepsia** – lifestyle and diet modification, Antacids
- **Constipation** – diet modification, fibre supplementation
- **Haemorrhoids** – no evidence of effective Tx, ... creams
- **Varicose veins** - common symptom, compression stockings alleviate symptoms
- **Vaginal discharge** – common, itch, soreness, smell, candidiasis
- **Backache** – common, individualize care, painkillers

1st trimester maternal and embryo monitoring tasks

- Establish Gestational age by LMP / TVU: CRL
- Evaluate maternal risks (history + examination)
- Rule out embryo chromosomal abnormalities (placental hormones + TVU scanning)
- Rule out embryo morphological defects (TVU: head, extremities, placenta position, twin pregnancy)
- Confirm embryo normal development and growth
- Blood tests check for Hg, VDRL, Hepatitis, VZV, Toxoplasmosis, Blood Group Rh, HIV, Rubella, CMV



TVS in early pregnancy

Gestational sac

Pregnancy sac under investigation



Characteristic Halo of the pregnancy sac



Corpus Luteum Function neo-angiogenesis



TVS in early pregnancy

Miscarriage

- The most common indication for early pregnancy TVS, more accurate than TAS
- Careful menstrual history-directs interpretation of US findings
 - How does she know date of LMP?
 - Pregnancy or hormonal contraception in 3/12 prior to LMP?
 - When she missed her period did she consider pregnancy?
 - When did she do first pregnancy test?
 - Repeated tests? First negative and 1 week later positive
 - Quantify blood loss, </> period
 - Pain with vaginal bleeding



TVS in early pregnancy

Normal sonoembryology-1

- 4/40 - gestation sac seen within the decidua (Chorio-decidual thickening)
- 5/40 – Gestation (Chorionic) sac (always), yolk sac and fetal pole (not always), short connecting stalk so they are in close proximity
- 6/40 - fetal pole, yolk sac and heart beat always seen (initially 100 then 130 BPM), CRL 4-8mm
- 7/40 - CRL 9-14 mm, limbs short and paddle like outgrowths, HR 160 BPM, fetal movement



Occasionally Dubious images



6 weeks



8+3 weeks

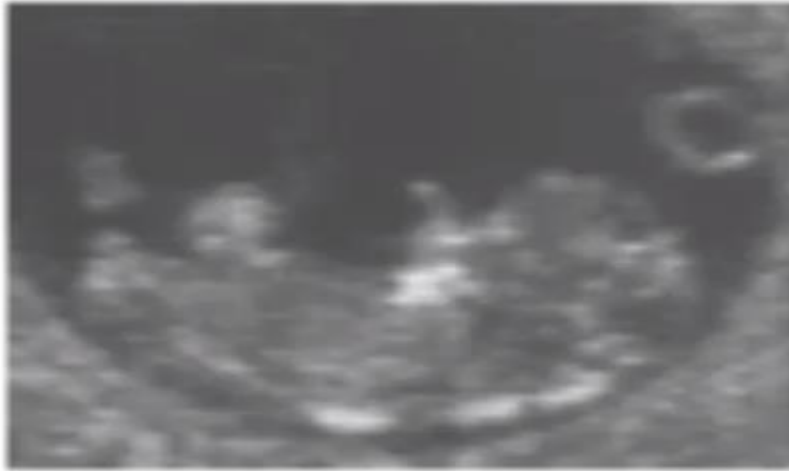


Embryo limbs and umbilical cord can easily visualized at an early pregnancy stage



