The Journey of Maternal and Fetal Medicine

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&
Wellington Hospital Women's Ultrasound
Wellington Regional Hospital

About

Clinical Leader of Maternal and Fetal Medicine

Wellington Hospital

Private Obstetrician

Clinical Lecturer UOG

Mother of two boys

Nothing to declare

What is a MATERNAL-FETAL MEDICINE (MFM) subspecialist?

A physician who has advanced knowledge and training in

medical, surgical, obstetrical, fetal, and genetic complications of pregnancy

& their effects on both the woman and fetus.

MFM Subspecialists provide

1. **consultations**
2. **co-management**
3. **transfer of care**

for **women with complex conditions before, during, and after pregnancy.**

MFM Subspecialists provide **peer and patient education**;

AND

perform research on innovative approaches and treatments.

MFM subspecialists work with **ALL OBSTETRIC PROVIDERS**

including physician assistants, nurses, NPs, CNMs/CMs, family physicians, and obstetrician-gynecologists to manage **HIGH-RISK PREGNANCIES.**

What is a HIGH-RISK PREGNANCY?

SICK WOMEN get pregnant

One that threatens the **HEALTH OR LIFE** of the **WOMAN OR HER FETUS.**

PREGNANT WOMEN get sick

1 EXISTING CONDITIONS,

such as **high blood pressure, obesity, diabetes,** or being **HIV-positive**

Rates of **Gestational Diabetes (GDM) and pre-GDM** have **DOUBLED** in the last 14 years.

Over the last 30 years, **first trimester use of prescription medications has increased** more than 60%

60% of women of reproductive age are **obese or overweight.**

2 COMPLICATIONS from PREVIOUS PREGNANCIES

e.g. preterm birth, preeclampsia, IUGR

3 MULTIPLE GESTATION

In 2014, **3.5% of all babies born** were **TWINS, TRIPLETS OR HIGHER-ORDER MULTIPLES,** accounting for almost **140,000 births** in the U.S.

The number of **MULTIPLES Born in The U.S.** is at an **ALL-TIME HIGH,** according to the National Center for Health Statistics.

4 PROBLEMS with THE FETUS

Birth defects affect **one in every 33 babies** born in the U.S. each year.

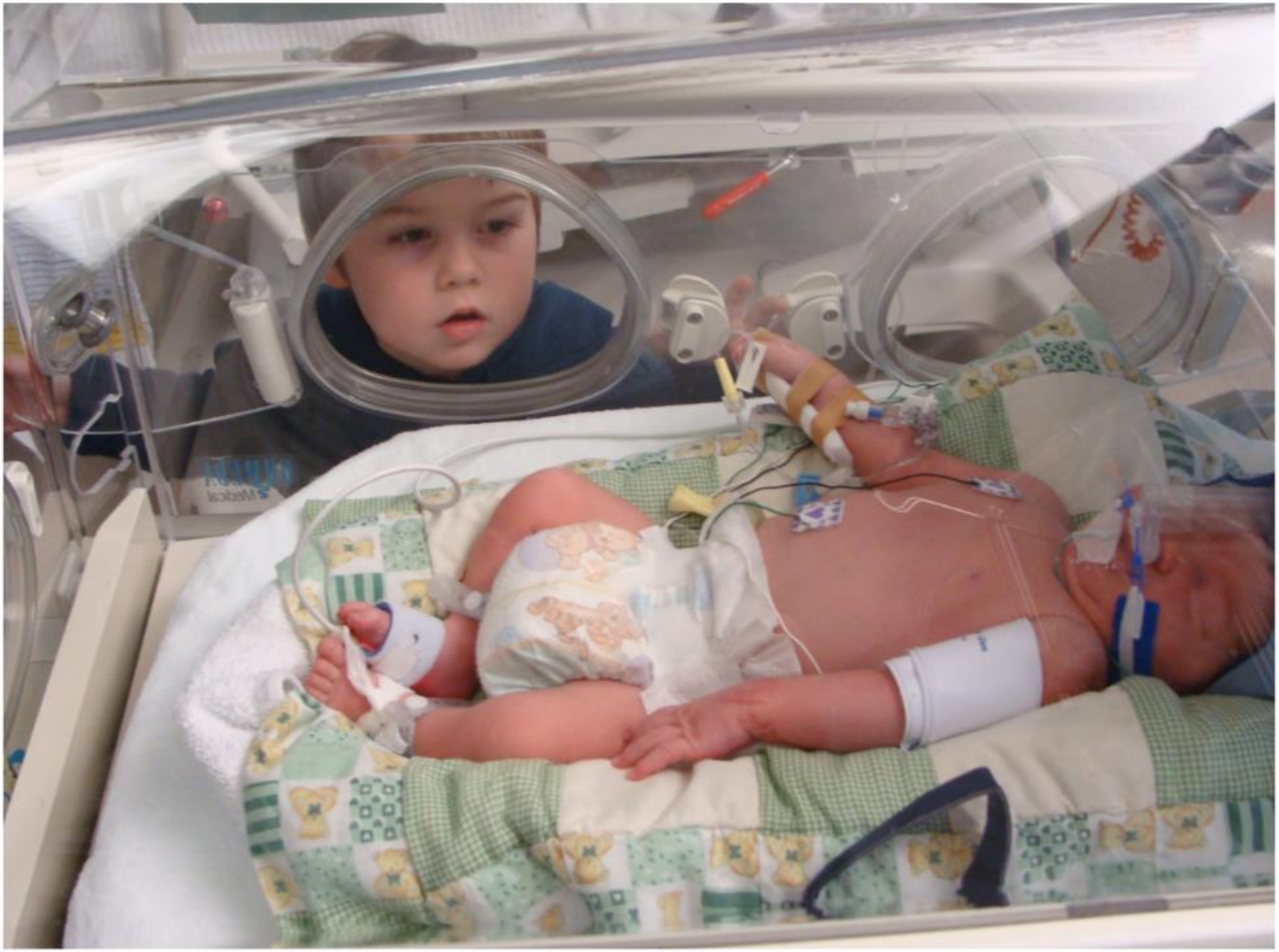
Birth defects are the leading cause of infant deaths, accounting for **20% of all infant deaths.**

Society for Maternal-Fetal Medicine

MFM

- Broad field
- Maternal
- Fetal
- Interventional

- Prediction
- Prevention
- Treatment



The patient journey

Get pregnant

Get an LMC

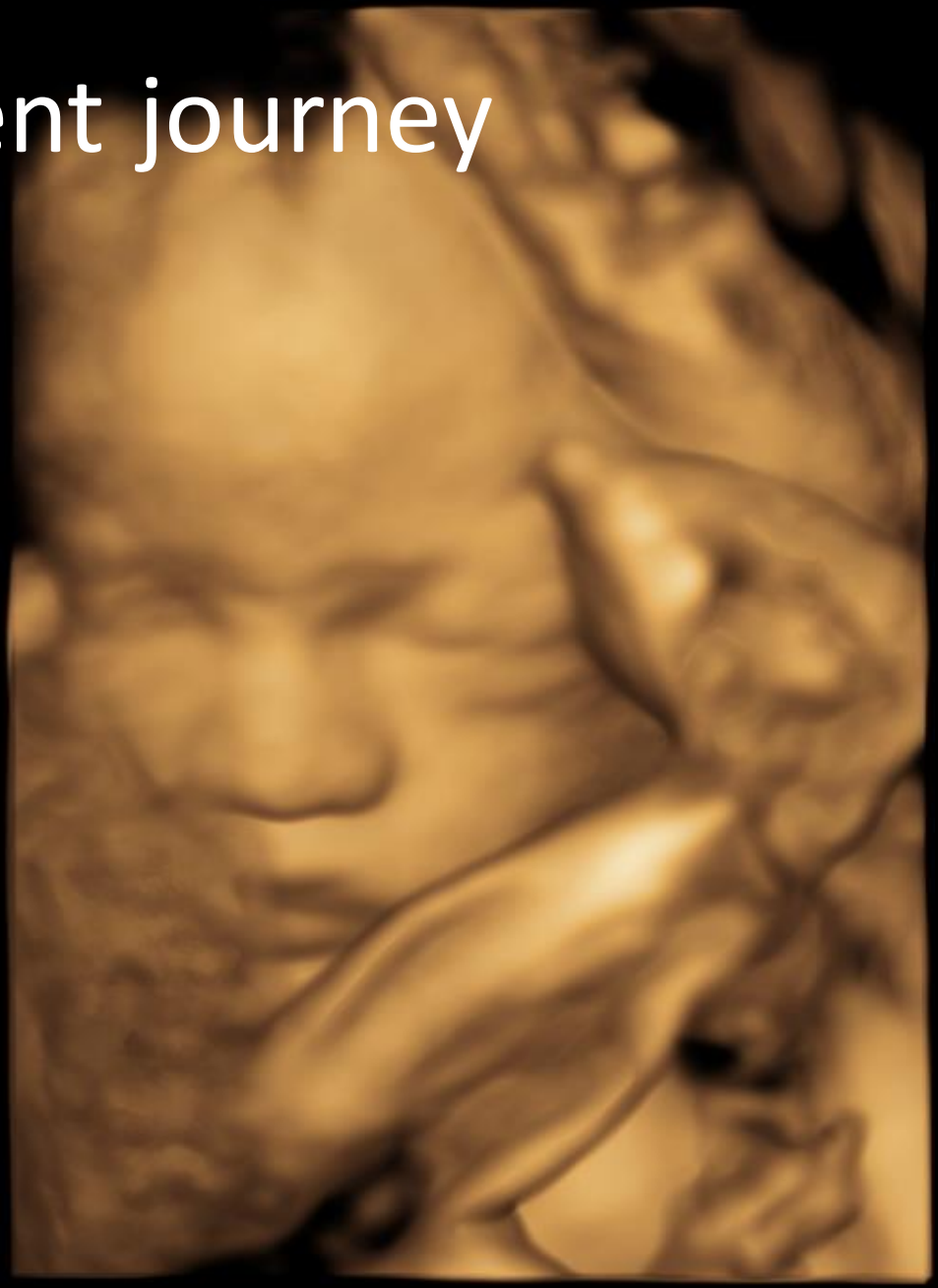
Routine screening

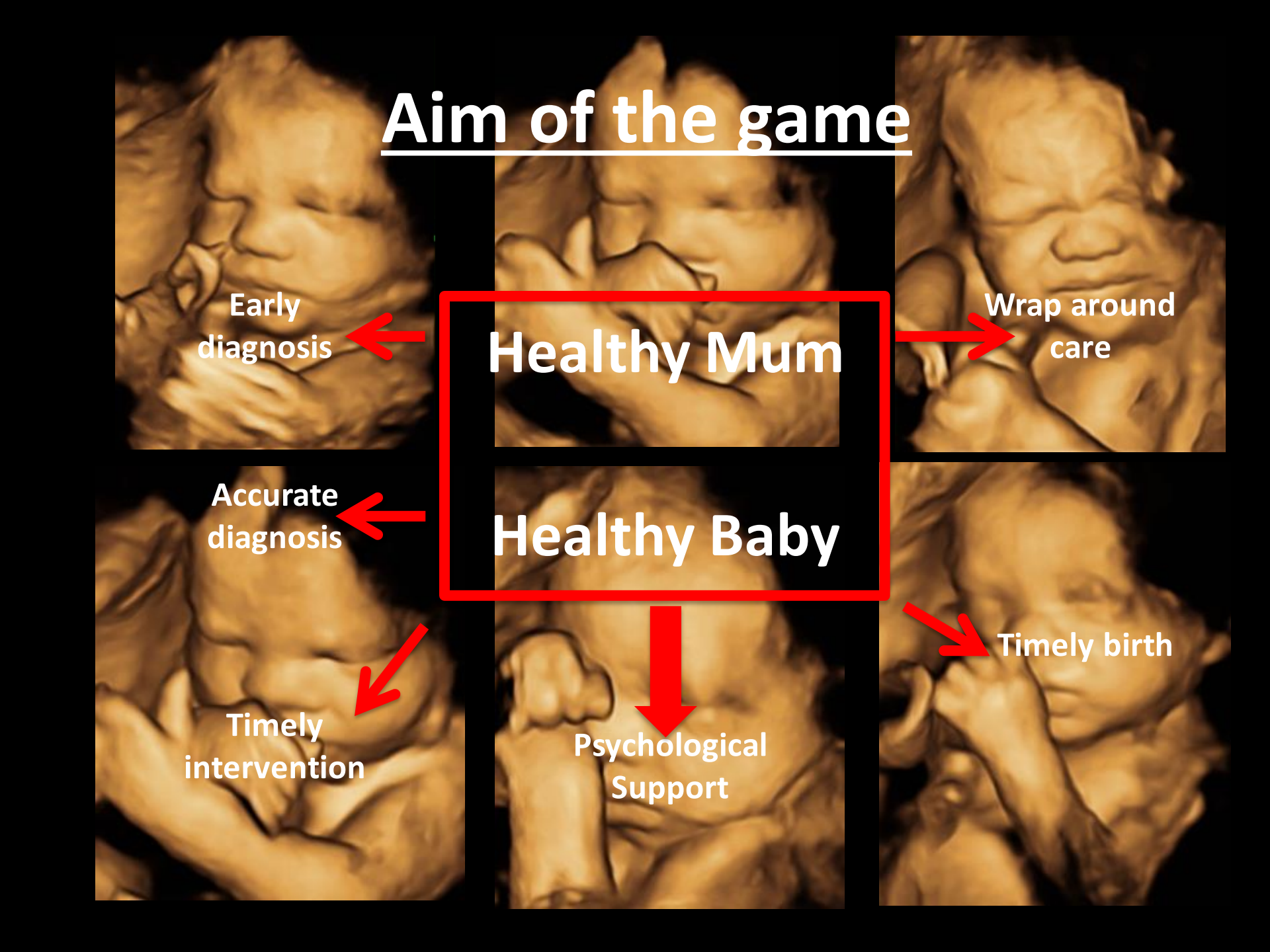
Concerns identified

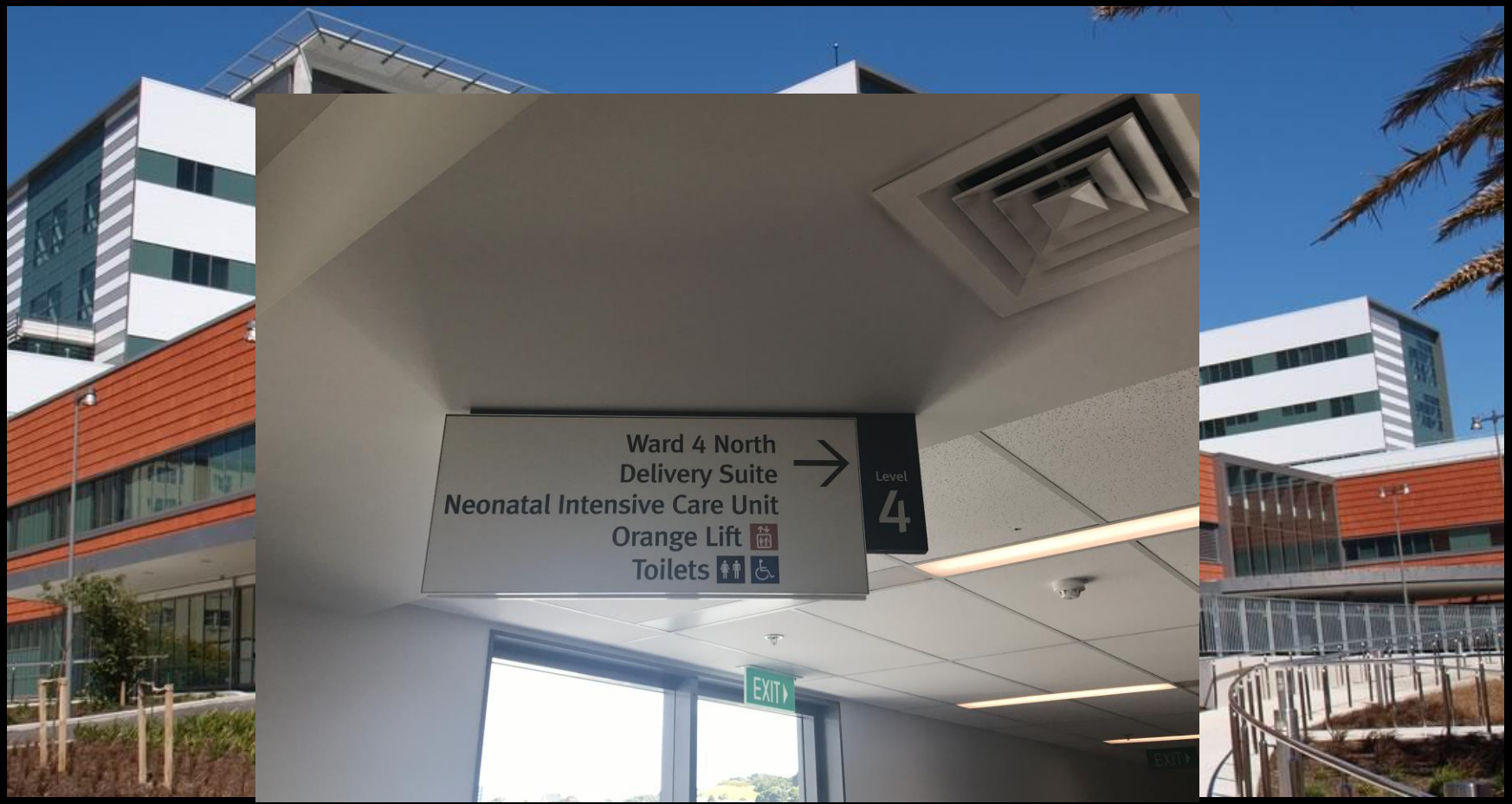
Referred to hospital

Evaluated

Management




Aim of the game
Early diagnosis
Healthy Mum
Wrap around care
Accurate diagnosis
Healthy Baby
Timely birth
Timely intervention
Psychological Support



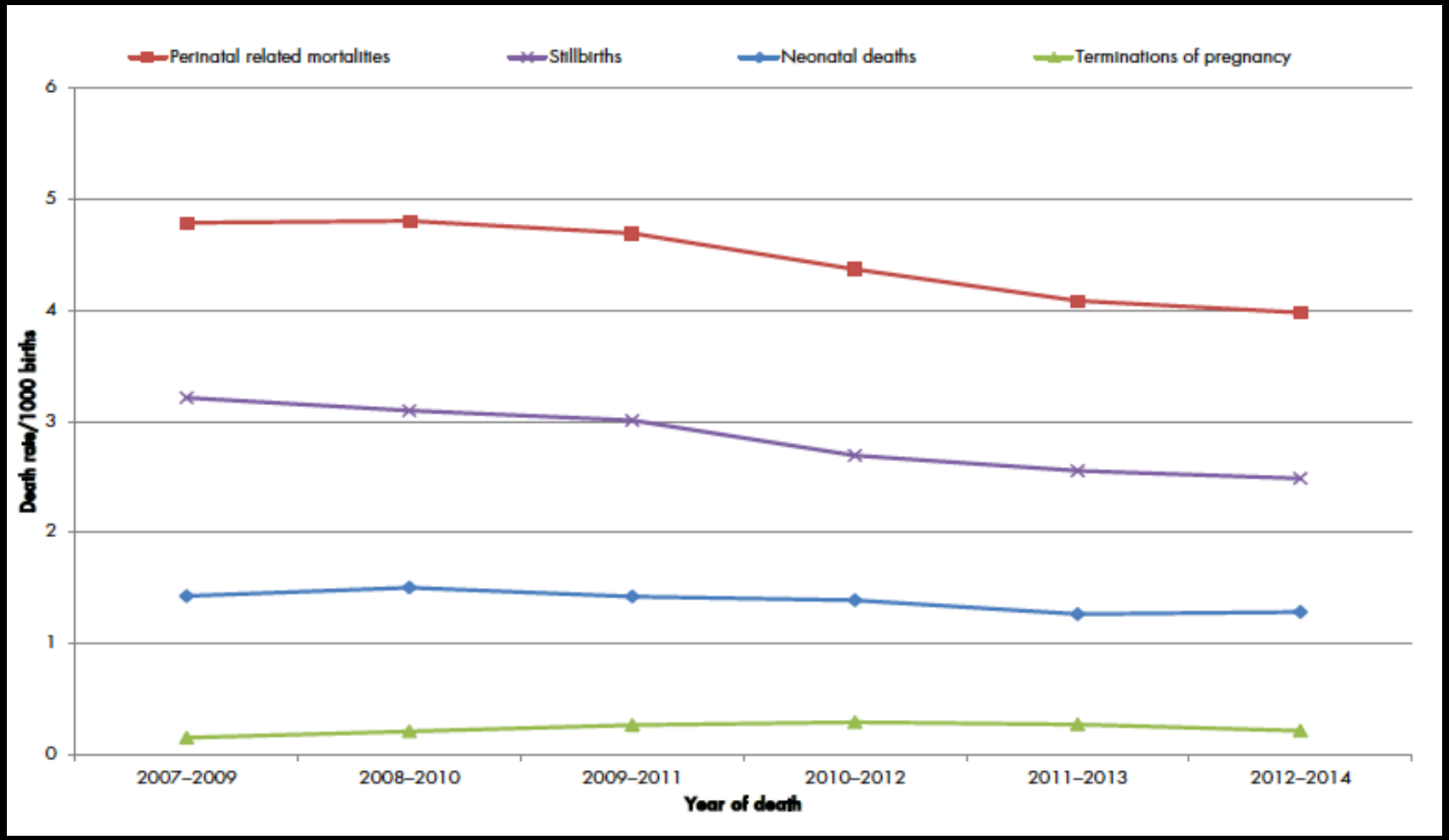
Delivery at best place possible

Tools

A Short History

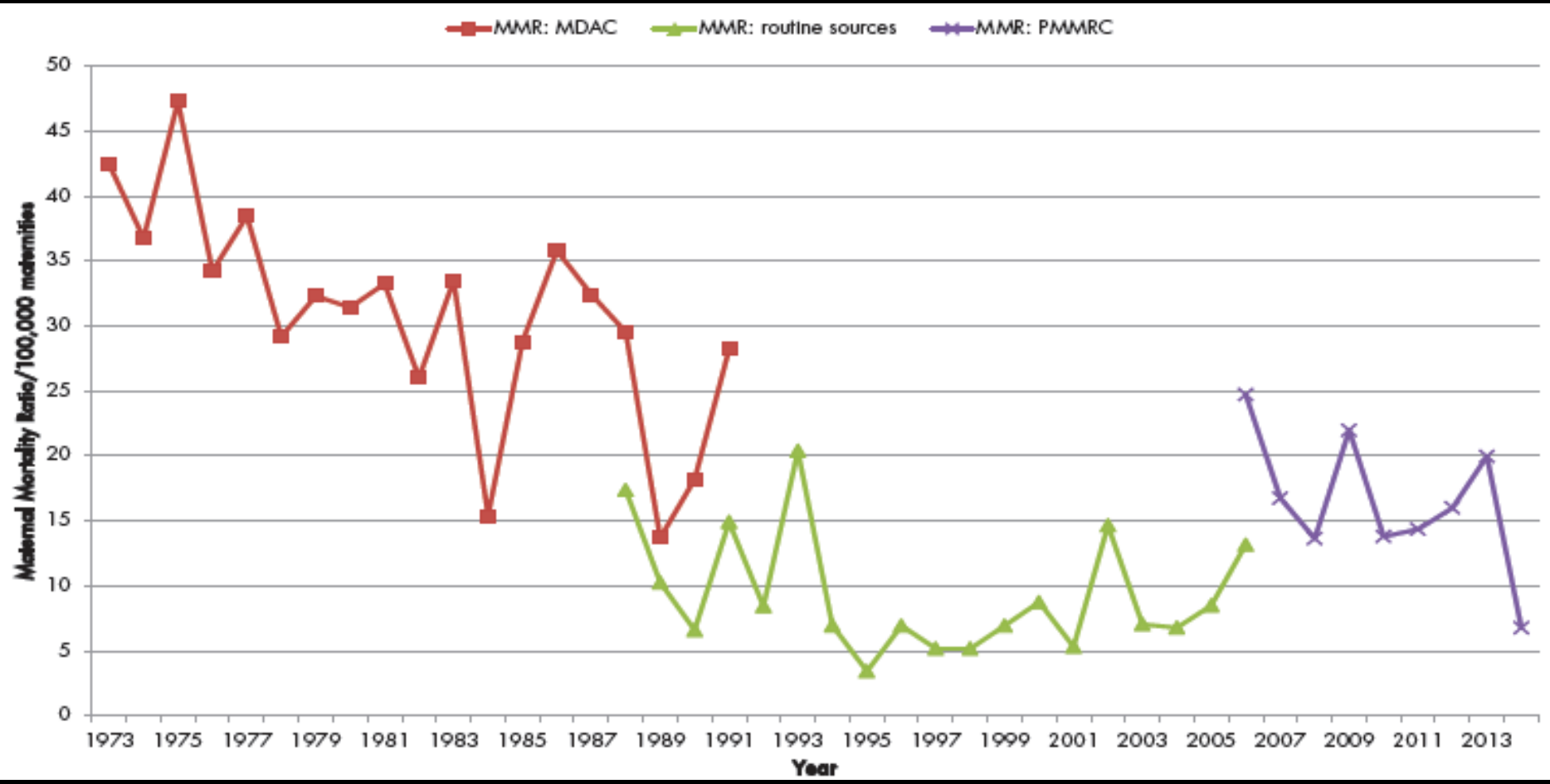
1952	• Amniocentesis
1963	• Intrauterine Transfusion • Prof Liley, NWH
1968	• Precise fetal heart rate monitoring in labour
1970?	• Antenatal corticosteroids for prevention of RDS • Prof Liggins, NWH
1971	• Real time ultrasound

Perinatal Mortality



PERINATAL AND MATERNAL MORTALITY REVIEW COMMITTEE: TENTH ANNUAL REPORT

Maternal Mortality



PERINATAL AND MATERNAL MORTALITY REVIEW COMMITTEE: TENTH ANNUAL REPORT

More recently

1988	• Laser TTTS • Dr Julian De Lia, Milwaukee
1994	• Low dose aspirin for prevention of PET and FGR
1997	• In-utero spina bifida surgery
2004	• FETO for CDH
2009	• Antenatal Progesterone for prevention of PTL

Tools:

ANTENATAL ULTRASOUND

1958

- Donald, McVicar, Brown
  - Lancet 1958
    - Physics, safety, images (fetus, ovary)

1963

- Early pregnancy and complications

1966

- Accurate placental location
  - High maternal mortality due to haemorrhage

1969

- Dating by Cephalometry
  - Campbell

1971

- Concept of IUGR/slowing of by growth biparietal diameter

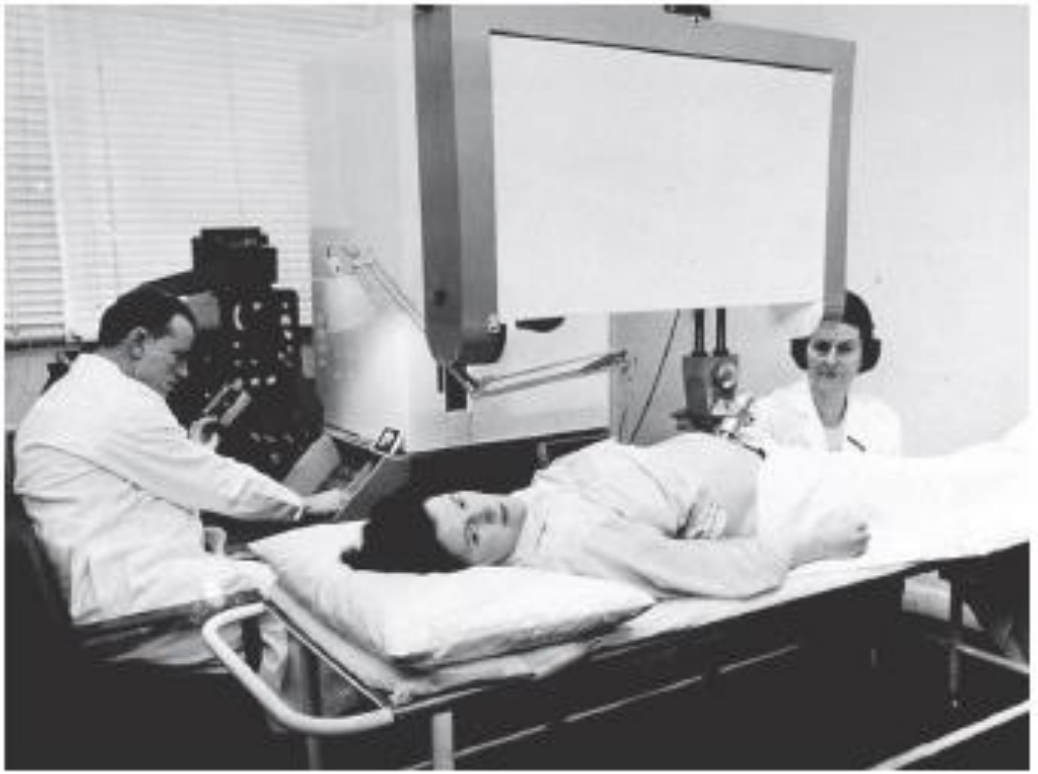
INVESTIGATION OF ABDOMINAL MASSES BY PULSED ULTRASOUND

IAN DONALD
M.B.E., B.A. Cape Town, M.D. Lond., F.R.F.P.S., F.R.C.O.G.
REGIUS PROFESSOR OF MIDWIFERY IN THE UNIVERSITY OF GLASGOW

J. MACVICAR
M.B. Glasg., M.R.C.O.G.
GYNAECOLOGICAL REGISTRAR, WESTERN INFIRMARY, GLASGOW

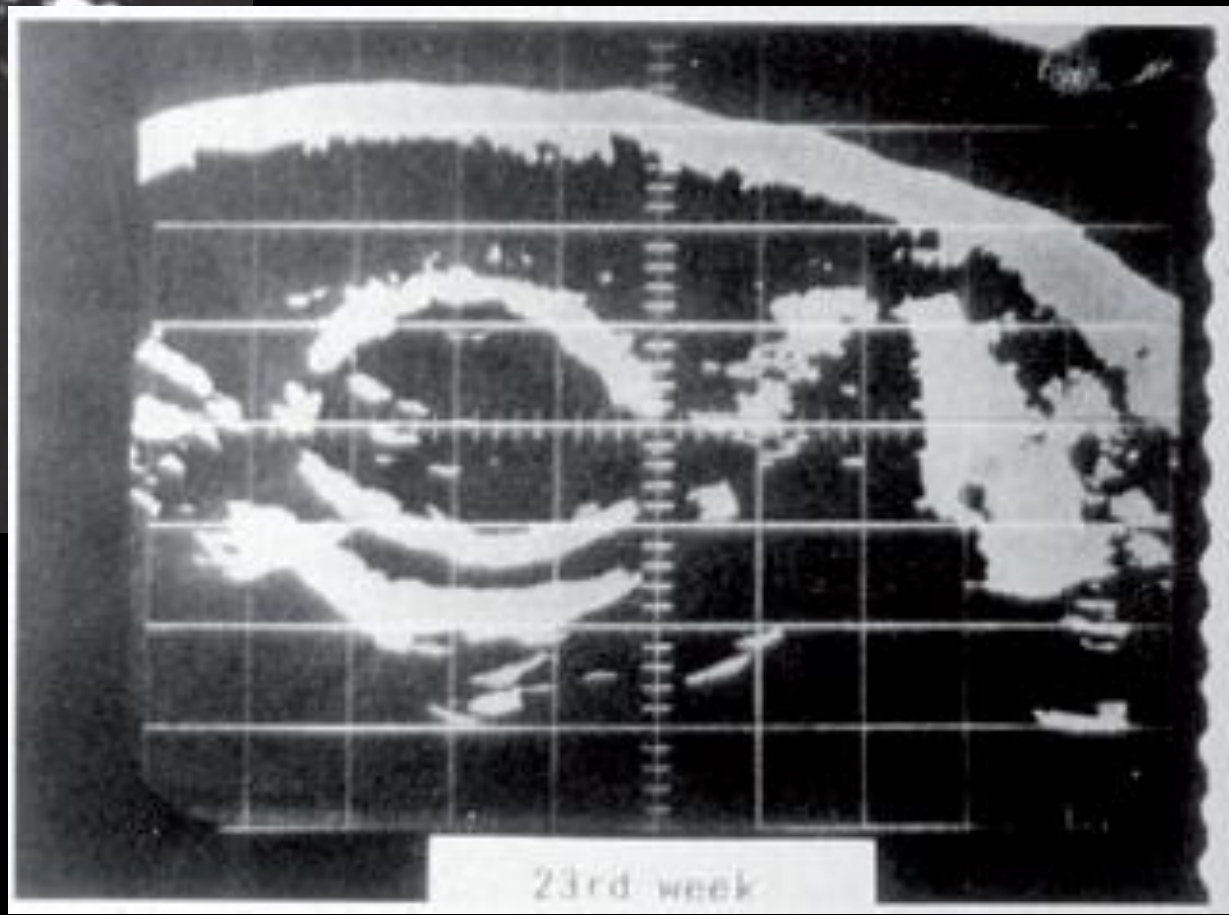
T. G. BROWN
OF MESSRS. KELVIN HUGHES LTD.