TVS in early pregnancy

Normal fetal anatomy

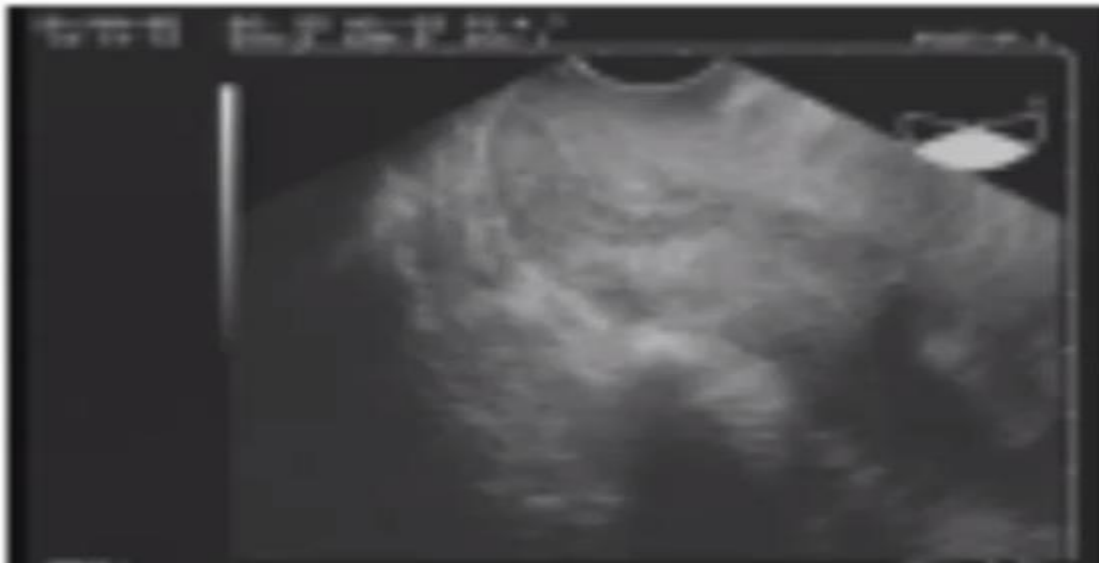


TVS in early pregnancy

Cervix

- Measurement of cervical length
- Usually $> 25\text{mm}$ from 10/40

Normal cervix



Funnelling and shortening

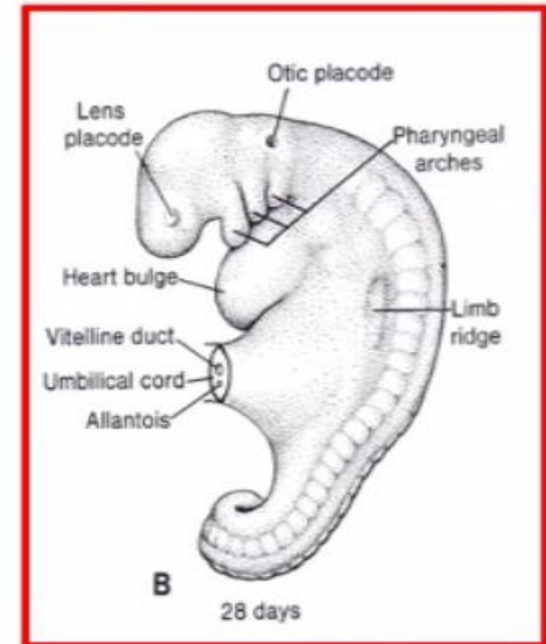


Pregnancy Earliest Seen with Ultrasonography

EARLY INTRAUTERINE PREGNANCY	Trans VAGINAL	Trans ABDOMINAL
Gestational sac seen		
Gestational sac size	0.5 cm	0.5 cm
Gestational sac age	4.3 w	4.3 w
Double Decidual outline		
Gestational sac size	0.6-0.7 cm	1.0 cm
Gestational sac age	4.4 w	5.0 w
Yolk sac seen		
Gestational sac size	0.7 cm	1.0 cm
Gestational sac age	4.6 w (34 d)	5.0 w (35 d)
Fetal pole seen		
Gestational sac size	0.7 cm	1.7 cm
Gestational sac age	4.6 w	6.0 w
Fetal heart motion seen		
Crown-rump length	0.3 cm	0.6 cm
Gestational sac age	4.6 w (34 d)	.5 w (47 d)

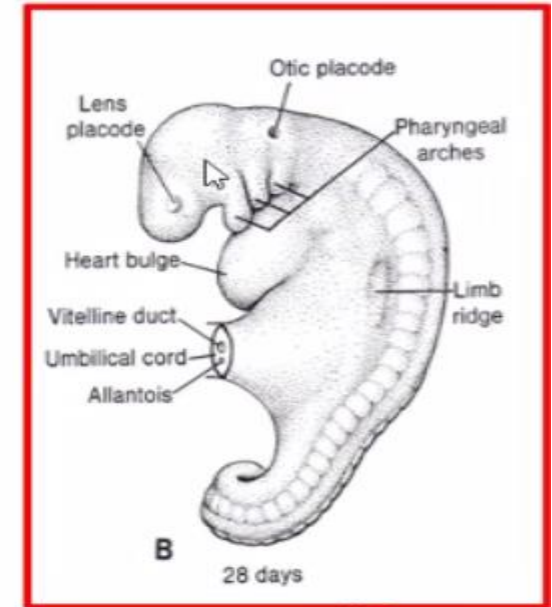
Assessment of gestation stage

- Original data from “Carnegie Institute Collection” started in 1887, leading to “23 Carnegie stages”
- Approximately 600 sectioned embryos
- Source of information for current knowledge:
 - spontaneous miscarriages fixed then forwarded to the institute
 - CRL measurements of IVF pregnancies compared with established data
 - IVF vs. GIFT post-ovulation data
 - Ovulation timing with ultrasound or LH surge vs CRL
- Embryos grow at the same rate through embryonic period seen on ultrasound (Dickey et al, 94)

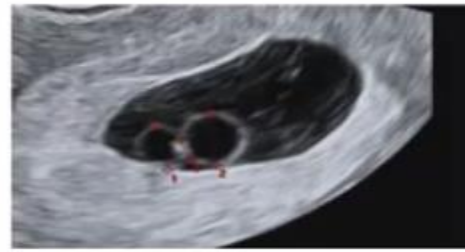


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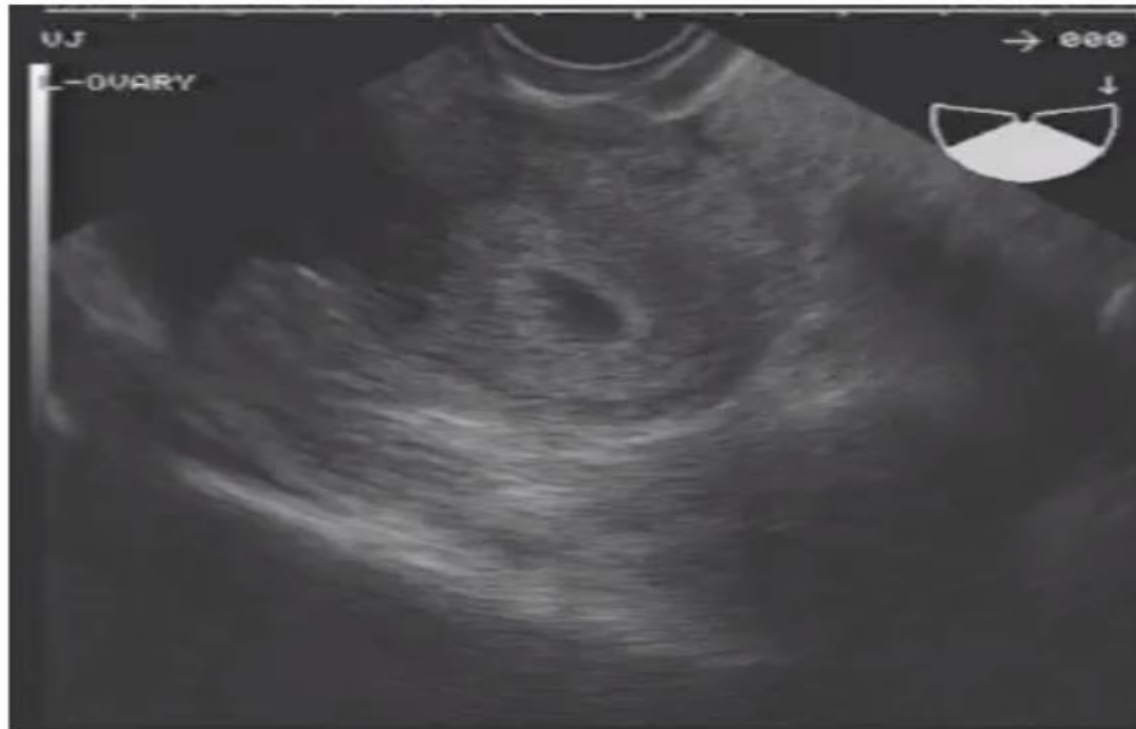
Embryo development