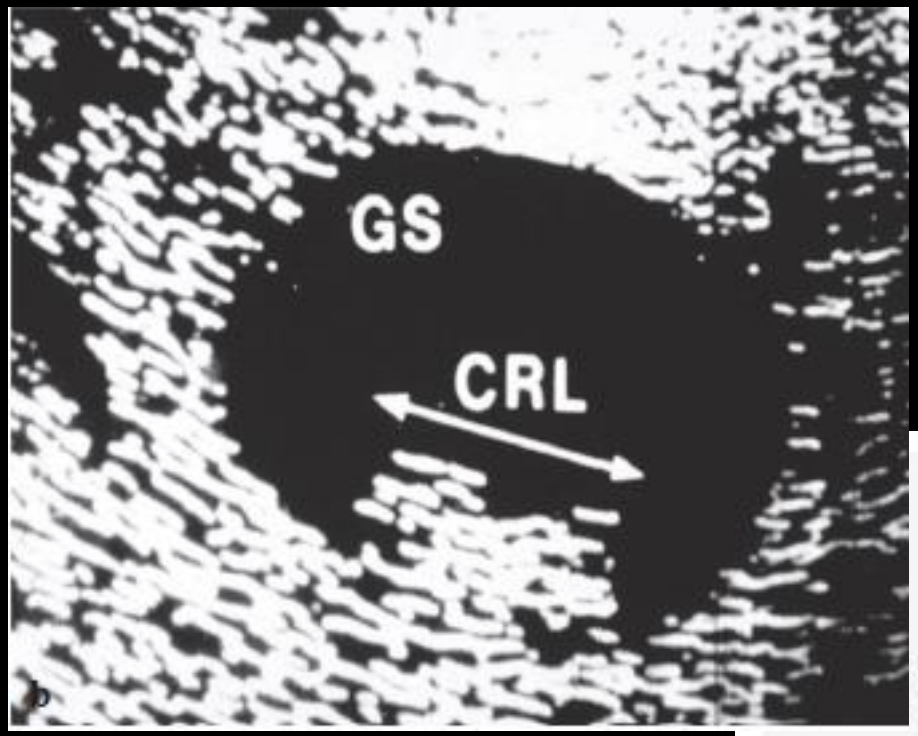
VIBRATIONS whose frequency exceeds 20,000 per
are beyond the range of hearing and therefore
" ultrasonic ". One of the properties of ultrasound
it can be propagated as a beam. When such
crosses an interface between two substances of d
specific acoustic impedance (which is defined
product of the density of the material and the velo
the sound wave in it), five things happen:



Campbell, 1970

USA 1970s





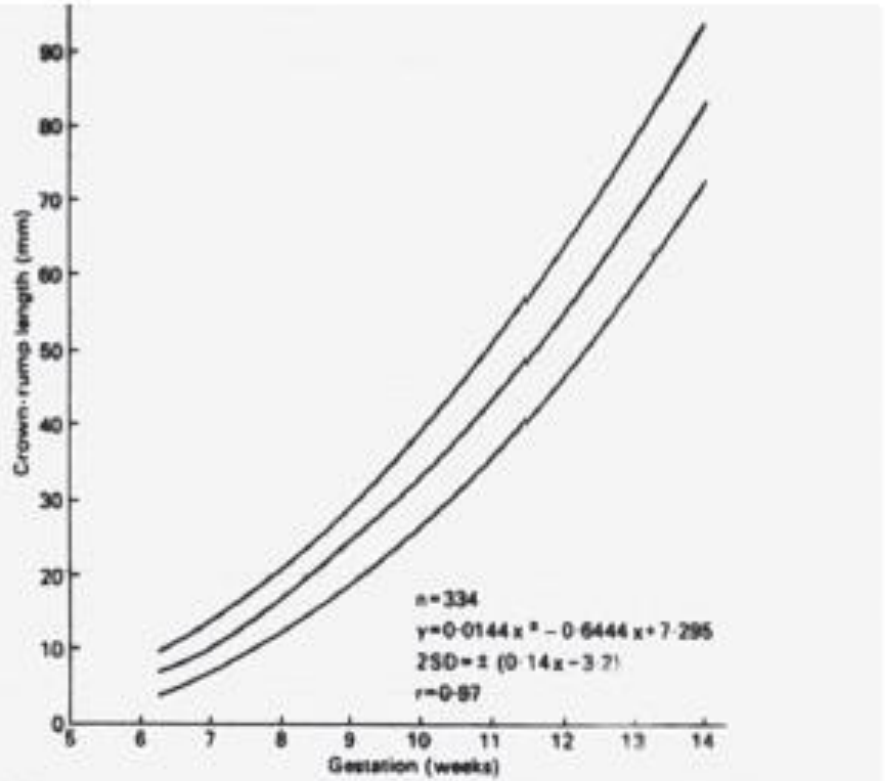
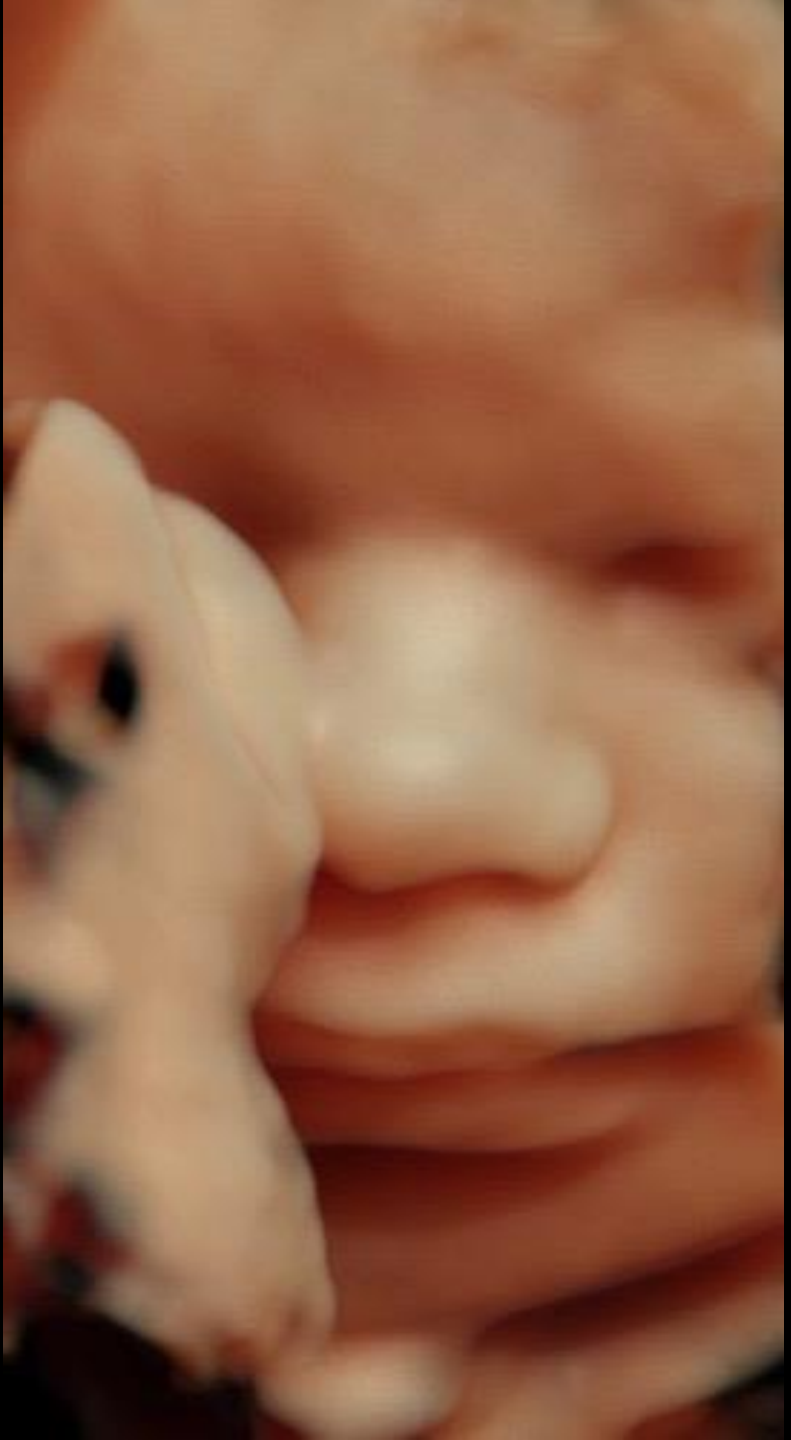
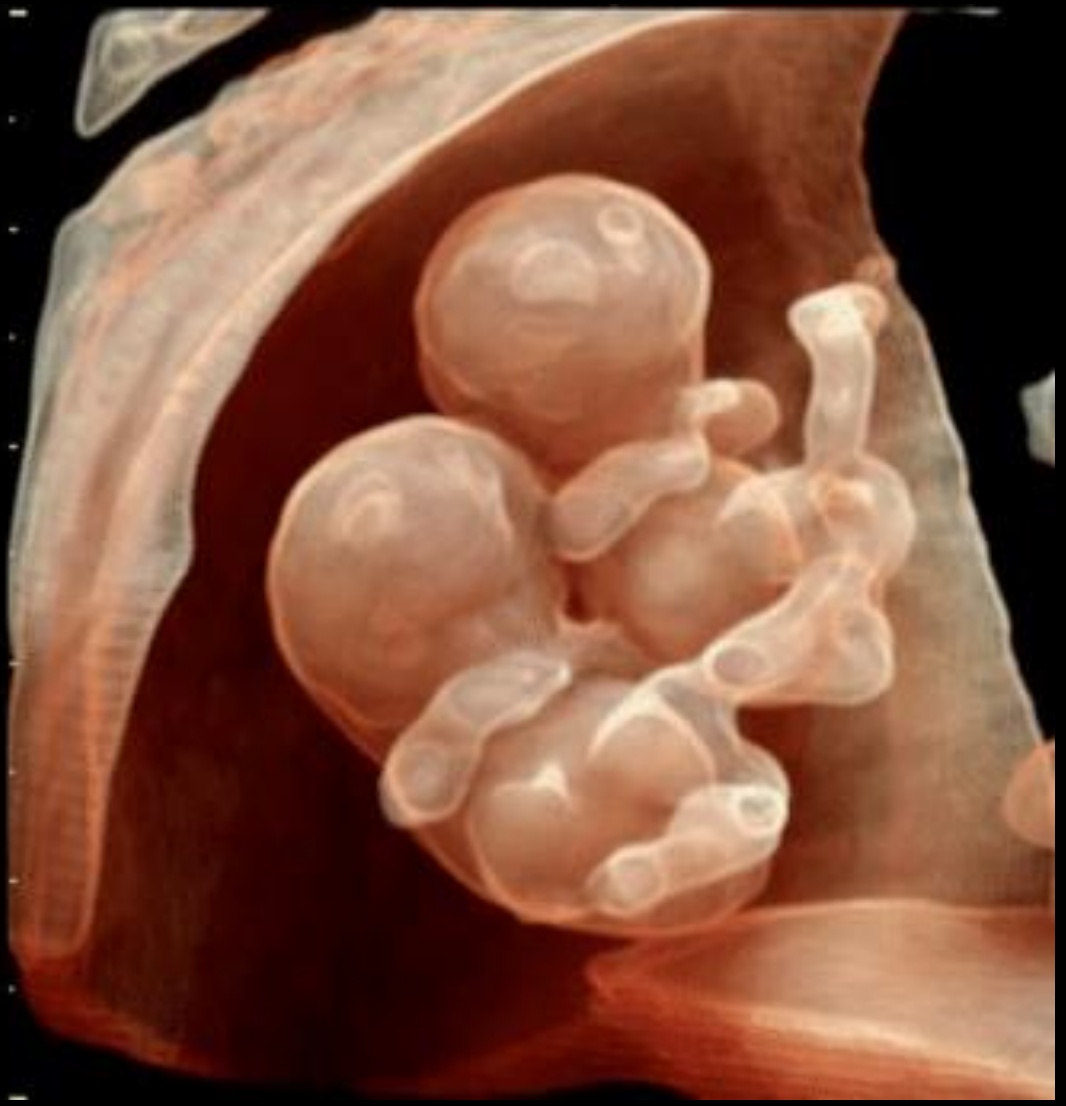


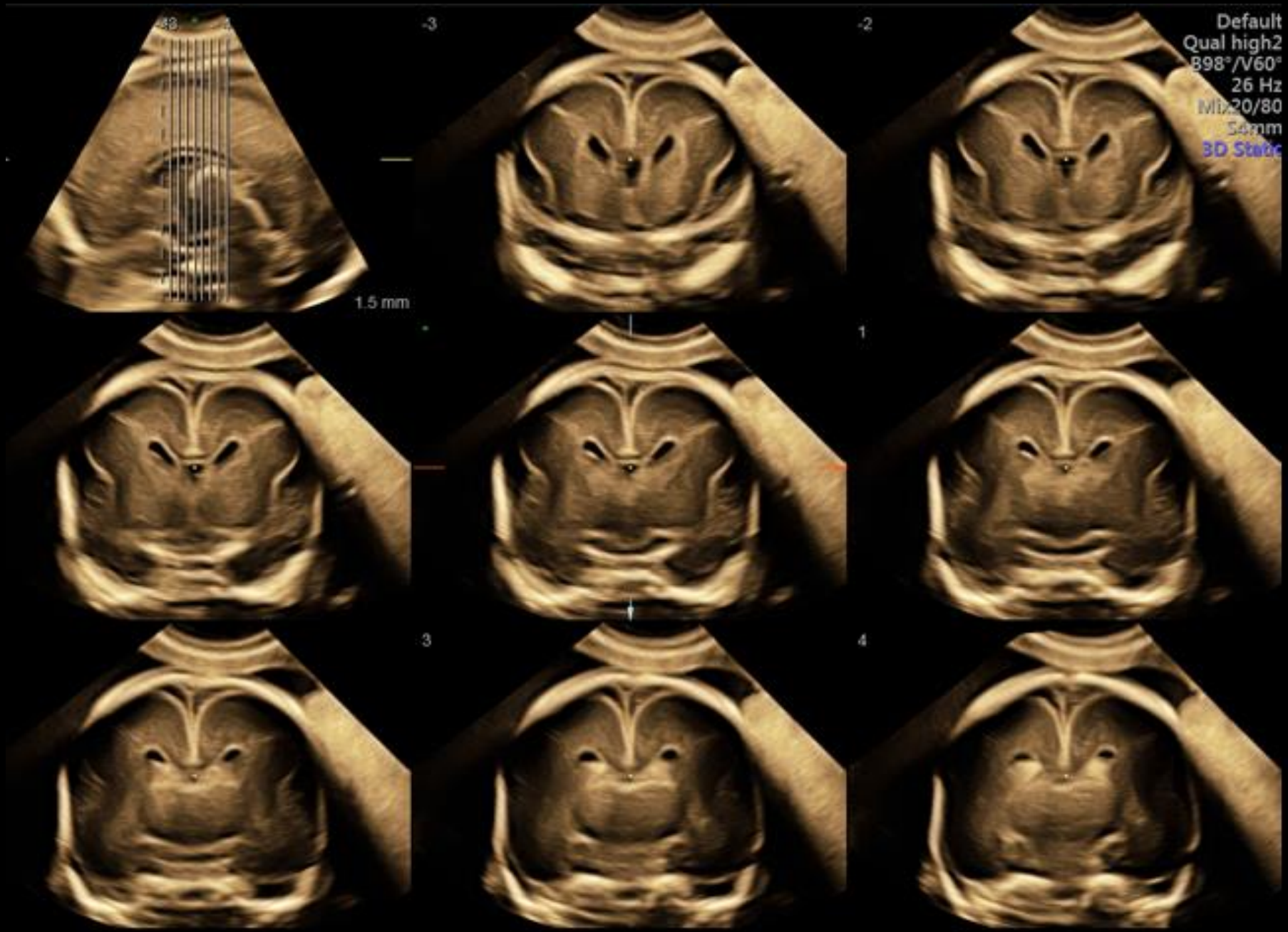
Figure 15.8. The mean growth of the embryonic CR length ± 2 s.d. from 6 to 14 weeks menstrual age as determined by a weighted non-linear regression analysis. From Robinson and Fleming (1975) with kind permission of the authors and the editor of *British Journal of Obstetrics and Gynaecology*.