- 3w - brain, spinal cord, heart, GIT
- 4-5w – arm & leg buds visible, not clearly distinguishable, steady rhythm pulse, CRL3mm
- 6w - formation of lungs, jaw, nose, hand and feet buds have webbed structures, forming the fingers and toes CRL 5mm
- 7w – trunk is more straight, elbows and toes are more visible
- 8w - bones begin to form, and muscles can contract, everything that is present in an adult human is now present in the small embryo
- 10 w - the end of the embryonic period and begins the fetal period, CRL 46mm, head is nearly half the size of the entire fetus

TVS in early pregnancy

Normal Sonoembryology – 4 1/2 – 5 weeks gestation



Courtesy Prof N Amso

TVS in early pregnancy

Measurement of CRL

- Correct measurements of CRL offer the most accurate dating of pregnancy (reducing the risk for preterm delivery, false SGA foetus, unnecessary or false induction of labour, CS etc.)
- Accuracy of first trimester dates ± 3 days, if dates are very certain don't alter dates if difference < 7 days
- True un-flexed longitudinal section of foetus with end points of crown and rump clearly defined.



TVS in early pregnancy

Measurement of CRL

- Can be difficult as a fetus moves!!
- Obtain fetus with full length of its spine
- When fetus $> 10/40$ TAS measurements easier as have more flexibility with probe
- After 13 weeks, flexed and rotated position of fetus makes measurement difficult and inaccurate
- 3D scan and post image acquisition processing



TVS in early pregnancy

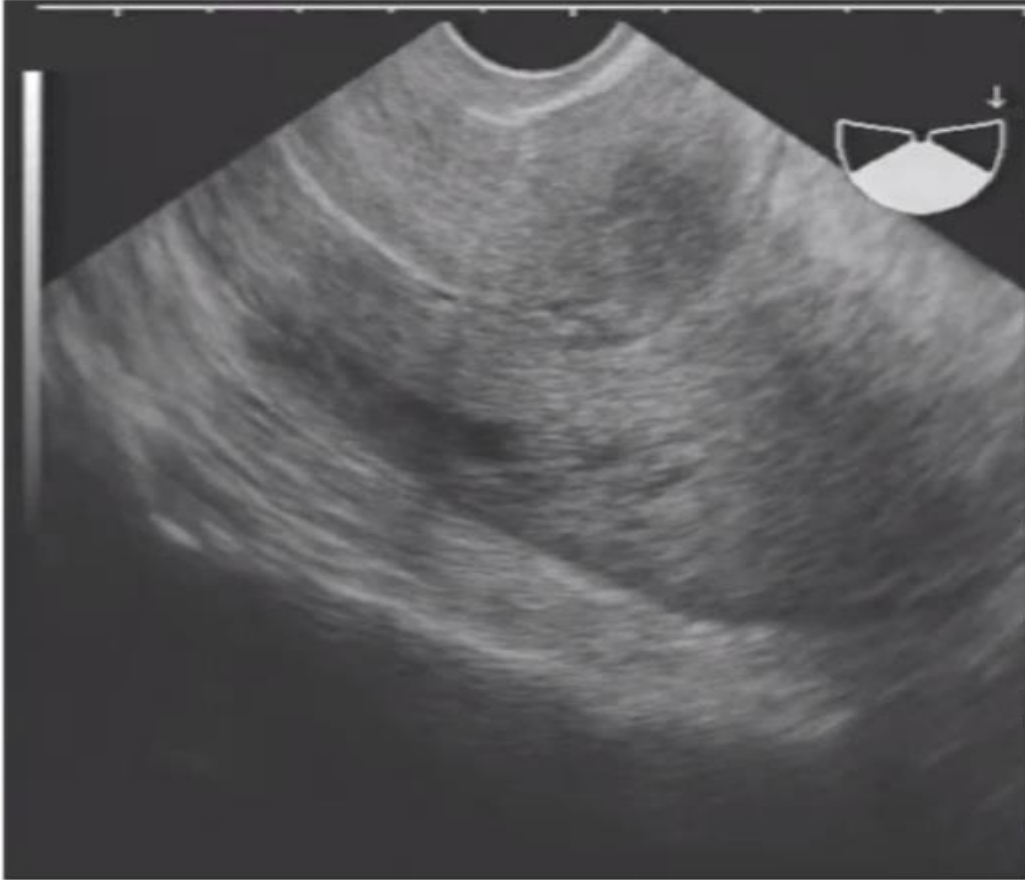
Measurement of CRL – Twin pregnancy ~ 6 weeks



Courtesy Prof N Amso

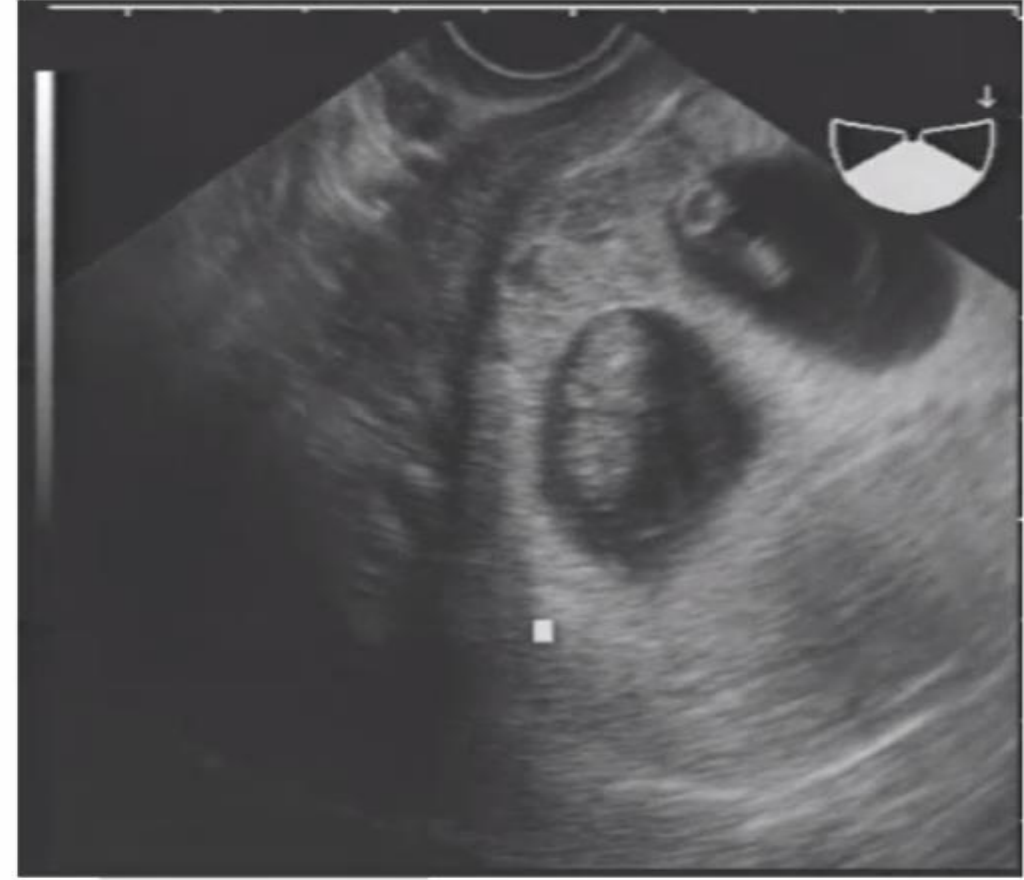
TVS in early pregnancy

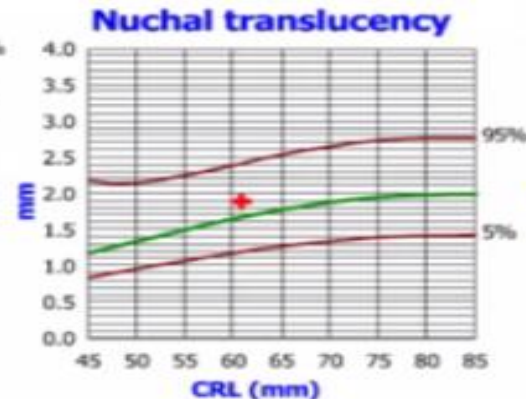
Live fetus and an IM fibroid !