Robinson, 1973

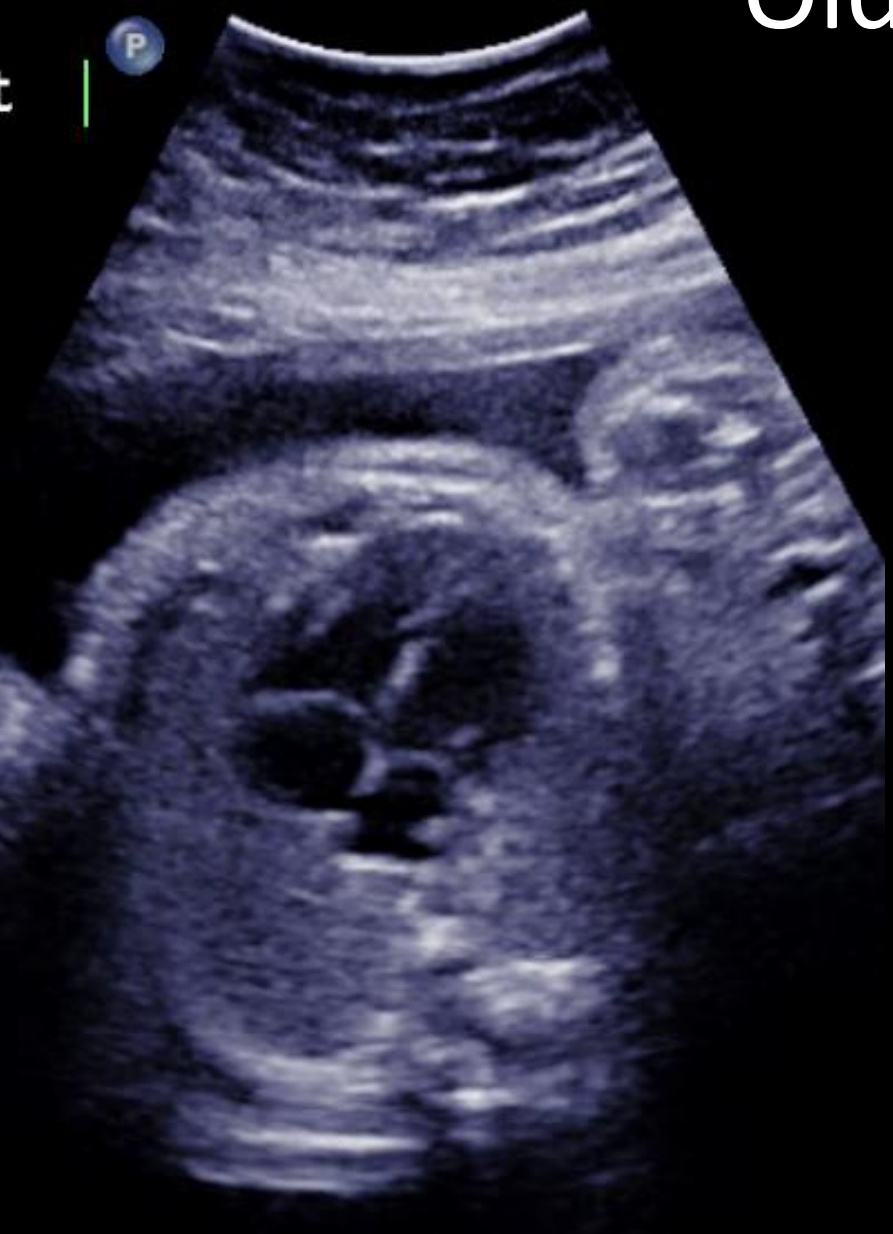

Voluson E10

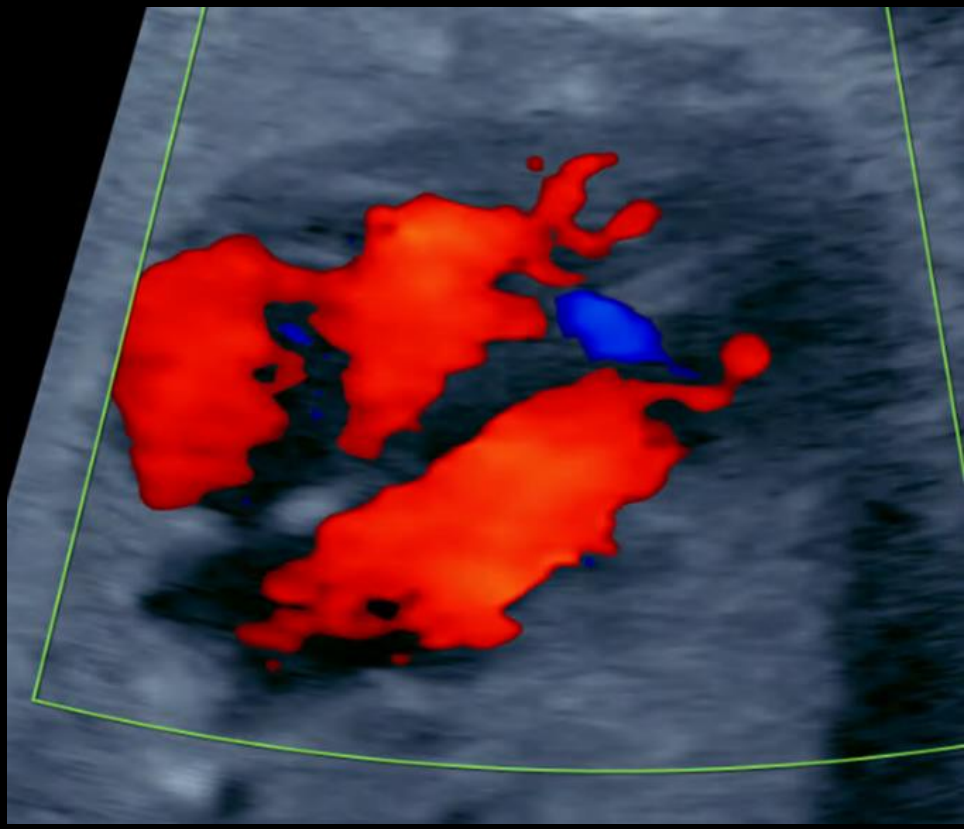


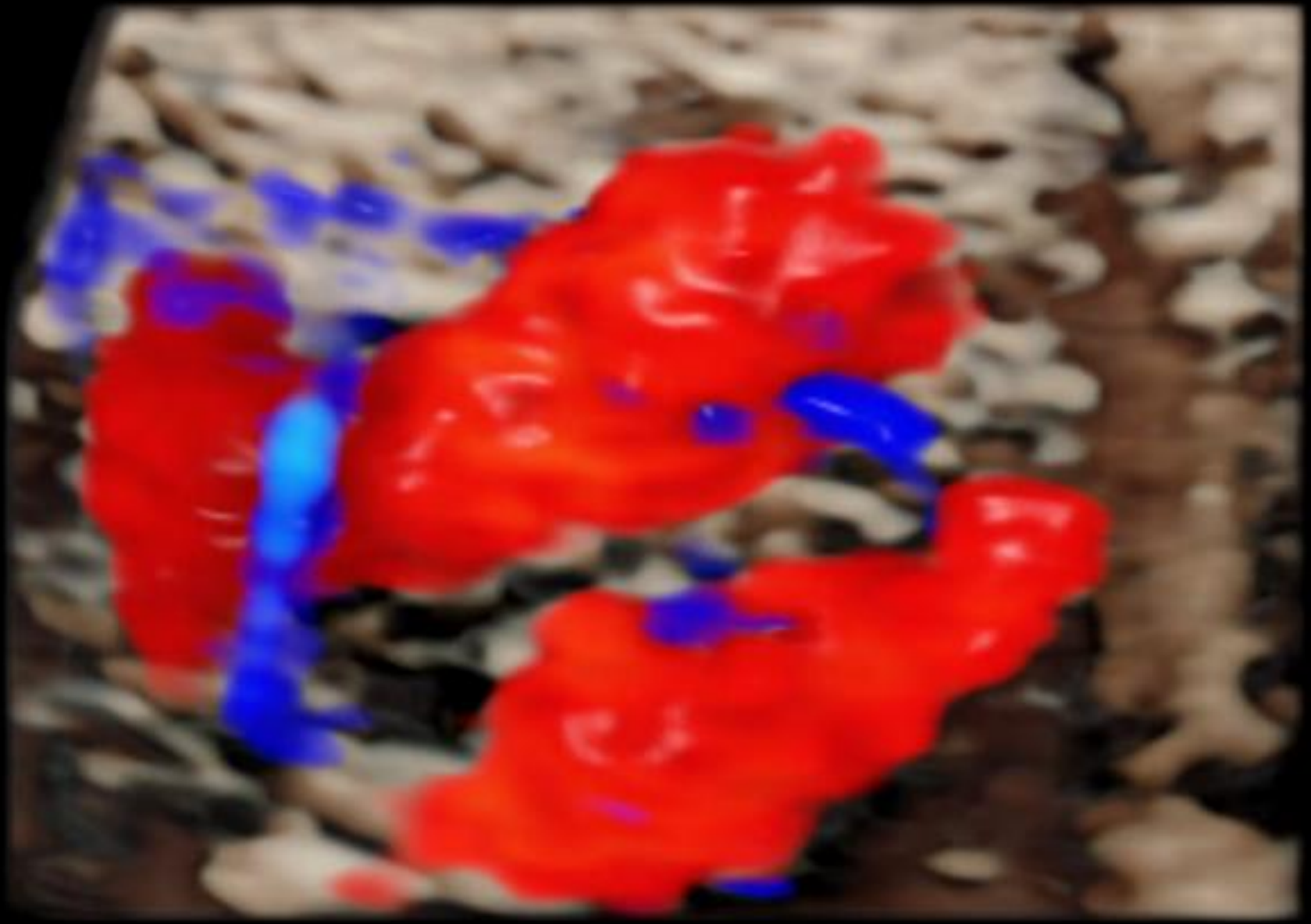


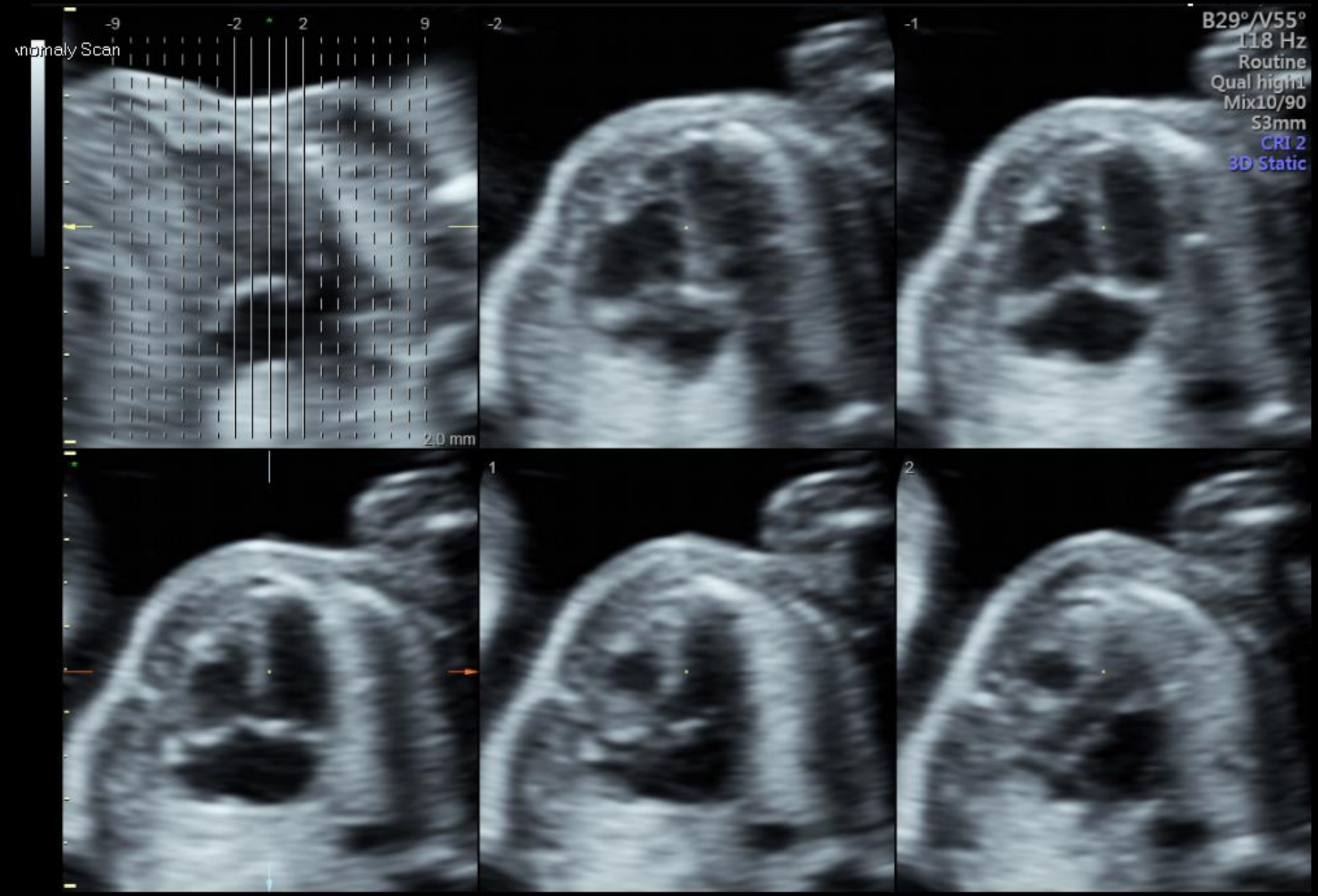

-3
-2
Default
Qual high2
B98°/V60°
26 Hz
Mix 20/80
54mm
3D Static
1.5 mm
1
3
4

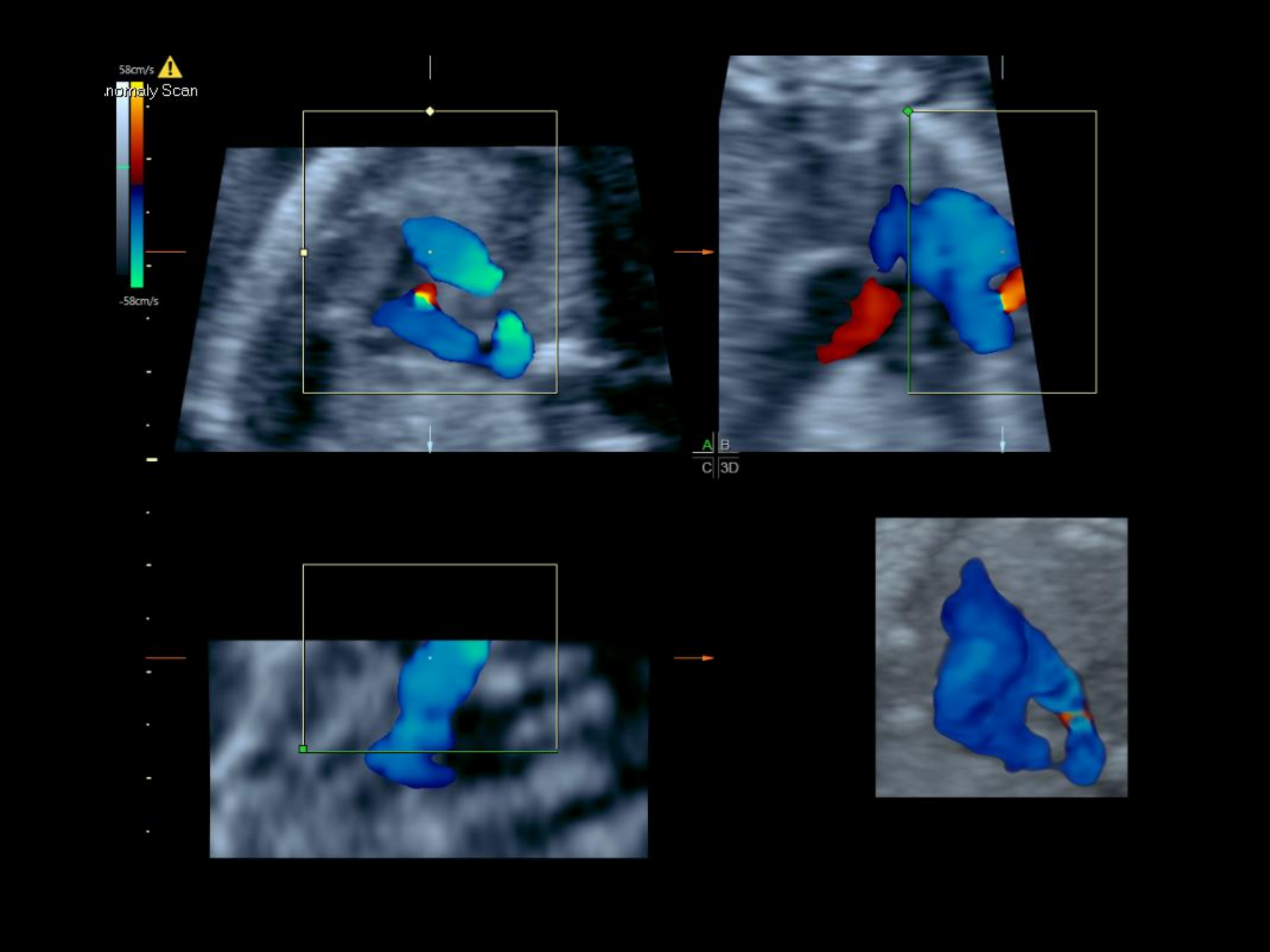
Old heart, new heart



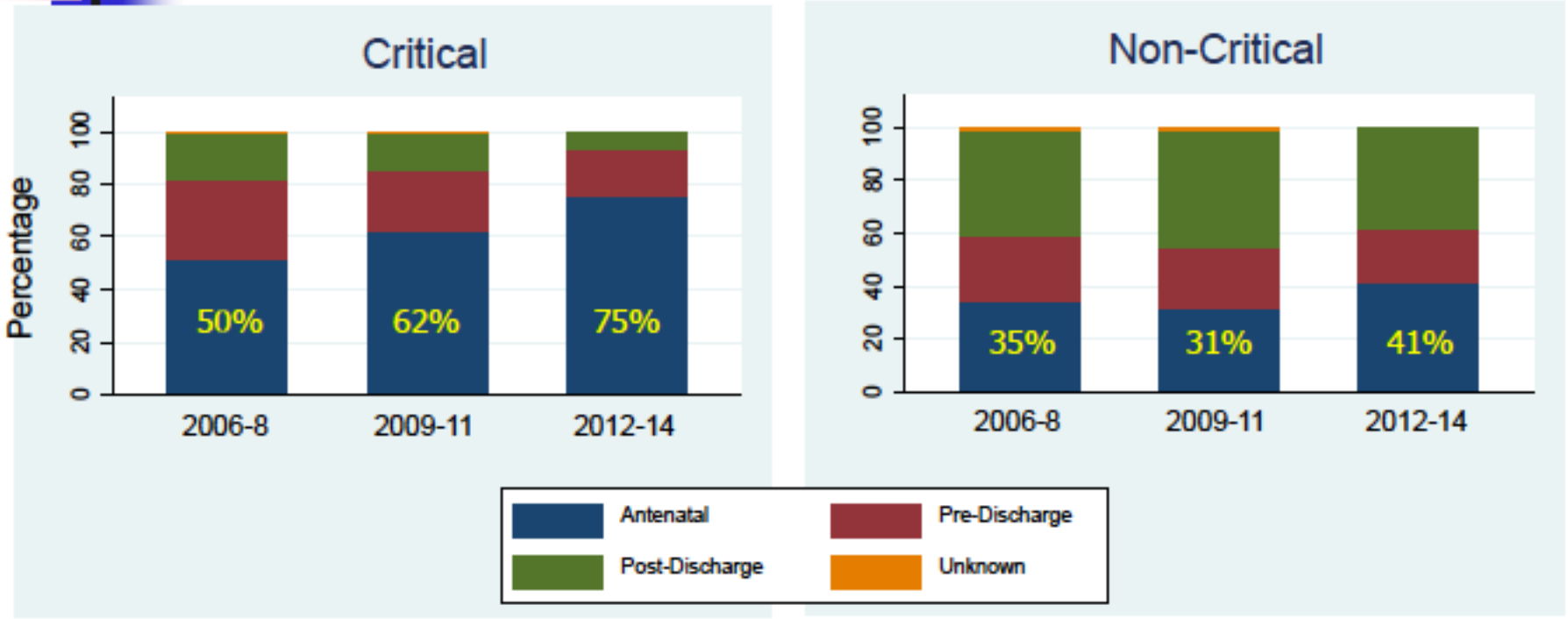





-9
-2
2
9
Anomaly Scan
2.0 mm
-2
-1
B29°/V55°
118 Hz
Routine
Qual high1
Mix10/90
S3mm
CRI 2
3D Static
1
2


58cm/s
normaly Scan
-58cm/s
A
B
C
3D

Timing of Diagnosis

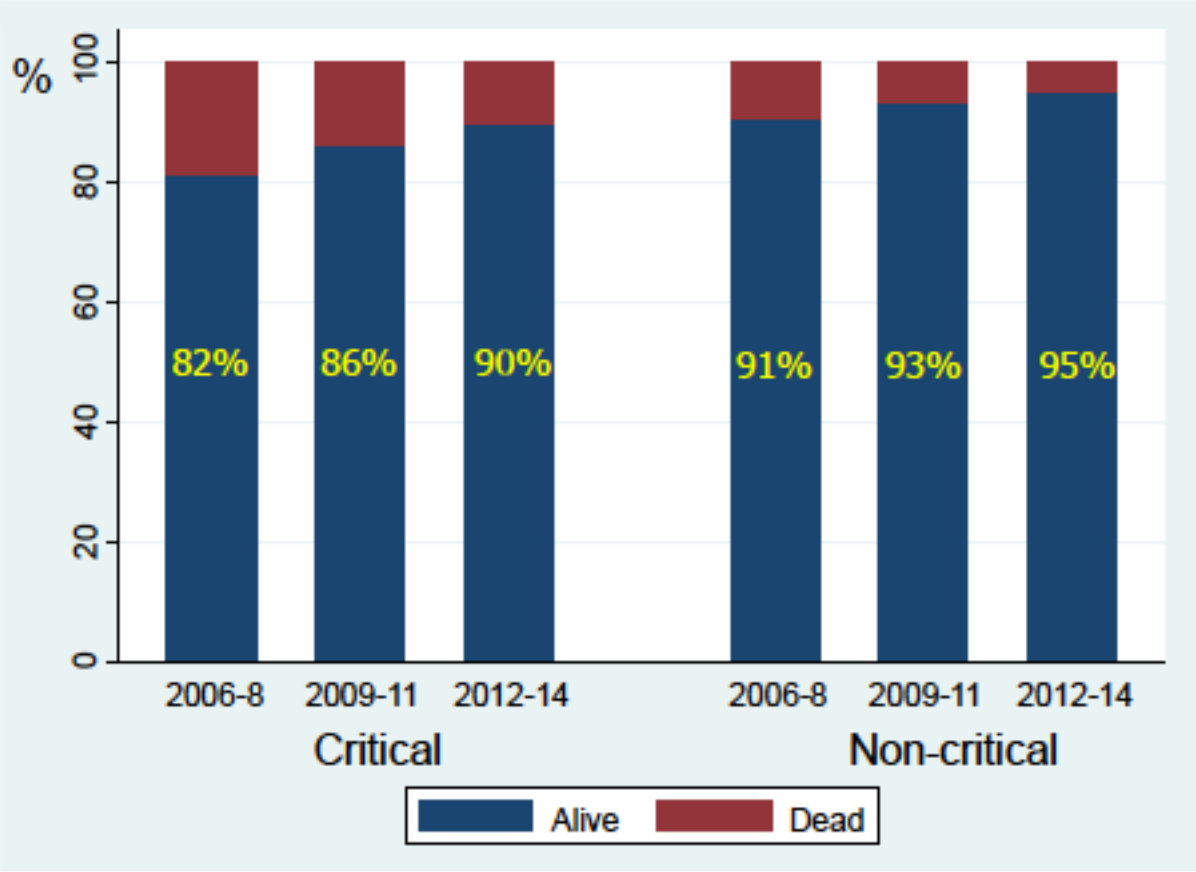


Increase in antenatal diagnosis rate in critical heart disease with time ($p<0.001$)

- no change in noncritical

Survival to one year

- live birth with intention to treat



ANTENATAL DIAGNOSIS

Changes

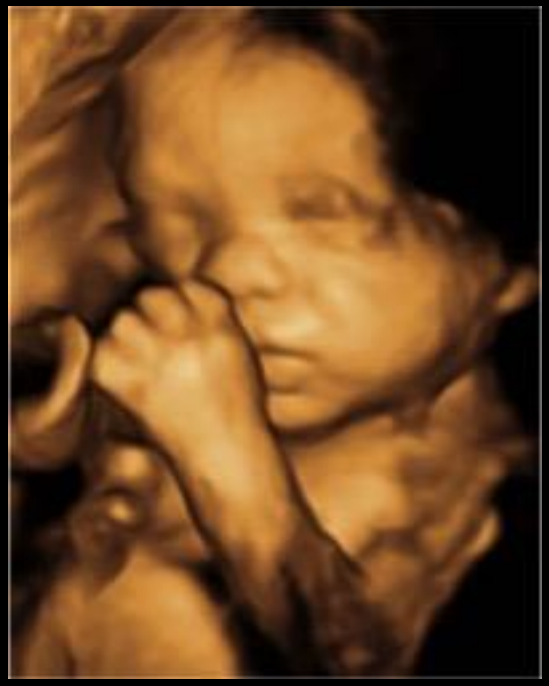
Rapid advancement in fetal medicine

Ultrasound technology
Antenatal MRI

Better understanding of late onset growth restriction

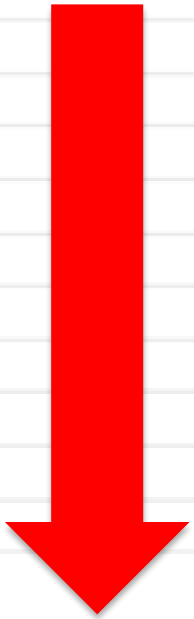
Screening and prevention of preterm labour

Molecular diagnosis
Less invasive testing

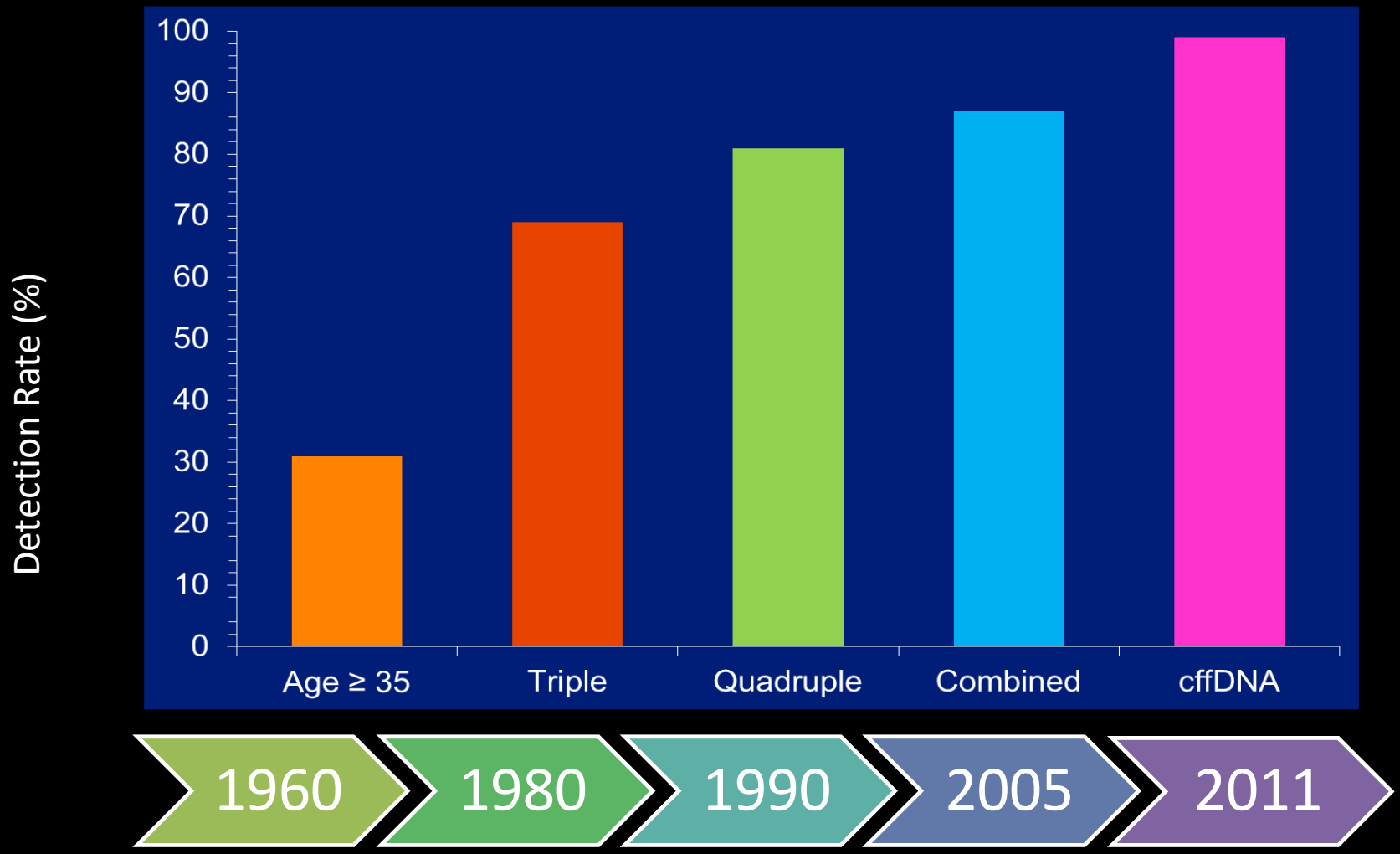


Maternal Risk of T21 increases with age

Age (yrs)	Risk for trisomy 21	
	At Birth	At 12 weeks
20	1 in 1527	1 in 898
25	1 in 1352	1 in 795
30	1 in 895	1 in 526
32	1 in 659	1 in 388
34	1 in 446	1 in 262
36	1 in 280	1 in 165
38	1 in 167	1 in 98
40	1 in 97	1 in 57
42	1 in 55	1 in 32
44	1 in 30	1 in 18

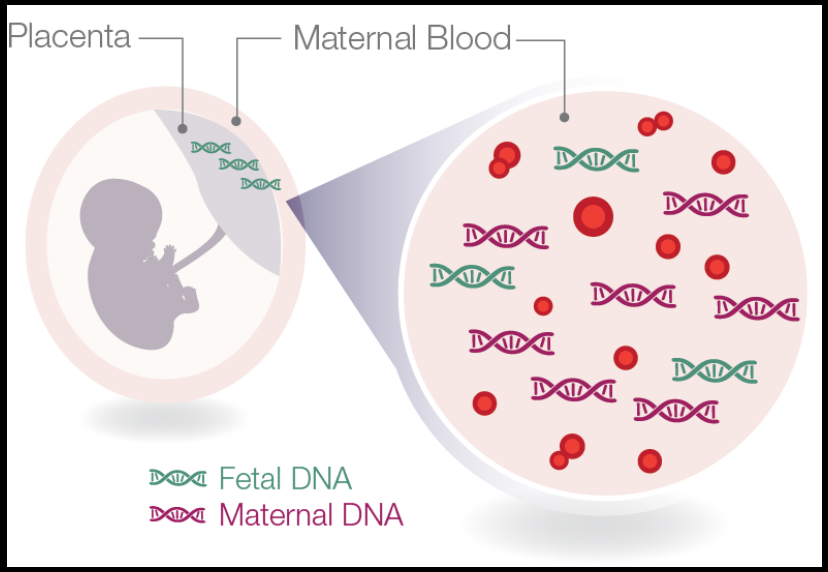


Aneuploidy Screening Approach: Observed Detection Rates



NIPT

- Measures circulating cell-free DNA (cfDNA) from placenta present in maternal blood
- ~10% of DNA in maternal blood
  - *Increases with gestational age*
- As early as 9-10 weeks gestation
  - *(company specific)*
- Dating U/S –
  - *viability, accurate GA, exclude multiples*



cfDNA comes from apoptotic cells derived from:

Maternal Circulation

- *Adipocytes*
- *White Blood Cells*

- *Fetal*
  - *Placental cells (trophoblasts) in the maternal circulation*

Table 2 Down syndrome and Edwards syndrome results in seven cell-free DNA studies carried out in high-risk pregnancies

	Down syndrome		*Edwards syndrome*	
Trial	*DR* (n *(%)*)	*FPR* (n *(%)*)	*DR* (n *(%)*)	*FPR* (n *(%)*)
Chiu *et al.*[65]*	86/86 (100)	3/146 (2.1)	—	—
Ehrich *et al.*[66]	39/39 (100)	1/410 (0.24)	—	—
Palomaki *et al.*[67,72]	209/212 (98.6)	3/1471 (0.20)	59/59 (100)	5/1688 (0.30)
Bianchi *et al.*[68]	89/90 (98.9)	0/410 (0.00)	35/38 (92.1)	0/463 (0.00)
Sparks *et al.*[70]	36/36 (100)	1/123 (0.81)	8/8 (100)	1/123 (0.81)
Ashoor *et al.*[69]	50/50 (100)	0/297 (0.00)	49/50 (98.0)	0/297 (0.00)
Norton *et al.*[71]	81/81 (100)	1/2888 (0.03)	37/38 (97.4)	2/2888 (0.06)
Total	590/594 (99.3)	9/5745 (0.16)	188/193 (97.4)	8/5459 (0.15)

*2-plex and 8-plex data were reported but only the more favorable 2-plex results are included here. DR, detection rate; FPR, false-positive rate.

- By far most accurate performance for T21/18

Benn et al, Ultras Obstet Gynecol 2013, 42: 15-33

Common microdeletions included on panels

- 22q11.2 deletion/DiGeorge

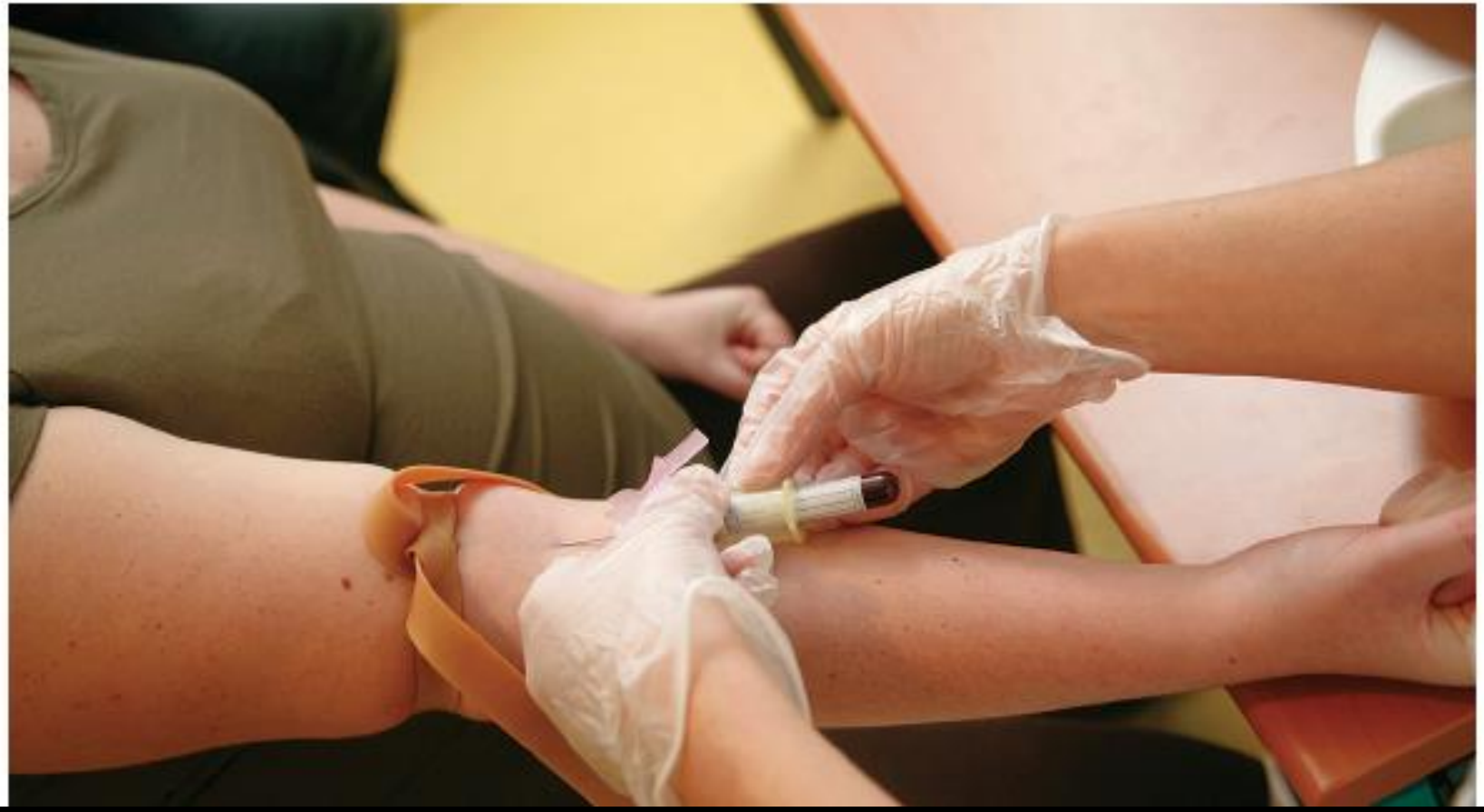
Cardiac indications on ultrasound but many missed