TVS in early pregnancy

*Multiple Pregnancy with IUCD
Chorionicity*





First Trimester Ultrasound

US system: GE VOLUSON E 10.

Gestational age: 12 weeks + 2 days from dates

EDD by scan: 29 January 2019

Findings
 Heart activity
 FHR
 Crown-rump length (CRL)
 Nuchal translucency (NT)
 Intracranial translucency

alive fetus
 visualised
 162 bpm
 60.8 mm
 1.90 mm
 present



Chromosomal markers:

Nasal bone: present; Tricuspid Doppler: normal.

Fetal anatomy:

Skull/brain: appears normal; Abdomen: appears normal; Stomach: visible; Bladder / Kidneys: visible; Hands: both visible; Feet: both visible.

Maternal Serum Biochemistry

Sample **P1807099**, taken on: 06 July 2018, analysed on: 09 July 2018. Equipment: BRAHMS Kryptor.

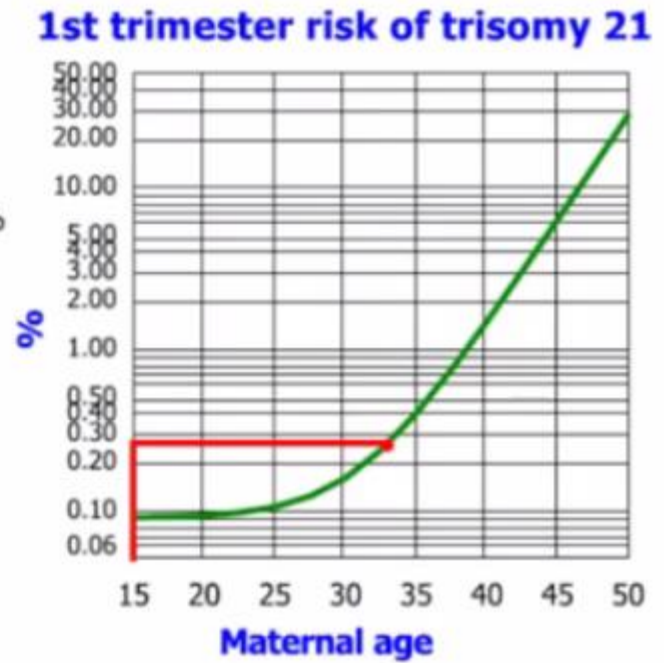
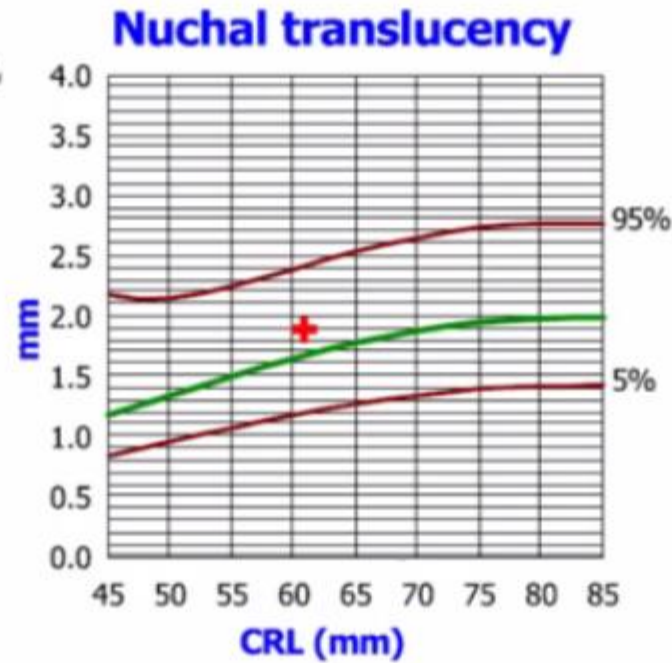
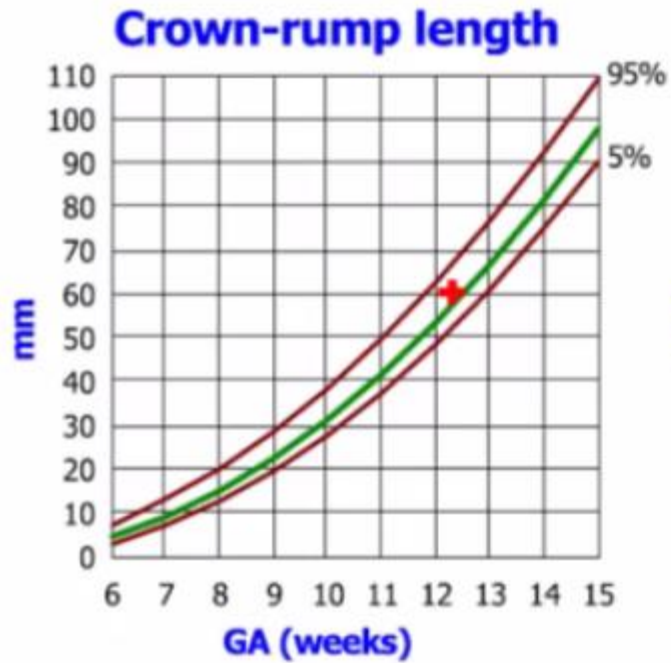
Free β -hCG	28.03 IU/l	equivalent to 0.505 MoM
PAPP-A	1.427 IU/l	equivalent to 1.007 MoM
Uterine artery mean PI:	1.780	equivalent to 1.084 MoM

Risk calculation

Patient counselled and consent given.

FMF Operator: Aphrodite Aristidou-Kallikas, FMF Id: 12371

<i>Condition</i>	<i>Background risk</i>	<i>Adjusted risk</i>
Trisomy 21	1: 408	1: 8158
Trisomy 18	1: 982	1: 19631
Trisomy 13	1: 3083	<1: 20000
Preeclampsia before 34 weeks		1: 5295



Comments

The result was discussed with the patient and options given: 1: have the 2nd trim U/S scan and then decide whether there is a need for further investigation, 2: NIPT (screening test), 3: CVS (diagnostic test, risk of miscarriage of 1%).

PATIENT INFORMATION		REFERRAL INFORMATION	
[REDACTED]		CLINIC NAME	Artaeio Hospital
ID NUMBER	797680	CLINIC ID	1010
DATE OF BIRTH (DD/MM/YYYY)	19/02/1978	REFERRING CLINICIAN	Dr. Vasilios Tanos
IVF STATUS	No	CLINIC FAX	22512371
GESTATIONAL AGE		Week: 12 Day: 4	
NUMBER OF FETUSES		One	
SAMPLE INFORMATION			
ORDER NUMBER	7482	LAB NUMBER	173601
DATE OF COLLECTION (DD/MM/YYYY)		01/08/2017	
DATE RECEIVED (DD/MM/YYYY)		01/08/2017	

VERACITY RESULTS			
<p>No Aneuploidy Detected</p> <p>FETAL FRACTION 11.9%</p> <p>INTERPRETATION</p> <p>The results show very low risk for all tested conditions. The fetal fraction is 11.9%, which is sufficient for analysis. The results should be communicated by the referring clinician with appropriate counselling.</p>		CONDITION	RESULT
		Trisomy 21	No trisomy 21 detected
		Trisomy 18	No trisomy 18 detected
		Trisomy 13	No trisomy 13 detected
		Trisomy X	No trisomy X detected
		Monosomy X	No monosomy X detected
		XXY Constitution	No XXY constitution detected
YY Constitution	No YY constitution detected		
Y Chromosome	No Y chromosome detected		
<p>REMARK</p> <p>The results show very low risk for trisomy 21</p> <p>The results show very low risk for trisomy 18</p> <p>The results show very low risk for trisomy 13</p> <p>The results show very low risk for trisomy X</p> <p>The results show very low risk for monosomy X</p> <p>The results show very low risk for XXY constitution</p> <p>The results show very low risk for YY constitution</p> <p>The results show the absence of Y chromosome</p>			