- 1p36 deletion
- Angelman
- Prader-Willi
- Cri-du-chat

Vast majority missed on ultrasound

Simple blood test can detect genetic diseases early in pregnancy

Together, single-gene disorders are more common than Down's syndrome. Now there's a safe prenatal test that can help prospective parents decide what to do



"What kind of society do you want to live in?": Inside the country where Down syndrome is disappearing

Agusta, age 7. On average, Iceland has two people with Down syndrome born each year. / CBS NEWS

INTERVENTION

A NZ Connection

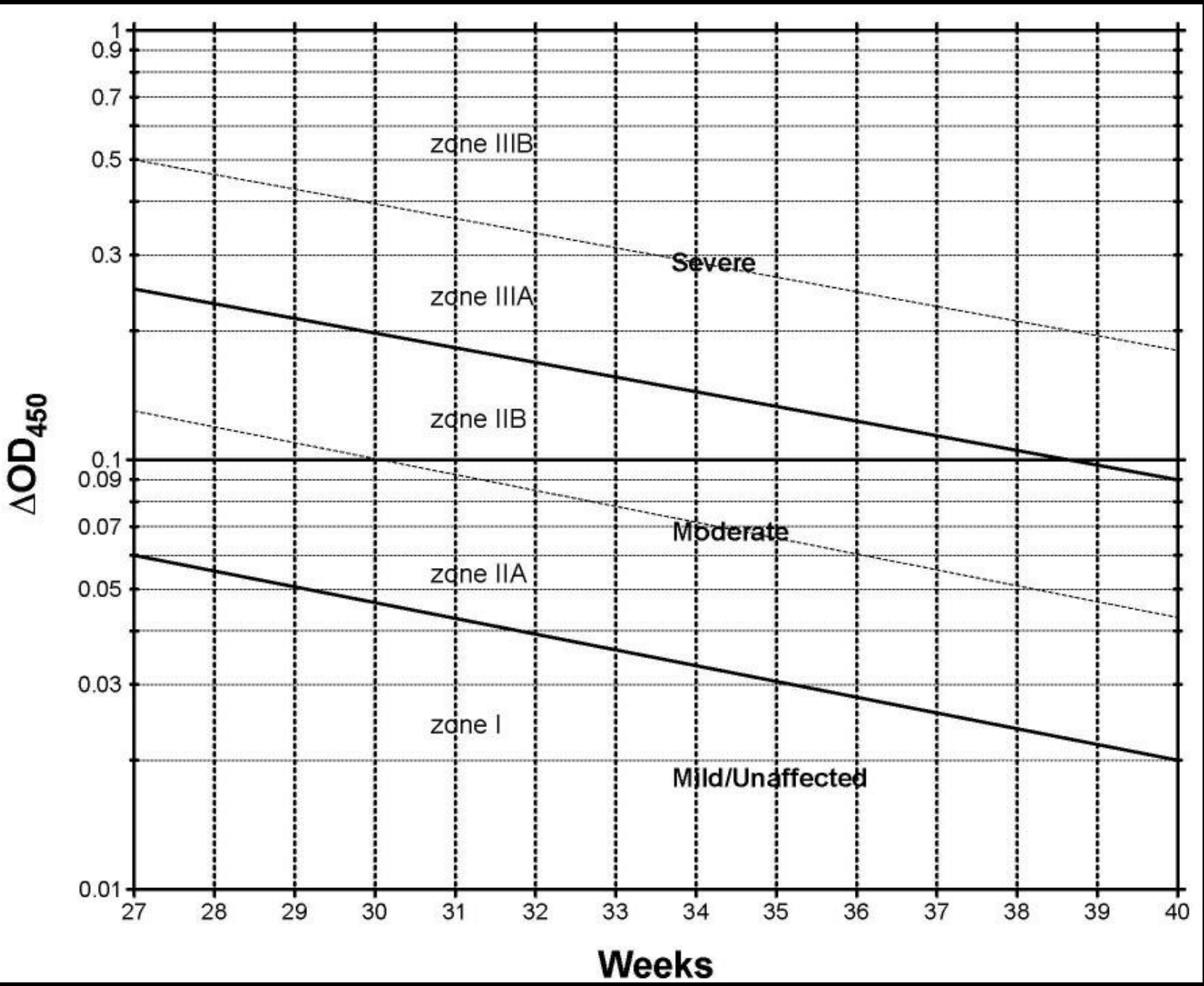
Sir William Liley

National Women's Hospital

Antenatal diagnosis of rhesus disease

- Amniocentesis
- Liley Curve

Latter: Rx of isoimmunisation


ΔOD450
1
0.9
0.7
0.5
0.3
0.1
0.09
0.07
0.05
0.03
0.01
zone IIIB
Severe
zone IIIA
zone IIB
Moderate
zone IIA
zone I
Mild/Unaffected
27
28
29
30
31
32
33
34
35
36
37
38
39
40
Weeks

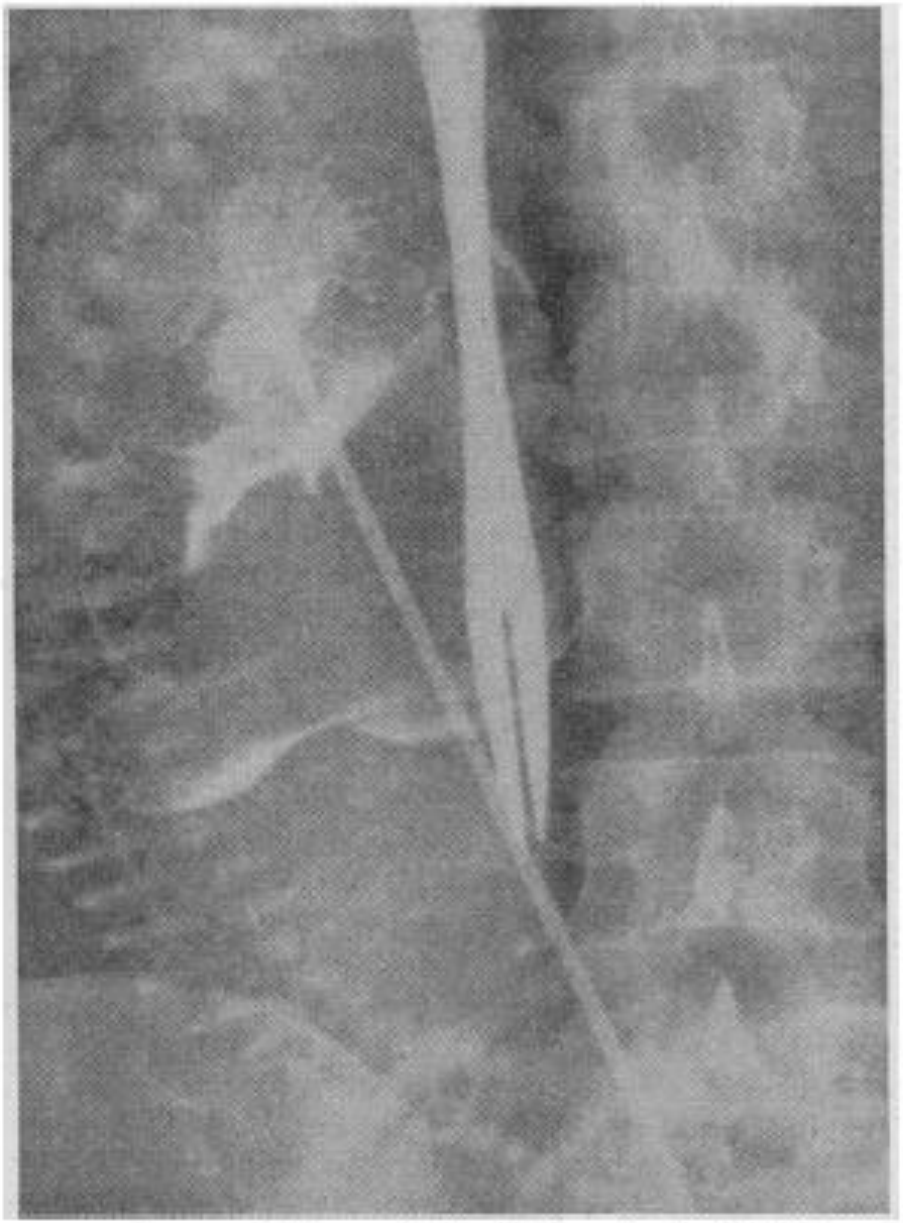
Preliminary Communications

Intrauterine Transfusion of Foetus in Haemolytic Disease

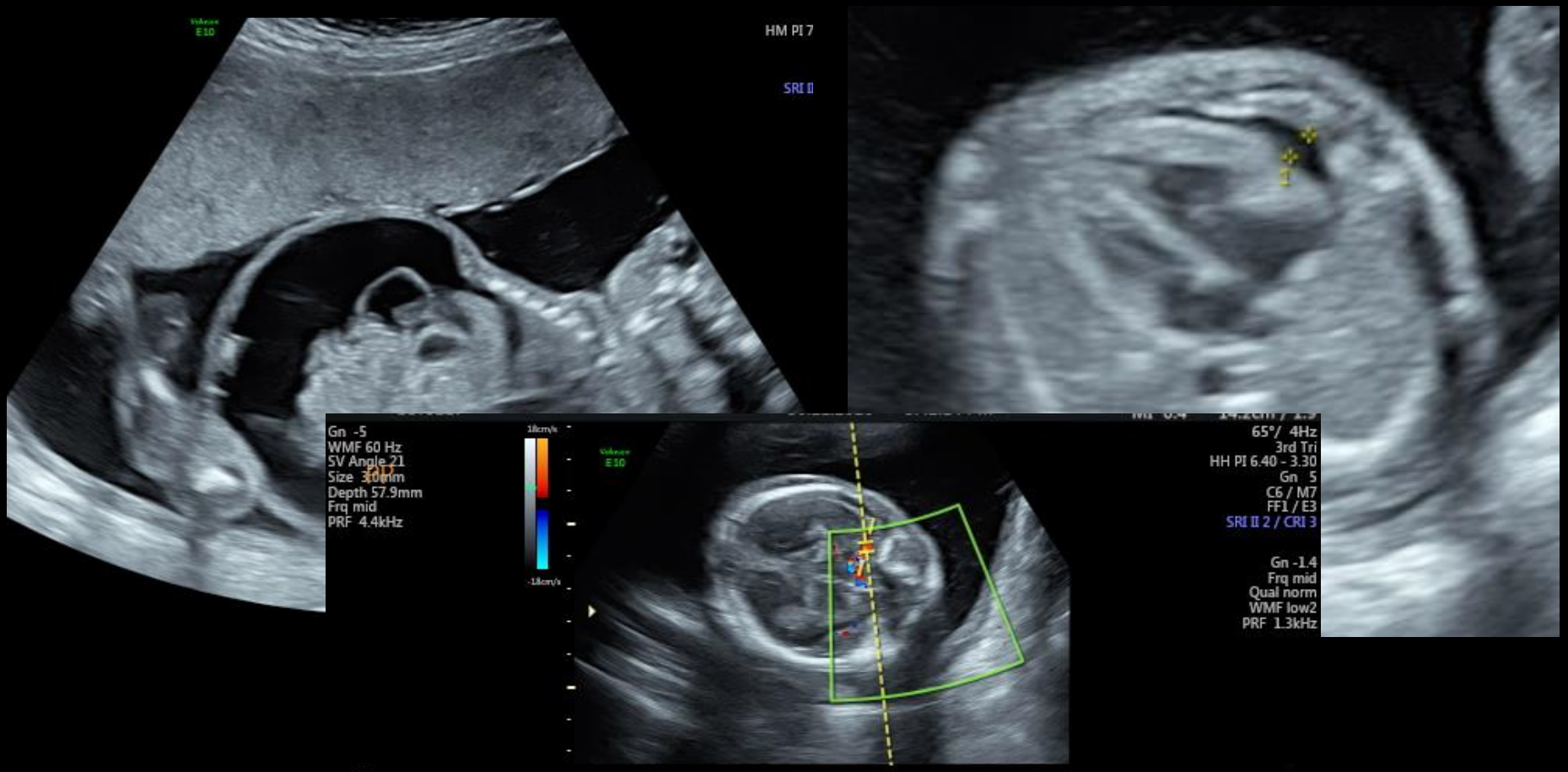
In the management of the pregnancy complicated by rhesus sensitization the guidance given by amniotic-fluid pigmentation (Bevis, 1956; Walker, 1957; Mackay, 1961; Liley, 1961, 1963) has greatly reduced the perinatal mortality from haemolytic disease. In the National Women's Hospital, Auckland, with a policy of selective induction based on amniocentesis findings, this perinatal mortality has fallen steadily from 22% in 1957–8 to 9% in 1962. It was obvious that no further reduction could be expected from conventional treatment when of 7 perinatal deaths in 80 consecutive rhesus-sensitized pregnancies one baby had multiple congenital abnormalities and the other six were all hydropic before 34 weeks' gestation. Transfusion *in utero* appeared the logical procedure for these very severely affected babies early in the third trimester, and intraperitoneal transfusion seemed the simplest technique.

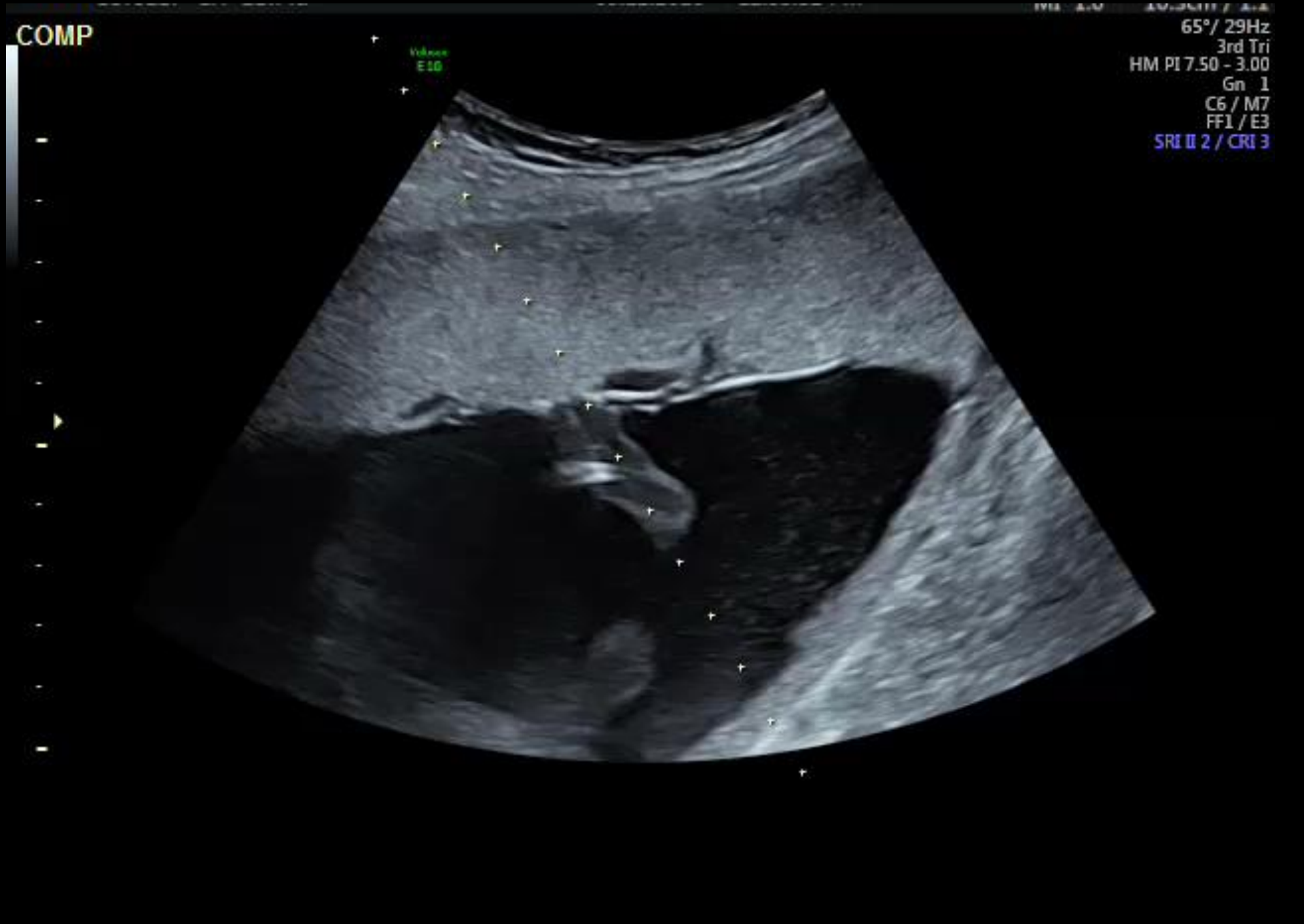
Case Report

The mother, aged 32, was pregnant for the fourth time. Her first pregnancy was normal, with a surviving 4,090-g. male infant. In her second pregnancy intrauterine death occurred a few days before delivery at term. Antibodies were present at 10 weeks in her third pregnancy and reached a titre of 1:64 by indirect Coombs test at 29 weeks. Mild hypertension had developed and stillborn macerated twins were delivered at 30 weeks. In her fourth pregnancy at 30 weeks by menstrual dates a specimen of bright yellow amniotic fluid was sent by post to this hospital. The spectral absorption curve (Bevis,



Contrast medium and the coiled catheter in the foetal peritoneal cavity. The Tuohy needle has been withdrawn and lies on the mother's abdominal skin.


HM PI 7
SRI II
Gn -5
WMF 60 Hz
SV Angle 21
Depth 57.9mm
Frq mid
PRF 4.4kHz
65°/ 4Hz
3rd Tri
HH PI 6.40 - 3.30
Gn 5
C6 / M7
FF1 / E3
SRI II 2 / CRI 3
Gn -1.4
Frq mid
Qual norm
WMF low2
PRF 1.3kHz
MCA-PS
60
45
30
15
cm/s
-15
-30
-45
-60
Rt MCA-PS 46.58cm/s


COMP
65°/ 29Hz
3rd Tri
HM PI 7.50 - 3.00
Gn 1
C6 / M7
FF1 / E3
SRI II 2 / CRI 3

Fetal Endoscopic Tracheal Occlusion (FETO)

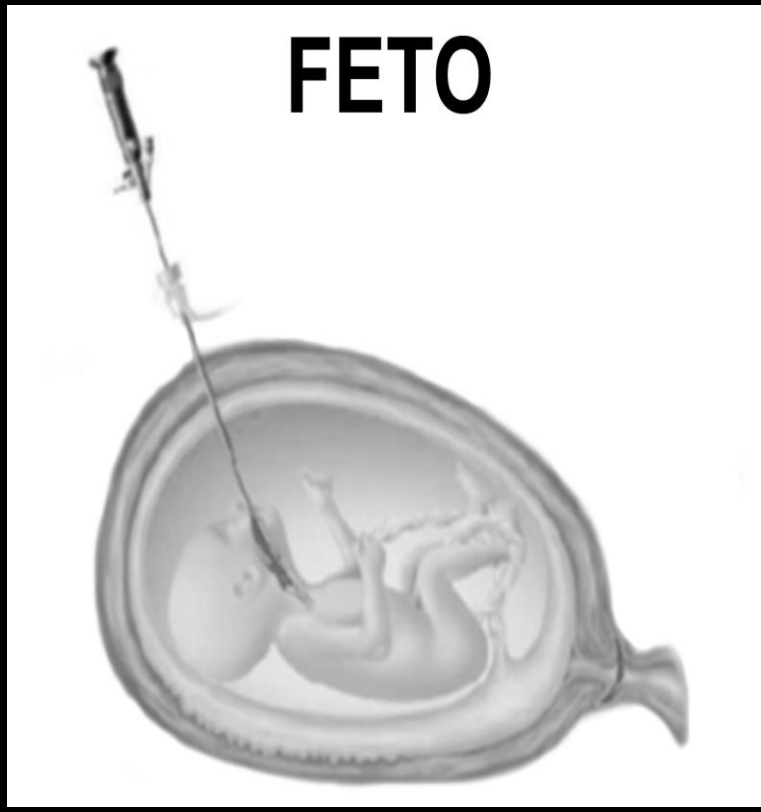
Minimally invasive fetoscopic procedure whereby a balloon is inserted into the fetal trachea with the purpose of blocking the trachea to allow the lungs to expand with the lung secretions.

Ruano et al. UOG 2012

RCT

Severe CDH

Survival at 6 months was 52.6% in the FETO group compared with 5.3% in the control group, i.e. a 10-fold survival rate.



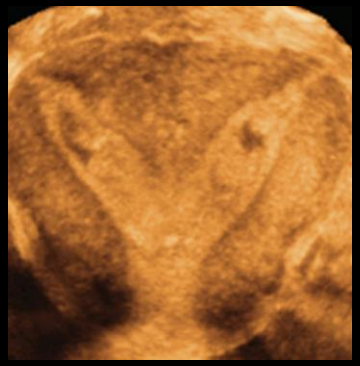
Current International Multicentre randomised controlled trial “TOTAL” (Tracheal Occlusion To Accelerate Lung growth)

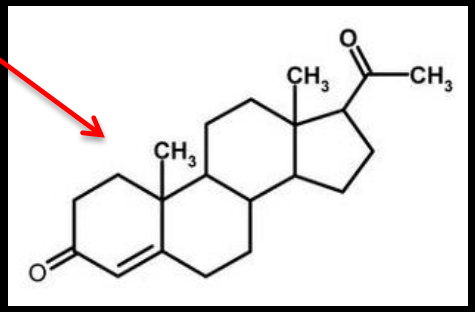
- Led by Eurofetus group

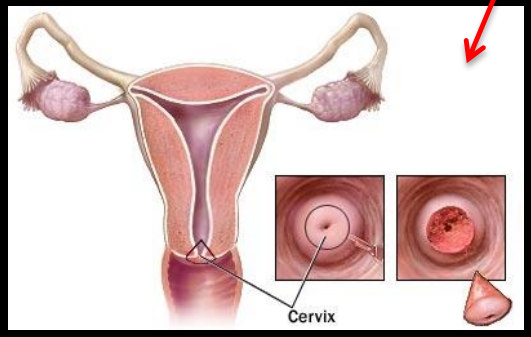
Tools:

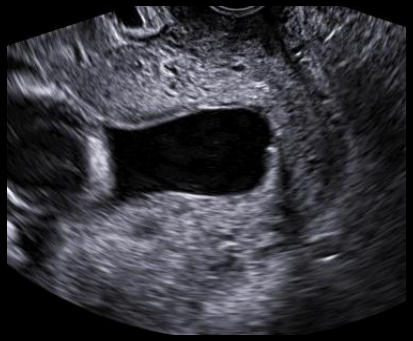
PREVENTION OF DELIVERY

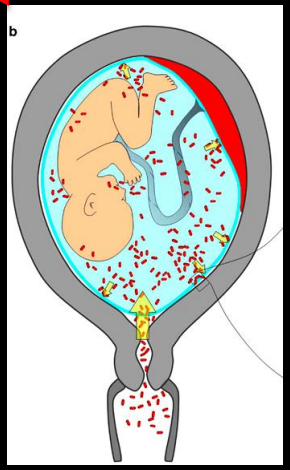
SHORT CERVIX









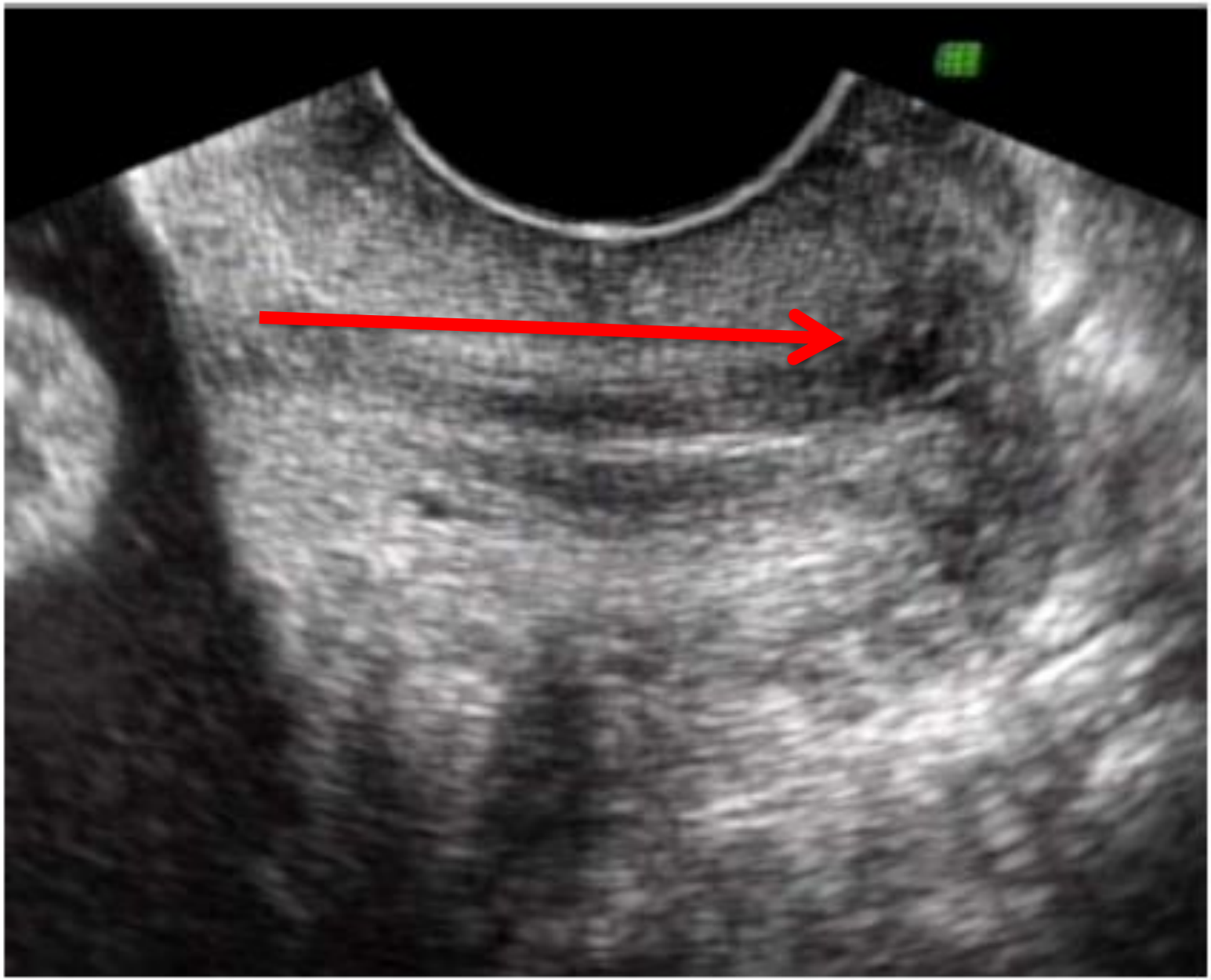


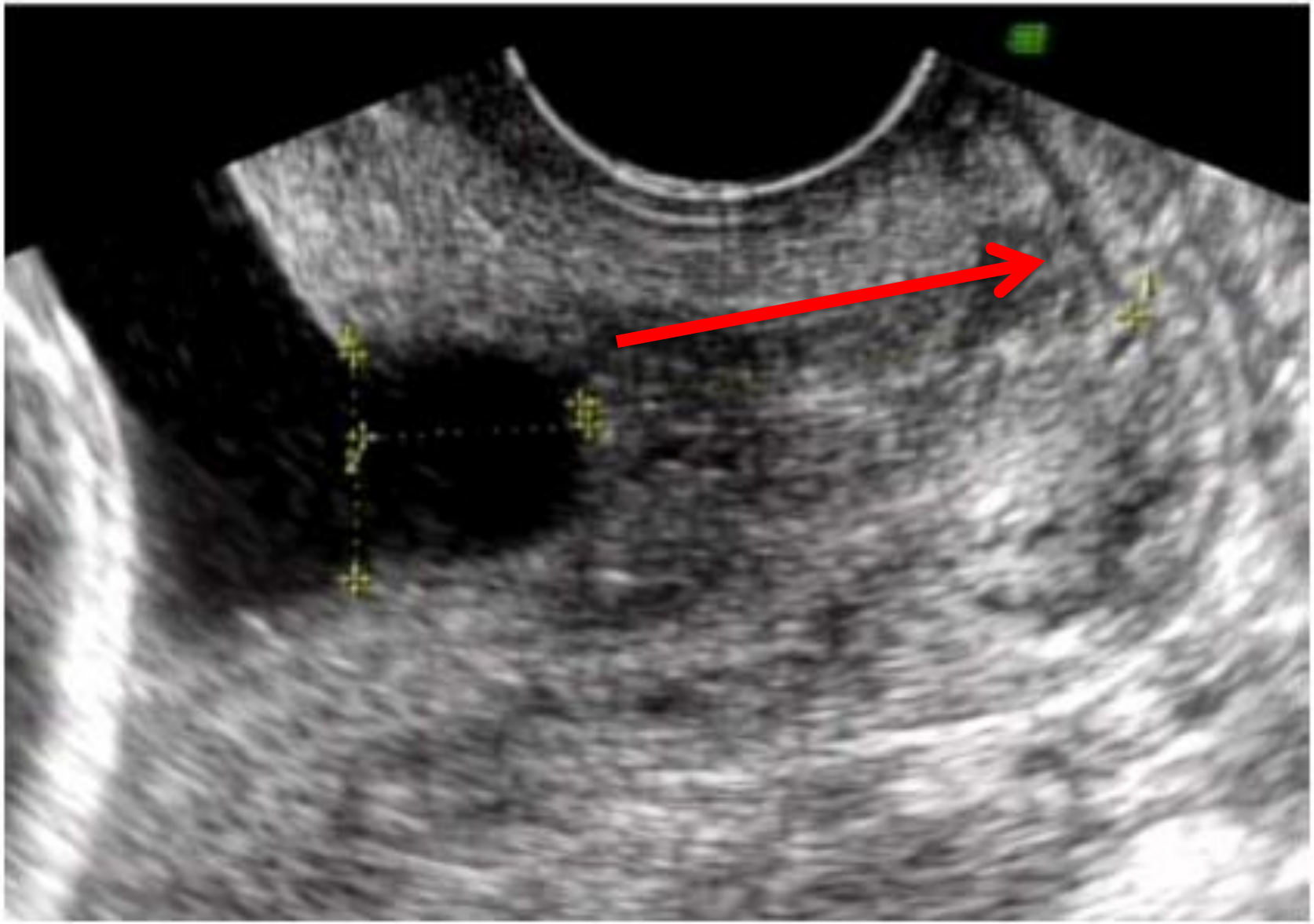
Risk Factors

- Prior hx of PTB
- Maternal age <20, >35
- Low BMI <19.8 kg/m^2
- Ethnicity: African-American

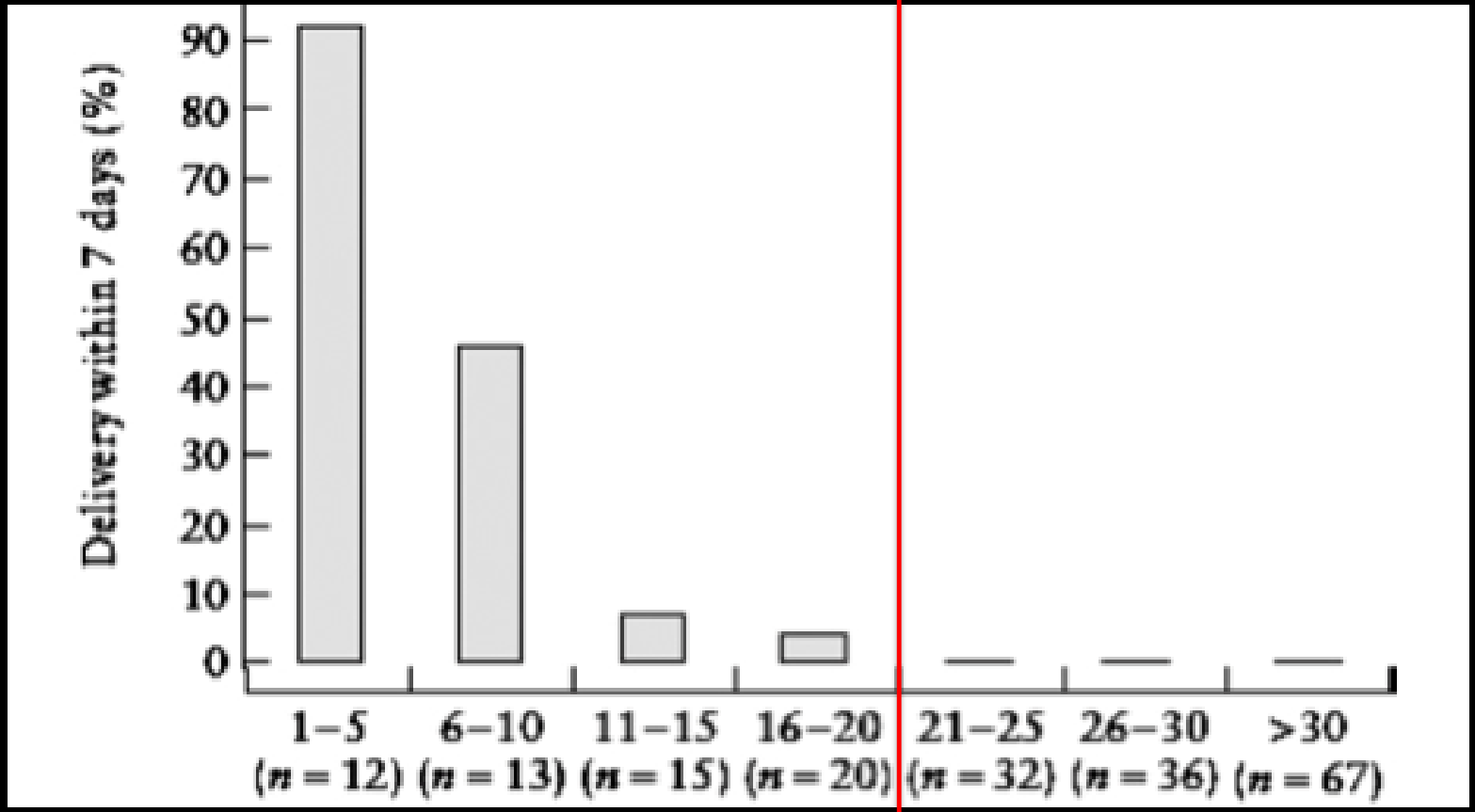
High Risk Groups

- Hx of spontaneous PTB in prior pregnancy
- Short Cx <25mm at <24 weeks current pregnancy
- Untreated
  - 15-20% recurrent PTB <28 weeks
  - 25-30% recurrent PTB <32 weeks
  - 50-60% recurrent PTB <37 weeks
    - *Iams et al AJOG 2010*
- Risks are higher:
  - The earlier the GA of PTB
  - The shorter the Cx length
  - Earlier in pregnancy the short Cx was diagnosed