TEST METHOD

VERACITY is a Laboratory Developed Test (LDT) from NIPD Genetics that analyses cell-free DNA from maternal plasma. Multiplexed parallel analysis of specific regions of interest was applied for the copy number determination of chromosomes 13, 18, 21, aneuploidies of X,Y and Y detection.

TEST DESCRIPTION

Test performance is valid only for full chromosomal aneuploidies and only for chromosomes 21, 18, and 13 and upon request aneuploidies of X, Y and Y detection. It does not exclude other chromosomal abnormalities, birth defects or other complications. VERACITY is available for singleton, twin and vanished twin pregnancies including in-vitro fertilization (IVF) pregnancies of at least 10 weeks of gestation. Singleton pregnancies conceived by IVF with egg donation are also eligible. Sex chromosome aneuploidies are not reportable for twin and vanished twin gestations. Patients with malignancy or a history of malignancy, patients with bone marrow or organ transplant, as well as twin and vanished twin pregnancies conceived through in-vitro fertilization (IVF) with egg donation or use of a surrogate mother are not eligible for the test. The test is not intended and not validated for mosaicism, triploidy, partial trisomy or translocations. A positive result for twin pregnancies indicates the presence of at least one affected fetus. In twin pregnancies, detection of Y indicates the presence of at least one Y chromosome. Although this test is highly accurate, there is still a possibility that not all aneuploid fetuses will be detected. A negative result does not always ensure an unaffected pregnancy due to test limitations related to biological reasons. In addition, there is a small possibility that the detected chromosomal abnormality is caused by true or confined placental mosaicism or maternal chromosomal changes or other rare molecular events. The VERACITY test is not diagnostic and results should be considered in the context of other clinical criteria. Clinical correlation with ultrasound findings, and other clinical data and tests is recommended. If definitive diagnosis is desired, amniocentesis is necessary. The referral clinician is responsible for counselling before and after the test including the provision of advice regarding the need for additional invasive genetic testing. The VERACITY non-invasive prenatal test development and performance evaluation was carried out by NIPD Genetics Public Company Limited, which is regulated under the Clinical Laboratory Improvement Act of 1998 (CLIA) as qualified to perform high-complexity testing.

VERACITY is intended for clinical purposes and should not be regarded as investigational or for research. The test has not been cleared or approved by the U.S. Food and Drug Administration (FDA), which does not require this test to go through premarket FDA review.

TEST PERFORMANCE

CONDITION	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)
Trisomy 21	100 % (93.2-100)	100 % (99.3-100)
Trisomy 18	100 % (79.4-100)	100 % (99.4-100)
Trisomy 13	100 % (47.8-100)	100 % (99.4-100)
Sex Chromosome Aneuploidies	100 % (93.2-100)	100 % (99.9-100)
Y Chromosome	Accuracy: 100%	95% C.I.: 99.2-100

LABORATORY DIRECTOR: ELENA KYPRI, Ph.D.



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Phone: +357 22266888 Fax: +357 22266899

DATE OF REPORT (DD/MM/YYYY): 11/08/2017

Web: www.nipd.com
Email: info@nipd.com



Conclusions

- The correct gestational age is of paramount importance, directs pregnancy follow up
- Accurate measurements of the gestational sac or CRL, where applicable, are necessary for accurate assessment of GA
- Clinical assessment of a pregnant woman at early stage of pregnancy identifies patients at high risk.
- Early pregnancy US can detect an intrauterine pregnancy with confidence.
- Knowledge of Sono-embryological structures is essential for efficient diagnosis.
- Early pregnancy US is essential since can diagnose an asymptomatic miscarriage, anencephaly etc.
- The management tasks during the 1st trimester are to identify the clinical status of the pregnant woman and r/o embryo chromosomal abnormalities