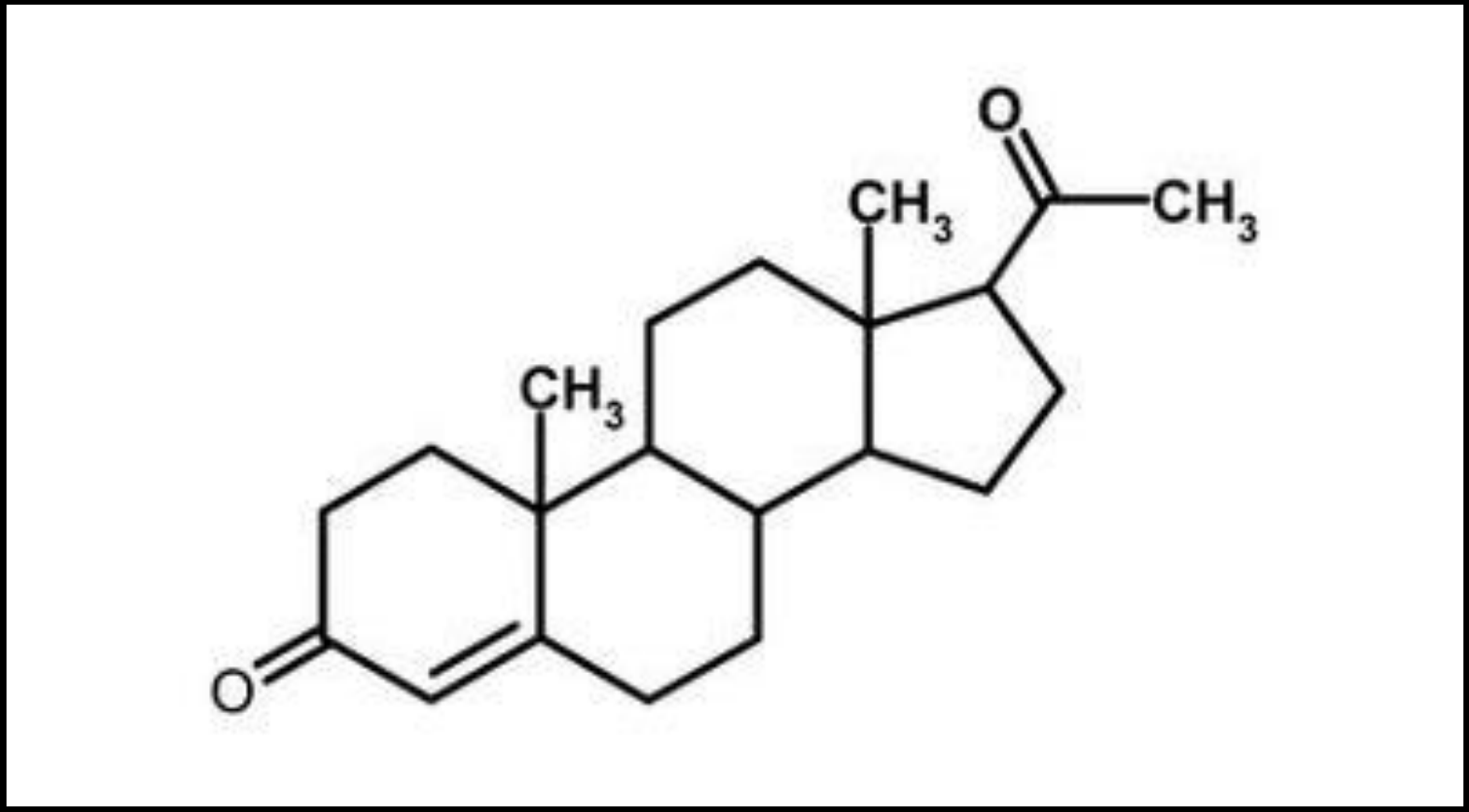




Delivery within 7 days



PROGESTERONE



Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data

Roberto Romero, MD; Kypros Nicolaides, MD; Agustin Conde-Agudelo, MD, MPH; Ann Tabor, MD; John M. O'Brien, MD; Elcin Cetingoz, MD; Eduardo Da Fonseca, MD; George W. Creasy, MD; Katharina Klein, MD; Line Rode, MD; Priya Soma-Pillay, MD; Shalini Fusey, MD; Cetin Cam, MD; Zarko Alfirevic, MD; Sonia S. Hassan, MD

OBJECTIVE: To determine whether the use of vaginal progesterone in asymptomatic women with a sonographic short cervix (≤25 mm) in the midtrimester reduces the risk of preterm birth and improves neonatal morbidity and mortality.

STUDY DESIGN: Individual patient data metaanalysis of randomized controlled trials.

RESULTS: Five trials of high quality were included with a total of 775 women and 827 infants. Treatment with vaginal progesterone was associated with a significant reduction in the rate of preterm birth <33 weeks (relative risk [RR], 0.58; 95% confidence interval [CI], 0.42–0.80), <35 weeks (RR, 0.69; 95% CI, 0.55–0.88), and <28 weeks (RR, 0.50; 95% CI, 0.30–0.81); respiratory distress syndrome (RR, 0.48; 95% CI, 0.30–0.76); composite neonatal morbidity and mortality (RR, 0.57; 95% CI, 0.40–0.81); birthweight <1500 g (RR, 0.55; 95% CI, 0.38–0.80); admission to neonatal intensive care unit (RR, 0.75; 95% CI, 0.59–0.94); and requirement for mechanical ventilation (RR, 0.66; 95% CI, 0.44–0.98). There were no significant differences between the vaginal progesterone and placebo groups in the rate of adverse maternal events or congenital anomalies.

CONCLUSION: Vaginal progesterone administration to asymptomatic women with a sonographic short cervix reduces the risk of preterm birth and neonatal morbidity and mortality.

Key words: admission to neonatal intensive care unit, birthweight <1500 g, mechanical ventilation, prematurity, preterm birth, progestin, respiratory distress syndrome, transvaginal ultrasound, uterine cervix, 17α-hydroxyprogesterone caproate

Cite this article as: Romero R, Nicolaides K, Conde-Agudelo A, et al. Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data. Am J Obstet Gynecol 2012;206:124.e1-19.

Results

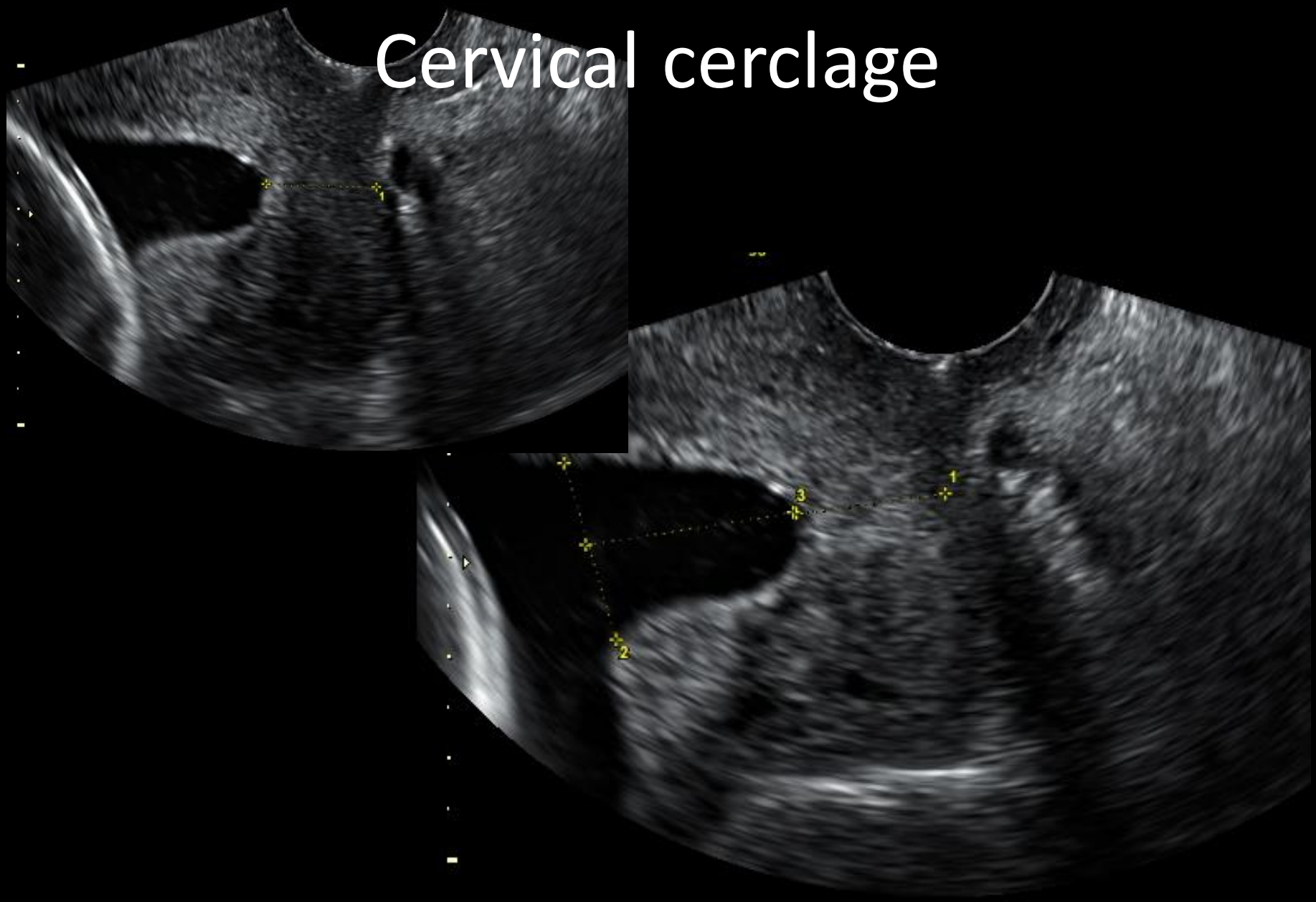
Preterm Birth

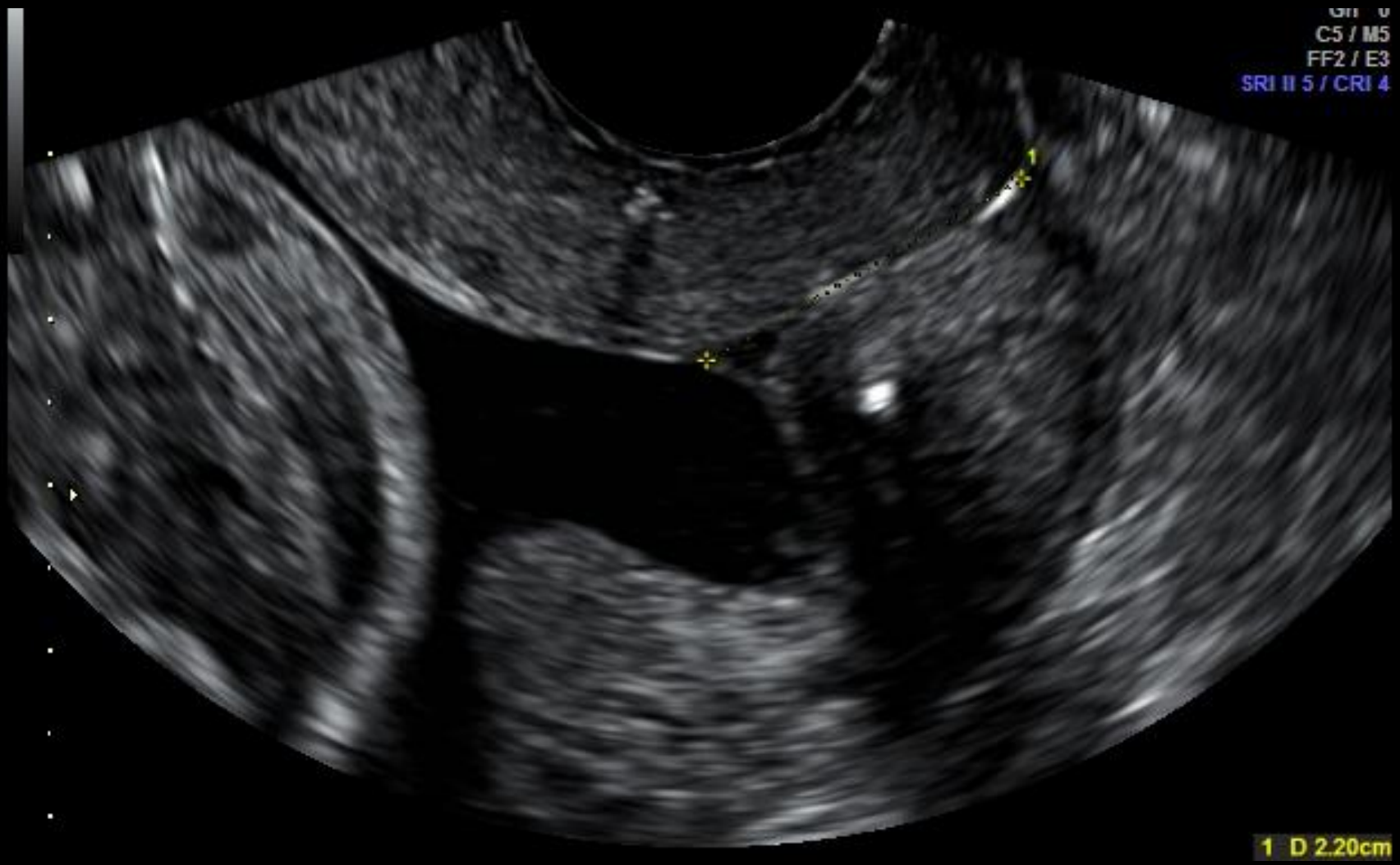
- Reduced
  - <28 weeks by 50%
  - <33 weeks by 40%
  - <35 weeks by 30%

Neonatal Outcomes

- Reduced
  - RDS
    - RR 0.48 (0.30-0.70)
  - NICU Admission
    - RR 0.75 (0.59-0.94)
  - Need for mechanical ventilation
    - RR 0.66 (0.44-0.98)
  - Lower rate of LBW <1500g
    - RR 0.55 (0.38-0.80)

Cervical cerclage




C5 / M5
FF2 / E3
SRI II 5 / CRI 4
1
1 D 2.20cm

Vaginal progesterone vs cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis

Agustin Conde-Agudelo, MD, MPH; Roberto Romero, MD, DMedSci; Kypros Nicolaides, MD; Tinnakorn Chaiworapongsa, MD; John M. O'Brien, MD; Elcin Cetingoz, MD; Eduardo da Fonseca, MD; George Creasy, MD; Priya Soma-Pillay, MD; Shalini Fusey, MD; Cetin Cam, MD; Zarko Alfirevic, MD; Sonia S. Hassan, MD

OBJECTIVE: No randomized controlled trial has compared vaginal progesterone and cervical cerclage directly for the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous spontaneous preterm birth. We performed an indirect comparison of vaginal progesterone vs cerclage using placebo/no cerclage as the common comparator.

STUDY DESIGN: Adjusted indirect metaanalysis of randomized controlled trials.

RESULTS: Four studies that evaluated vaginal progesterone vs placebo (158 patients) and 5 studies that evaluated cerclage vs no cerclage (504 patients) were included. Both interventions were associated with a statistically significant reduction in the risk of preterm birth at <32 weeks of gestation and composite perinatal morbidity and mortality compared with placebo/no cerclage. Adjusted indirect metaanalyses did not show statistically significant differences between vaginal progesterone and cerclage in the reduction of preterm birth or adverse perinatal outcomes.

CONCLUSION: Based on state-of-the-art methods for indirect comparisons, either vaginal progesterone or cerclage are equally efficacious in the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous preterm birth. Selection of the optimal treatment needs to consider adverse events, cost and patient/clinician preferences.

Key words: birthweight, cervix, neonatal intensive care unit, perinatal mortality, perinatal morbidity, premature, prematurity, progestin, 17α-hydroxyprogesterone caproate, 17P

Cite this article as: Conde-Agudelo A, Romero R, Nicolaides K, et al. Vaginal progesterone vs cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. Am J Obstet Gynecol 2013;208:42.e1-18.

Tools:

PREPARATION FOR DELIVERY

Steroids

Drs Liggins and Howie

NWH

Prevention of:

Perinatal death RR 0.72

Neonatal death RR 0.69

RDS RR 0.66

NEC RR 0.55

IVH RR 0.50

Cochrane 2017

THE PATIENT

The art of medicine

Counselling

Support

Empathy

Multidisciplinary approach

Available

Memorial for Unborn Children

Martin Hudáček

Summary

Antenatal diagnosis

Counselling

Preparation

Delivery at best place possible


Thank you!